THE REACTIONS OF MONOMERIC STYRENES

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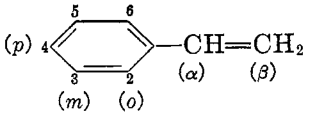
Even before its structural formula was known, Kopp (411) in 1844 and Blyth and Hofmann (87) in 1845 had examined certain chemical reactions of monomeric styrene. They reported that treatment with nitric acid yielded nitrostyrene, oxidation yielded benzoic acid, and treatment with chlorine or bromine yielded halogen addition products. After 1866, when Erlenmeyer (203) suggested that styrene was phenylethylene, the nature of these reactions became clearer. Subsequent experimenters have, of course, substantiated this formula in numerous ways and have added a host of reactions to those examined by the earliest investigators.

In considering the chemistry of styrene and its derivatives, the name "phenylethylene," used by Erlenmeyer to describe its structure, must be kept continually in mind. Styrene is a typical olefinic hydrocarbon and undergoes a great variety of reactions characteristic of compounds containing a carbon–carbon double bond. However, the phenyl group exerts a marked activating influence on this functional group, as is shown by the pronounced tendency for the compound to polymerize. Styrene readily undergoes a number of reactions which other, less reactive olefins undergo with difficulty or not at all.

The present review describes the reactions of monomeric styrenes. It includes nothing on the polymerization of styrene or its derivatives. The chemistry is limited to compounds having only two carbon atoms in the functional group attached to the benzene ring. α-Methylstyrene, β-methylstyrene, cinnamyl alcohol, cinnamaldehyde, cinnamic acid, etc. have been omitted purposely, as falling outside the scope of this review. Similarly the nuclearly substituted styrenes have been limited to those containing one benzene ring. This excludes purposely vinylnaphthalene, vinylbiphenyl, etc. Even with these artificial limitations the field covered is a large one. The literature has been covered as completely as possible through December 31, 1947 and a number of references have been added which have appeared since then.[1]

Nomenclature

The names "cinnamene," "phenethylene," "phenylethylene," "styrol," and "vinylbenzene" appear in the literature. At present in *Chemical Abstracts* styrene and its substitution products are indexed under *styrene* and the positions of substituents are indicated as follows:



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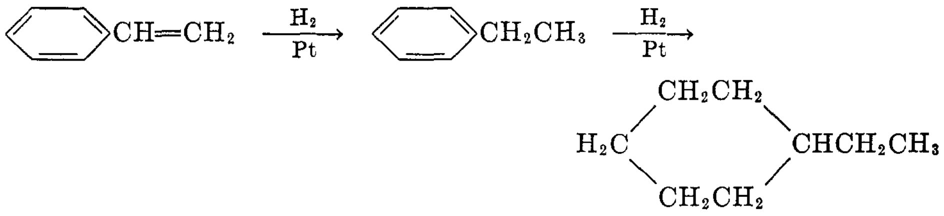
[1] Some additions inserted in manuscript to August 15, 1949.

I. REDUCTION

A. Catalytic hydrogenation

The most straightforward method of reduction is the direct addition of one or more molecules of hydrogen in the presence of a catalyst. In 1868 Berthelot (81) passed a mixture of styrene and hydrogen through a hot tube and detected ethylbenzene among the products of the reaction. However, under the conditions used (73, 79) pyrolysis predominated, so that the principal compounds isolated were benzene and ethylene together with smaller amounts of acetylene, toluene, and *p*-xylene.

In 1901 Sabatier and Senderens (644) studied the vapor-phase catalytic hydrogenation of styrene. When copper was used as the catalyst, ethylbenzene was formed, whereas over a nickel catalyst ethylcyclohexane, contaminated with a little methylcyclohexane, was obtained. Willstätter and King (779) used platinum as the catalyst and acetic acid as the solvent. Depending on the duration of the hydrogenation either ethylbenzene or ethylcyclohexane could be produced.



Since these early studies, a number of investigators have examined the reaction. Styrene has been hydrogenated to ethylbenzene in essentially quantitative yield in the presence of all the common hydrogenation catalysts. These include Raney nickel (176, 804), copper chromite (804), palladium black (771), platinum black (362, 438), platinum oxide (367), and palladium oxide (367). Copper is equally effective (403), and some reduction has been reported to take place in the presence of zinc, magnesium, aluminum, cupric chloride, zinc chloride, magnesium chloride, and aluminum chloride (403). These reductions in the presence of metal chlorides have not been confirmed. In fact, styrene reacts very readily with hydrogen, much more so than cinnamic acid, benzalacetone, or α-pinene (764, 765), and 900 times faster than benzene (458). Competitive hydrogenations of styrene with eugenol, oleic acid, and several other olefinic compounds have been studied (438, 439).

The heat of hydrogenation of styrene to ethylcyclohexane has been found to be $-77{,}893$ cal. per mole (164). The reaction rate is independent of styrene concentration, but proportional to the hydrogen pressure and to the platinum concentration (187). The reaction has, of course, served as an example in discussions of the theory of catalytic hydrogenation (148, 655).

Catalytic hydrogenation has proven equally effective for converting substituted styrenes to the corresponding ethylbenzenes. For convenience these reductions are summarized in tabular form (table 1).

v. Braun, Karpf, and Garn (113) reduced *m*-phenylenediacetonitrile with sodium and alcohol and then pyrolyzed the quaternary ammonium hydroxide obtained from the resulting amine. The product, which undoubtedly was a styrene, was reduced to the corresponding saturated aromatic hydrocarbon. Fries and Bestian (246) hydrogenated *o*-divinylbenzene in the presence of platinum oxide. Depending on whether one or two moles of hydrogen were absorbed, *o*-ethylstyrene or *o*-diethylbenzene was obtained.

TABLE 1

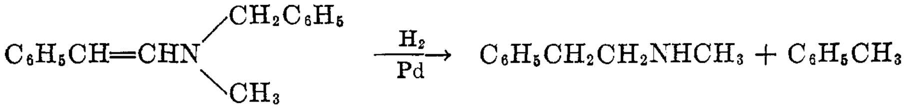
Hydrogenation of substituted styrenes

SUBSTITUTED STYRENE	CATALYST	YIELD	REFERENCE
		per cent	
o-Methyl	Pd		(186)
p-Methyl	Pd		(486)
m-Bromo	PtO_2	86	(125)
p-Phenoxy	Raney nickel	84	(234)
2,6-Dimethoxy	Pt	69	(667)
2,5-Dimethyl-3,6-dimethoxy	Raney nickel	86	(687)
4,5-Dimethoxy-2-carboxy	Pd		(406, 408)
o-(β-Dimethylaminoethyl)	Pd		(116)

With styrenes substituted in the side chain, hydrogenation proceeds in the normal manner if the substituent is not halogen. Thus, in the presence of palladium β-acetoxystyrene yielded 82.5 per cent of β-phenethyl acetate (678), in the

$$C_6H_5CH{=}CHOCOCH_3 \xrightarrow[Pd]{H_2} C_6H_5CH_2CH_2OCOCH_3$$

presence of platinum oxide α,β-diacetoxystyrene yielded styrene glycol diacetate (156), and in the presence of platinum *p*-methoxy-α-ethoxystyrene yielded α-ethoxyethylanisole (583). Similarly in the presence of platinum oxide β-diethylamino-, β-piperidino-, β-methylbenzylamino-, and β-dibenzylamino-styrenes yielded the corresponding ethylbenzenes (470). In the presence of a palladium catalyst the two latter compounds were debenzylated to give methyl-β-phenethylamine and β-phenethylamine, respectively.



$$C_6H_5CH{=}CHN\begin{matrix}\diagup CH_2C_6H_5\\ \diagdown CH_3\end{matrix} \xrightarrow[Pd]{H_2} C_6H_5CH_2CH_2NHCH_3 + C_6H_5CH_3$$

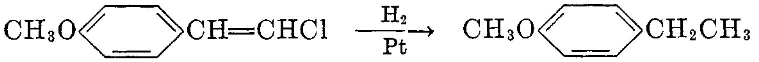
Treatment of *N*-methyl-*N*-β-(3,4-diacetoxystyryl)acetamide with hydrogen in the presence of palladium gave *N*-methyl-*N*-β-(3,4-diacetoxyphenyl)ethylacetamide (118).

The hydrogenation of *N*-methyl-*N*,β-styryl-*p*-toluenesulfonamide with a palladium catalyst proceeded normally to give *N*-methyl-*N*-β-phenethyl-*p*-toluenesulfonamide (375). *N*-Benzyl-*N*-β-styryl-*p*-toluenesulfonamide behaved similarly and *N*-β-styryl-*p*-toluenesulfonamide yielded *N*-β-phenethyl-*p*-toluenesulfonamide. In the presence of a platinum oxide catalyst sodium β-styrylsulfonate yielded sodium β-phenylethanesulfonate (373).

$$C_6H_5CH{=}CHSO_3Na \xrightarrow[PtO_2]{H_2} C_6H_5CH_2CH_2SO_3Na$$

Styrenephosphonic acid was hydrogenated in the presence of a palladium on barium sulfate catalyst to give β-phenylethanephosphonic acid (66).

If the styrene contains halogen in the side chain, catalytic hydrogenation removes it whether it is in the active α- or the unreactive β-position. Thus, both *p*-methoxy-α-chloro- and *p*-methoxy-β-chloro-styrenes yielded *p*-ethylanisole on treatment with hydrogen in the presence of platinum (583).



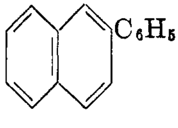
Similarly in the presence of palladium *p*-methoxy-β-chlorostyrene yielded 90 per cent of *p*-ethylanisole, 3,4-methylenedioxy-β-chlorostyrene yielded 65 per cent of 3,4-methylenedioxyethylbenzene, and β-bromostyrene yielded 62 per cent of ethylbenzene (99). When β-bromostyrene was treated with hydrogen at 140°C. in the presence of palladium, potassium hydroxide, and hydrazine hydrate in methanol solution, the product was 52 per cent of 1,4-diphenylbutadiene (132). This is really a coupling reaction but it is described here because the conditions are those of reduction.

B. Chemical methods of reduction

Again, Berthelot (1867) was the first to describe the reduction of styrene by chemical means (74, 77, 82). On treating the compound with hydriodic acid in a sealed tube at 280°C. ethylbenzene, plus a little benzene and ethane, was formed. With a larger excess of hydriodic acid the products were octane, a little hexane, and ethane. Stoermer and Kippe (711) later reported obtaining ethylbenzene by treating styrene with hydriodic acid. Under the same conditions they reported β-phenoxystyrene as giving phenol and styrene diiodide, since their ultimate product was β-phenylnaphthalene.

$$C_6H_5CH{=}CHOC_6H_5 + 2HI \rightarrow$$

$$C_6H_5OH + C_6H_5CHICH_2I \rightarrow$$



When heated to 200°C. with phosphorus and hydriodic acid, vinylmesitylene yielded mesitylene (393).

Klages and Keil (392) used sodium and alcohol very successfully for the reduction of styrene and its homologs. With styrene itself the yield of ethylbenzene was 82 per cent. Other styrenes reduced by the same method are summarized in table 2. While he does not say so specifically, Semmler (665) probably used sodium and alcohol to reduce β-acetoxystyrene to β-phenethyl alcohol. With sodium and alcohol β-phenoxystyrene gave a 65 per cent yield of ethylbenzene (710).

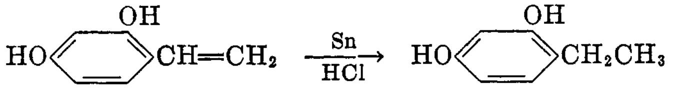
Sodium in liquid ammonia has been reported as a means of slowly reducing styrene to ethylbenzene (436). The yield given was 50 per cent, with polystyrene as the by-product (787). No reaction was obtained when styrene was treated with sodium amalgam and water (712); with this same reagent (*o*-vinylbenzyl)-trimethylammonium chloride yielded *o*-methylstyrene (188).

Metal and acid combinations have been utilized successfully for the reduction of substituted styrenes. Thus, 4-vinylresorcinol has been reduced to 4-ethylresorcinol with tin and hydrochloric acid (223). Similarly, *N*-methyl-*N*-β-styryl-*p*-toluenesulfonamide was reduced to *N*-methyl-*N*-β-phenethyl-*p*-toluenesulfonamide with iron and alcoholic hydrochloric acid (375). Zinc and acetic acid have been used to reduce what was probably 2-carboxy-4-methoxy-β,β-dichlorostyrene to 2-ethyl-5-methoxybenzoic acid (321) and a compound postulated as 2-methyl-4-methoxy-5-carboxy-α-hydroxy-β,β-dichlorostyrene to 2-hydroxy-4-methyl-5-ethylbenzoic acid (666).

TABLE 2

Reduction of styrenes with sodium and alcohol

STYRENE	YIELD	REFERENCE
	per cent	
p-Methyl		(186, 392)
2,4-Dimethyl	74	(392)
2,5-Dimethyl		(392)
2,4,5-Trimethyl	82	(392)
2,4,6-Trimethyl	90	(392)
p-Ethyl	85	(392)
2,5-Diethyl		(392)
2,4,5-Triethyl		(392)
p-Isopropyl		(392)
o-Methoxy		(390)
m-Methoxy		(390)
p-Methoxy		(390)
p-Ethoxy		(390)
3,4-Methylenedioxy		(390)



On the other hand, since stannous chloride and hydrochloric acid have no effect on the vinyl group in styrene, this reagent may be used for the reduction of other groups in the styrene molecule. These reactions are discussed in detail in the section devoted to reactions not involving the vinyl group.

C. Reduction of β-nitrostyrenes

Because of the importance of β-phenethylamines in biological and medicinal chemistry and because of their utility as starting materials for the synthesis of isoquinolines, the preparation of these compounds by the reduction of β-nitrostyrenes has occupied the attention of many chemists. The wide applicability of such a synthesis from the requisite aromatic aldehyde is obvious:

$$\mathrm{ArCHO} + \mathrm{CH_3NO_2} \rightarrow \mathrm{ArCH{=}CHNO_2} \xrightarrow{(H)} \mathrm{ArCH_2CH_2NH_2}$$

Unfortunately the reduction proved extremely difficult and it was a long time before it could be effected in good yields.

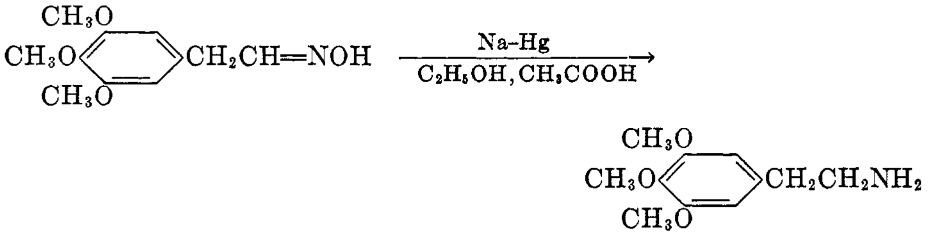
In 1873 Alexeyev (13), the first investigator in the field, treated nitrostyrene with sodium amalgam and isolated a red oil which might have been azostyrene. A red solution was obtained by treating nitrostyrene with zinc and alcoholic sodium hydroxide. Priebs (571), who first elucidated the chemistry of β-nitrostyrene, was unable to isolate anything from reduction experiments.

Bouveault and Wahl were the first to make any progress with the problem. In 1902 they reported obtaining *p*-methoxyphenylacetaldehyde and 3,4-methylenedioxyphenylacetaldehyde by treating the corresponding β-nitrostyrenes with zinc and acetic acid (107). Later the intermediate phenylacetaldoxime was isolated after treating β-nitrostyrene with aluminum amalgam or zinc and acetic acid (106). The yield when zinc and acetic acid in ether was used was 22 per cent (108).

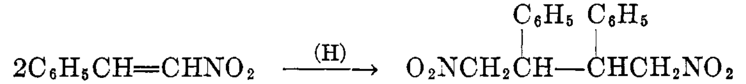
$$\mathrm{ArCH{=}CHNO_2} \xrightarrow[\mathrm{CH_3COOH}]{\mathrm{Zn}} \mathrm{ArCH_2CH{=}NOH} \xrightarrow{\mathrm{H_2O}} \mathrm{ArCH_2CHO}$$

Medinger (488) reduced 3,4-methylenedioxy-β-nitrostyrene with zinc and aqueous acetic acid and obtained a 70 per cent yield of 3,4-methylenedioxyphenylacetaldoxime. Zinc and ammonium chloride also was used successfully, but aluminum amalgam was not active. Rosenmund obtained a 20 per cent yield of *p*-methoxyphenylacetaldoxime as well as a little *p*-methoxy-β-phenethylamine by treating *p*-methoxy-β-nitrostyrene with aluminum amalgam in moist ether (623). With zinc and alcoholic acetic acid the yield of oxime was 33–48 per cent. This latter method was used to reduce 3,4-methylenedioxy-β-nitrostyrene to the desired aldoxime in 75 per cent yield and also was used successfully for the similar reduction of 3,4-dimethoxy-β-nitrostyrene (624). About this time two patents were issued to Bayer and Company, the first (58) describing the reduction of 3,4-methylenedioxy-β-nitrostyrene to 3,4-methylenedioxyphenylacetaldoxime by means of zinc and alcoholic acetic acid and to the aldoxime and 3,4-methylenedioxy-β-phenethylamine by means of aluminum and alcohol. The second patent (59) described the electrolytic reduction of the same nitro compound to the corresponding amine by means of a lead cathode in aqueous sulfuric and acetic acids.

Späth was the first investigator to reduce successfully the phenylacetaldoximes to the corresponding phenethylamines. Using sodium amalgam and alcoholic acetic acid he converted 3,4,5-trimethoxyphenylacetaldoxime to 3,4,5-trimethoxyphenethylamine (698). The overall yield from the corresponding nitrostyrene was 25 per cent. Later Späth and Dobrowsky (699) obtained a 16 per cent yield of 3-methoxy-4-ethoxy-β-phenethylamine from 3-methoxy-4-ethoxy-β-nitrostyrene by utilizing the same technique.

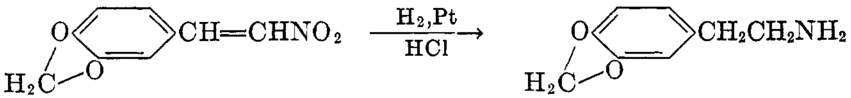


The early attempts to reduce nitrostyrenes with hydrogen and a catalyst yielded dimeric products. Thus, in the presence of platinum black Sonn and Schellenberg (693) obtained from β-nitrostyrene two compounds in 19 and 44 per cent yields, respectively, which presumably are the stereoisomeric forms of 2,3-diphenyl-1,4-dinitrobutane.



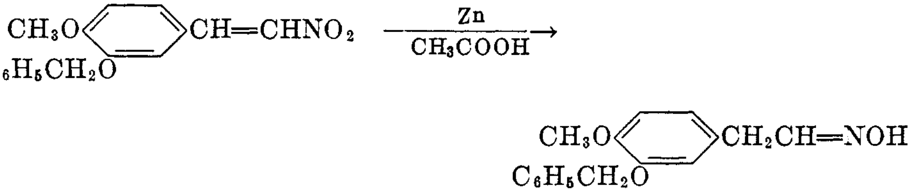
$$2C_6H_5CH{=}CHNO_2 \xrightarrow{(H)} O_2NCH_2\underset{}{\overset{C_6H_5}{C}}H{-}\overset{C_6H_5}{C}HCH_2NO_2$$

Two isomeric dimers also were obtained from 3,4-methylenedioxy-β-nitrostyrene. Using a mixture of ether and acetic acid instead of alcohol as the solvent, Banus and Vila (50) obtained low yields of both the diphenyldinitrobutane and phenylacetaldoxime from β-nitrostyrene. In either alcohol or ether Kohler and Drake (398) for the most part obtained the diphenyldinitrobutane, although the phenylacetaldoxime became the principal reaction product if hydrochloric acid was present. The same results were observed with a nickel catalyst. Skita (676) first reported the successful catalytic reduction of β-nitrostyrenes to β-phenethylamines. β-Phenethylamine and bis(β-phenethyl)amine were obtained from β-nitrostyrene and 3,4-methylenedioxy-β-phenethylamine from 3,4-methylenedioxy-β-nitrostyrene using a platinum catalyst, and *p*-methoxy-β-phenethylamine from *p*-methoxy-β-nitrostyrene using a palladium and then a platinum catalyst.



In all cases hydrochloric acid was included in the reaction mixture.

Of the three successful methods whose development has just been outlined—namely, catalytic reduction, electrolytic reduction, and reduction through the phenylacetaldoxime—the last mentioned has been the least used. It has the disadvantage of involving two steps and of giving low yields. Thus, Shoesmith and Connor (668) obtained a very small yield of *m*-methoxy-β-phenethylamine from *m*-methoxy-β-nitrostyrene by this technique. Incidentally, De (157) was unsuccessful in subsequent attempts to reduce this particular nitrostyrene. Kobayashi (395) used this method to obtain 10 per cent of 3-methoxy-4-hydroxy-β-phenethylamine from either 3-methoxy-4-hydroxy-β-nitrostyrene or its acetate. The method was not effective for the reduction of 3-methoxy-4-methoxymethyleneoxy-β-nitrostyrene to the corresponding amine, and the reduction of 3-methoxy-4-benzyloxy-β-nitrostyrene proceeded only as far as the phenylacetaldoxime. Jansen (352, 353) obtained only 20 per cent of 2,4,5-trimethoxyphenylacetaldoxime by treating 2,4,5-trimethoxy-β-nitrostyrene with zinc and acetic acid. The amine was obtained by treatment with sodium amalgam. On the other hand Späth, Orechoff, and Kuffner (700) obtained 95 per cent of 3-benzyloxy-4-methoxyphenylacetaldoxime from 3-benzyloxy-4-methoxy-β-nitrostyrene.



Probably the most widely used technique for reducing β-nitrostyrenes to β-phenethylamines is the electrolytic method. It achieved particularly extensive application for the seven years preceding the development of satisfactory catalytic techniques, but has not been employed as much since that time. The usual technique was to use a lead cathode and a mixture of alcohol, acetic acid, and hydrochloric acid as the electrolyte. In table 3 are listed the β-nitrostyrenes which have been reduced to β-phenethylamines by this method. Under the same conditions *m*,β-dinitrostyrene yielded 54 per cent of *m*-amino-β-phenethylamine, 4-methoxy-β,3-dinitrostyrene 47 per cent of 3-amino-4-methoxy-β-phenethylamine, and 4,5-dimethoxy-3,β-dinitrostyrene 49 per cent of 3-amino-4,5-dimethoxy-β-phenethylamine (684).

Subsequent to Skita's first description of the catalytic hydrogenation of β-nitrostyrene to β-phenethylamine, Sawai (648) hydrogenated 3-methoxy-4-ethoxy-β-nitrostyrene to 3-methoxy-4-ethoxy-β-phenethylamine with a platinum catalyst. Skita and Keil (677) reduced *p*-methoxy-β-nitrostyrene (16 per cent yield), 3,4-dimethoxy-β-nitrostyrene, and 3,4,5-trimethoxy-β-nitrostyrene (28 per cent yield) to the corresponding β-phenethylamines with hydrogen in the presence of a catalyst.

Kindler, Brandt, and Gehlhaar (380) were the first to effect this type of reduction in good yields. They used a palladium catalyst and dissolved their β-nitrostyrene in glacial acetic acid containing sulfuric acid. At 15°C. 90 per cent of the hydrogenation was complete in 2 min. and the reaction was over in 10 min. Their yield of β-phenethylamine was 84 per cent. In the absence of sulfuric acid, 90 per cent of the reaction was complete in 10 hr. and the yield of β-phenethylamine was only 8 per cent.

TABLE 3

Electrolytic reduction of β-nitrostyrenes

β-NITROSTYRENE	YIELD	REFERENCE
	per cent	
p-Methoxy		(409)
3,4-Dimethoxy		(52, 406, 408)
2,5-Dimethoxy	51	(718)
2,3,4-Trimethoxy	87	(683)
2,4,5-Trimethoxy		(352, 353)
3,4,5-Trimethoxy	77	(683)
3-Methoxy-4-ethoxy		(410)
3,4-Diethoxy	60.5	(679)
2,3,4-Triethoxy	73	(683)
3,4,5-Triethoxy	78	(683)
3,4-Methylenedioxy	76	(729, 730)
3,4-Methylenedioxy	67	(679)
3-Benzyloxy-4-methoxy	60	(622)
3-Methoxy-4-benzoxy	40–60	(752)
m-Bromo		(407)
3-Bromo-4-methoxy		(407)
3,4-Dimethoxy-5-bromo	42	(752)
m-Carbomethoxy	52	(682)
p-Carbomethoxy	49	(682)
m-Carbethoxy	53.5	(682)
p-Carbethoxy	46	(682)

TABLE 4

Catalytic hydrogenation of β-nitrostyrenes

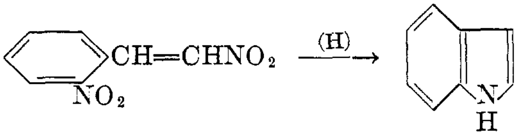
β-NITROSTYRENE	YIELD	REFERENCE
	per cent	
p-Methoxy	77	(379)
3,4-Dimethoxy	61	(379)
3,4-Dimethoxy	23	(487)
3,4,5-Trimethoxy	84	(279)
3,4,5-Trimethoxy	62	(379)
3,4-Methylenedioxy	93	(649, 650)
3,4-Methylenedioxy	76	(379)
3,4-Methylenedioxy	70	(487)
3-Methoxy-4,5-methylenedioxy	76	(379)
m-Nitro (to *m*-amino)	41	(649)
o-Hydroxy	79	(280)
m-Hydroxy	72.5	(280)
p-Hydroxy	85	(280)
3-Hydroxy-4-methoxy	68	(279)
3-Methoxy-4-hydroxy	84.5	(280)
p-Acetoxy	80	(280)

This technique immediately received wide application with both palladium and platinum catalysts. By means of this procedure the β-nitrostyrenes listed in table 4 were reduced to the corresponding β-phenethylamines.

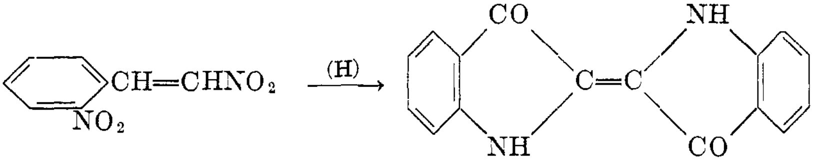
Recently it has been shown that β-nitrostyrene may be reduced to β-phenethylamine in 60 per cent yield by means of lithium aluminum hydride (534a).

Meanwhile Reichert and Koch (609) discovered that hydrogenation in pyridine solution gave the corresponding phenylacetaldoxime in excellent yield. They used a palladium catalyst on a charcoal carrier. The following β-nitrostyrenes were reduced by this technique: *o*-methoxy- (90 per cent) (607, 609), *p*-methoxy- (almost quantitative) (609), 2,4-dimethoxy- (92 per cent) (607, 609), 3,4-dimethoxy- (609), and 3,4,5-trimethoxy- (90 per cent) (606, 607). Several of these phenylacetaldoximes subsequently were reduced to the corresponding β-phenethylamines by means of hydrogen in the presence of a platinum catalyst. Alcohol was used as the solvent and oxalic acid was added to the reaction mixture. The yields were as follows: *o*-methoxy- (60 per cent) (607), 2,4-dimethoxy- (60 per cent) (607), and 3,4,5-trimethoxy- (80 per cent) (606, 607).

With a variety of reducing agents *o*,β-dinitrostyrene gave low yields of indole.

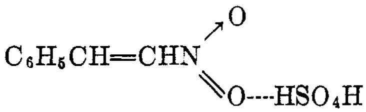


The results are as follows: iron and acetic acid, 9.4 per cent (440), 32 per cent (532); zinc and acetic acid, 11 per cent (440), low (532); and aluminum amalgam, some (440), trace (532). Alkaline sodium hydrosulfite yielded indigo (532).



No tribromoindole was obtained when β,2-dinitro-3,4,5-tribromostyrene was treated with iron and acetic acid. However, with more active 2,β-dinitrostyrenes the method appears to have considerable synthetic utility. Thus, 4-acetoxyindole (29–35 per cent) (59a), 5-acetoxyindole (50–55 per cent) (59a), and 5,6-methylenedioxyindole (81 per cent) (131a) have been prepared in this way.

It is to be noted that all reductions of β-nitrostyrenes to β-phenethylamines which were effected in good yield were conducted in the presence of a strong acid. In the absence of such acid the reduction proceeded only as far as the phenylacetaldoxime. Kindler, Brandt, and Gehlhaar (380) postulated that in the presence of sulfuric acid they were actually reducing a molecular compound of the β-nitrostyrene and the acid.



$$C_6H_5CH{=}CHN\begin{matrix}\nearrow O\\ \searrow O\text{---}HSO_4H\end{matrix}$$

The effect of the acid was to polarize the molecule by drawing the electrons away from the benzene ring. This concentrated the unsaturation at the far end of the chain (on the carbon atom attached to the ring) and thereby facilitated reduction at this point. It particularly avoided the formation of radicals of the type

$$C_6H_5\underset{|}{C}HCH_2NO_2$$

which could dimerize to give the bimolecular reduction products described by Sonn and Schellenberg (693). Apparently the general effect of a strong acid is just this type of polarization which weakens the double bonds and facilitates the addition of hydrogen. It is equally applicable to the β-nitrostyrenes or the phenylacetaldoximes. In the absence of such polarization the oxime is stable to further reduction under most of the conditions which have been tried. In pyridine solution particularly high yields of the oxime have been obtained. It would be expected that pyridine would form a loose molecular complex with the oxime

$$C_6H_5CH_2CH{=}NOH{\leftarrow}NC_5H_5$$

which would give the reverse polarization from that produced by a strong acid and therefore would increase the difficulty of further reduction.

II. OXIDATION

A. Oxidation to aromatic acids

The first application of oxidation in the field of styrene chemistry was in structure proof where the side chain was oxidized to a carboxyl group. Location of the side chain by this means subsequently has been utilized very often.

In 1844 Kopp first oxidized styrene to benzoic acid by means of chromic acid (411). With boiling concentrated nitric acid the product was nitrobenzoic acid.

$$C_6H_5CH{=}CH_2 \xrightarrow{CrO_3} C_6H_5COOH$$

Blyth and Hofmann (87) also obtained nitrobenzoic acid when they oxidized styrene with nitric acid. Benzoic acid and benzaldehyde were obtained as by-products. With potassium dichromate and sulfuric acid benzoic acid was produced. Oxidation to benzoic acid was one means utilized by Dykstra to identify styrene (181). With nitric acid and bromine styrene yielded a mixture of bromonitromethanes (154).

In table 5 are summarized the oxidations of some substituted styrenes to the corresponding aromatic acids. However, when the p-hydroxyl group in 3,4-

dimethoxystyrene was not etherified, dilute nitric acid removed the side chain, so that the product of the oxidation was methoxyquinone (249).

Styrenes with halogen in the β-position in the side chain are oxidized with greater difficulty than unsubstituted styrenes. Thus, β-bromostyrene is oxidized with difficulty by potassium permanganate (303), since it is more resistant than unsaturated aliphatic bromides to this reagent. Similarly chromic and sulfuric acids at 95°C. did not affect β-chlorostyrene and while some benzoic and formic acids were obtained from β-bromostyrene, 60 per cent of the styrene was recovered unchanged (147). β-Chlorostyrene was oxidized to benzoic acid by potassium dichromate and nitric acid (269). In table 6 are summarized the oxidations of some other halogenated and nitrated styrenes to the corresponding aromatic acids.

TABLE 5

Oxidation of styrenes to aromatic acids

STYRENE	OXIDIZING AGENT	BENZOIC ACID PRODUCED	REFERENCE
p-Methyl	HNO_3	*p*-Methyl	(215)
2,4-Dimethyl	$KMnO_4$	2,4-Dimethyl	(483)
3,4-Dimethyl	$KMnO_4$	3,4-Dimethyl	(483)
tert-Butyl	Cold CrO_3	(No oxidation)	(551)
p-Methoxy	$KMnO_4$	*p*-Methoxy	(581)
2-Methyl-4-methoxy	$KMnO_4$	2-Methyl-4-methoxy	(582)
3-Methyl-4-methoxy	$KMnO_4$	3-Methyl-4-methoxy	(582)
5-Methyl-2-methoxy	$KMnO_4$	5-Methyl-2-methoxy	(582)
2-Methyl-4-methoxy-5-isopropyl	$KMnO_4$	2-Methyl-4-methoxy-5-isopropyl	(582)
2,6-Dimethoxy	$KMnO_4$	2,6-Dimethoxy	(667)
3-Nitro-4-methoxy	$KMnO_4$	3-Nitro-4-methoxy	(184)
2,4-Dimethoxy	$KMnO_4$	2,4-Dimethoxy	(223)
	HNO_3	2,4-Dimethoxy	(223)
3,4-Dimethoxy	$KMnO_4$	3,4-Dimethoxy	(249)
	HNO_3	3,4-Dimethoxy	(249)
p-Dimethylamino	$KMnO_4$	(Not isolated)	(111)
o-Dimethylaminomethyl	$KMnO_4$	(Not isolated)	(188)
o-(β-Dimethylaminoethyl)	$KMnO_4$	(Not isolated)	(116)
β-(*N*-Methyl-*N*-acetyl)-3,4-diacetoxy	$KMnO_4$	(Not isolated)	(118)
p-*N*,*N*-Dimethylsulfonamido	$KMnO_4$	*p*-*N*,*N*-Dimethylsulfonamido	(349)

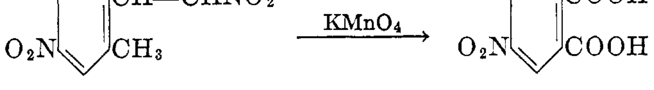
Treatment of what was probably 3-carboxy-4-methoxy-β,β-dichlorostyrene with fuming nitric acid at 100°C. yielded 4-methoxyisophthalic acid (321). Both β,β-dichlorostyrene and α,β,β-trichlorostyrene gave a mixture of benzoic and *p*-nitrobenzoic acids when treated with nitrogen tetroxide at 100°C. (86).

With methylated nitrostyrenes potassium permanganate has given variable results. Thus, Worrall has used it to oxidize 4-methyl-β,3-dinitrostyrene to 3-nitro-4-methylbenzoic acid (790). On the other hand, Hanzlik and Bianchi (284) obtained nitroterephthalic acid from 4-methyl-β,3-dinitrostyrene using permanganate but got 3-nitro-4-methylbenzoic acid using nitric acid. Franzen and Schneider (235) obtained 4-nitrophthalic acid by treating 2-methyl-β,4-dinitrostyrene with potassium permanganate.

TABLE 6

Oxidation of halogenated and nitrated styrenes

STYRENE	OXIDIZING AGENT	PRODUCT OBTAINED	REFERENCE
2-Bromo-4-trifluoromethyl	$KMnO_4$	2-Bromo-4-trifluoromethylbenzoic acid	(43)
α,β-Dibromo	$KMnO_4$	Benzoic acid	(17)
β,*p*-Dibromo	$KMnO_4$	*p*-Bromobenzoic acid	(614)
2-Methoxy-β,3,5-tribromo	$KMnO_4$	2-Methoxy-3,5-dibromobenzoic acid	(248)
3-Methoxy-β,6-dibromo	$KMnO_4$	(Not isolated)	(612)
p-Methoxy-β-chloro	$KMnO_4$	Anisic acid	(583)
p-Methoxy-α-chloro	$KMnO_4$	Anisic acid	(583)
4-Methyl-β,2-dichloro	$KMnO_4$	2-Chloro-4-methylbenzoic acid	(32)
2,4-Dimethyl-β-chloro	$KMnO_4$	2,4-Dimethylbenzaldehyde	(42)
2,4-Dimethyl-β,6-dichloro	$KMnO_4$	2,4-Dimethyl-6-chlorobenzaldehyde	(42)
β-Nitro	$K_2Cr_2O_7 + H_2SO_4$	Benzoic acid	(571)
β,*o*-Dinitro	$KMnO_4$	*o*-Nitrobenzoic acid	(571)
β,*p*-Dinitro	CrO_3	*p*-Nitrobenzoic acid	(571)
β-Chloro-β,*p*-dinitro	$CrO_3 + CH_3COOH$	*p*-Nitrobenzoic acid	(560)
4-Methoxy-β,3-dinitro	$KMnO_4$	3-Nitroanisic acid	(184)
2-Bromo-β,5-dinitro	$KMnO_4$	2-Bromo-5-nitrobenzoic acid	(794)
2-Iodo-β,5-dinitro	$KMnO_4$	2-Iodo-5-nitrobenzoic acid	(793)



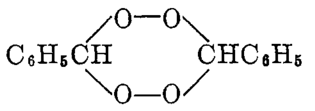
B. Ozonization

The first ozonization of styrene itself was reported in 1930, by Brus and Peyresblanques (127), who showed that ozone was absorbed quantitatively by the side chain before the nucleus was attacked. Briner and Gelbert (122) ozonized styrene in carbon tetrachloride solution. Decomposition of the ozonide with hot water yielded benzaldehyde and formic acid. When allowed to stand for 10 hr., styrene ozonide slowly evolved a gas which consisted of 40 per cent hydrogen, 45 per cent carbon dioxide, and 15 per cent methane. Benzoic acid was isolated from the non-volatile residue. Styrene ozonide was too unstable to permit the measurement of the heat of ozonization of styrene (123). Since Marvel and Nichols (481) isolated dibenzaldehyde peroxide (I) from the ozonization of styrene even under strictly anhydrous conditions, they postulated that styrene ozonide decomposed directly to the ozonization products without ever passing through an intermediate dihydroxydibenzaldehyde peroxide (II) whose presence they were never able to detect.

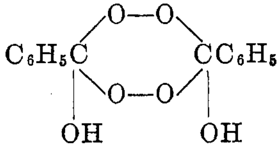
TABLE 7

Molecular weight of styrene ozonide

SOLVENT	$(C_8H_8O_3)_6$	$(C_8H_8O_3)_4$	$(C_8H_8O_3)_2$
	per cent	*per cent*	*per cent*
CCl_4	56	33	
C_6H_6	59	29	
$CHCl_3$		57	35
$(C_2H_5)_2O$			74



I



II

Kawamura (366) obtained benzaldehyde, formaldehyde, and hydrogen peroxide by decomposing styrene ozonide with hot water. He reported the ozonide to be largely polymeric, with the molecular weight depending on the solvent used. These results are summarized in table 7.

Semmler (665) was the first to use ozonization for structure proof in the styrene series. β-Acetoxystyrene was oxidized to a mixture of benzaldehyde and benzoic acid by this method. Subsequently a number of styrenes were ozonized and the corresponding benzaldehydes isolated in each case. These include a mixture of *o*- and *p*-methoxystyrenes (581), β-chloro-*p*-methoxystyrene (583), α-chloro-*p*-methoxystyrene (583), 3-hydroxy-4-ethoxystyrene (359), 2-methoxy-5-isopropylstyrene (585), and 3-methoxy-4-hydroxystyrene (62–74 per cent yield) (652).

C. Air oxidation

Moureu and Dufraisse (523), who were the first to investigate this reaction, found that the following substances were positive catalysts for the air oxidation of styrene: I_2, KI, NaI, LiI, MgI_2, ZnI_2, FeI_2, NH_4I, $CH_3NH_2 \cdot HI$, $(CH_3)_2NH \cdot HI$, $(CH_3)_3N \cdot HI$, CHI_3. This effect was investigated further (524) and the following compounds added to the list: Sb_2O_5, SbI_3, $SbBr_3$, $SbCl_3$, $(C_6H_5)_2SbCl$, $(C_6H_5)_3SbCl_2$, $Bi(NO_3)_3$, $BiBr_3$, BiI_3, $(C_2H_5)_3Bi$, $(C_3H_7)_3Bi$, V_2O_3, V_2O_5, $VOCl_3$, NH_4VO_3. The following substances inhibited the air oxidation of styrene: tartar emetic, $(C_6H_5)_3Sb$, Bi, Bi_2O_3, $[(CH_3)_2CH(CH_2)_2]_3Bi$, $(C_6H_5)_3Bi$. Triphenylmethyl also is a catalyst for the air oxidation of styrene (806).

Styrene is a fairly strong inhibitor for the oxidation of benzaldehyde in the presence of light (594). In this case styrene oxide was isolated after blowing a mixture of benzaldehyde and styrene with oxygen. A careful study of the oxidation and polymerization of styrene at 70–90°C. in the presence of benzaldehyde, formaldehyde, polystyrene, or benzoyl peroxide showed that the oxidation of styrene consists of two chain reactions involving peroxides and propagated through free radicals (489). The direct oxidation of styrene with air over a nickel–chromium gauze catalyst at 110°C. yielded formaldehyde as one of the products (539).

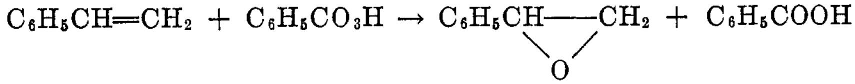
The oxidation of an α-halostyrene with oxygen is particularly interesting in that it leads directly to the corresponding benzoyl halide and formaldehyde.

$$C_6H_5CCl{=}CH_2 + O_2 \rightarrow C_6H_5COCl + HCHO$$

These products have been isolated in the case of α-chlorostyrene (174). In the case of *p*-methoxy-α-chlorostyrene it was shown that the anisic acid which was isolated came from anisoyl chloride (583). For the air oxidation of α-bromostyrene, sodium iodide and methylammonium iodide have been shown to be positive catalysts, while iodine, ferrous iodide, and iodoform are negative (523).

D. Epoxidation

Böeseken and Derx (93) originally showed that styrene formed an epoxide on treatment with perbenzoic acid more easily than did 1,4-dihydronaphthalene,



$$C_6H_5CH{=}CH_2 + C_6H_5CO_3H \rightarrow C_6H_5\underbrace{CH{-}CH_2}_{O} + C_6H_5COOH$$

indene, or 1,2-dihydronaphthalene. Hibbert and Burt obtained 70–75 per cent yields of styrene oxide by conducting this oxidation in chloroform at 0°C. (297, 298). Golumbic and Cottle (273) found their product to be contaminated with a little phenylacetaldehyde. The epoxidation also can be effected with peracetic acid (728); in this case the reaction has been shown to be bimolecular as a result of rate studies made with a number of olefins (97, 716).

E. Miscellaneous oxidations

When styrene was treated with hydrogen peroxide at 0°C. in *tert*-butyl alcohol solution in the presence of osmium tetroxide, the product was a 50 per cent yield of styrene glycol (511). Treatment of styrene with potassium permanganate in

$$C_6H_5CH{=}CH_2 + H_2O_2 \xrightarrow{OsO_4} C_6H_5CHOHCH_2OH$$

the presence of very dilute sodium hydroxide produced a 69 per cent crude yield (55 per cent pure) of phenylglyoxylic acid, together with a 7 per cent yield of benzoic acid (320). Styrene and chromyl chloride reacted to form an addition compound which decomposed on treatment with water to give benzaldehyde, chlorinated products, and a trace of phenylacetaldehyde (290). Styrene did not react with selenium dioxide at 140°C. and yielded complex products at higher temperatures (620). It has been reported that when styrene and oxygen are passed over active carbon at 100–110°C. very small amounts of pentoses are produced (538). Oxidation of 3-methoxy-4-acetoxystyrene with sodium dichromate and sulfuric acid at 50°C. yielded 71 per cent of vanillin (652).

$$C_6H_5CH{=}CH_2 \xrightarrow[\text{aqueous NaOH}]{KMnO_4} C_6H_5COCOOH + C_6H_5COOH$$

III. CHLORINATED DERIVATIVES

A. Addition of chlorine

Laurent (435) in 1844 was the first to add chlorine to styrene. He also described a chlorinated styrene where one hydrogen atom was replaced by chlorine (probably α-chlorostyrene). It was obtained by treating styrene dichloride with potassium hydroxide. A derivative also was mentioned from which two hydrogen atoms were lost and to which eight chlorine atoms were added. Blyth and Hofmann (87) also added chlorine to styrene and mentioned that the resulting styrene dichloride lost hydrogen chloride on treatment with alcoholic potassium hydroxide. Berthelot (72, 77) mentions the addition of chlorine as one of the characteristic reactions of styrene. Biltz (85) found chloroform to be a suitable solvent for this addition. In carbon tetrachloride solution with no particular precautions for the exclusion of light, the product was about three parts of styrene dichloride to one of β-chlorostyrene (197).

$$C_6H_5CH{=}CH_2 + Cl_2 \rightarrow C_6H_5CHClCH_2Cl$$

Styrene dichloride has been obtained in several other ways. It constitutes 10 per cent of the product when styrene is treated with bromine chloride (759). It is obtained in 50 per cent yield, along with 36 per cent of β-styrenephosphonic acid, when styrene is treated with phosphorus trichloride and chlorine in anhydrous benzene (412). It is one of the products of the reaction between styrene and nitrosyl chloride (555) and also is formed by the chlorination of ethylbenzene at its boiling point. In this latter reaction Evans, Mabbot, and Turner (213) have postulated its formation as the addition of chlorine to styrene formed by dehydrochlorination of chloroethylbenzene in the mixture. Styrene dichloride

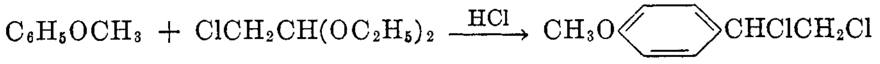
$$C_6H_5CH{=}CH_2 \xrightarrow[C_6H_6]{PCl_3 + Cl_2} C_6H_5CHClCH_2Cl + C_6H_5CH{=}CHPO_3H_2$$

$$C_6H_5C_2H_5 \xrightarrow{Cl_2} C_6H_5C_2H_4Cl \xrightarrow{-\,HCl} C_6H_5CH{=}CH_2 \xrightarrow{Cl_2} C_6H_5CHClCH_2Cl$$

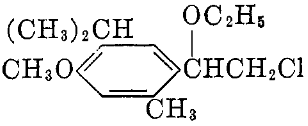
has been postulated as the initial product of the reaction between benzene and *s*-dichloroethylene in the presence of an aluminum-mercury couple (91). The styrene dichloride reacts further with another molecule of benzene to give as the final product 2-chloro-1,1-diphenylethane.

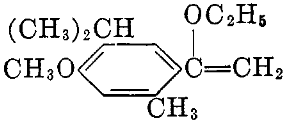
$$C_6H_6 + CHCl{=}CHCl \xrightarrow{AlCl_3} [C_6H_5CHClCH_2Cl] \xrightarrow{C_6H_6} (C_6H_5)_2CHCH_2Cl$$

3,4-Methylenedioxystyrene readily yields the dichloride when treated with chlorine in carbon tetrachloride solution (51 (72 per cent yield), 100, 495, 496). *p*-Methoxystyrene dichloride has been prepared in 25–30 per cent yield by treating anisole with chloroacetal and hydrogen chloride at 60–70°C. (583). With *o*-cresyl methyl ether, *p*-cresyl methyl ether, and thymol methyl ether the yields

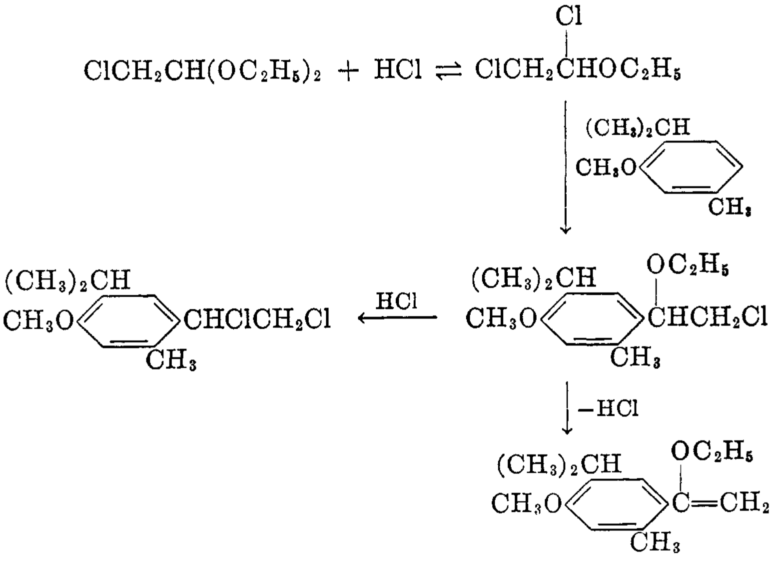


fell to 5 per cent. In the case of thymol two other compounds were isolated from the reaction mixture.



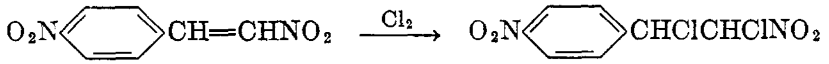


These products suggest that the reaction with β-chloroacetal involves the active *p*-hydrogen and the α,β-dichloro ether:



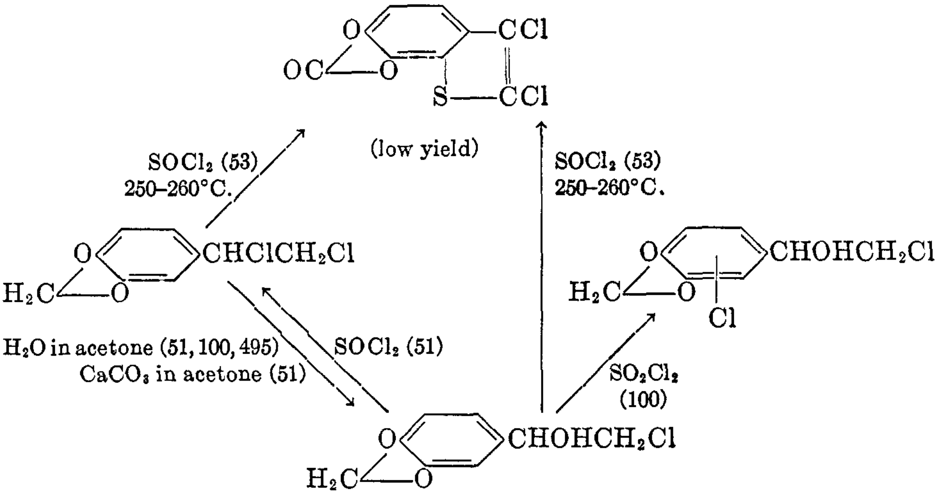
All four of these dichlorides (*p*-methoxystyrene dichloride, 3-methyl-4-methoxystyrene dichloride, 2-methoxy-5-methylstyrene dichloride, and 2-methyl-4-methoxy-5-isopropylstyrene dichloride) were prepared in 25 per cent yield by treating the corresponding styrene with chlorine.

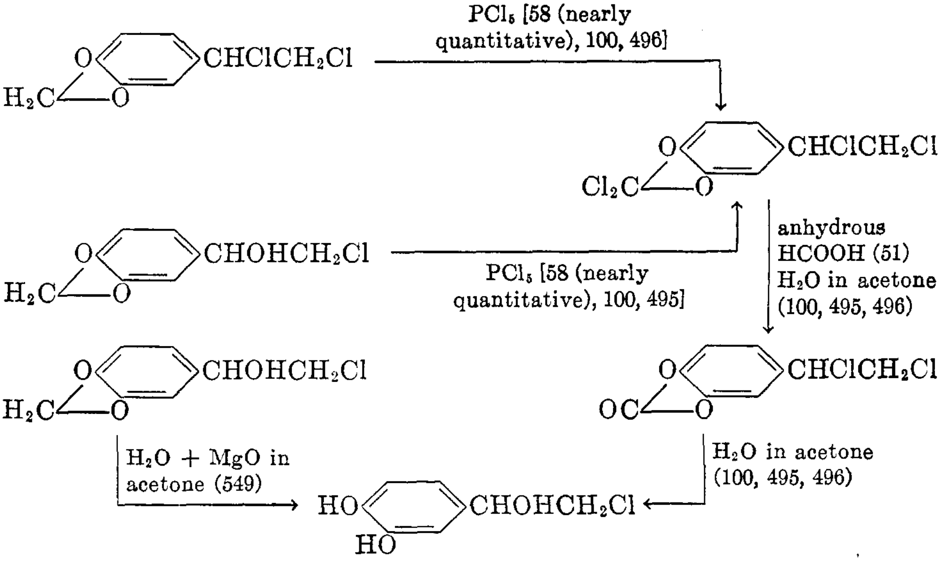
Priebs (571) found that β-nitrostyrene readily added chlorine in chloroform solution. Pfeiffer (560) found the same to be true of β,p-dinitrostyrene (53 per cent yield), and Worrall and Finkel (794) extended the reaction to β,5-dinitro-2-bromostyrene.



When styrene dichloride was heated for several hours at 120°C. with aqueous calcium carbonate, there was obtained a 70 per cent yield of styrene chlorohydrin

$$C_6H_5CHClCH_2Cl \xrightarrow[CaCO_3]{H_2O} C_6H_5CHOHCH_2Cl + C_6H_5CHOHCH_2OH$$





contaminated with a trace of styrene glycol (330). With sodium acetate the yield was 70–80 per cent, with sodium carbonate 40 per cent, and with calcium hydroxide "good."

In the case of the last-named reagent styrene glycol was obtained exclusively if one mole of calcium hydroxide was used instead of the one-half mole necessary for chlorohydrin formation. When this type of hydrolysis was utilized as an analytical procedure (647), the styrene dichloride was boiled with potassium hydroxide in benzyl alcohol, cooled, diluted with water, and the liberated halide titrated with silver nitrate.

The conversion of 3,4-methylenedioxystyrene dichloride to the corresponding chlorohydrin has been examined as a route to 3,4-dihydroxystyrene chlorohydrin. The various transformations studied are shown in the chart on page 201.

When styrene dichloride was distilled from pyridine, a 90 per cent yield of β-chlorostyrene was obtained (329). This reaction also has been employed for

$$C_6H_5CHClCH_2Cl \xrightarrow{\text{pyridine}} C_6H_5CH{=}CHCl$$

(90 per cent)

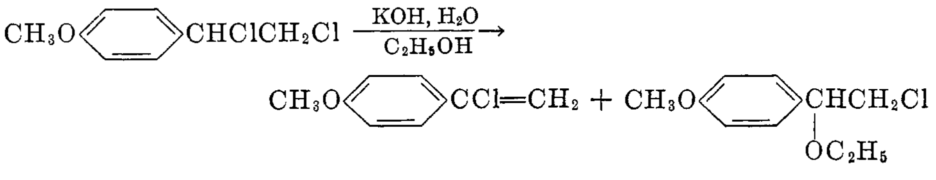
the preparation of p-methoxy-β-chlorostyrene, 3-methyl-4-methoxy-β-chlorostyrene, 2-methoxy-5-methyl-β-chlorostyrene, and 2-methyl-4-methoxy-5-isopropyl-β-chlorostyrene from the corresponding substituted styrene dichlorides (583). A yield of 92 per cent of β-chlorostyrene has been obtained by passing styrene dichloride vapors together with steam over alumina at 360–400°C. (197).

On the other hand, treatment of styrene dichloride with alcoholic sodium hydroxide yielded 89 per cent of α-chlorostyrene (197). As mentioned previously, this reaction had been observed by the earliest investigators (87, 435). Glaser

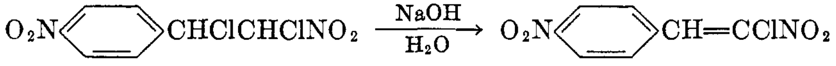
$$C_6H_5CHClCH_2Cl \xrightarrow[C_2H_5OH]{NaOH} C_6H_5CCl{=}CH_2$$

(89 per cent)

(269) obtained α-chlorostyrene by boiling styrene dichloride with calcium oxide. Alcoholic sodium ethoxide has been used similarly to prepare p-methoxy-α-chlorostyrene, 3-methyl-4-methoxy-α-chlorostyrene, 2-methoxy-5-methyl-α-chlorostyrene, and 2-methyl-4-methoxy-5-isopropyl-α-chlorostyrene from the corresponding substituted styrene dichlorides (583). When p-methoxystyrene dichloride was treated with potassium hydroxide in aqueous ethanol, both p-methoxy-α-chlorostyrene and p-methoxy-α-ethoxy-β-chloroethylbenzene were obtained. The latter compound was the sole product obtained by treating p-methoxystyrene dichloride with alcoholic potassium cyanide.



Priebs (571) reported that treatment of β-nitrostyrene dichloride with dilute sodium hydroxide yielded α-chloro-β-nitrostyrene. Subsequent investigators have always obtained the β-halostyrene in this type of reaction. Since Thiele and Haeckel (737) showed Priebs to be wrong in the case of the bromo compound, his formulation here probably was incorrect also. Thus Pfeiffer (560) obtained β-chloro-β,*p*-dinitrostyrene by treating β,*p*-dinitrostyrene dichloride with aqueous sodium hydroxide, and Worrall and Finkel (794) obtained β-chloro-2-bromo-β,5-dinitrostyrene by treating 2-bromo-β,5-dinitrostyrene dichloride with alcoholic potassium acetate. Similarly, *p*-methyl-β-nitrostyrene dichloride yielded *p*-methyl-β-chloro-β-nitrostyrene (790).



B. β-Chlorostyrene chemistry

The preparation of β-chlorostyrenes from styrene dichlorides has been described above. While a very convenient method, it has not been as widely used as the various routes from cinnamic acid. In 1845 Stenhouse (708, 709) first obtained a chlorine-containing oil by treating cinnamic acid with bleaching powder, potassium hypochlorite, or chlorine and hot water. In 1864 Erlenmeyer (201) showed that it had the empirical formula C_8H_7Cl. Glaser (269) added hypochlorous acid to cinnamic acid and then boiled the adduct with aqueous sodium carbonate. He placed the chlorine in the product in the α-position. Erlenmeyer (204) later showed Glaser's compound to be β-chlorostyrene, since it did not have the same properties as the α-chlorostyrene which Friedel obtained by treating acetophenone with phosphorus pentachloride followed by potassium hydroxide.

$$C_6H_5CH{=}CHCOOH \xrightarrow{HOCl} C_6H_5CHOHCHClCOOH \xrightarrow[Na_2CO_3]{aqueous} C_6H_5CH{=}CHCl$$

$$C_6H_5COCH_3 \xrightarrow{PCl_5} C_6H_5CCl_2CH_3 \xrightarrow{KOH} C_6H_5CCl{=}CH_2$$

Erlenmeyer (207) obtained a 97 per cent yield of β-chlorostyrene by treating cinnamic acid dichloride with cold aqueous sodium carbonate.

$$C_6H_5CHClCHClCOOH \xrightarrow[Na_2CO_3]{aqueous} C_6H_5CH{=}CHCl$$

Biltz (85, 449) used hot carbonate and v. Auwers (34) found cold or hot carbonate equally useful. Durrans (178) used aqueous sodium hydroxide to decompose his cinnamic acid dichloride, while Dann, Howard, and Davies (150) used aqueous sodium acetate (60 per cent yield). This alkaline decomposition of a cinnamic acid dichloride has been found equally suitable for the preparation of *p*-methyl-β-chlorostyrene (40), *o*-iodo-β-chlorostyrene (774), and β,*p*-dinitro-β-chlorostyrene (560).

When Read and Andrews treated cinnamic acid with cold dilute chlorine water a 91 per cent yield of α-chloro-β-hydroxycinnamic acid was obtained

$$\begin{aligned} C_6H_5CH{=}CHCOOH \xrightarrow[H_2O]{Cl_2} {} & C_6H_5CHOHCHClCOOH \\ & + C_6H_5CHClCHClCOOH + C_6H_5CH{=}CHCl \end{aligned}$$

(596). By-products included 1 per cent of cinnamic acid dichloride and 8 per cent of β-chlorostyrene. The same reaction has been observed by other investigators (94), who have isolated such other by-products as phenylacetaldehyde (210) and α-hydroxy-β,β-dichloroethylbenzene (228). In the latter case the yield of α-chloro-β-hydroxycinnamic acid was 73.5 per cent, of β-chlorostyrene 1.8 per cent, and of α-hydroxy-β,β-dichloroethylbenzene 16 per cent. When cold sodium hypochlorite was used in place of cold chlorine water the yield of acid was 72 per cent and of β-chlorostyrene 28 per cent. It is interesting to note that the decomposition of α-chloro-β-hydroxycinnamic acid yielded mostly phenylacetaldehyde plus a little β-chlorostyrene (40).

TABLE 8

β-Chlorostyrenes from alkali cinnamates

ALKALI CINNAMATE	YIELD OF β-CHLOROSTYRENE OBTAINED	REFERENCE
	per cent	
p-Methoxy	57	(99)
3,4-Methylenedioxy	60	(99)
o-Nitro		(453)
	16	(404, 405)
	5–15	(150)
m-Nitro	5–15	(150)
p-Nitro	5–15	(150)

$$C_6H_5CHOHCHClCOOH \rightarrow C_6H_5CH_2CHO + C_6H_5CH{=}CHCl$$

Recently it has been reported that treatment of sodium cinnamate with sodium hypochlorite and alcohol yielded chloroform, benzoic acid, and chlorostyrene (719). No chlorostyrene was obtained in the absence of alcohol.

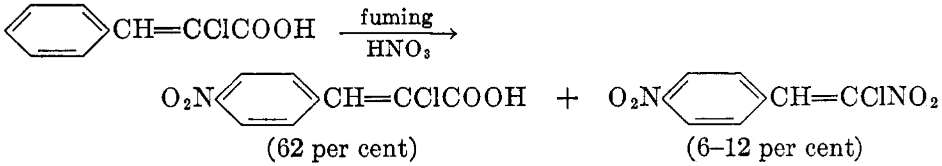
With sodium *p*-nitrocinnamate and hypochlorous acid, not only was α-hydroxy-β-chloro-*p*-nitrophenylpropionic acid isolated, but also epoxy *p*-nitrocinnamic acid and *p*-nitro-β-chlorostyrene (207). With other substituted alkali cinnamates hypochlorous acid or sodium hypochlorite gave the β-chlorostyrene as the principal product of the reaction, as shown in table 8. In the case of sodium *o*-methoxycinnamate both mono- and di-chlorinated derivatives of *o*-methoxystyrene were obtained (552).

This same reaction was responsible for the by-product in another degradation. Treatment of styryl methyl ketone with sodium hypochlorite yielded besides

65–71 per cent of the expected cinnamic acid a small amount of β-chlorostyrene (669).

$$C_6H_5CH{=}CHCOCH_3 \xrightarrow{NaOCl} \underset{(65\text{–}71\text{ per cent})}{C_6H_5CH{=}CHCOOH} + C_6H_5CH{=}CHCl$$

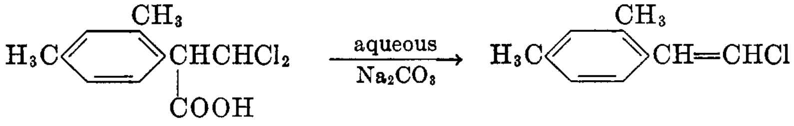
A related reaction is the nitration of α-chlorocinnamic acid with fuming nitric acid (560). At −10°C. there was obtained 62 per cent of *p*-nitro-α-chlorocinnamic acid together with a 6–12 per cent yield of β,*p*-dinitro-β-chlorostyrene. At 20–25°C. the yield of the styrene rose to 28 per cent, while the yield of nitro acid fell to 8 per cent.



Forrer (227) showed that β,β-dichloroethylbenzene, from phenylacetaldehyde and phosphorus pentachloride, gradually lost hydrogen chloride on standing. With alcoholic potassium hydroxide at 120°C. the product was β-chlorostyrene.

$$C_6H_5CH_2CHO \xrightarrow{PCl_5} C_6H_5CH_2CHCl_2 \xrightarrow{KOH} C_6H_5CH{=}CHCl$$

However, β,β-dichloroethylbenzene is less reactive toward potassium hydroxide than is α,α-dichloroethylbenzene (558). v. Auwers used this reaction to prepare a number of substituted β-chlorostyrenes. These included *p*-methyl- (37, 40), 2,4-dimethyl- (41), 3,4-dimethyl- (41), 2,4,5-trimethyl- (41), 2-chloro-4-methyl- (32), and 2,4-dimethyl-6-chloro- (32). He also prepared 2,4-dimethyl-β-chlorostyrene by the simultaneous decarboxylation and dehydrochlorination of α-dichloromethyl-2,4-dimethylphenylacetic acid with aqueous sodium carbonate (42).



It also has been reported (666) that 2-methyl-4-methoxy-5-carboxy-β-chlorostyrene can be prepared by heating 2-methyl-4-methoxy-5-carboxy-β,β-dichloroethylbenzene with sodium hydroxide or by heating 2-methyl-4-hydroxy-5-carboxy-β,β-dichloroethylbenzene with methyl sulfate and sodium hydroxide.

When styrene chlorohydrin vapors, together with steam, were passed over a phosphoric acid on silica gel catalyst held at 370–400°C., a 63 per cent yield of β-chlorostyrene was obtained (197).

$$C_6H_5CHOHCH_2Cl \xrightarrow[370\text{–}400°C.]{H_2O,\ HPO_3,\ SiO_2} \underset{(63\text{ per cent})}{C_6H_5CH{=}CHCl}$$

3,4-Methylenedioxy-β-chlorostyrene also has been prepared merely by heating the corresponding chlorohydrin (549). *p*-Methoxy-β-chlorostyrene was obtained by heating the ethyl ether of the corresponding chlorohydrin (583).

When styrylmagnesium bromide was treated with benzenesulfonyl chloride, a 40 per cent yield of β-chlorostyrene was obtained along with 34 per cent of 1,4-diphenylbutadiene and 33.6 per cent of styrene (from the unreacted Grignard reagent) (260). β-Chlorostyrene was also a by-product of the reaction between phenylmagnesium bromide and 1,1,2,2-tetrachloroethane or 1,1-dichloro-2,2-difluoroethane (723).

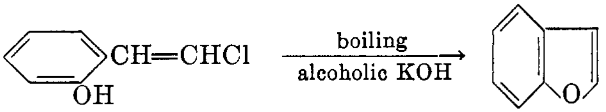
p-Methyl-β-chlorostyrene was the only product isolated from the treatment of *p*-methylstyrene with nitrosyl chloride (555). β-Chlorostyrene and styrene were the products obtained by treating α-hydroxy-β,β,β-trichloroethylbenzene with zinc in alcohol (799).

When heated with concentrated alcoholic potassium hydroxide at 180°C. in a sealed tube β-chlorostyrene yielded β-ethoxystyrene (207, 227). This same result has been effected with alcoholic sodium ethoxide (207) with a yield of 67 per cent (197).

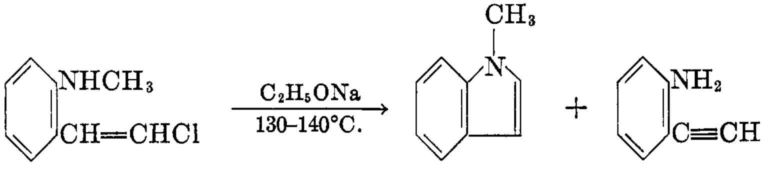
$$C_6H_5CH{=}CHCl + C_2H_5ONa \xrightarrow[180°C.]{C_2H_5OH} C_6H_5CH{=}CHOC_2H_5 + NaCl$$

(67 per cent)

In the case of *o*-hydroxy-β-chlorostyrene boiling with alcoholic potassium hydroxide produced benzofuran (404, 405).



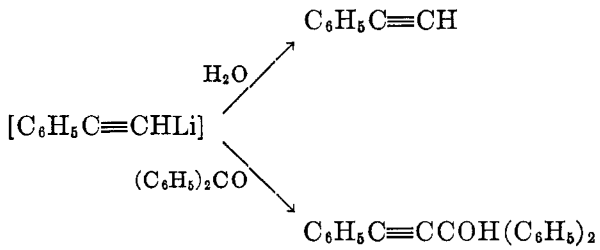
When *o*-amino-β-chlorostyrene was heated with sodium ethoxide at 160–170°C., indole was obtained (453). With *o*-methylamino-β-chlorostyrene, *N*-methylindole and *o*-aminophenylacetylene were produced (454).



However, toward most hydrolytic agents β-chlorostyrene is comparatively inert. Toward potassium hydroxide the order of ease of hydrolysis is as follows: $C_6H_5CCl{=}CHCl > C_6H_5CCl{=}CH_2 > C_6H_5CH{=}CCl_2 > C_6H_5CH{=}CHCl$; toward piperidine: $C_6H_5CCl{=}CHCl > C_6H_5CH{=}CHCl > C_6H_5CCl{=}CH_2 > C_6H_5CH{=}CCl_2$; and toward silver nitrate: $C_6H_5CCl{=}CH_2 > C_6H_5CCl{=}CHCl > C_6H_5CH{=}CHCl > C_6H_5CH{=}CCl_2$ (559). At 41°C. the order of ease of hydrolysis with alcoholic potassium hydroxide of the nitro-β-chlorostyrenes was: *p*-nitro > *o*-nitro > *m*-nitro> unsubstituted (150). At 81°C. the last two were reversed. Which halogen atoms were removed was not determined.

Phenyllithium in ether solution dehydrohalogenated β-chlorostyrene to give a 70 per cent yield of phenylacetylene (782). With butyllithium the yield of phenylacetylene was 82 per cent (781). The following mechanism was advanced, since the ether solution, when treated with benzophenone before hydrolysis, yielded 93 per cent of triphenylpropargyl alcohol:

$$C_6H_5CH{=}CHCl + C_4H_9Li \rightarrow [C_6H_5CLi{=}CClLi] \longrightarrow$$



$$[C_6H_5C{\equiv}CHLi] \begin{cases} \xrightarrow{H_2O} C_6H_5C{\equiv}CH \\ \xrightarrow{(C_6H_5)_2CO} C_6H_5C{\equiv}CCOH(C_6H_5)_2 \end{cases}$$

When heated with butyllithium in benzene at 50°C. for 22 hr., β-chlorostyrene yielded 20 per cent of phenylacetylene and 53 per cent of β-butylstyrene.

When β-chlorostyrene was heated with hydrochloric acid at 170–180°C., the product was β-phenylnaphthalene (40). With *p*-methyl-β-chlorostyrene or *p*-methyl-β,β-dichloroethylbenzene and water at 170–180°C., the product was 2-(*p*-methylphenyl)-7-methylnaphthalene.

Pyrolysis of β-chlorostyrene in a porcelain tube at 550–600°C. yielded hydrogen chloride and acetylene (209). Phenylacetylene was postulated as one of the intermediates.

With nitrosyl chloride β-chlorostyrene yielded difficultly separable mixtures (555).

C. α-Chlorostyrene chemistry

α-Chlorostyrene probably was first prepared by Laurent (435) in 1844 by treating styrene dichloride with potassium hydroxide. Shortly thereafter Blyth and Hofmann (87) observed the same reaction. The correct structure for α-chlorostyrene was first postulated by Friedel (237, 239, 240) in 1868, who prepared it by treating acetophenone with phosphorus pentachloride. Generally the product isolated was a mixture of α-chlorostyrene and α,α-dichloroethylbenzene. Treatment of the latter with alcoholic potassium hydroxide yielded α-chlorostyrene. In 1870 Glaser (269) prepared α-chlorostyrene by distilling styrene dichloride from lime. He formulated the compound as the β-isomer. Erlenmeyer (204) later showed this to be wrong, since the properties were the same as those of Friedel's α-chlorostyrene.

The preparation of α-chlorostyrene from styrene dichloride has been mentioned above and discussed in detail under the reactions of the latter compound.

The commonest route to α-chlorostyrenes has been from the corresponding acetophenones with or without the isolation of the intermediate α,α-dichloroethyl-

$$ArCOCH_3 \xrightarrow{PCl_5} ArCCl_2CH_3 \xrightarrow[KOH + C_2H_5OH]{\text{heat or}} ArCCl{=}CH_2$$

benzene. If the reaction is conducted below 40°C., the dichloroethylbenzene is the only product of the reaction (430, 431). By-products have included dypnone (732) and ω,ω-dichloro-ω-tetrachlorophosphinoacetophenone. A number of investigators (34, 103, 104, 449, 632) have prepared α-chlorostyrene by this method and have given yields of 54 per cent (174) to 91 per cent (531). The substituted α-chlorostyrenes listed in table 9 also have been prepared in this way.

TABLE 9

α-Chlorostyrenes from substituted acetophenones

SUBSTITUTED ACETOPHENONE	YIELD OF α-CHLOROSTYRENE	REFERENCE
	per cent	
p-Methyl		(39, 354)
2,4-Dimethyl	82	(762)
	86	(276)
2,4,6-Trimethyl*	50	(4)
	78	(762)
2,3,4,6-Tetramethyl*	73	(4)
p-Chloro		(803)
	60	(762)
p-Bromo		(173, 803)
2,4,6-Trimethyl-3-bromo*	63	(5)
o-Nitro		(259)
p-Nitro		(166)

* In the case of 2,4,6-trimethyl, 2,3,4,6-tetramethyl, and 2,4,6-trimethyl-3-bromo, 19, 22, and 11.5 per cent, respectively, of the corresponding phenacyl chlorides were isolated as by-products (4, 5).

α-Chlorostyrene has been prepared in 70 per cent yield by treating α-chloro-β-bromoethylbenzene with alcoholic potassium hydroxide at 0°C. (759). It is also a by-product of the coupling of phenylacetylene (802).

$$C_6H_5C{\equiv}CH \xrightarrow[HCl]{CuCl,\,NH_4Cl} C_6H_5C{\equiv}C{-}C{\equiv}CC_6H_5 + C_6H_5CCl{=}CH_2$$

α-Chlorostyrene and its homologs have been used primarily as intermediates for the preparation of phenylacetylenes. This reaction was observed first by

Friedel (237, 239, 240), who obtained phenylacetylene by treating α-chlorostyrene or a mixture of α-chlorostyrene and α,α-dichloroethylbenzene with alcoholic potassium hydroxide at 120°C. While such mixtures have been used, most investigators have preferred to isolate the α-chlorostyrene before proceeding with further dehydrohalogenation. The yields of phenylacetylene from α,α-dichloroethylbenzene are low using aqueous potassium hydroxide (516), soda lime (516), or red-hot sodium hydroxide (522), even though α,α-dichloroethylbenzene is more reactive toward potassium hydroxide than is β,β-dichloroethylbenzene (558).

With α-chlorostyrene 38 per cent of the halogen was removed in 1 hr. by 24 per cent alcoholic potassium hydroxide at 80°C. and 78 per cent in 3 hr. by the same reagent at 120°C. (174). Other investigators have used alcoholic sodium ethoxide at 110–130°C. (37–43 per cent yield) (531) and sodium amide in liquid ammonia (57 per cent yield) (763). In the former case a small amount of β-ethoxystyrene appeared as a by-product (531). With sodium in liquid ammonia the only product isolated was 15 per cent of ethylbenzene (761).

TABLE 10

Phenylacetylenes from α-chlorostyrenes

SUBSTITUTED α-CHLOROSTYRENE	REAGENT	YIELD	REFERENCE
		per cent	
p-Methyl	$NaNH_2$ in liquid NH_3	49	(763)
	Na in liquid NH_3	63	(761)
	Alcoholic KOH	25	(354)
2,4-Dimethyl	$NaNH_2$	70–72	(276)
	$NaNH_2$ at 150°C.	75	(762)
2,4,6-Trimethyl	$NaNH_2$ at 150°C.	71	(762)
2,3,4,6-Tetramethyl	$C_2H_5ONa + C_2H_5OH$, 110°C.	65	(4)
p-Chloro	25% alcoholic KOH	36	(762)
p-Chloro*	25% alcoholic KOH		(803)
p-Bromo*	25% alcoholic KOH		(803)
p-Bromo†	25% alcoholic KOH	53	(173)
2,4,6-Trimethyl-3-bromo	$C_2H_5ONa + C_2H_5OH$	57	(5)

* From the monohalide and dihalide mixture.

† From the dichloride only.

$$C_6H_5CCl{=}CH_2 \xrightarrow[C_2H_5OH]{KOH} C_6H_5C{\equiv}CH$$

Substituted α-chlorostyrenes have been converted to the corresponding phenylacetylenes by means of a variety of reagents (see table 10).

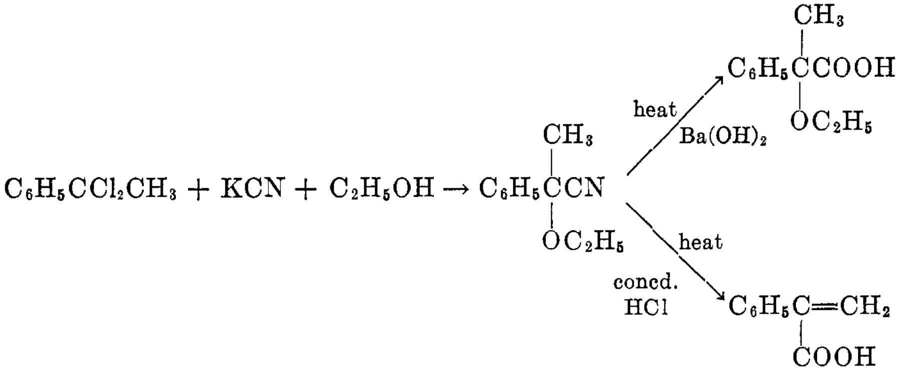
In the presence of hot water (206) or hot aqueous acids, α-chlorostyrene is hydrolyzed to acetophenone. With concentrated hydrochloric acid alone (60), yields of 30 per cent (193) to 77 per cent (759) have been reported. With hydrochloric acid and metal halides the yields were 74–78 per cent (193) and with 80 per cent sulfuric acid at 60°C. 81 per cent (192, 197). With saturated aqueous hydrochloric acid the reaction also has been reported to proceed with explosive violence to give appreciable quantities of 1,3,5-triphenylbenzene. This compound also has been prepared by treating α-chlorostyrene with boron fluoride (479) and by heating α,α-dichloroethylbenzene with water (60).

$$C_6H_5CCl{=}CH_2 \xrightarrow[\text{HCl}]{\text{concd.}} \underset{\text{(30–77 per cent)}}{C_6H_5COCH_3}$$

When treated with nitrosyl chloride α-chlorostyrene yielded α,β,β-trichlorostyrene and α,β-dichloro-β-nitrostyrene (555). α-Chlorostyrene reacted with alcoholic potassium cyanide at 200–220°C. to give in low yield a compound which could be hydrolyzed with barium hydroxide to phenylsuccinic acid (632).

$$C_6H_5CCl{=}CH_2 \xrightarrow{NOCl} C_6H_5CCl{=}CCl_2 + C_6H_5CCl{=}CClNO_2$$

Besides the α,α-dichloroethylbenzene chemistry discussed in connection with α-chlorostyrene it should be mentioned that α,α-dichloroethylbenzene also has been obtained by chlorinating ethylbenzene in the sunlight (588). Treatment with aqueous silver oxide yielded acetophenone. In the cold α,α-dichloroethylbenzene reacted with alcoholic potassium cyanide to give α-methyl-α-ethoxyphenylacetonitrile, some of whose chemistry follows (430, 431).



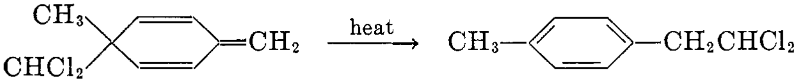
$$C_6H_5CCl_2CH_3 + KCN + C_2H_5OH \rightarrow C_6H_5\overset{\displaystyle CH_3}{\underset{\displaystyle OC_2H_5}{C}}CN$$

$$C_6H_5\overset{\displaystyle CH_3}{\underset{\displaystyle OC_2H_5}{C}}CN \xrightarrow[\text{Ba(OH)}_2]{\text{heat}} C_6H_5\overset{\displaystyle CH_3}{\underset{\displaystyle OC_2H_5}{C}}COOH$$

$$C_6H_5\overset{\displaystyle CH_3}{\underset{\displaystyle OC_2H_5}{C}}CN \xrightarrow[\text{concd. HCl}]{\text{heat}} C_6H_5\underset{\displaystyle COOH}{C}{=}CH_2$$

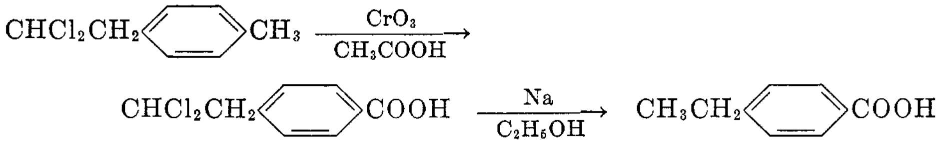
D. More highly chlorinated styrene derivatives

As has been mentioned previously, β,β-dichloroethylbenzene can be obtained by treating phenylacetaldehyde with phosphorus pentachloride (40, 227). A number of substituted β,β-dichloroethylbenzenes have been prepared by heating 1-methyl-1-dichloromethyl-4-methylenedihydrobenzenes.

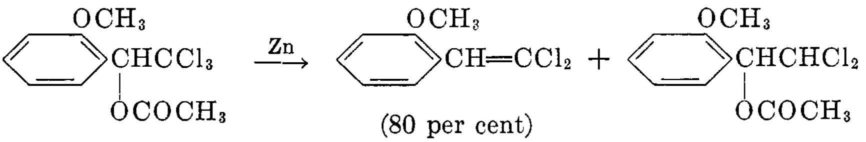


The analogs prepared in this way include *p*-methyl- (37), 2,4-dimethyl- (41), 3,4-dimethyl- (41), 2,4,5-trimethyl- (41), 2-chloro-4-methyl- (32), 2,6-dichloro-4-methyl- (32), and 2,4-dimethyl-6-chloro- (32). α,*p*-Dimethoxy-β,β-dichloroethylbenzene has been obtained by treating α,*p*-dimethoxy-β,β,β-trichloroethylbenzene with zinc and acetic acid (501).

The conversion of these compounds to β-chlorostyrenes has been mentioned previously. Otherwise they are quite inert. Treatment of *p*-methyl-β,β-dichloroethylbenzene with chromic acid in acetic acid yielded *p*-(β,β-dichloroethyl)-benzoic acid (40). This was reduced to *p*-ethylbenzoic acid with sodium and alcohol.

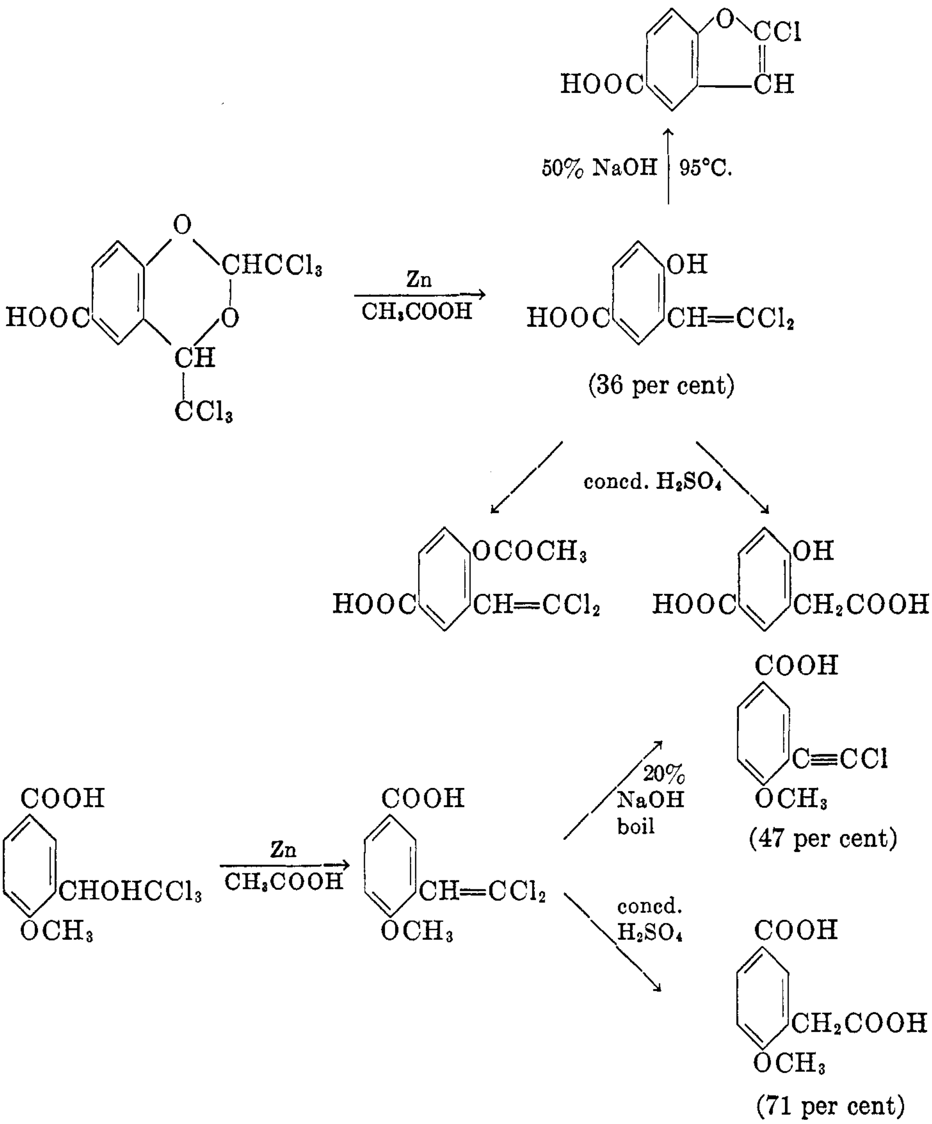


Meldrum and coworkers have described a large number of compounds as derivatives of β,β-dichloroethylbenzene which they obtained by treating β,β,β-trichloro-α-hydroxyethylbenzenes with zinc and acetic acid. In 1940 Dharwarkar and Alimchandani (160) showed that all of these compounds are actually β,β-dichlorostyrenes. This is not surprising, since as early as 1897 Biltz (84) showed that β,β-dichlorostyrene was one of the products obtained by treating benzene with chloral in the presence of aluminum chloride. Very shortly thereafter the acetates of β,β,β-trichloro-α-hydroxyethylbenzene (800) and *o*-methoxy-β,β,β-trichloro-α-hydroxyethylbenzene (437) were treated with zinc to give 90 per cent and 80 per cent, respectively, of the corresponding β,β-dichlorostyrenes. In the latter case a little of the acetate of the corresponding β,β-dichloro-α-hydroxyethylbenzene also was isolated.



In 1905 Dinesmann (163) obtained β,β-dichlorostyrene by treating β,β,β-trichloro-α-hydroxyethylbenzene with zinc and acetic acid. 3-Carboxy-4-hydroxy-β,β-dichlorostyrene has been prepared similarly (133).

Dharwarkar and Alimchandani used the following reactions to prove the structures of their β,β-dichlorostyrenes:

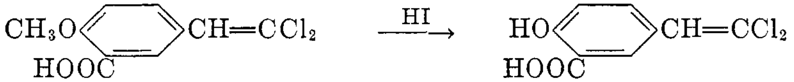


Besides the 2-hydroxy-5-carboxy- and 2-methoxy-5-carboxy-β,β-dichlorostyrenes shown above, the 3-carboxy-4-hydroxy- (86 per cent yield), 3-carboxy-4-methoxy-, 2-carboxy-4-hydroxy-, and 2-carboxy-4-methoxy- analogs also were prepared. Both the 2-hydroxy-5-carboxy- and the 3-carboxy-4-hydroxy-β,β-dichlorostyrenes were converted to the corresponding phenylacetic acids by means of concentrated sulfuric acid. These two styrenes also were acetylated and were converted to the methoxy compounds with methyl sulfate. 3-Carboxy-4-methoxy-β-chlorophenylacetylene was prepared from the corresponding β,β-dichlorostyrene by treatment with hot aqueous sodium hydroxide.

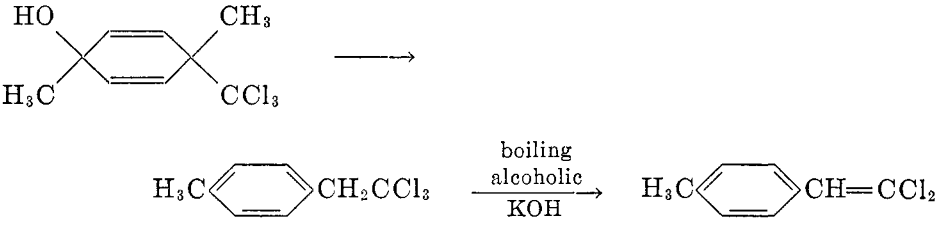
β,β-Dichlorostyrenes formulated as β,β-dichloroethylbenzenes, which were prepared by Meldrum and coworkers, are listed in table 11. These β,β-dichlorostyrenes were prepared by treating the indicated starting compound with zinc and acetic acid.

A number of β,β-dichlorostyrenes, formulated as β,β-dichloroethylbenzenes, were converted to the corresponding phenylacetic acids, as shown in table 12.

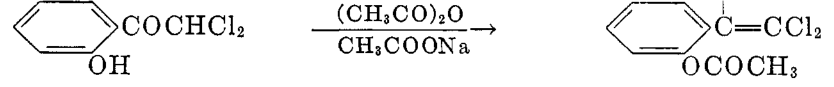
Other than the reactions described above with concentrated sulfuric acid and with hot alkali, Meldrum and coworkers found these compounds to be surprisingly inert. Thus 2-carboxy-4,5,6-triacetoxy-β,β-dichlorostyrene was easily deacetylated by means of sulfuric acid in methanol (502). 2-Carboxy-4-methyl-6-hydroxy-β,β-dichlorostyrene was acetylated with acetic anhydride containing sulfuric acid (503). 3-Carboxy-4-methoxy-β,β-dichlorostyrene yielded a methyl ester, amide, anilide, and *p*-toluidide (321). It was demethylated with hydriodic acid. Treatment with aqueous sodium hydroxide at 165°C. was reported to yield 3-carboxy-4-methoxyphenylacetaldehyde.



Besides the route from β,β,β-trichloro-α-hydroxyethylbenzene, β,β-dichlorostyrene has been prepared by treating α,β,β-trichloroethylbenzene (from β-chlorostyrene and chlorine) with alcoholic potassium hydroxide (85). *p*-Methyl-β,β-dichlorostyrene has been prepared similarly from *p*-methyl-β,β,β-trichloroethylbenzene (38, 815).



α,2-Diacetoxy-5-carboxy-β,β-dichlorostyrene was obtained by treating 2-hydroxy-5-carboxy-β,β-dichloroacetophenone with acetic anhydride and sodium acetate (138).



β,β-Dichlorostyrene adds chlorine or bromine (85). With alcoholic potassium hydroxide at 100°C. the chief product (41 per cent yield) was β-chlorophenylacetylene along with some β-chloro-β-ethoxystyrene (531). The latter compound

TABLE 11

Preparations of β,β-dichlorostyrenes

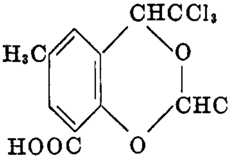
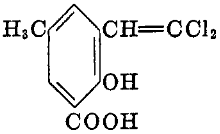
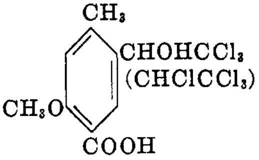
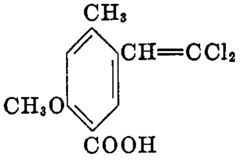
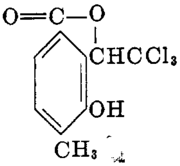
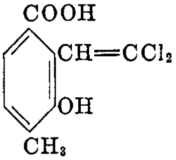
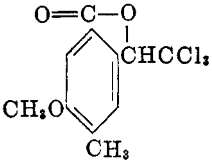
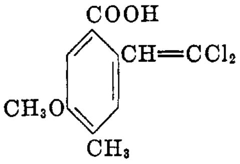
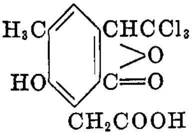
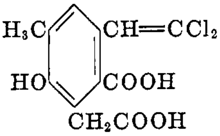
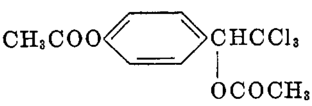
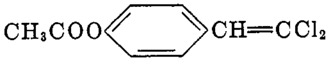
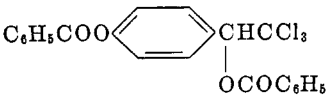
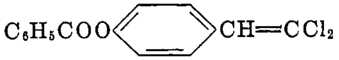
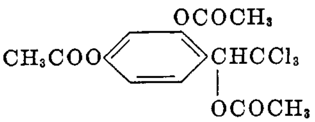
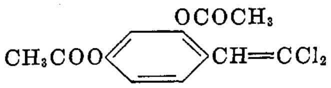
STARTING COMPOUND	β,β-DICHLOROSTYRENE OBTAINED	YIELD	REFERENCE
		er cent	
			(14)
			(498, 499)
			(500)
			(500)
			(500)
			(501)
			(501)
			(501)

TABLE 11—*Continued*

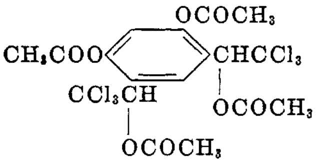
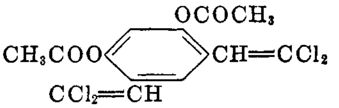
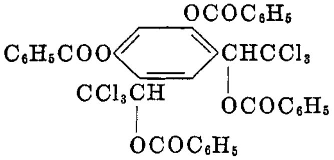
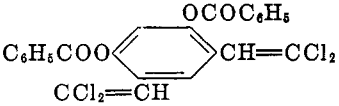
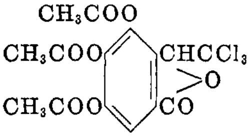
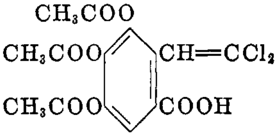
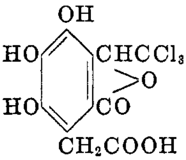
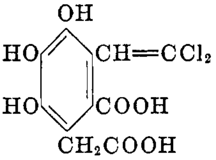
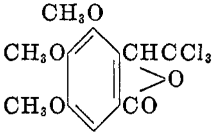
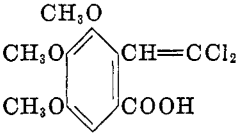
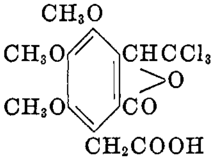
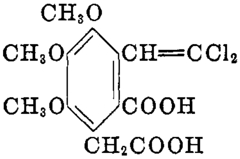
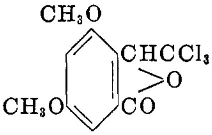
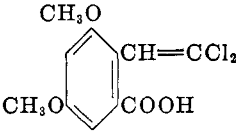
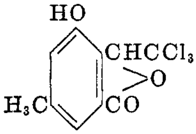
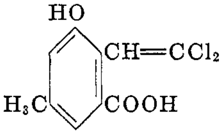
STARTING COMPOUND	β,β-DICHLOROSTYRENE OBTAINED	YIELD	REFERENCE
		per cent	
			(501)
			(501)
			(502)
			(502)
			(502)
			(502)
			(502)
		75	(503)

TABLE 11—*Continued*

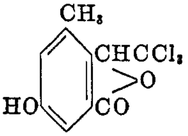
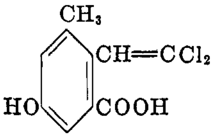
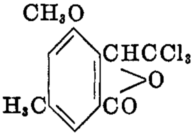
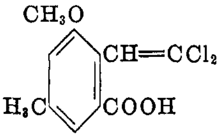
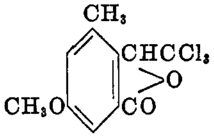
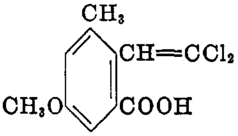
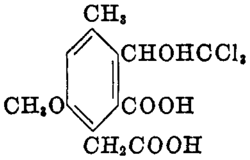
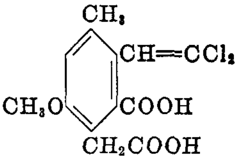
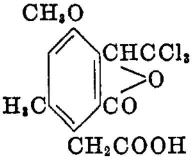
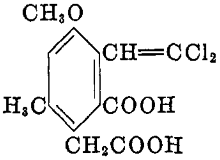
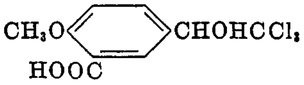
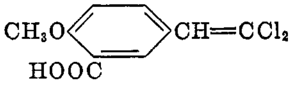
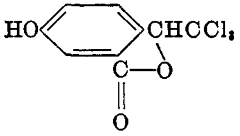
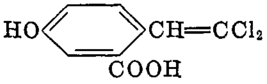
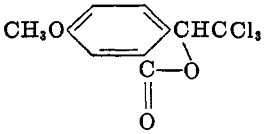
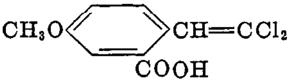
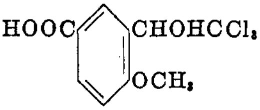
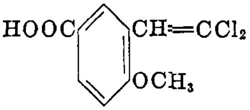
STARTING COMPOUND	β,β-DICHLOROSTYRENE OBTAINED	YIELD	REFERENCE
		per cent	
			(503)
		75	(503)
		70	(503)
		67	(503)
		33	(503)
		69	(321)
			(321)
			(321)
			(321)

TABLE 12

Phenylacetic acids from β,β-dichlorostyrenes

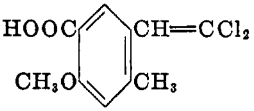
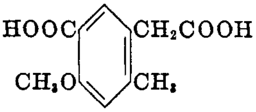
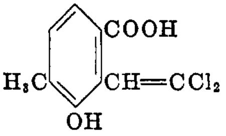
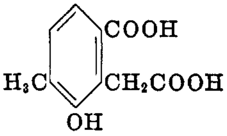
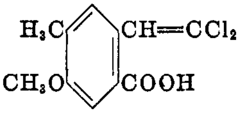
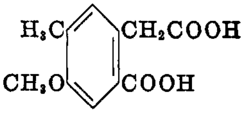
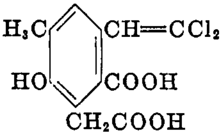
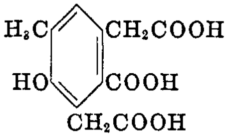
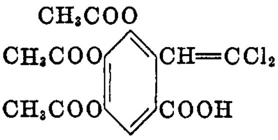
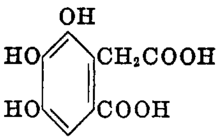
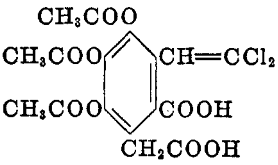
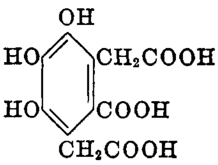
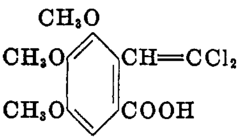
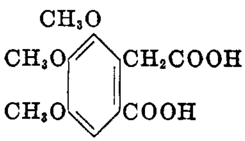
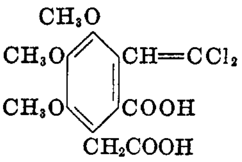
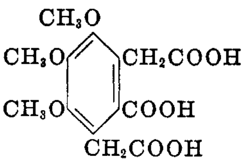
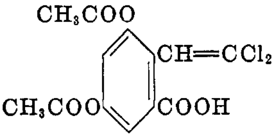
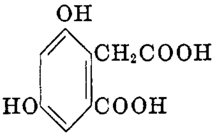
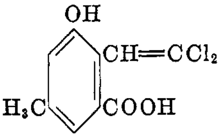
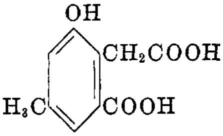
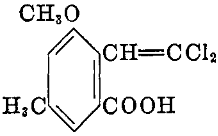
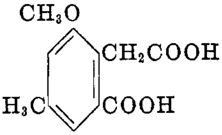
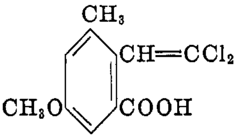
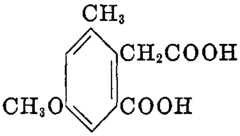
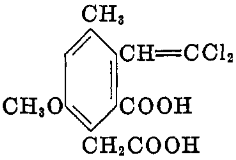
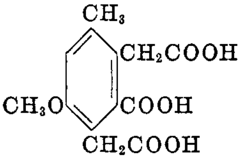
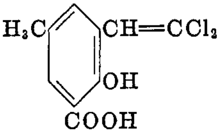
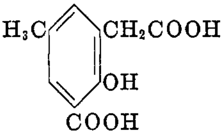
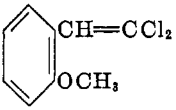
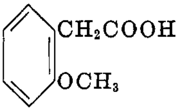
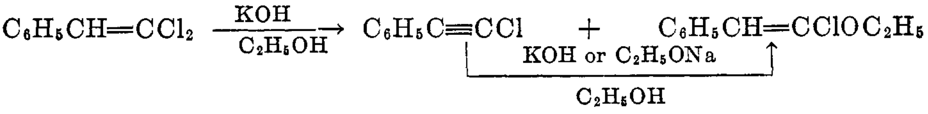
β,β-DICHLOROSTYRENE	PHENYLACETIC ACID OBTAINED	REAGENT	YIELD *per cent*	REFERENCE
		Concentrated H_2SO_4		(499)
		Concentrated H_2SO_4		(500)
		Concentrated H_2SO_4		(500)
		Concentrated H_2SO_4		(500)
		Concentrated H_2SO_4		(502)
		Concentrated H_2SO_4		(502)
		Concentrated H_2SO_4		(502)
		Concentrated H_2SO_4		(502)

TABLE 12—*Continued*

β,β-DICHLOROSTYRENE	PHENYLACETIC ACID OBTAINED	REAGENT	YIELD	REFERENCE
			per cent	
		Concentrated H_2SO_4		(502)
		Concentrated H_2SO_4		(503)
		Concentrated H_2SO_4	82	(503)
		Concentrated H_2SO_4	82	(503)
		Concentrated H_2SO_4	68	(503)
		KOH, 250–260°C.		(14)
		KOH, C_2H_5OH		(437)

was obtained from the acetylene by treatment with alcoholic sodium ethoxide or potassium hydroxide.



$$C_6H_5CH{=}CCl_2 \xrightarrow[C_2H_5OH]{KOH} C_6H_5C{\equiv}CCl + C_6H_5CH{=}CClOC_2H_5$$

KOH or C_2H_5ONa

C_2H_5OH

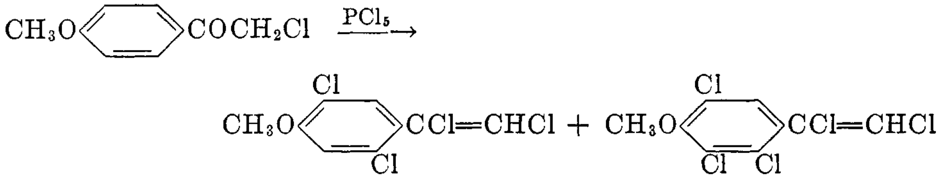
In 1877 Dyckerhoff found that treatment of phenacyl chloride with phosphorus pentachloride yielded α,α,β-trichloroethylbenzene, which decomposed on distillation to give α,β-dichlorostyrene (179, 180). The compound added chlorine

$$C_6H_5COCH_2Cl + PCl_5 \rightarrow POCl_3 + C_6H_5CCl_2CH_2Cl \xrightarrow{\text{distillation}} C_6H_5CCl{=}CHCl$$

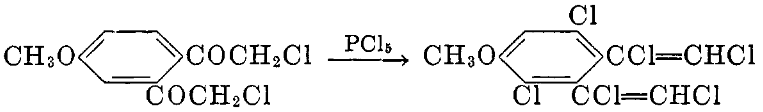
and bromine, but did not react with alcoholic potassium cyanide (180). The study of these compounds was extended in considerable detail by Kunckell and coworkers.

Most α,β-dichlorostyrenes have been prepared by treating the corresponding phenacyl chloride with phosphorus pentachloride, as shown above. The compounds thus prepared are listed in table 13.

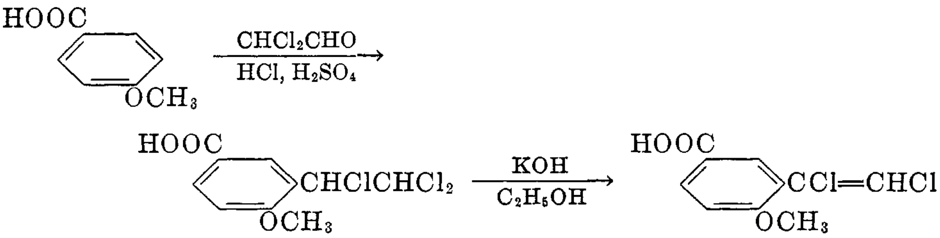
The following divinyl compounds also were prepared (423): 4-methoxy-1,2-di(α,β-dichlorovinyl)benzene, 2,4,6-trimethyl-1,3-di(α,β-dichlorovinyl)benzene, 2,4,6-triethyl-1,3-di(α,β-dichlorovinyl)benzene, and 4,4′-di(α,β-dichlorovinyl)phenyl ether. When *p*-methoxyphenacyl chloride was heated with phosphorus pentachloride over a free flame, some ring chlorination also occurred.



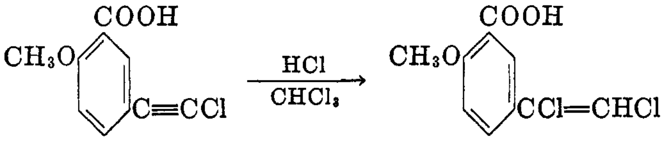
The same reaction was observed with 3,4-di(chloroacetyl)anisole.



α,β-Dichlorostyrene has been prepared by treating α,β-diiodostyrene with mercurous chloride (550). 2-Methoxy-5-carboxy-α,β-dichlorostyrene and 2-methoxy-5-nitro-α,β-dichlorostyrene have been obtained from the corresponding α,β,β-trichloroethylbenzenes (prepared by treating anisic acid and *p*-nitroanisole, respectively, with dichloroacetaldehyde in the presence of sulfuric and hydrochloric acids) by treatment with alcoholic potassium hydroxide (137).



3-Carboxy-4-methoxy-α,β-dichlorostyrene was produced by treating 3-carboxy-4-methoxy-β-chlorophenylacetylene with hydrogen chloride in chloroform solution (160).



When α,β-dichlorostyrenes are treated with alcoholic potassium hydroxide, β-chlorophenylacetylenes are produced.

$$\mathrm{ArCCl{=}CHCl} \xrightarrow[C_2H_5OH]{KOH} \mathrm{ArC{\equiv}CCl}$$

The following substituted β-chlorophenylacetylenes have been prepared in this way: p-methyl- (423, 424), 2,5-dimethyl- (423, 424), p-ethyl- (425), p-isopropyl- (425), 2,4,6-trimethyl- (425), 2-methyl-5-isopropyl- (425), p-methoxy- (422) in 10 per cent yield (423), 2-methyl-5-methoxy- (423), and 2,4-6-triethyl- (423). When α,β-dichlorostyrenes are treated with sodium in ether, phenylacetylenes are produced. This method has been used for the preparation of the following

TABLE 13

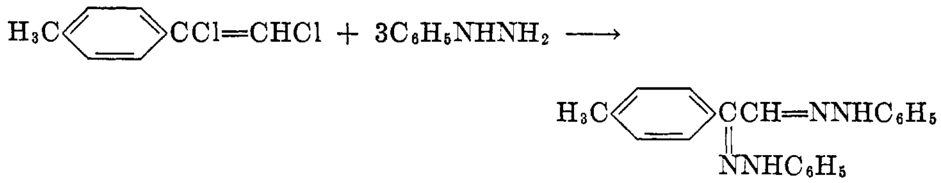
α,β-Dichlorostyrenes from phenacyl chlorides

α,β-DICHLOROSTYRENE	REFERENCES
p-Methyl	(424, 803)
p-Methyl (65 per cent yield)	(423)
2,4-Dimethyl	(423, 424)
2,5-Dimethyl	(423, 424)
3-Chloro-4-methyl	(424)
p-Ethyl	(423, 425)
p-Isopropyl	(423, 425)
2,4,6-Trimethyl	(425)
2-Methyl-5-isopropyl	(423, 425)
p-Methoxy	(421, 423)
2-Bromo-5-methoxy	(423)
p-Ethoxy	(423)
2-Methyl-5-methoxy	(423)
2,4-Dimethoxy	(423)
2,4,6-Triethyl	(423)

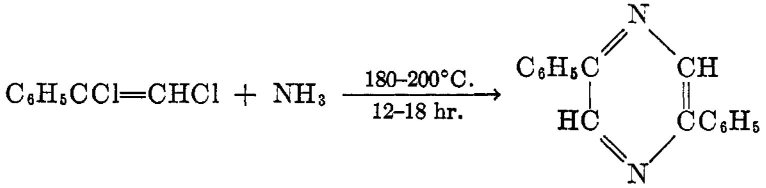
$$\mathrm{ArCCl{=}CHCl} \xrightarrow[\text{ether}]{Na} \mathrm{ArC{\equiv}CH}$$

phenylacetylenes: p-methyl- (423, 424, 803), p-ethyl- (423, 425), p-isopropyl- (423, 425), 2,4,6-trimethyl- (425), 2-methyl-5-isopropyl- (423, 425), p-methoxy- (422, 423), 2-methyl-5-methoxy- (423), and 2,4,6-triethyl- (423).

With phenylhydrazine or *N*-methyl-*N*-phenylhydrazine *p*-methyl-α,β-dichlorostyrene yielded the corresponding bisphenylhydrazone of phenylglyoxal (426).



With ammonia both α,β-dichlorostyrene and *p*-methyl-α,β-dichlorostyrene gave a symmetrically substituted pyridazine (427).



2-Methoxy-5-nitro-α,β-dichlorostyrene added chlorine to give 2-methoxy-5-nitro-α,α,β,β-tetrachloroethylbenzene (137). Treatment of this latter compound with alcoholic potassium hydroxide yielded 2-methoxy-5-nitro-α,β,β-trichlorostyrene. α,β,β-Trichlorostyrene itself has been prepared from β,β-dichlorostyrene by a similar series of reactions (85). The same method has been used for

$$C_6H_5CH{=}CCl_2 \xrightarrow[CHCl_3]{Cl_2} C_6H_5CHClCCl_3 \xrightarrow[C_2H_5OH]{KOH} C_6H_5CCl{=}CCl_2$$

the preparation of 2-methyl-4-methoxy-5-carboxy-α,β,β-trichlorostyrene (499) and 2-methoxy-5-nitro-α,β,β-trichlorostyrene (136). In these two latter cases the α,β,β,β-tetrachloroethylbenzenes were obtained from the α-hydroxy-β,β,β-trichloroethylbenzenes by treatment with hydrogen chloride and sulfuric acid.

α,β,β-Trichlorostyrene also was one of the products of the reaction between benzoyl peroxide and tetrachloroethylene (616). It was the principal product

$$(C_6H_5COO)_2 + C_2Cl_4 \xrightarrow{110\text{–}115^\circ C.} C_6H_5Cl + 2CO_2 + C_6H_5CCl{=}CCl_2$$

(27 per cent yield) when pentachloroethylbenzene and hydrogen fluoride were heated in an iron vessel (772, 773). Some fluorodichlorostyrene (14 per cent) also was obtained. In a nickel vessel the trichlorostyrene was the by-product and the principal product was 65 per cent of difluorotrichloroethylbenzene (772).

α,β,β-Trichlorostyrene adds both chlorine and bromine, although the reactions are quite slow (85). The preparation of many of the side-chain chlorinated derivatives of *p*-chlorostyrene has been described recently (786a).

IV. BROMINATED DERIVATIVES

A. Addition of bromine

Probably the most widely used reaction for the characterization of styrene and substituted styrenes is the addition of bromine. The reaction proceeds easily and the dibromides thus obtained are crystalline solids with characteristic melting points.

$$RCH{=}CH_2 + Br_2 \rightarrow RCHBrCH_2Br$$

Styrene dibromide was first prepared by Kopp in 1844 (411). In 1845 Blyth and Hofmann (87) also added bromine to styrene. This reaction was reported by all of the earlier investigators: Erlenmeyer (1866) (203), Swarts (1866) (722), Berthelot (1866–68) (72, 75, 76, 77, 78, 80), Friedel (1868) (238), and Glaser (1870) (269). The alternative preparation by the bromination of ethylbenzene was first mentioned by Thorpe in 1871 (739) and by Radziszewski in 1873 (589).

Since these early reports the addition of bromine to styrene has been described in numerous articles. (These include the following references: 31, 63, 105, 117, 175, 177, 181, 214, 215, 222, 253, 256, 283, 320, 392, 513, 543, 569, 629, 640, 645, 691, 710, 797, 811.) Many inert solvents have been used, but the best conditions seem to be an ether solvent at 0°C. (98 per cent yield) (214) or −10°C. (quantitative yield) (177), a chloroform solvent in the cold (theoretical bromine absorption) (253), or a liquid sulfur dioxide solvent (theoretical yield) (628a, 629). If properly conducted, the addition evidently is quantitative.

The addition of bromine to styrene is practically instantaneous (535) and the heat of the reaction has been measured (459). The kinetics have been studied, although in glacial acetic acid solution the addition is too fast for detailed measurements (749). The reaction has been included in several studies of competitive bromine addition (22, 345). In the presence of oxygen some of the latter element also is absorbed (89). The products were styrene dibromide and an unidentified oil.

In methanol solution side reactions occur and the addition is not complete. Bromine absorption has been shown to be 85 per cent of theory (254). Under the same conditions (bromine and sodium bromide in methanol) another investigator found the products to be 50 per cent styrene dibromide and 50 per cent bromostyrene, together with some hydrogen bromide (356). Some addition of the methoxyl radical also has been observed (490).

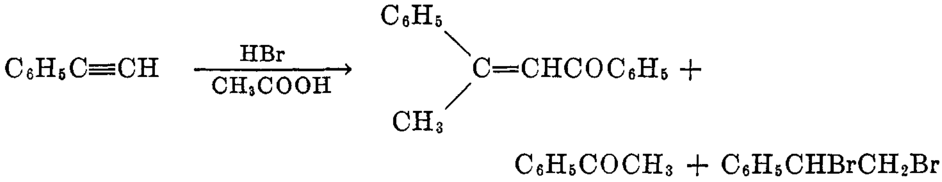
Unlike the chlorination, the bromination of ethylbenzene in the dark at its boiling point gives primarily styrene dibromide (661). In the light α,α-dibromoethylbenzene is obtained. The first bromine enters the α-position. This bromination of ethylbenzene or of α-bromoethylbenzene has been utilized by several investigators for the preparation of styrene dibromide (26, 105, 242, 308, 811; in 90 per cent yield, 115).

$$C_6H_5CH_2CH_3 \xrightarrow{Br_2} C_6H_5CHBrCH_3 \xrightarrow{Br_2} C_6H_5CHBrCH_2Br$$

Styrene dibromide constituted 20 per cent of the product obtained by treating styrene with bromine chloride (759).

$$C_6H_5CH{=}CH_2 + BrCl \xrightarrow{-10°C.} C_6H_5CHClCH_2Cl + \underset{(65\text{–}70\ \text{per cent})}{C_6H_5CHClCH_2Br} + \underset{(20\ \text{per cent})}{C_6H_5CHBrCH_2Br}$$

It has been obtained by treating styrene with *N*-bromoacetamide in acetone solution (783) and has been reported as a by-product of the reaction between phenylacetylene and hydrobromic acid in acetic acid solution (733).



$$C_6H_5C\equiv CH \xrightarrow[CH_3COOH]{HBr} (C_6H_5)(CH_3)C{=}CHCOC_6H_5 + C_6H_5COCH_3 + C_6H_5CHBrCH_2Br$$

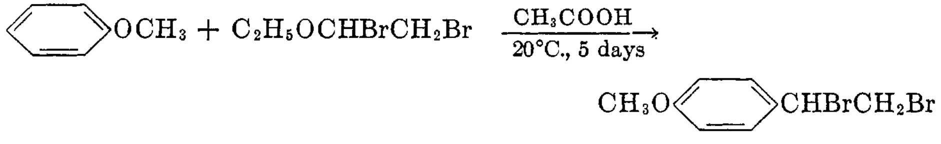
Treatment of styrene oxide with phosphorus pentabromide gave styrene dibromide (743).

As shown in table 14 a great many nuclear-substituted styrenes have been characterized as their dibromides.

The *o*- (158), *m*- (158), and *p*-divinylbenzenes (342, 445) all add two molecules of bromine to give the corresponding tetrabromides. v. Braun and Engel (112) reduced 5-methyl-1,3-phenylenediacetonitrile with sodium in alcohol and pyrolyzed the quaternary methylammonium hydroxide obtained from the resulting amine. The unsaturated hydrocarbon thus produced added bromine.

p-Methylstyrene dibromide also has been prepared by brominating *p*-methyl-α-bromoethylbenzene in the dark (662). In the presence of light the product was *p*-methyl-α,α-dibromoethylbenzene. Similarly, both *o*- and *p*-bromostyrene dibromides were prepared by brominating the corresponding ethylbenzenes in the absence of light.

p-Methoxystyrene dibromide also has been obtained in 68 per cent yield by allowing anisole and α,β-dibromoethyl ether to stand in glacial acetic acid solution for 5 days (584). The reaction was applied with equal success to phenyl ether, phenoxyacetic acid, and veratrole. In all three cases the dibromoethyl group appeared in the position para to the functional group already present, and in phenyl ether two dibromoethyl groups were introduced.



In the case of 3,4-methylenedioxystyrene dibromide further treatment with bromine introduced a third bromine atom (549).

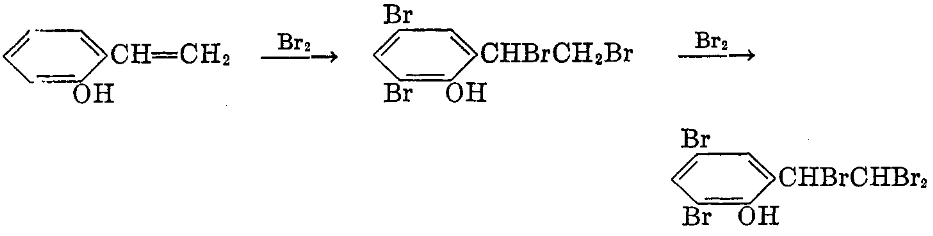
When vinylphenols are treated with bromine, not only does bromine add to

TABLE 14

Substituted styrene dibromides

SUBSTITUTED STYRENE	REFERENCES
m-Methyl	(525, 750)
p-Methyl	(24, 117, 256, 392, 645, 662, 750)
2,5-Dimethyl	(392, 483)
3,5-Dimethyl	(483)
2,4,5-Trimethyl	(391)
o-Ethyl	(246)
p-Ethyl	(256, 392)
Isopropyl	(551)
p-Isopropyl	(392)
p-Fluoro	(229)
Chloro	(544)
p-Chloro	(215)
3,5-Dichloro	(482)
2,3,4,5,6-Pentachloro	(341, 446)
Bromo	(544)
p-Bromo	(579, 662, 809)
o-Bromomethyl	(110)
o-Nitro	(183)
m-Nitro	(404, 567)
p-Nitro	(56, 283, 317, 404)
2-Nitro-4-isopropyl	(185)
p-Dimethylamino	(111)
o-Dimethylaminomethyl	(188, 217)
m-Cyano	(778b)
m-Carboxy	(404)
o-Methoxy	(586)
m-Methoxy	(234)
p-Methoxy	(551, 742, 758)
3-Nitro-4-methoxy	(184)
p-Phenoxy	(234)
3,4-Dimethoxy	(54, 234, 474)
3,4-Methylenedioxy	(54, 474, 549)
3,4-Carbonyldioxy	(548, 549)
3-Methoxy-4-acetoxy	(619)

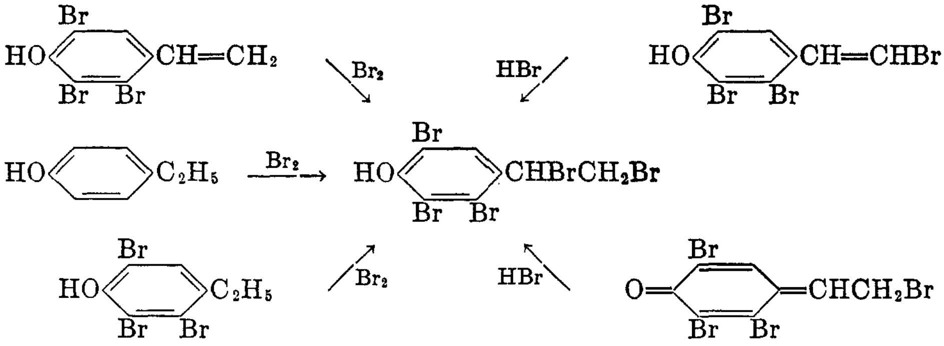
the double bond, but the reactive positions in the ring also are substituted. Thus, treatment of *o*-vinylphenol yielded 2-hydroxy-3,5-dibromostyrene dibromide (247, 248, 686).



Further treatment with bromine yielded 2-hydroxy-α,β,β,3,5-pentabromoethylbenzene. When the reactive 3- and 5-positions were blocked, as in 2-hydroxy-3,5-dimethyl- (6) and 2-hydroxy-3,5-dibromo-styrenes (248), addition proceeded normally to give the corresponding styrene dibromide.

With 3-hydroxy-4-isopropylstyrene a tribromide (probably α,β,2-tribromo-4-isopropyl-5-hydroxyethylbenzene) was obtained (117). Precipitates also have been observed in the case of 3-hydroxy-4-ethoxy- (359) and 3,4-dihydroxystyrenes (428).

Treatment of 2,3,5-tribromo-4-hydroxystyrene with bromine yielded the expected styrene dibromide (816). The compound also was prepared in 40–50 per cent yield by treating *p*-ethylphenol with a large excess of bromine, by brominating the ethyltribromophenol, and by adding hydrogen bromide to the quinoid and normal forms of the corresponding β-bromostyrene.



Further bromination of the ethylphenol (75 per cent yield), ethyltribromophenol (70–80 per cent yield), or tribromostyrene dibromide gave α,β,β,2,3,5-hexabromo-4-hydroxyethylbenzene. Bromination of 2,3,5,6-tetrabromo-4-hydroxyethylbenzene gave a low yield of 2,3,5,6-tetrabromo-4-hydroxystyrene dibromide. Under more extreme conditions α,β,β,2,3,5,6-heptabromo-4-hydroxyethylbenzene was obtained in 80–85 per cent yield.

Styrenes substituted in the side chain also add bromine. Dibromides have been obtained from β-chloro- (85, 719), β,β-dichloro- (85), α,β,β-trichloro- (85), and

$$C_6H_5CH{=}CCl_2 + Br_2 \rightarrow C_6H_5CHBrCCl_2Br$$

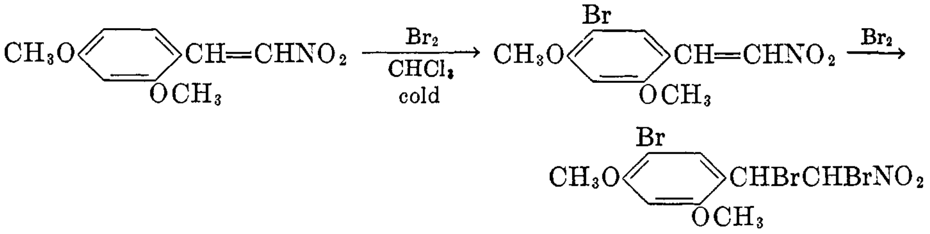
p-bromo-α-chlorostyrenes (173). 3,4-Dimethoxy-β-bromostyrene added bromine quantitatively (474), and bromine addition was observed with β,2,3,5-tetrabromo-4-hydroxy- and β,2,3,5,6-pentabromo-4-hydroxy-styrenes (816).

α-Ethoxystyrene reacted instantly with bromine (508), and an unstable dibromide was obtained from β-phenoxystyrene (710). Treatment of α-phenoxystyrene with bromine gave only tar (635). α-Acetoxystyrene added bromine (479).

Besides β-nitrostyrene itself (199, 200, 571, 737), the substituted β-nitrostyrenes listed in table 15 have been shown to form dibromides.

In the case of 2,4-dimethoxy-β-nitrostyrene the first product isolated was

2,4-dimethoxy-5-bromo-β-nitrostyrene, which then reacted further to form the dibromide (608). .



The addition of bromine to β-nitrostyrene was very much slower than the addition of bromine to styrene (749). This reaction also was catalyzed by sulfuric and by hydrobromic acids.

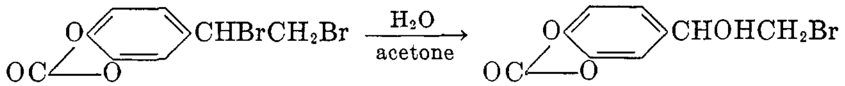
TABLE 15

Dibromides of β-nitrostyrenes

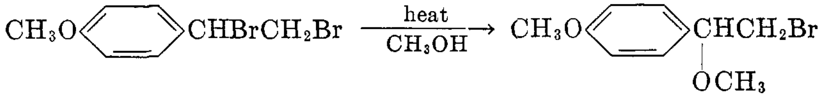
β-NITROSTYRENE	YIELD	REFERENCES
	per cent	
o-Nitro		(45, 571)
m-Nitro		(45)
p-Nitro		(571)
3-Nitro-4-methoxy		(184)
o-Methoxy	90	(608)
p-Methoxy		(608, 627)
3,4-Dimethoxy		(608)
2,3,4-Trimethoxy		(608)
3,4-Methylenedioxy		(530, 608, 627)
p-Methyl		(790)
o-Fluoro		(795)
o-Chloro		(791)
2-Chloro-5-nitro		(791)
2-Bromo-5-nitro		(794)
2-Iodo-5-nitro		(793)

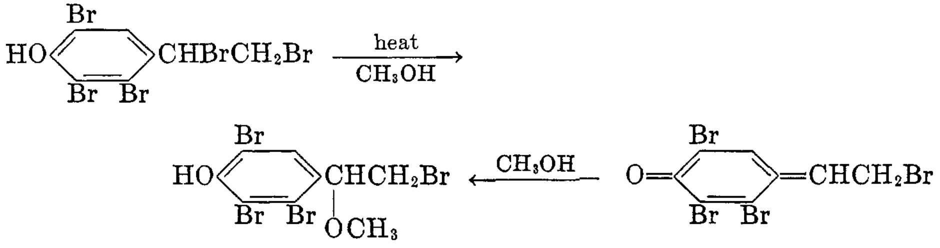
Styrene dibromide has been hydrolyzed to styrene bromohydrin in 59 per cent yield by heating for 6 hr. at 90°C. with an aqueous suspension of calcium carbonate (330). The same reaction has been effected in the case of *p*-methoxystyrene dibromide (758) and 2,3,5-tribromo-4-hydroxystyrene dibromide (816).

While no bromohydrin was obtained in attempts to hydrolyze 3-methoxy-4-acetoxystyrene dibromide (619), the hydrolysis of 3,4-dimethoxystyrene dibromide (54) by means of aqueous acetone proceeded in nearly quantitative yield (474). The hydrolysis of 3,4-methylenedioxystyrene dibromide similarly was effected (54, 497) in good yield (474). In the case of 3,4-carbonyldioxystyrene dibromide the yield of bromohydrin was 90 per cent (549).

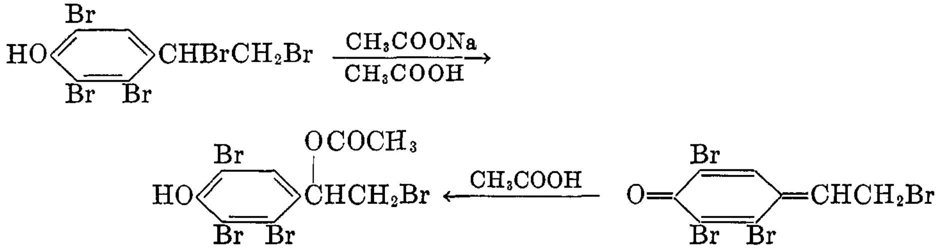


Replacement of the α-bromine atom by alkoxy and acyloxy groups has been effected similarly. Thus, when heated in methanol solution *p*-methoxystyrene dibromide (584), 3,4-dimethoxystyrene dibromide (474, 584), and 3,4-methylenedioxystyrene dibromide (474) all yielded methyl ethers of the corresponding bromohydrins. The reaction proceeded in the same fashion with 2-hydroxy-3,5-dibromostyrene dibromide (248) and 2,3,5-tribromo-4-hydroxystyrene dibromide (816). The latter bromohydrin ether also was prepared by adding methanol to the quinoid form of the corresponding β-bromostyrene. When *o*-methoxystyrene dibromide was treated with an ethanol solution of potassium cyanide, the product was the ethyl ether of *o*-methoxystyrene bromohydrin (586).

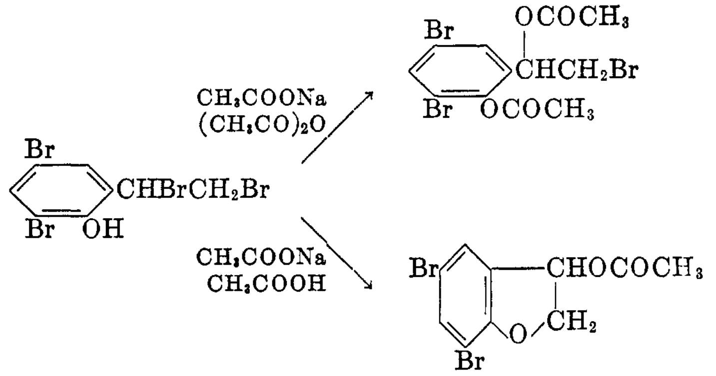




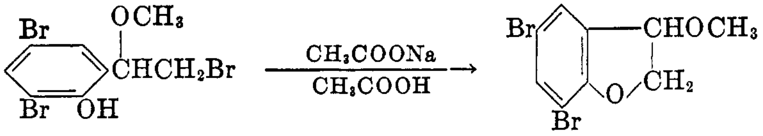
Treatment of 2,3,5-tribromo-4-hydroxystyrene dibromide with sodium acetate in hot acetic acid gave the corresponding bromohydrin acetate (816). Here again the compound was prepared by adding acetic acid to the quinoid form of the corresponding β-bromostyrene.



When 2-hydroxy-3,5-dibromostyrene dibromide was heated with sodium acetate and acetic anhydride, not only was the hydroxyl group acetylated, but the α-bromine atom also was replaced by the acetoxyl group (248). Treatment of the same dibromide with sodium acetate and acetic acid gave an acetoxydihydrocoumarone.

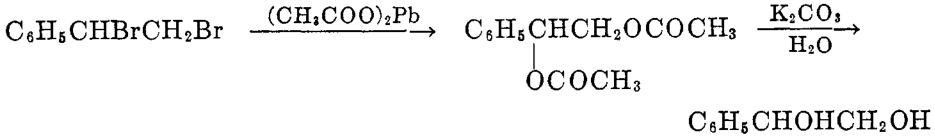


This same type of ring closure has been effected with the bromohydrin ether.



The conversion of both bromine atoms in styrene dibromide to hydroxyl groups has been effected both directly and indirectly by means of a number of reagents. Zincke and Breuer (120, 810, 811) tried a wide variety of combinations, including silver nitrate in acetic acid, potassium acetate in acetic acid, potassium acetate in ethanol, silver benzoate in ethanol, silver acetate in ethanol, silver acetate in acetic acid, silver benzoate in toluene, and aqueous potassium carbonate. In all cases a mixture of styrene glycol, the corresponding ester, α-bromostyrene, and tar was obtained. The combined yield of glycol and ester varied between 5 per cent and 31 per cent except in the case of silver benzoate and toluene, where 50 per cent of styrene glycol dibenzoate was isolated.

Evans and Morgan (214) obtained 47 per cent of styrene glycol by boiling styrene dibromide for 3 days with aqueous potassium carbonate. A 97 per cent yield of the diacetate was produced by treating the dibromide with lead acetate in boiling acetic acid. This diacetate was hydrolyzed to the glycol in 64 per cent yield with dilute sulfuric acid, 74 per cent yield with aqueous calcium carbonate, and 90 per cent yield with aqueous potassium carbonate. This lead acetate-potassium carbonate method has been utilized subsequently (543). *p*-Bromostyrene dibromide was hydrolyzed to *p*-bromostyrene glycol by means of aqueous potassium carbonate (662). The bromine in styrene dibromide has been determined by boiling the compound with potassium hydroxide in benzyl alcohol,



$$C_6H_5CHBrCH_2Br \xrightarrow{(CH_3COO)_2Pb} C_6H_5\underset{\displaystyle OCOCH_3}{CH}CH_2OCOCH_3 \xrightarrow[H_2O]{K_2CO_3} C_6H_5CHOHCH_2OH$$

diluting with water, and then titrating the halide ion with silver nitrate (647).

In 1845 Blyth and Hofmann (87) observed that treatment of styrene dibromide with alcoholic potassium hydroxide removed a molecule of hydrogen bromide. Subsequently this preparation of α-bromostyrene has been employed by a number of investigators (31, 238, 242, 269, 722, 733) to give yields as high as 85 per cent (105). Styrene bromohydrin ethyl ether has been observed as a by-product (733). This same reaction has been effected by heating styrene dibromide with water at 190°C. (589).

$$C_6H_5CHBrCH_2Br \xrightarrow[C_2H_5OH]{KOH} C_6H_5CBr{=}CH_2$$

TABLE 16

Phenylacetylene from styrene dibromide

REAGENT	YIELD	REFERENCE
	per cent	
Sodium amide	70	(102)
Potassium hydroxide	40–50	(102)
Sodium amide	40–60	(105)
Sodium amide in toluene	62	(105)
Sodium amide in kerosene	40	(105)
Sodium amide	64	(763)
Sodium in liquid ammonia	66	(761)
Sodium aniline	45	(90)

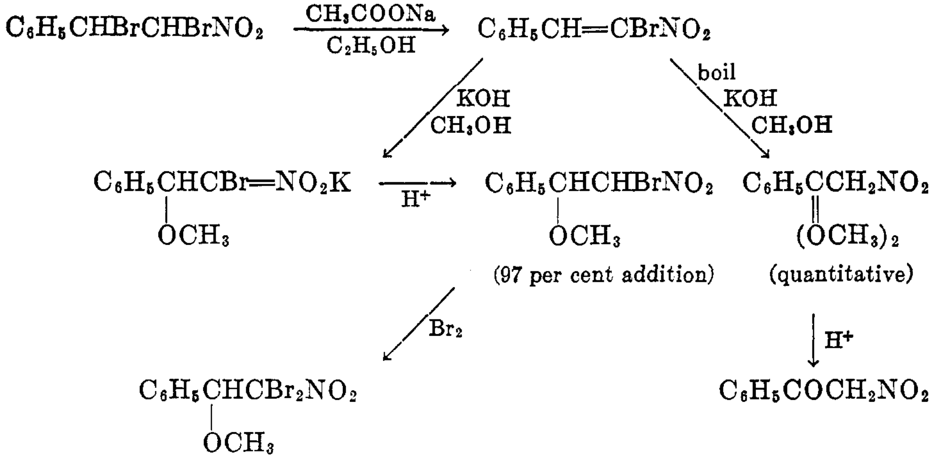
When styrene dibromide vapors were passed over calcium oxide at dull red heat, phenylacetylene was obtained (589). This reaction has been effected in fair yield by means of a number of other reagents, as shown in table 16.

$$C_6H_5CHBrCH_2Br \xrightarrow{NaNH_2} C_6H_5C{\equiv}CH$$

Isopropylstyrene dibromide lost hydrogen bromide on treatment with alcoholic potassium hydroxide to give a bromostyrene (probably α) (551). Under the same conditions *m*-methylstyrene dibromide gave *m*-methyl-α-bromostyrene (525). On heating at reduced pressure β-phenoxystyrene dibromide also lost hydrogen bromide, giving a compound postulated as β-bromo-β-phenoxystyrene (710).

Treatment of *m*- (158) and *p*-divinylbenzene tetrabromide (445) with alcoholic potassium hydroxide gave *m*- and *p*-phenylenediacetylene, respectively. Under the same conditions the ortho isomer gave a variety of products, including naphthalene (158). With sodium ethoxide *o*-divinylbenzene tetrabromide gave a mixture of *o*-phenylenediacetylene, *o*-(α-bromovinyl)phenylacetylene, and *o*-di(α-bromovinyl)benzene.

In the case of β-nitrostyrene dibromides the α-bromine is removed by alkaline reagents. Priebs (571) originally postulated the β-bromine atom as being removed by alcoholic sodium hydroxide, but Thiele and Haeckel (737) showed that it was the α-bromine which was removed. The reactions used are given below:



(Since this is alkali-insoluble, both bromine atoms must be on the same carbon atom.)

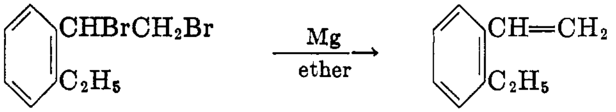
A parallel series of reactions was conducted with β,*p*-dinitrostyrene dibromide. An alcoholic solution of sodium or potassium acetate has been used by all subsequent investigators to convert β-nitrostyrene dibromides to β-bromo-β-nitrostyrenes. The compounds listed in table 17 have been prepared in this way. In the case of the 3,4-methylenedioxy compound one group of investigators (530) formulated their product as the α-bromo compound, but this seems unlikely since in every other case the β-compound was produced.

TABLE 17

β-Bromo-β-nitrostyrenes from β-nitrostyrene dibromides

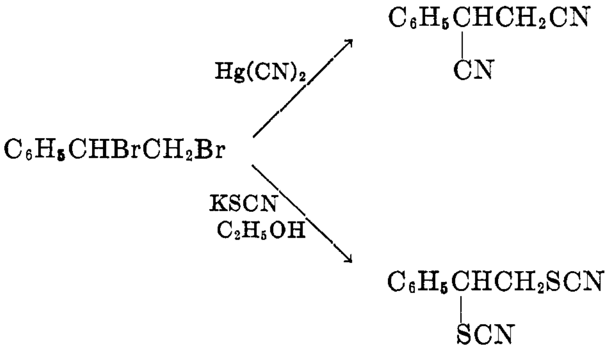
β-BROMO-β-NITROSTYRENE OBTAINED	REFERENCE
o-Methoxy	(608)
p-Methoxy	(608, 627)
3,4-Dimethoxy	(608)
3,4-Methylenedioxy	(530, 608, 627)
2,4-Dimethoxy-5-bromo	(608)
2,3,4-Trimethoxy	(608)
m-Nitro	(45)
p-Nitro	(45)
p-Methyl	(790)
o-Fluoro	(795)
o-Chloro	(791)
2-Chloro-5-nitro	(791)
2-Bromo-5-nitro	(794)
2-Iodo-5-nitro	(793)

Both styrene dibromide (115) and *o*-ethylstyrene dibromide (246) have been dehalogenated in 70 per cent yield by means of magnesium in ether. With zinc



in ether styrene dibromide gave mostly polymer (115). The same reaction is brought about by iodide ion (175), and it has been shown to be first order with respect to both dibromide and iodide-ion concentration (569). Although no reaction occurred in ether at 25°C. (534a), in tetrahydrofuran styrene dibromide reacted with lithium aluminum hydride to give a 71 per cent yield of styrene (756a).

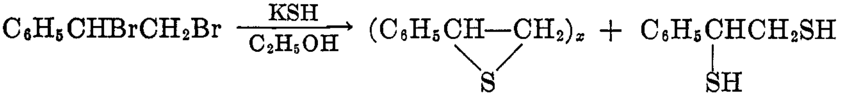
Treatment of styrene dibromide with mercuric cyanide gave a low yield of phenylsuccinonitrile (529). Potassium thiocyanate in boiling alcohol produced styrene dithiocyanate.



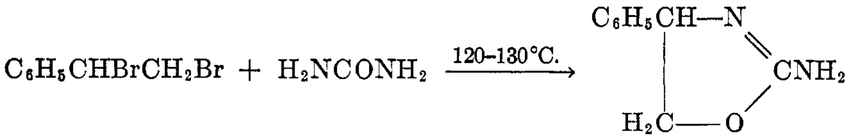
$$C_6H_5CHBrCH_2Br \xrightarrow{Hg(CN)_2} \underset{\displaystyle CN}{C_6H_5\overset{}{C}H}CH_2CN$$

$$C_6H_5CHBrCH_2Br \xrightarrow[C_2H_5OH]{KSCN} \underset{\displaystyle SCN}{C_6H_5CH}CH_2SCN$$

Similarly, sodium sulfite gave disodium ethylbenzene-α,β-disulfonate (377). Alcoholic potassium hydrogen sulfide at 120–130°C. gave a mixture of α,β-dimercaptoethylbenzene and polymeric styrene sulfide (703).



The sodium salt of bis-thioglycolic acid removed hydrogen bromide and gave indefinite products (310). Treatment of styrene dibromide with urea at 120–130°C. gave a product formulated as 2-amino-4-phenyloxazoline (727).



Styrene dibromide did not react with diazoacetic ester (129); with diethylamine at 180°C. it gave a mixture presumably containing both α- and β-diethylaminostyrenes (63). With benzene and aluminum chloride in carbon disulfide the product was diphenylethane (26).

B. *β-Bromostyrene chemistry*

Except for the β-nitro-β-bromostyrenes, β-bromostyrenes have not been prepared from styrene dibromides. The routes from cinnamic acid almost invariably have been employed.

In 1863 Schmitt (656) obtained a bromine-containing oil by treating cinnamic acid dibromide with boiling water. In 1864 Erlenmeyer (201) showed that this compound had the empirical formula C_8H_7Br and therefore was a monobromostyrene, for which he suggested the two possible formulas two years later (203). In 1870 Glaser (269) obtained both β-bromostyrene and α-bromo-β-hydroxycinnamic acid from cinnamic acid dibromide and boiling water. He converted the latter product to the former by heating with water at 200°C.

TABLE 18

β-Bromostyrene from cinnamic acid dibromide

REAGENT	YIELD OF β-BROMOSTYRENE	BY-PRODUCT	YIELD OF BY-PRODUCT	REFERENCE
	per cent		*per cent*	
Hot water		Both bromocinnamic acids		(34, 205, 220)
Alcoholic KOH				(55)
Aqueous Na_2CO_3	65–75			(8)
Aqueous Na_2CO_3				(34, 168, 171, 292, 450, 522, 717)
Aqueous NaOH				(531)
Alcoholic $AgNO_3$		Bromocinnamic acid		(444)
Alcoholic CH_3COONa				(34)
Alcoholic CH_3COOK	92			(713)
Aqueous $BaCO_3$				(717)
Aqueous NH_3				(717)
Alcoholic dimethylaniline		Cinnamic acid		(717)
Aqueous pyridine	65–75			(8)
Pyridine	37	Cinnamic acid α-Bromocinnamic acid	34 15	(8)

Since these early experiments a number of investigators have used the decomposition of cinnamic acid dibromide for the preparation of β-bromostyrene. The various reagents used are summarized in table 18.

An 81 per cent yield of β-bromostyrene was reported from the bromination of

$$C_6H_5CH{=}CHCOOH \xrightarrow[\text{ether}]{Br_2} C_6H_5CH{=}CHBr$$

cinnamic acid in ether solution (413). The same product has been reported from bromination in chloroform or carbon tetrachloride (669). Bromination of cinnamic acid in aqueous suspension gave very low yields of β-bromostyrene (596). The principal products were cinnamic acid dibromide (17 per cent) and α-bromo-β-hydroxycinnamic acid (83 per cent) (599). Bromination of aqueous sodium cinnamate gave 5 per cent of cinnamic acid dibromide, 53 per cent of α-bromo-β-hydroxycinnamic acid, and 43 per cent of β-bromostyrene. Later investigators reported somewhat different yields with sodium carbonate present: 49 per cent of α-bromo-β-hydroxycinnamic acid, 5 per cent of cinnamic acid dibromide, and 7 per cent of β-bromostyrene (44).

β-Bromostyrene also has been prepared by heating benzalbromoacetophenone with solid sodium hydroxide (168). Some phenylacetylene is obtained in this reaction (171).

$$C_6H_5CH{=}CBrCOC_6H_5 \xrightarrow[\text{NaOH}]{\text{heat}} C_6H_5COONa$$

$$+\ C_6H_5CH{=}CHBr \xrightarrow{\text{NaOH}} C_6H_5C{\equiv}CH$$

Treatment of α-hydroxy-β,β,β-tribromoethylbenzene with zinc and alcohol gave β-bromostyrene (800) as well as some by-product styrene (799).

$$C_6H_5CHOHCBr_3 \xrightarrow[C_2H_5OH]{\text{Zn}} C_6H_5CH{=}CHBr + C_6H_5CH{=}CH_2$$

Dufraisse (168, 169, 171) prepared both isomeric forms of β-bromostyrene and studied their properties in detail. He showed that light changed both to an equilibrium mixture containing 90 per cent of the A form. On the basis of physical properties v. Auwers (35) showed that the A and B forms studied by Dufraisse were the *trans* and *cis* forms, respectively.

In general, substituted β-bromostyrenes also have been prepared from the corresponding cinnamic acids. Again the most widely used procedure was to decompose the cinnamic acid dibromide. These preparations are summarized below (table 19).

It is to be noted that Dann, Howard, and Davies (150) obtained different melting points for their *o*-, *m*-, and *p*-nitro-β-bromostyrenes than did Reich and coworkers (600, 601, 603, 604).

Certain substituted β-bromostyrenes have been prepared by the bromination of the corresponding sodium cinnamate. This is true of *m*-methyl- (525), *p*-methyl- in 41 per cent yield (in the presence of sodium hydroxide) (40), and *p*-nitro- (in the presence of sodium carbonate, product mostly α-bromo-β-hydroxy-*p*-nitrocinnamic acid) (44). The 2,4,6-trimethyl homolog was prepared by bromination of the cinnamic acid in carbon disulfide, acetic acid, chloroform, or carbon tetrachloride (88). When *p*-aminocinnamic acid was treated with bromine in acetic acid a *p*-acetaminobromostyrene, which was probably the β-isomer, was obtained (252).

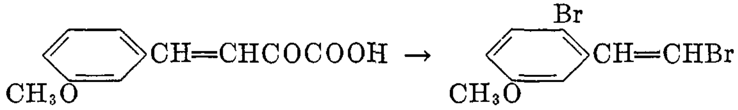
TABLE 19

Preparations of substituted β-bromostyrenes

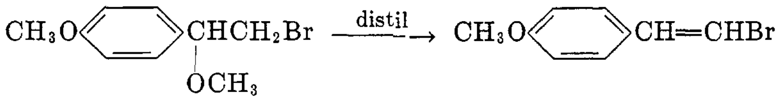
CINNAMIC ACID DIBROMIDE	DECOMPOSITION REAGENT	YIELD	REFERENCE
		per cent	
p-Bromo	$Na_2CO_3 + H_2O$		(614)
p-Bromo	2% $Na_2CO_3 + H_2O$	70	(615)
p-Bromo (A)*	H_2O		(615)
o-Nitro	$CH_3COONa + H_2O$		(603)
o-Nitro	$CH_3COONa + C_2H_5OH$		(603)
o-Nitro	30% $CH_3COONa + H_2O$	20	(150)
m-Nitro	H_2O	60	(786)
m-Nitro (B)	H_2O	15	(604)
m-Nitro	$Na_2CO_3 + H_2O$		(600, 601)
m-Nitro (C)	$KOH + C_2H_5OH$	A little	(600)
m-Nitro	30% $CH_3COONa + H_2O$	35	(150)
p-Nitro	$CH_3COONa + H_2O$		(603)
p-Nitro	$Na_2CO_3 + H_2O$		(603)
p-Nitro	$CH_3COONa + C_2H_5OH$		(603)
p-Nitro	30% $CH_3COONa + H_2O$	50	(150)
p-Methoxy	30% $KOH + H_2O$		(182)
p-Methoxy	$Na_2CO_3 + H_2O$		(354)
p-Methoxy	$Na_2CO_3 + H_2O$	75	(469)
o-Ethoxy	H_2O		(221)
Bromo-*o*-methoxy	$CH_3COONa + H_2O$		(552)
2,4-Dimethoxy-5-bromo (D)	$KOH + CH_3OH$	80	(613)
3,4-Methylenedioxy	$CaCO_3 + H_2O$		(218)
3,4-Methylenedioxy	$Na_2CO_3 + H_2O$	90	(469)
3,4-Dibromomethylenedioxy (E)	$KOH + H_2O$		(553)
3,5-Dibromo-4-hydroxy	$KOH + C_2H_5OH$		(814)

* By-products: (A) *p*-bromobenzaldehyde and *p*-bromocinnamic acid; (B) *m*-nitro-α-bromocinnamic acid; (C) *m*-nitro-α-bromocinnamic acid; (D) β,2,4-trimethoxy-α,5-dibromophenylpropionic acid; (E) the corresponding styrene and both the α- and the β-bromocinnamic acids.

β,2-Dibromo-5-methoxystyrene has been obtained by brominating *m*-methoxybenzalpyruvic acid in chloroform solution, followed by treatment with potassium acetate in methanol (612).

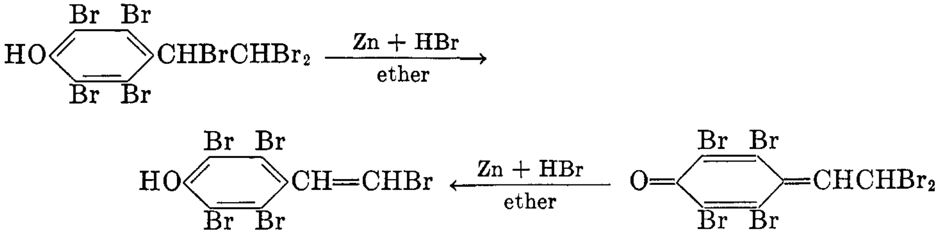


A few β-bromostyrenes have been prepared by distilling the corresponding bromohydrin methyl or ethyl ethers. This is true of *o*-methoxy- (586), *p*-methoxy-



(584), and 3,4-dimethoxy-β-bromostyrenes (474, 584).

β,2,3,5-Tetrabromo-4-hydroxystyrene was prepared by treating α,β,β,2,3,5-hexabromo-4-hydroxyethylbenzene with zinc and hydrobromic acid in ether (816). The same reaction was used to prepare β,2,3,5,6-pentabromostyrene. This compound also was prepared by treating the quinoid form of β,β,2,3,5,6-hexabromo-4-hydroxystyrene with the same reagent.



β-Bromo-β, *p*-dinitrostyrene was a by-product obtained in the preparation of α-bromo-*p*-nitrocinnamic acid by the nitration of α-bromocinnamic acid (560). A mixture of *o*- and *p*-nitro-β-bromo-β-nitrostyrenes was obtained by nitrating β-bromostyrene (224).

β-Bromostyrene has served as a convenient source of phenylacetylene. In table 20 are shown the reagents used and the yields obtained.

The same procedures have been used to convert substituted β-bromostyrenes to the corresponding phenylacetylenes. Thus alcoholic potassium hydroxide has been used in the case of *p*-methoxy-β-bromostyrene (354) with an 84 per cent yield (519) and 3,4-methylenedioxy-β-bromostyrene (218) with a 60.5 per cent yield (469). Sodium amide gave a poor yield of *o*-methoxyphenylacetylene from *o*-methoxy-β-bromostyrene (586).

In the experiment marked (A) in table 20 there was obtained as a by-product 17 per cent of β-ethoxystyrene (448, 531). By-product β-methoxystyrene in experiment (B) has been noted above (456). With potassium hydroxide and ethanol at 180°C. the yield of β-ethoxystyrene was nearly quantitative (292).

It has been shown that the hydrolysis of β-bromostyrene by chromic acid and sulfuric acid at 90–95°C. for 2 hr. amounted to 4.3 per cent (147). When heated with water β-bromostyrene yielded phenylacetaldehyde (206).

β-Bromostyrene did not react with sodium malonic ester, sodium acetoacetic ester, or sodium cyanoacetic ester in alcohol, benzene, or xylene (452). It gave a color with antimony trichloride in chloroform (646) and with nitrosyl chloride a nitrosochloride from which hydroxylamine hydrochloride was obtained by heating with hydrochloric acid (556). It did not react with phosphorus pentachloride (68).

Styrylmagnesium bromide and styryllithium, both prepared from β-bromostyrene, have served as agents for the introduction of styryl groups into a large number of compounds. While the Grignard reagent is quite difficult to prepare, it can be made in 90 per cent yield under the proper conditions (267). In this

$$C_6H_5CH{=}CHBr + Mg \xrightarrow{\text{ether}} C_6H_5CH{=}CHMgBr$$

detailed study the other yields varied between 42 per cent and 78 per cent. Because of this yield variation, β-bromostyrene has been used for the evaluation of different forms of magnesium and methods for their activation (262). By-products in the preparation of styrylmagnesium bromide include styrene (509, 740), phenylacetylene (509, 740), and 1,4-diphenylbutadiene (509, 640, 740, 797, 798, 807).

In contrast to *p*-bromoallyl- and *p*-bromopropenyl-benzenes, *p*-bromostyrene was inert to magnesium in ether (578, 580).

TABLE 20

Phenylacetylene from β-bromostyrene

REAGENT	YIELD	REFERENCE
	per cent	
KOH + C_2H_5OH	40	(305)
KOH + C_2H_5OH, 120–130°C	18	(531)
Na in ether	24	(531)
KOH + C_2H_5OH, 130–135°C. (A)*	60	(531)
KOH + C_2H_5OH	37	(522)
Na		(740)
KOH + C_2H_5OH, 100°C	61	(712)
KOH + C_2H_5OH, 125–130°C	76	(469)
KOH + C_2H_5OH		(168)
KOH + C_2H_5OH		(171)
KOH, 200–215°C	80	(295)
KOH, 200–230°C	67	(296)
KOH + NaOH, 200–215°C., copper vessel	70	(641)
CH_3ONa (B)*	28	(456)
Na in liquid NH_3	96	(761)
$NaNH_2$ in liquid NH_3	75	(763)
C_6H_5NHNa in ether	45	(90)
$NaNH_2$ + $C_6H_5NH_2$ (small amount)	89	(90)

* (A) In this experiment 17 per cent of β-ethoxystyrene was obtained as a by-product.

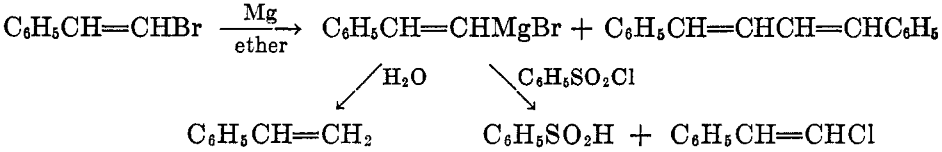
(B) In this experiment there was a 55 per cent recovery of β-bromostyrene and 12 per cent of β-methoxystyrene.

Treatment of styrylmagnesium bromide with water of course gives styrene (640, 798). Carbonation produces cinnamic acid (740, 797, 798) with some phenylpropiolic acid as a by-product (740). A mixture of the *cis* and *trans* acids was

$$C_6H_5CH{=}CHMgBr \xrightarrow{CO_2} C_6H_5CH{=}CHCOOH + C_6H_5C{\equiv}CCOOH$$

obtained from either the *cis* or the *trans* bromide (797). With acetaldehyde 30 per cent of methylstyrylcarbinol was obtained and with benzophenone 14 per cent of diphenylstryrylcarbinol (509) (isolated as the methyl ether after crystallization from methanol) (714). Other investigators were not able to separate this latter carbinol or the one from methyl *p*-tolyl ketone from the by-product diphenylbutadiene, but showed their presence by means of the color with concentrated sulfuric acid (807). Styrylmagnesium bromide also has been condensed with the following ketones and the resulting carbinols isolated as the perchlorates: *p*-methoxybenzophenone in 40 per cent yield (807), xanthone in 56 per cent yield (807) (as the chloride in 58 per cent yield) (808), 1-methoxyxanthone (807), and 2,3,5,6-dinaphthalenepyrone (807) in 52 per cent yield (808). Reaction also occurred with estrone acetate (651).

Styrylmagnesium bromide reacted with benzenesulfonyl chloride to give benzenesulfinic acid and β-chlorostyrene (260). Unreacted Grignard reagent was recovered as styrene and some by-product diphenylbutadiene was isolated.



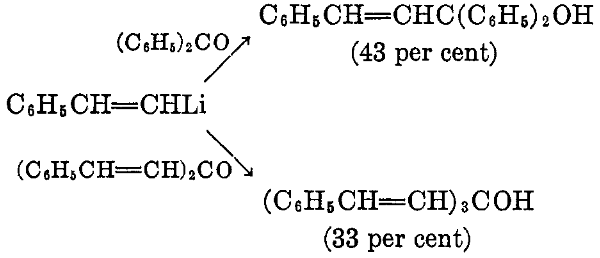
$$C_6H_5CH{=}CHBr \xrightarrow[\text{ether}]{Mg} C_6H_5CH{=}CHMgBr + C_6H_5CH{=}CHCH{=}CHC_6H_5$$

$$C_6H_5CH{=}CHMgBr \xrightarrow{H_2O} C_6H_5CH{=}CH_2$$

$$C_6H_5CH{=}CHMgBr \xrightarrow{C_6H_5SO_2Cl} C_6H_5SO_2H + C_6H_5CH{=}CHCl$$

Styrylmagnesium bromide and β-bromostyrene have served as the raw materials for the preparation of a number of organometallic compounds. These reactions are discussed in connection with the various metallic derivatives of styrene.

When β-bromostyrene was treated with lithium in ether 34 per cent of the organo-lithium compound was obtained (266). Since no cinnamic acid was obtained on carbonation, the authors did not believe that they had obtained styryllithium. Subsequently styryllithium was obtained in 68 per cent yield by this method (797). Treatment with water gave principally styrene plus a little phenylacetylene. Carbonation gave cinnamic acid and phenylpropiolic acid in the ratio of four to one. Styryllithium has been added to benzophenone and to distyryl ketone to give the corresponding carbinols (480).



$$C_6H_5CH{=}CHLi \xrightarrow{(C_6H_5)_2CO} C_6H_5CH{=}CHC(C_6H_5)_2OH \quad \text{(43 per cent)}$$

$$C_6H_5CH{=}CHLi \xrightarrow{(C_6H_5CH{=}CH)_2CO} (C_6H_5CH{=}CH)_3COH \quad \text{(33 per cent)}$$

With cholestanone the olefin was obtained (651).

When β-bromostyrene was allowed to stand in petroleum ether for 38 days with butyllithium; the products were 1-phenyl-1-hexene and 1,4-diphenylbutadiene (478). After boiling in petroleum ether, carbonation of the products of the same reaction yielded 23 per cent of cinnamic acid, 27 per cent of recovered β-bromostyrene, and a trace of phenylbutadiene (263). In ether solution

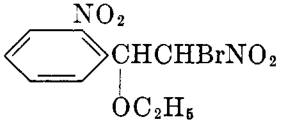
$$C_6H_5CH{=}CHBr + C_4H_9Li \rightarrow C_6H_5CH{=}CHC_4H_9 + C_6H_5CH{=}CHCH{=}CHC_6H_5$$

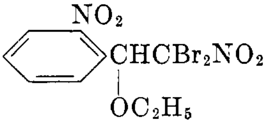
15 per cent of β-bromostyrene was recovered and the carbonated product was 42.5 per cent of phenylpropiolic acid. When β-bromostyrene was treated with phenyllithium in ether solution and then with benzophenone, 95 per cent of triphenylpropargyl alcohol was produced (782).

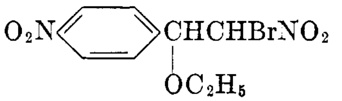
$$C_6H_5CH{=}CHBr \xrightarrow[\text{then } (C_6H_5)_2CO]{\text{ether, } C_6H_5Li} (C_6H_5)_2COHC{\equiv}CC_6H_5$$

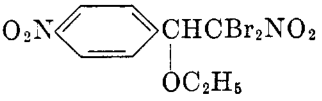
β-Bromostyrene was dehalogenated by lithium aluminum hydride to yield 49 per cent of styrene (756a).

On page 230 are shown several reactions which Thiele and Haeckel (737) conducted with β-bromo-β-nitrostyrene and with β-bromo-β,*p*-dinitrostyrene. This same conversion of a β-bromo-β-nitrostyrene to an ω-nitroacetophenone has been utilized by other investigators to prepare the following ω-nitroacetophenones: *m*-nitro- (45), *p*-nitro- (45), *o*-methoxy- (608), *p*-methoxy- (608), 3,4-dimethoxy- (608), and 3,4-methylenedioxy- (530, 608). The reaction was not applicable to the 2,4-dimethoxy-5-bromo analog. In the case of the *o*- and *p*-nitro compounds the mono- and dibromo-ethyl ethers and for the *p*-nitro compound the mono- and dibromo-methyl ethers (441) also have been prepared (224). For the *m*-nitro compound the analogous mono- and dibromo-methyl (243, 441) and ethyl (243, 441) ethers have been obtained.









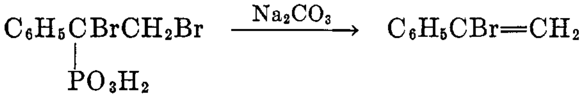
C. α-Bromostyrene chemistry

The preparation of α-bromostyrenes by the dehydrohalogenation of styrene dibromides has already been described. This has been by far the most widely used method of preparation.

α-Bromostyrene has been prepared by adding hydrogen bromide to phenylacetylene in glacial acetic acid solution at 0°C. (168, 171, 531). One investigator preferred dry ice temperatures, since at room temperature he obtained primarily dypnone, acetophenone, and a small amount of styrene dibromide (733). The

$$C_6H_5C{\equiv}CH + HBr \xrightarrow{\text{cold}} C_6H_5CBr{=}CH_2 + C_6H_5CBr_2CH_3$$

by-product in this reaction is α,α-dibromoethylbenzene, which can be converted to α-bromostyrene by means of cold alcoholic potassium hydroxide (531) or by heating with anhydrous ethyl alcohol or with sodium ethoxide in alcohol at 55°C. (733). In the latter case dypnone and acetophenone acetal also were obtained. α-Bromostyrene has been prepared by treating acetophenone with phosphorus pentabromide. A 68 per cent yield of α-bromostyrene was obtained by treating α,β-dibromo-α-phenethylphosphonic acid with saturated aqueous sodium carbonate at 0°C. (145).



$$\underset{\displaystyle PO_3H_2}{C_6H_5CBrCH_2Br} \xrightarrow{Na_2CO_3} C_6H_5CBr{=}CH_2$$

As with β-bromostyrene, α-bromostyrene has served as a source of phenylacetylene. In table 21 are summarized the various reagents which have been used to effect this dehydrohalogenation.

Treatment of phenylacetylene with aqueous hydrogen bromide at 100°C. gave α-bromostyrene and acetophenone in the ratio of two to one (531). α-Bromostyrene has been converted to acetophenone by heating with water (241), by means of 50–67 per cent sulfuric acid (242), concentrated sulfuric acid (241), and boiling formic acid in 92 per cent yield (31). α-Bromostyrene was not affected by zinc dust in alcohol and gave no sodium phenylacetylide with sodium in ether (431). Swarts (722) stated that treatment with sodium followed by carbonation gave a mixture of cinnamic and phenylpropionic acids. Erlenmeyer (208) later said the reaction yielded a mixture of phenylpropiolic and phenylpropionic acids. Both of these investigators must have obtained some sodium phenylacetylide, in spite of Nef's (531) subsequent statement that no such reaction occurred.

TABLE 21

Phenylacetylene from α-bromostyrene

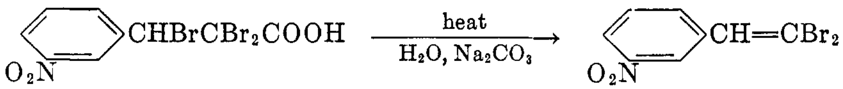
REAGENT	YIELD	REFERENCE
	per cent	
KOH + C_2H_5OH, 110°C.		(238)
KOH + C_2H_5OH		(268)
KOH + C_2H_5OH, 120°C.		(269)
KOH + C_2H_5OH, 130°C.	31	(242)
C_2H_5ONa + C_2H_5OH, 120°C.		(531)
$NaNH_2$ + kerosene, 160°C.	78	(105)
KOH + C_2H_5OH		(168)
KOH + C_2H_5OH		(171)

$$C_6H_5CBr{=}CH_2 \xrightarrow{HCOOH} C_6H_5COCH_3$$

The air oxidation of α-bromostyrene has been mentioned previously. ω-Bromoacetophenone has been isolated as a product of this reaction (170).

D. More highly brominated styrene derivatives

β,β-Dibromostyrene has been prepared by treating α,β,β-tribromoethylbenzene with alcoholic potassium hydroxide (469, 531). Some α,β-dibromostyrene also was isolated from the reaction mixture (531). *m*-Nitro-β,β-dibromostyrene was obtained by heating *m*-nitro-α,α,β-tribromophenylpropionic acid with aqueous sodium carbonate (601).



β,β-Dibromostyrene yielded β-bromophenylacetylene on treatment with alcoholic potassium hydroxide (469, 531) and reacted slowly with zinc and alcohol at 100°C. (531). When the vapors of β,β-dibromostyrene were passed over glowing copper, a good yield of phenylacetylene was obtained (531).

α,β-Dibromostyrene has been prepared by treating phenylacetylene with

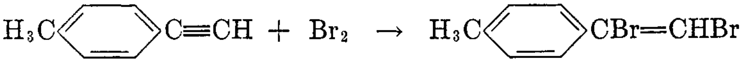
$$C_6H_5C{\equiv}CH + Br_2 \rightarrow C_6H_5CBr{=}CHBr$$

bromine (238; 78 per cent yield, 531) or phosphorus pentabromide (34 per cent yield) (68). Alternate syntheses include treating phenacyl bromide with phosphorus pentabromide (180) or phosphorus dibromotrichloride (some by-product ω,ω-dibromoacetophenone) (732), treating dibromobenzalacetophenone with alkali (167), and heating β-bromo-β-nitrostyrene to 190–200°C. (67 per cent yield)

$$C_6H_5COCBr{=}CBrC_6H_5 \xrightarrow{OH^-} C_6H_5CBr{=}CHBr + C_6H_5COOH$$

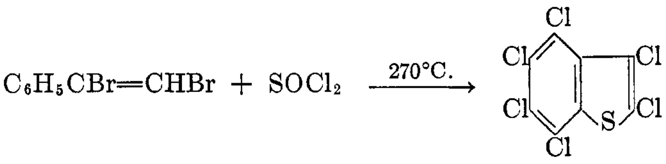
(17). When acetophenone was treated with phosphorus dibromotrichloride, α,β-dibromostyrene was obtained along with phenacyl bromide, ω,ω-dibromoacetophenone, and α,α-dibromoethylbenzene (732).

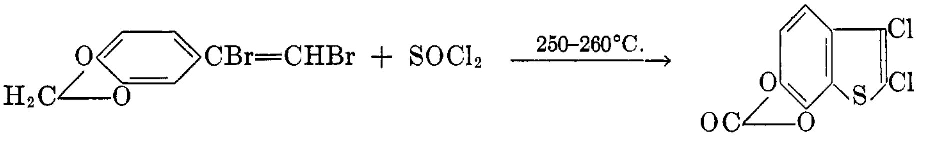
Treatment of the corresponding phenylacetylene with bromine has been used as a means of preparing the following α,β-dibromostyrenes: *p*-methyl- (423), *p*-ethyl- (423), 2-methyl-5-isopropyl- (423), *m*-nitro- (601), and 2,6-dichloro- (602).



m-Nitro-α,β-dibromostyrene also has been prepared by heating *m*-nitro-α,β,β-tribromophenylpropionic acid with aqueous sodium carbonate (601).

Treatment of α,β-dibromostyrene with zinc (17) or zinc and alcohol (531) yielded phenylacetylene. Treatment with alcoholic potassium hydroxide yielded primarily β-bromophenylacetylene (531). When α,β-dibromostyrene and 3,4-methylenedioxy-α,β-dibromostyrene were heated with thionyl chloride, chlorinated benzothiophenes were produced (53).





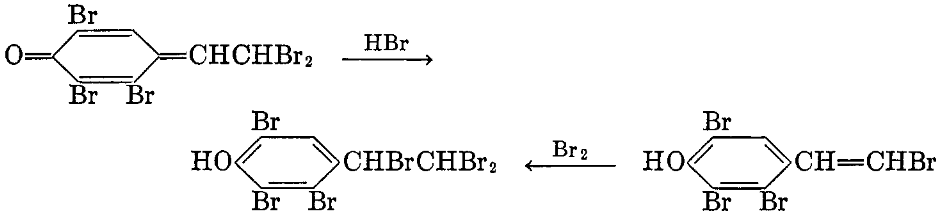
(70 per cent)

The preparation of α,α-dibromoethylbenzene by the addition of hydrogen bromide to phenylacetylene, together with its conversion to α-bromostyrene, has been described previously. When heated with alcohol or alcoholic potassium hydroxide, α,α-dibromoethylbenzene yielded acetophenone.

Both α,β,β-tribromoethylbenzene (168, 171, 220, 450, 605, 717) and its substituted analogs have been prepared by the addition of bromine to the corresponding β-bromostyrenes. These substituted analogs include o-nitro- (603), p-nitro- (603), o-ethoxy- (221), 2,4-dimethoxy-5-bromo- (613), 3,4-dimethoxy- (474),

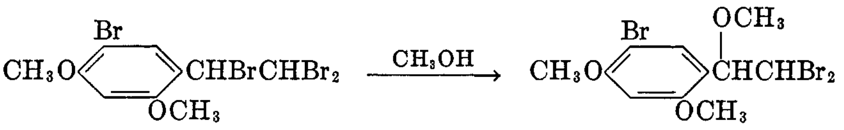
$$C_6H_5CH{=}CHBr + Br_2 \rightarrow C_6H_5CHBrCHBr_2$$

3,5-dibromo-4-hydroxy- (814), 2,3,5-tribromo-4-hydroxy- (816), and 2,3,5,6-tetrabromo-4-hydroxy- (816). The last two named also have been prepared by the addition of hydrogen bromide to the quinoid form of the corresponding β,β-dibromostyrene.

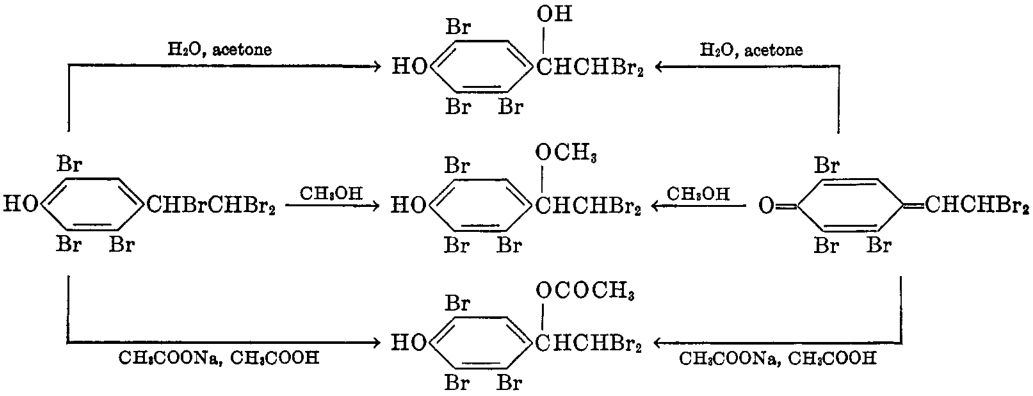


Treatment of α,β,β-tribromoethylbenzene with alcoholic potassium hydroxide yielded mostly β,β-dibromostyrene, together with some α,β-dibromostyrene (531). Treatment with potassium iodide resulted in dehalogenation to give presumably β-bromostyrene (175). α,β,β-Tribromoethylbenzene reacted with benzene in the presence of aluminum chloride to give s-tetraphenylethane (25).

When boiled with potassium hydroxide in methanol or in methanol alone, 2,4-dimethoxy-α,β,β,5-tetrabromoethylbenzene yielded α,2,4-trimethoxy-β,β,5-tribromoethylbenzene (613). Similar results were obtained with ethanol. When



heated in methanol 2-hydroxy-α,β,β,3,5-pentabromoethylbenzene also gave the α-methoxy derivative (248). With α,β,β,3,5-pentabromo-4-hydroxyethylbenzene this same replacement of the α-bromine atom has been effected with methanol and with water and acetone to give the α-methoxy and α-hydroxy derivatives, respectively (814). Both reactions have been conducted successfully with α,β,β,2,3,5-hexabromo-4-hydroxyethylbenzene and with α,β,β,2,3,5,6-heptabromo-4-hydroxyethylbenzene (816). Treatment of these last two compounds with sodium acetate in acetic acid gave the α-acetoxy derivatives. All six of these last-named substitution products have been prepared by adding the appropriate reagent to the quinoid form of the corresponding β,β-dibromostyrene.

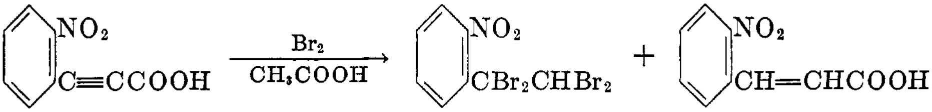


On treatment with zinc and hydrobromic acid in ether α,β,β,3,5-pentabromo-α,β,β,2,3,5-hexabromo-, and α,β,β,2,3,5,6-heptabromo-4-hydroxyethylbenzene all gave the corresponding β-bromostyrenes (814, 816).

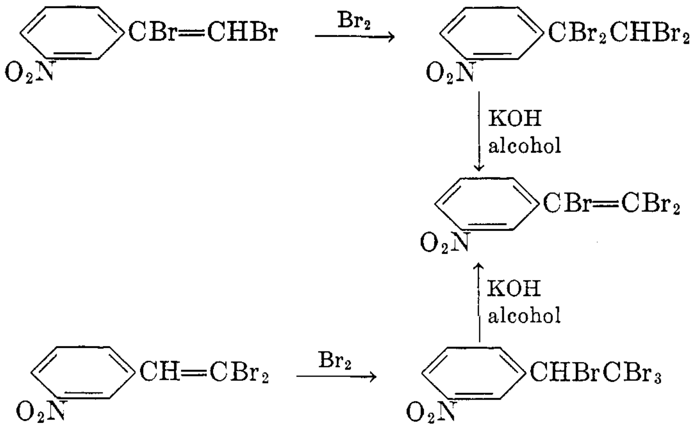
α,α,β-Tribromoethylbenzene has been prepared by the addition of bromine to α-bromostyrene (168, 171).

$$C_6H_5CBr{=}CH_2 + Br_2 \rightarrow C_6H_5CBr_2CH_2Br$$

Besides α,α,β,β-tetrabromoethylbenzene itself (180), the following substituted analogs have been prepared by the addition of bromine to the corresponding α,β-dibromostyrenes: *p*-methyl- (423), *p*-ethyl- (423), and *m*-nitro- (601). The *o*-nitro compound was obtained in 15–20 per cent yield along with 15 per cent of the corresponding cinnamic acid by treating *o*-nitrophenylpropiolic acid with bromine in acetic acid (289).



Distillation of α,α,β,β-tetrabromoethylbenzene yielded α,β,β-tribromostyrene (180). *m*-Nitro-α,β,β-tribromostyrene was prepared by treating the corresponding tetrabromoethylbenzene with alcoholic potassium hydroxide (601). This styrene, which was inert to bromine, was prepared in the same way from *m*-nitro-α,β,β-tetrabromoethylbenzene.



V. MISCELLANEOUS HALOGENATED STYRENE DERIVATIVES

A. Mixed fluoro, chloro, and bromo compounds

Treatment of phenylmagnesium bromide with 1,1-difluoro-2,2-dichloroethane yielded small amounts of β-fluorostyrene, β-chlorostyrene, α-fluoro-β,β-dichloroethylbenzene, bromobenzene, and biphenyl (723). Phenylmagnesium bromide and 1,1-difluoro-2,2-dibromoethane yielded mostly bromobenzene and biphenyl, plus small amounts of fluorobenzene and β-fluorostyrene. Treatment of the last-named compound with bromine gave β-fluoro-α,β-dibromoethylbenzene.

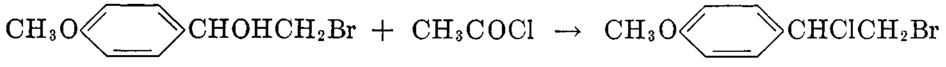
When α,α,β,β,β-pentachloroethylbenzene was heated with hydrogen fluoride at 150°C. in a nickel vessel, the product was 65 per cent of difluorotrichloroethylbenzene plus a little α,β,β-trichlorostyrene (772). In an iron vessel the product was 14 per cent of difluorotrichloroethylbenzene and 27 per cent of α,β,β-trichlorostyrene (772, 773).

Treatment of styrene with bromine chloride at −10° to −12°C. gave 65–70 per cent of α-chloro-β-bromoethylbenzene, 20 per cent of styrene dibromide, and 10 per cent of styrene dichloride (759). α-Chloro-β-bromoethylbenzene reacted with alcoholic potassium hydroxide at 0°C. to give 70 per cent of α-chlorostyrene.

$$C_6H_5CHClCH_2Br \xrightarrow[C_2H_5OH]{KOH} C_6H_5CCl{=}CH_2$$

(70 per cent)

p-Methoxy-α-chloro-β-bromoethylbenzene was prepared by treating *p*-methoxystyrene bromohydrin with acetyl chloride (758). β-Chlorostyrene added bromine



to give 64 per cent of β-chloro-α,β-dibromoethylbenzene in 13 min. (605).

$$C_6H_5CH{=}CHCl + Br_2 \rightarrow C_6H_5CHBrCHClBr$$

(64 per cent)

3,4-Methylenedioxy-β-chlorostyrene also formed a dibromide (549).

B. Iodinated derivatives

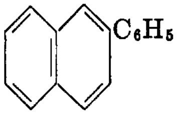
Treatment of styrene with iodine monochloride gave α-chloro-β-iodoethylbenzene (92, 343, 344) in yields as high as 95 per cent (346). This latter compound reacted with water to give styrene iodohydrin (344) and with potassium iodide

$$C_6H_5CH{=}CH_2 \xrightarrow{ICl} \underset{(95\text{ per cent})}{C_6H_5CHClCH_2I} \xrightarrow{H_2O} C_6H_5CHOHCH_2I$$

to give styrene, iodine, and potassium chloride (343). With silver nitrate the silver chloride precipitated before the silver iodide.

Berthelot reported that styrene yielded an unstable crystalline iodide on treatment with iodine in potassium iodide (72, 75, 76, 77, 78). The compound decomposed readily to iodine and polystyrene (75, 78). Styrene diiodide has been postulated as the intermediate in the formation of β-phenylnaphthalene from the reaction between hydriodic acid and β-phenoxystyrene or 3-phenyldihydrocoumarone (711).

$$C_6H_5CH{=}CHOC_6H_5 \xrightarrow{HI} C_6H_5OH + [C_6H_5CHICH_2I] \rightarrow$$



β-Nitrostyrene did not add iodine (571).

When styrylmercuric bromide was treated with iodine in chloroform solution, a 79 per cent yield of β-iodostyrene was obtained (797).

$$C_6H_5CH{=}CHHgBr \xrightarrow[CHCl_3]{I_2} \underset{(79\text{ per cent})}{C_6H_5CH{=}CHI}$$

β-Bromophenylacetylene added iodine to give β-bromo-α,β-diiodostyrene (531).

$$C_6H_5C{\equiv}CBr + I_2 \rightarrow C_6H_5CI{=}CBrI$$

α,β-Diiodostyrene has been prepared by the addition of iodine to phenylacetylene (155, 550) or by the addition of hydrogen iodide to β-iodophenylacetylene (550). With mercurous chloride α,β-diiodostyrene yielded α,β-dichlorostyrene (550).

$$\begin{tikzcd}
C_6H_5C{\equiv}CH + I_2 \arrow[dr] & & \\
 & C_6H_5CI{=}CHI \arrow[r, "HgCl"] & C_6H_5CCl{=}CHCl \\
C_6H_5C{\equiv}CI + HI \arrow[ur] & &
\end{tikzcd}$$

α,β,β-Triiodostyrene has been obtained by a variety of methods such as the reaction between silver phenylacetylide or β-iodophenylacetylene with iodine (451), the reaction between phenylacetylene and nitrogen triiodide (155), and, along with β-iodo-α-phenylacetylene, from the reaction between silver phenylpropiolate and iodine in benzene solution (777).

$$C_6H_5C{\equiv}CCOOAg \xrightarrow[C_6H_6]{I_2} C_6H_5C{\equiv}CI + C_6H_5CI{=}CI_2$$

α,β,β-Triiodostyrene and acetophenone were the products obtained by heating α,β-diiodocinnamic acid to 140°C. (550).

VI. STYRENE HALOHYDRIN CHEMISTRY

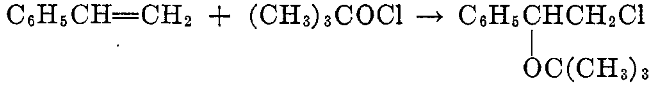
A. Addition of hypohalous acids

The preparation of styrene halohydrins (defined as β-halo-α-hydroxyethylbenzenes) by the hydrolysis of styrene dihalides, usually by means of a mixture of water and acetone, has been described in detail in connection with the various styrene dihalides.

A number of methods have been adopted to effect the addition of hypochlorous acid to styrene. The earliest (159) utilized chlorourea in acetic acid solution

$$C_6H_5CH{=}CH_2 + HOCl \rightarrow C_6H_5CHOHCH_2Cl$$

to give a 95 per cent yield of crude and a 70 per cent yield of pure styrene chlorohydrin. Subsequent investigators (282) were able to obtain only 52 per cent by this method. Other methods included calcium hypochlorite and carbon dioxide (76 per cent yield) (189), sodium hypochlorite and nitric acid (32 per cent yield) (282), and *tert*-butyl hypochlorite in acetic acid (70 per cent conversion, 84 per cent yield) (282). In the last case omission of the acetic acid led to direct addition of the *tert*-butyl hypochlorite to the styrene.



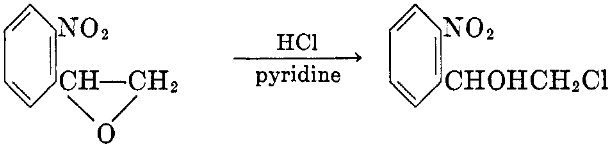
$$C_6H_5CH{=}CH_2 + (CH_3)_3COCl \rightarrow C_6H_5\underset{\displaystyle |\atop \displaystyle OC(CH_3)_3}{CH}CH_2Cl$$

Treatment of styrene with hypochlorous acid in the presence of sodium chloride at 90°C. or sodium carbonate at 40–50°C. gave negligible yields. Styrene chlorohydrin also has been prepared in 58 per cent yield by the reaction between phenylmagnesium bromide and chloroacetaldehyde (697),

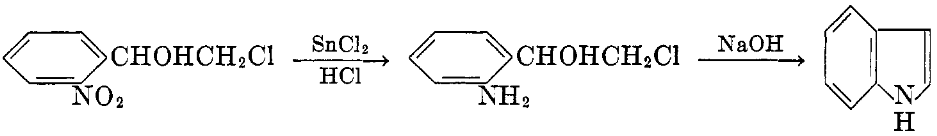
$$C_6H_5MgBr + ClCH_2CHO \rightarrow C_6H_5CHOHCH_2Cl$$

and in 86 per cent yield by the reduction of ω-chloroacetophenone with aluminum isopropoxide (260a).

p-Methylstyrene chlorohydrin has been prepared by treating *p*-methylstyrene with *tert*-butyl hypochlorite in water or aqueous acetic acid or with chlorourea in aqueous acetic acid (689). When the reaction with *tert*-butyl hypochlorite was conducted in glacial acetic acid, the product was largely the chlorohydrin acetate. *p*-Methyl- (696), 3,4-dimethyl- (697), and *p*-chloro-styrene (65 per cent yield) (696) chlorohydrins all have been prepared by treating the corresponding substituted phenylmagnesium bromide with chloroacetaldehyde. Both 3,4-methylenedioxy- and 3,4-carbonyldioxy-styrenes added hypochlorous acid in petroleum ether and benzene solutions, respectively, to give the corresponding chlorohydrins (549). In the first case the crude product was contaminated with chlorinated chlorohydrin, so that the yield of pure product was only 14 per cent; in the second case the yield was 60 per cent. *o*-Nitrostyrene chlorohydrin in 49 per cent yield resulted from the addition of hydrogen chloride in pyridine solution to *o*-nitrostyrene oxide (29).



Reduction of *o*-nitrostyrene chlorohydrin with stannous chloride and hydrochloric acid gave *o*-aminostyrene chlorohydrin, which yielded a little indole on treatment with alkali (29).



Styrene chlorohydrin has been oxidized to ω-chloroacetophenone by means of potassium dichromate in sulfuric acid (159) in yields as high as 83 per cent

$$C_6H_5CHOHCH_2Cl \xrightarrow[H_2SO_4]{K_2Cr_2O_7} \underset{\text{(83 per cent)}}{C_6H_5COCH_2Cl}$$

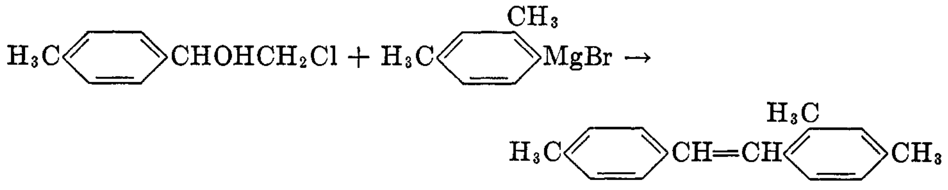
(282). This same oxidation has been effected in the case of *o*-nitrostyrene chlorohydrin (29).

Treatment of styrene chlorohydrin with acetic anhydride gave a 66 per cent yield of the acetate (282). The *p*-nitrobenzoate also has been prepared. The acetate of *o*-nitrostyrene chlorohydrin has been prepared by treating *o*-nitrostyrene oxide with acetyl chloride in pyridine (29). The benzoate was prepared in the same way, as well as by benzoylation of the chlorohydrin by the Schotten–Baumann method.

When the vapors of styrene chlorohydrin together with steam were passed over an alumina catalyst held at 360–390°C., a 67 per cent yield of acetophenone was obtained (194, 197). Over a silica catalyst impregnated with calcium carbonate, 51 per cent of phenylacetaldehyde contaminated with some β-chlorostyrene was obtained (195, 197).

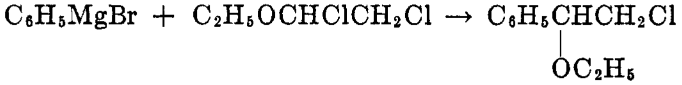
$$C_6H_5CHOHCH_2Cl \xrightarrow[CaCO_3]{H_2O,\ SiO_2} C_6H_5CH_2CHO + C_6H_5CH{=}CHCl$$

p-Methylstyrene chlorohydrin reacted with 2,4-dimethylphenylmagnesium bromide to give, after boiling with 40 per cent sulfuric acid, a 70 per cent yield of 2,4,4′-trimethylstilbene (696). In the same way a 59 per cent yield of 4-methyl-



4′-chlorostilbene was obtained from *p*-chlorostyrene chlorohydrin and *p*-tolylmagnesium bromide.

The ethyl ether of styrene chlorohydrin has been obtained by treating phenylmagnesium bromide with α,β-dichloroethyl ether (744). A yield of 65 per cent has been reported (314).



$$C_6H_5MgBr + C_2H_5OCHClCH_2Cl \rightarrow C_6H_5\underset{\displaystyle OC_2H_5}{CH}CH_2Cl$$

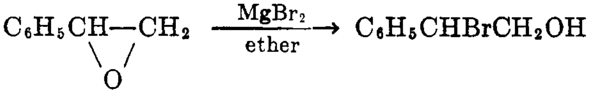
Several investigators have added hypobromous acid to styrene. The best conditions involve the use of bromine water at 90°C. (21, 597, 598, 721), although the only yields given were 91 per cent crude and 55 per cent pure (598). Styrene bromohydrin has been prepared in 90 per cent yield by the reduction of phenacyl bromide with aluminum isopropoxide (461, 462). Reduction with sodium borohydride yielded 71 per cent of styrene bromohydrin (135a).

$$C_6H_5COCH_2Br \xrightarrow[CH_3CHOHCH_3]{(i\text{-}C_3H_7O)_3Al} C_6H_5CHOHCH_2Br$$

(90 per cent)

Mixtures of *o*- and *p*-ethyl- and *o*- and *p*-chloro-styrene bromohydrins have been prepared by treating the corresponding styrene mixtures with hot bromine water (21). In the case of 3,4-methylenedioxystyrene, besides bromohydrin formation, one of the nuclear hydrogens was replaced by bromine (54, 100, 466). The first investigator (466) postulated the reaction as the addition of bromine, but subsequently (54) he was shown to be wrong. In attempts to prepare the bromohydrin of 3-methoxy-4-acetoxystyrene, only tars were obtained when the styrene was treated with hypobromous acid or when the phenacyl bromide was treated with aluminum isopropoxide (619).

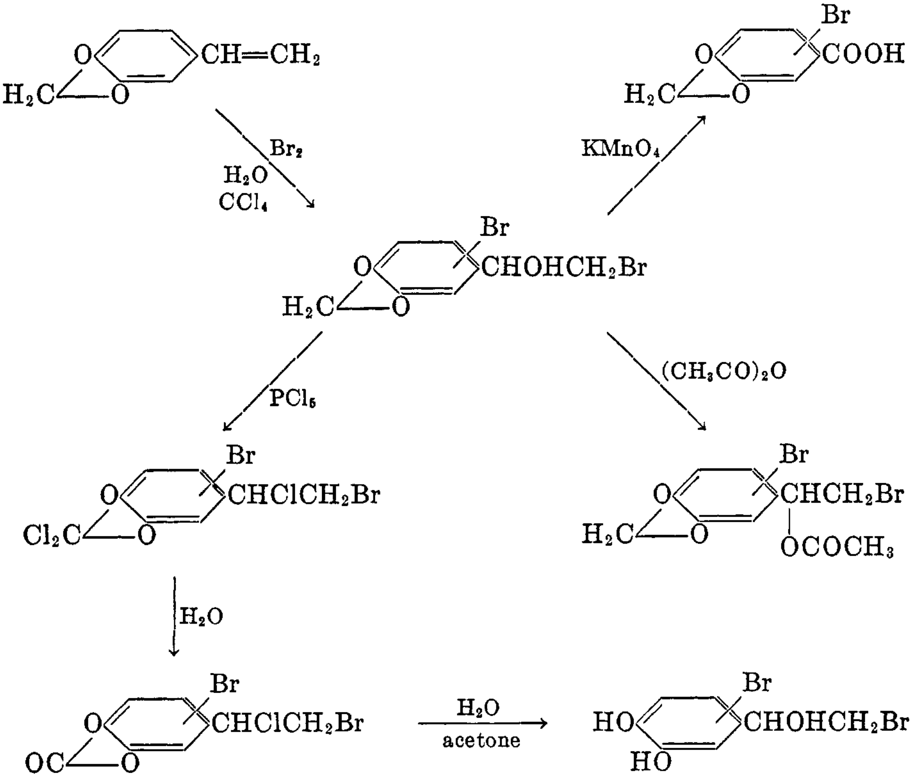
α-Bromo-β-hydroxyethylbenzene has been prepared by treating styrene oxide with the magnesium bromide–ether complex (747). It has been characterized as its *p*-nitrobenzoate and dinitrobenzoate.



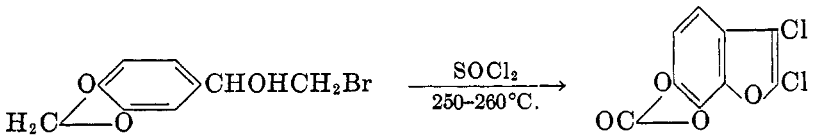
$$\underbrace{C_6H_5CH\text{—}CH_2}_{O} \xrightarrow[ether]{MgBr_2} C_6H_5CHBrCH_2OH$$

Contrary to the reaction reported with *p*-methoxystyrene bromohydrin (758), styrene bromohydrin reacted with acetyl chloride to give 91 per cent of the acetate (479). Treatment of 3,5-dibromo-4-hydroxystyrene bromohydrin (814), β,β,3,5-tetrabromo-α,4-dihydroxyethylbenzene (814), 2,3,5-tribromo-4-hydroxystyrene bromohydrin (816), β,β,2,3,5-pentabromo-α,4-dihydroxyethylbenzene (816), and β,β,2,3,5,6-hexabromo-α,4-dihydroxyethylbenzene (816) with acetic anhydride led to the formation of diacetyl derivatives. The preparation of α-acetyl derivatives of the last three named by both acetolysis and addition reactions has been mentioned in connection with the chemistry of the corresponding bromo compounds.

3,4-Methylenedioxystyrene bromohydrin reacted with sulfuryl chloride to give a nuclear-chlorinated analog (100). A similarly brominated 3,4-methylenedioxystyrene bromohydrin was obtained by treating the corresponding styrene with bromine water. Both of these compounds were acetylated with acetic anhydride. In addition the bromo compound underwent the series of reactions shown below.



Styrene bromohydrin reacted with sodium sulfite to give sodium β-hydroxy-β-phenylethanesulfonate (377). 3,4-Methylenedioxystyrene bromohydrin gave a benzothiophene derivative on treatment with thionyl chloride at 250–260°C. (53).

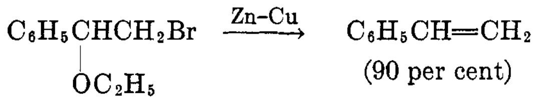


Besides the alcoholysis methods discussed in connection with styrene dibromide and related compounds, β-bromo-α-methoxyethylbenzene has been prepared by treating phenylmagnesium bromide with α-chloro-β-bromoethyl methyl ether (465).

$$C_6H_5MgBr + CH_3OCHClCH_2Br \rightarrow C_6H_5\underset{\underset{\displaystyle OCH_3}{|}}{C}HCH_2Br$$

β-Bromo-α-ethoxyethylbenzene has been prepared similarly from phenylmagnesium bromide and α,β-dibromoethyl ether (433) in 90 per cent yield (771) and from phenylmagnesium bromide and β-bromoacetal in 22 per cent yield (696). Treatment of β-phenyl-β-methoxyethylmercuric bromide with bromine in methanol at 0°C. yielded 70 per cent of β-bromo-α-methoxyethylbenzene (796).

β-Bromo-α-ethoxyethylbenzene reacted with a zinc–copper couple in ethanol to give 90 per cent of styrene (771). The same compound gave 74 per cent of



$$C_6H_5\underset{\underset{\displaystyle OC_2H_5}{|}}{C}HCH_2Br \xrightarrow{Zn\text{-}Cu} \underset{\text{(90 per cent)}}{C_6H_5CH{=}CH_2}$$

4-methylstilbene when treated with *p*-tolylmagnesium bromide followed by 40 per cent sulfuric acid (696).

Styrene iodohydrin has been prepared by treating styrene with mercuric oxide, iodine and water (70, 233, 273, 741, 742, 744). The only yield reported was 48

$$C_6H_5CH{=}CH_2 + HgO + I_2 + H_2O \rightarrow C_6H_5CHOHCH_2I$$

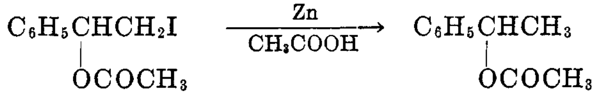
per cent (273). The first investigator to try this reaction reported the product as α-iodo-β-hydroxyethylbenzene (101). Under the same conditions with *p*-methoxystyrene the intermediate iodohydrin was not isolated and the product isolated was *p*-methoxyphenylacetaldehyde (742).

On distillation styrene iodohydrin decomposed (101) to acetophenone and hydrogen iodide (741). Treatment with silver nitrate gave phenylacetaldehyde (101, 741, 742).

$$C_6H_5CHOHCH_2I \xrightarrow{AgNO_3} C_6H_5CH_2CHO$$

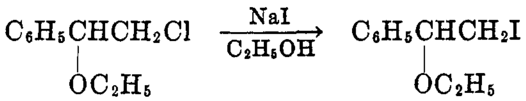
With acetic anhydride the compound was acetylated (742). Styrene iodohydrin reacted with sodium sulfite to give sodium β-phenyl-β-hydroxyethanesulfonate (377) and with methylmagnesium iodide to give β-phenethyl alcohol and a secondary alcohol (273).

Treatment of β-iodo-α-acetoxyethylbenzene with zinc and acetic acid gave α-phenethyl acetate (742).



$$C_6H_5\underset{\underset{\displaystyle OCOCH_3}{|}}{C}HCH_2I \xrightarrow[CH_3COOH]{Zn} C_6H_5\underset{\underset{\displaystyle OCOCH_3}{|}}{C}HCH_3$$

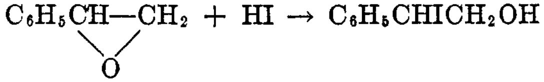
The methyl, ethyl, and amyl ethers of styrene iodohydrin were prepared by treating styrene with mercuric oxide and iodine in the appropriate alcohol (741). The ethyl ether has been prepared by boiling the ethyl ether of styrene chlorohydrin with sodium iodide in ethanol (314).



$$\underset{\displaystyle OC_2H_5}{C_6H_5CHCH_2Cl} \xrightarrow[C_2H_5OH]{NaI} \underset{\displaystyle OC_2H_5}{C_6H_5CHCH_2I}$$

Both the methyl and amyl ethers yield phenylacetaldehyde on treatment with silver nitrate.

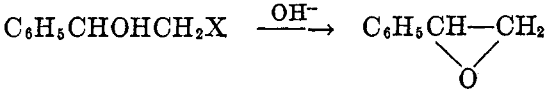
α-Iodo-β-hydroxyethylbenzene was obtained by the reaction between styrene oxide and hydriodic acid (273, 742, 744) or magnesium iodide in ether (273, 747). In the latter case if the reaction mixture was hot, phenylacetaldehyde also was obtained (747). The best yields were 34 per cent with hydriodic acid in ether, 60–85 per cent with hydriodic acid in petroleum ether, and 65 per cent with magnesium iodide in ether (273).



α-Iodo-β-hydroxyethylbenzene has been characterized as its *p*-nitrobenzoate and dinitrobenzoate (747). With methylmagnesium iodide the products were β-phenethyl alcohol and a secondary alcohol (273). α-Iodo-β-hydroxyethylbenzene reacted with *o*-aminothiophenol in the presence of alcoholic potassium hydroxide to give 2-phenyldihydrobenzothiazine (148a).

B. Styrene oxide

The preparation of styrene oxide by the epoxidation of styrene has been discussed under that heading. Another common method is to treat a styrene halohydrin with concentrated aqueous alkali or with concentrated alkali in a solvent.



Often the halohydrin is dissolved in a solvent also. These reactions are summarized in table 22.

Other styrene oxides which have been made from the corresponding chlorohydrin and sodium methoxide (697) are *p*-chloro- (74 per cent yield) and 3,4-dimethyl-. In the latter case considerable 3,4-dimethylstyrene glycol β-methyl ether also was reported. Treatment of *o*-nitrostyrene chlorohydrin or its acetate with sodium hydroxide gave *o*-nitrostyrene oxide (29). The method utilizing the bromohydrin and aqueous sodium hydroxide gave a 64 per cent yield of a mixture of *o*- and *p*-ethylstyrene oxides and was also used to prepare a mixture of *o*- and *p*-chlorostyrene oxides (21).

Impure and partly polymerized *d*-styrene oxide was obtained along with acetophenone and styrene glycol by treating *d*-β-phenyl-β-hydroxyethyltrimethylammonium iodide with water and silver oxide (597). *o*-Nitrostyrene oxide was prepared by treating *o*-nitrobenzaldehyde with diazomethane (29, 30). By-products included *o*-nitroacetophenone and *o*-nitrophenylacetone (29).

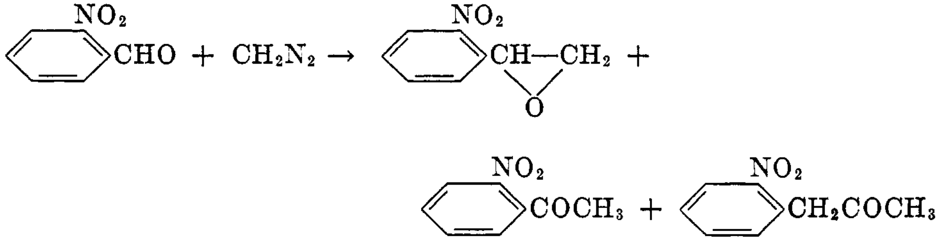


TABLE 22

Styrene oxide from styrene halohydrins

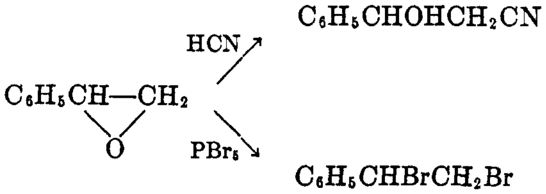
HALOHYDRIN USED	ALKALI	SOLVENTS	TEMPERATURE	YIELD	REFERENCE
			°C.	*per cent*	
Chlorohydrin	C_2H_5ONa	C_2H_5OH		*	(697)
	KOH	C_2H_5OH		†	(159)
	KOH	H_2O, C_6H_6	42	90	(324, 336)
Bromohydrin	NaOH	H_2O	60	73 from styrene	(21)
Iodohydrin	KOH	None		50 from styrene	(233)
	KOH	None			(741)
	KOH	$(C_2H_5)_2O$		50	(743)
	KOH	$(C_2H_5)_2O$		46 from styrene	(79)
	KOH	$(C_2H_5)_2O$		51 from styrene	(273)

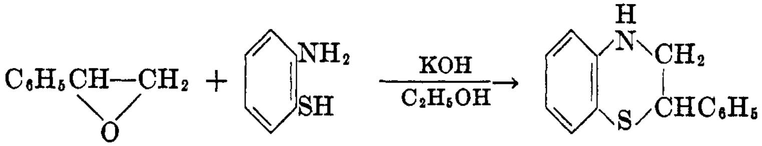
* The product was "mostly" styrene oxide with some by-product styrene glycol β-ethyl ether.

† In this same article it was reported that styrene chlorohydrin and sodium ethoxide gave only β-ethoxy-α-hydroxyethylbenzene.

While no phenylacetaldehyde was obtained when styrene oxide was heated with boiling 20 per cent sulfuric acid or with nitric acid or silver nitrate (742), the aldehyde was obtained when styrene oxide vapors were passed over a metallic catalyst at 200–250°C. (233, 743). Dilute acids gave mostly styrene oxide dimer (743). With such reducing agents as sodium in moist ether (743) or hydrogen and a nickel on calcium carbonate catalyst (322, 337, 455), β-phenethyl alcohol was obtained. In the latter case, besides some recovered oxide, a small amount of phenylacetaldehyde was produced. Reduction of styrene oxide with lithium aluminum hydride yielded from 75 per cent (756a) to 94 per cent (534a) of α-phenethyl alcohol.

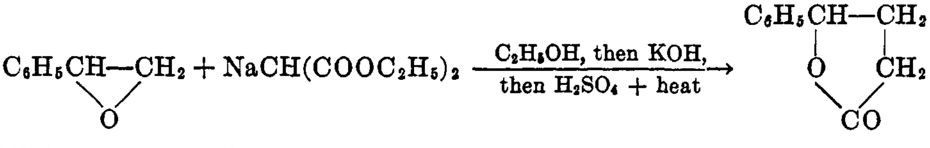
Besides the addition of hydrogen discussed above and that of hydrogen iodide mentioned previously, styrene oxide added hydrogen cyanide to give β-phenyl-β-hydroxypropionitrile (743). With phosphorus pentabromide styrene dibromide was obtained. Styrene oxide was less reactive toward hydroxylamine than was ethylene oxide (355). With crude pyridine styrene oxide gave a red color after 24 hr. heating at 50–60°C. (457). With pure pyridine the color was brown. Styrene oxide reacted with *o*-aminothiophenol in the presence of alcoholic potassium hydroxide to give 2-phenyldihydrobenzothiazine (148a).



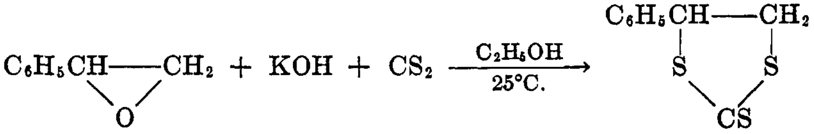


When styrene oxide was added to a solution of phenylmagnesium bromide, an 80–90 per cent yield of β,β-diphenylethyl alcohol was obtained (369). If the addition was reversed, an 80–90 per cent yield of α,β-diphenylethyl alcohol resulted. In each case there was always a trace of the other isomer formed. With methylmagnesium and ethylmagnesium bromides (743) or with methylmagnesium iodide (273), the products were the secondary alcohols. Treatment of styrene oxide with dimethylmagnesium gave a 60 per cent yield of 2-phenyl-1-propanol (273).

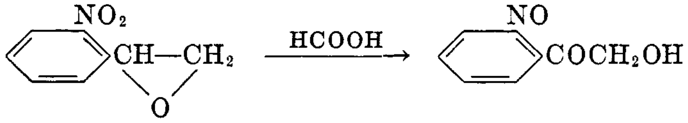
Styrene oxide reacted with sodium malonic ester to give a 72 per cent yield of δ-phenyl-δ-butyrolactone (642).



With potassium hydroxide and carbon disulfide the product was 77 per cent of a cyclic trithiocarbonate (149).



o-Nitrostyrene oxide reacted with formic acid to give 50–75 per cent of *o*-nitroso-ω-hydroxyacetophenone (30).



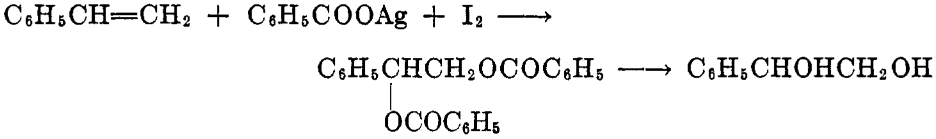
With acetic anhydride in the presence of a trace of ferric chloride the acetate was obtained (29). *o*-Nitrostyrene oxide did not react with phenyl isocyanate at 130–140°C., but gave a little indole on treatment with hydrazine hydrate in alcohol.

C. *Styrene glycol*

The preparation of styrene glycol by the hydrolysis of styrene dichloride or dibromide has been mentioned in connection with the chemistry of those compounds. Styrene chlorohydrin has been hydrolyzed to styrene glycol by boiling with aqueous sodium carbonate (211, 212) or bicarbonate (197).

$$C_6H_5CHOHCH_2Cl \xrightarrow[H_2O]{Na_2CO_3} C_6H_5CHOHCH_2OH$$

Treatment of styrene with hydrogen peroxide in *tert*-butyl alcohol in the presence of osmium tetroxide yielded 50 per cent of styrene glycol (511). Styrene glycol also has been prepared from styrene by the Prévost reaction (47, 570), in which styrene was treated with silver benzoate and iodine in boiling benzene followed by hydrolysis of the resulting styrene glycol dibenzoate.

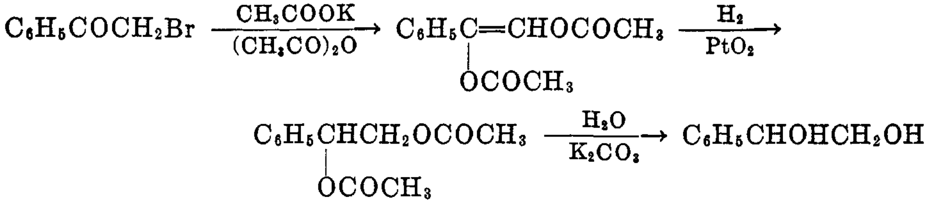


$$C_6H_5CH{=}CH_2 + C_6H_5COOAg + I_2 \longrightarrow \underset{\displaystyle OCOC_6H_5}{C_6H_5\overset{}{C}HCH_2OCOC_6H_5} \longrightarrow C_6H_5CHOHCH_2OH$$

Reduction of ω-hydroxyacetophenone with hydrogen in the presence of Raney nickel gave 85 per cent of styrene glycol (631). Reduction with aluminum amalgam gave styrene glycol and α-phenethyl alcohol (394). A 76 per cent yield was obtained by treating the corresponding acetate with acetone and aluminum isopropoxide, followed by hydrolysis with potassium hydroxide (277). Treatment

$$C_6H_5COCH_2OCOCH_3 \xrightarrow[CH_3COCH_3]{(i\text{-}C_3H_7O)_3Al} C_6H_5CHOHCH_2OCOCH_3 \xrightarrow{KOH} C_6H_5CHOHCH_2OH$$

of α,β-diacetoxystyrene (from phenacyl bromide and potassium acetate in acetic anhydride) with hydrogen in the presence of platinum oxide gave the diacetate, which was hydrolyzed to styrene glycol with aqueous potassium carbonate (156).

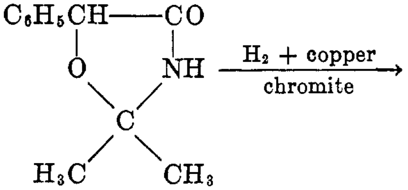


$$C_6H_5COCH_2Br \xrightarrow[(CH_3CO)_2O]{CH_3COOK} C_6H_5\underset{\displaystyle OCOCH_3}{\underset{|}{C}}{=}CHOCOCH_3 \xrightarrow[PtO_2]{H_2}$$

$$C_6H_5\underset{\displaystyle OCOCH_3}{\underset{|}{C}}HCH_2OCOCH_3 \xrightarrow[K_2CO_3]{H_2O} C_6H_5CHOHCH_2OH$$

In the presence of a palladium catalyst phenylglyoxal and *p*-methylphenylglyoxal have been hydrogenated to the corresponding glycols in 71 per cent and 68 per cent yields, respectively (225a).

A 62 per cent yield of styrene glycol was reported to have been obtained by boiling a benzene solution of 2,5-diphenyl-1,4-dioxane with aqueous potassium hydroxide (447). When 2,2-dimethyl-5-phenyloxazolidone was treated with hydrogen in the presence of copper chromite, styrene glycol was one of the products (161).



$$\xrightarrow[\text{chromite}]{H_2 + \text{copper}}$$

$$\underset{(35\text{ per cent})}{C_6H_5CHOHCONH_2} + \underset{(29\text{ per cent})}{C_6H_5CHOHCH_2OH}$$

$$+ \underset{(3\text{ per cent})}{C_6H_5CH_2CH_2OH} + \underset{(47\text{ per cent})}{[(CH_3)_2CH]_2NH}$$

Styrene glycol was a by-product of the reaction between styrene bromohydrin and sodium sulfite (721) and of the reaction between *d*-(β-phenyl-β-hydroxyethyl)-trimethylammonium iodide and wet silver oxide (597).

Reduction of styrene glycol with hydrogen in the presence of a palladium on charcoal catalyst gave β-phenethyl alcohol and perhaps some ethylbenzene (49).

$$C_6H_5CHOHCH_2OH \xrightarrow[Pd]{H_2} C_6H_5CH_2CH_2OH$$

Oxidation of styrene glycol with potassium permanganate, potassium ferricyanide, or silver oxide led to nearly quantitative yields of benzoic acid (214). *p*-Bromostyrene glycol behaved similarly with potassium permanganate (662). With lead tetraacetate styrene glycol gave a 78 per cent yield of benzaldehyde (277). The same product was obtained with chromic acid (811). When nitric acid was used as the oxidizing agent, an 80–90 per cent yield of ω-hydroxyacetophenone resulted. The yield was 41 per cent with aqueous bromine and potassium carbonate (214). In this case some benzoic acid also was obtained.

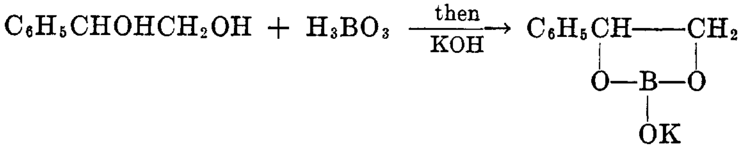
$$C_6H_5CHOHCH_2OH \xrightarrow{HNO_3} \underset{(80\text{–}90\text{ per cent})}{C_6H_5COCH_2OH}$$

Over platinum in the vapor phase styrene glycol was dehydrogenated to phenylglyoxal (757). The electrolytic oxidation gave a large number of products including benzaldehyde, benzoic acid, mandelic acid, phenylglyoxylic acid, formaldehyde, and ω-hydroxyacetophenone (753).

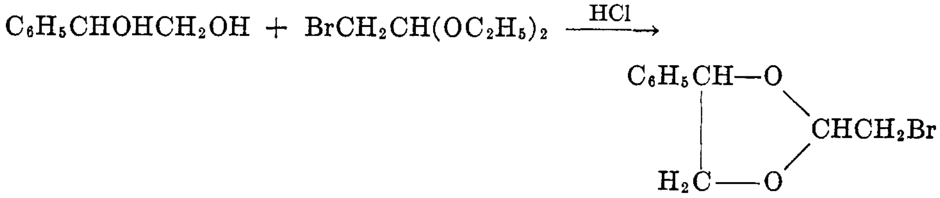
$$\mathrm{C_6H_5CHOHCH_2OH} \xrightarrow{\mathrm{Pt}} \mathrm{C_6H_5COCHO}$$

Styrene glycol reacted with formic acetic anhydride to give mostly the diformate, plus a little of the diacetate (61). With acetyl chloride or acetic anhydride the diacetate was obtained (810, 811). Similar results were obtained with benzoyl chloride and benzoic anhydride (161, 810, 811).

Styrene glycol reacted with phenyl isocyanate to give the diurethan (542). With allophanyl chloride both the β-mono- and the di-allophanate were obtained. Boric acid gave a cyclic borate which was isolated as its potassium salt (291).



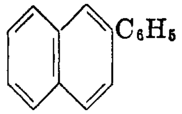
With bromoacetal in the presence of hydrogen chloride a cyclic acetal was produced (232).



When styrene glycol was heated with potassium hydroxide at 250°C., the products were benzoic acid and 38 per cent of α-phenethyl alcohol (543, 694). With 5 per cent of nickel at 250°C. acetophenone was obtained (281). When styrene glycol vapors together with steam were passed over silica gel impregnated with phosphoric acid, a 74 per cent yield of phenylacetaldehyde resulted (196a, 197). A little aldehyde was obtained in the liquid phase with 15–20 per cent sulfuric acid (120, 811). However, the principal product was β-phenylnaphthalene, which was obtained exclusively when 50 per cent sulfuric acid was used (812, 813) and in yields as high as 60–70 per cent (121). With 48 per cent hydrobromic acid the yield of β-phenylnaphthalene was 78 per cent (135).

$$\mathrm{C_6H_5CHOHCH_2OH} \xrightarrow[\mathrm{SiO_2}]{\overset{\mathrm{H_2O}}{\mathrm{HPO_3}}} \underset{\text{(74 per cent)}}{\mathrm{C_6H_5CH_2CHO}}$$

$$2C_6H_5CHOHCH_2OH \xrightarrow{\text{heat, }H^+}$$



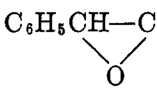
Styrene glycol β-monomethyl ether has been obtained by treating styrene iodohydrin with sodium methoxide or with sodium hydroxide in methanol (741) or by treating styrene chlorohydrin with potassium hydroxide in methanol (61 per cent yield) (189). The β-ethyl ether has been prepared similarly from styrene chlorohydrin and sodium ethoxide (159, 697) or potassium hydroxide in ethanol

$$C_6H_5CHOHCH_2Cl \xrightarrow[C_2H_5OH]{KOH} C_6H_5CHOHCH_2OC_2H_5$$

(65 per cent yield) (189) and from styrene bromohydrin and potassium hydroxide in ethanol (51 per cent yield). The β-*n*-butyl ether was obtained in 52 per cent yield from the chlorohydrin and potassium hydroxide in 1-butanol.

When styrene oxide was boiled with an alcohol containing a small amount of phosphoric or sulfuric acid, the corresponding monoether of styrene glycol was formed. By analogy with the above these compounds were formulated as β-ethers, although this structure has since been criticized on theoretical grounds and because hydrogen iodide adds to styrene oxide to give α-iodo-β-hydroxyethylbenzene (358). This method has been used to prepare the monoethyl (47 per cent yield) (189, 738), mono-*n*-butyl (738) (57 per cent yield) (189), mono-2-ethylhexyl (60 per cent yield) (738), and monolauryl ethers (738). In all cases a by-product, whose analysis indicated it to be a mixture of diphenyldioxanes, also was obtained.

Treatment of styrene oxide with sodium methoxide in methanol gave styrene glycol β-monomethyl ether (358a). The identity of this product was proven by oxidation with chromic acid to ω-methoxyacetophenone. In the case of 3,4-diacetoxystyrene the reverse addition occurred, so that the product obtained was 3,4-diacetoxystyrene glycol α-monomethyl ether.



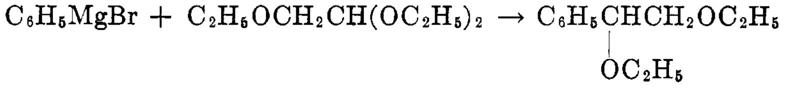
$$C_6H_5\underset{\diagdown\,O\,\diagup}{CH—CH_2} + CH_3OH \xrightarrow{CH_3ONa}$$

$$C_6H_5CHOHCH_2OCH_3 \xrightarrow{CrO_3} C_6H_5COCH_2OCH_3$$

Styrene oxide reacted with allyl alcohol in the presence of sodium to give an 81 per cent yield of a mixture comprising 90 per cent of styrene glycol α-monoallyl ether and 10 per cent of styrene glycol β-monoallyl ether (723a). When sulfuric acid was used as the catalyst, 83 per cent of styrene glycol β-monoallyl ether was obtained. With β-diethylaminoethyl γ-hydroxypropyl sulfide in the presence of potassium hydroxide, 15 per cent of the β-monoalkyl ether was obtained (260a).

By refluxing the appropriate monoether with acetic anhydride containing sodium acetate, acetates of the methyl (189), ethyl (189), *n*-butyl (189), and diethylaminoethyl (260a) ethers were obtained in yields of 82, 64, 79, and 78 per cent, respectively. Other esters were prepared by refluxing a toluene solution of the monoether and the acid together with a small amount of *p*-toluenesulfonic acid (189). The following compounds were prepared in this way in the yields given: caproate of the methyl ether, 55 per cent; butyrate of the ethyl ether, 61 per cent; laurate of the ethyl ether, 32 per cent; benzoate of the butyl ether, 51 per cent.

The diethyl ether of styrene glycol was prepared in 40 per cent yield by treating phenylmagnesium bromide with ethoxyacetal at 100–200°C. (695, 697).



$$C_6H_5MgBr + C_2H_5OCH_2CH(OC_2H_5)_2 \rightarrow C_6H_5\underset{\underset{OC_2H_5}{|}}{C}HCH_2OC_2H_5$$

By using *o*-tolylmagnesium iodide, *p*-tolylmagnesium bromide, 2,4-dimethylphenylmagnesium iodide, and *p*-chlorophenylmagnesium bromide in the same reaction, the diethyl ethers of the corresponding substituted styrene glycols were obtained (697). The product usually was contaminated with some of the β-ethoxystyrene. All of these diethyl ethers were converted to the corresponding phenylacetaldehydes by boiling with dilute sulfuric acid (695, 697).

Treatment of styrene bromohydrin with sodium methylmercaptide and sodium ethylmercaptide gave 70 per cent and 81 per cent, respectively, of the correpponding β-thioethers of styrene glycol (568). These compounds were prepared in 88 per cent and 58 per cent yields, respectively, by reducing the corresponding ketones with aluminum isopropoxide and isopropyl alcohol.

$$C_6H_5CHOHCH_2Br \xrightarrow{NaSCH_3}$$

$$C_6H_5CHOHCH_2SCH_3 \xleftarrow[CH_3CHOHCH_3]{(i\text{-}C_3H_7O)_3Al} C_6H_5COCH_2SCH_3$$

This latter method was used to prepare the following substituted styrene glycol β-thioethers in the yields shown: *p*-methyl methyl, 79 per cent; *p*-methyl ethyl, 77 per cent; *p*-methoxy ethyl, 57 per cent; 3,4-dimethoxy methyl, 94 per cent. Styrene bromohydrin also reacted with potassium *o*-aminothiophenoxide to give the corresponding thioether (148a). In the case of styrene chlorohydrin and sodium β-diethylaminoethylmercaptide, 78 per cent of the β-thioether was obtained (260a). Styrene oxide reacted with the corresponding potassium mercaptides to give the following styrene glycol β-thioethers in the yields specified: methyl, 22 per cent; β-diethylaminoethyl, 20 per cent; γ-diethylaminopropyl, 51 per cent; *p*-aminophenyl, 68 per cent. With potassium *o*-aminothiophenoxide, using either styrene oxide or α-iodo-β-phenethyl alcohol, the product was 2-phenyldihydrobenzothiazine (148a).

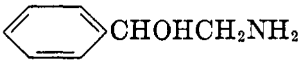
These compounds behave as typical thioethers, forming quaternary salts with methyl chloride, ethyl chloride, methyl iodide, ethyl iodide, and methyl sulfate. Picrates were prepared by treating the quaternary halides with sodium picrate. The β-ethyl thioether of styrene glycol was oxidized to the sulfoxide by means of hydrogen peroxide. The methyl (311), ethyl (311), phenyl (311), carboxymethyl (310, 311), and carbethoxymethyl dithioethers of styrene glycol have been prepared by treating styrene with the corresponding disulfide in the presence of iodine in anhydrous ether solution.

Styrene glycol β-monoacetate was prepared in 77 per cent yield by reducing ω-acetoxyacetophenone with hydrogen in the presence of a platinum oxide catalyst (671). A little α-phenethyl alcohol also was obtained. The epoxidation of styrene with peracetic acid in acetic acid solution gave styrene glycol or its acetate as the final product of the reaction (97). Styrene oxide was the intermediate.

As mentioned previously, styrene glycol diacetate and dibenzoate have been prepared from styrene dibromide. The dipropionate, di-*n*-butyrate, and dilaurate have been prepared by treating styrene oxide with an excess of the corresponding acid in boiling toluene containing *p*-toluenesulfonic acid (189).

D. Phenylethanolamines

Because of their importance as pressor amines (19), phenylethanolamines (α-hydroxy-β-aminoethylbenzenes) have been studied in great detail, particularly with respect to various methods of synthesis.



For phenylethanolamine itself the most widely investigated methods of preparation have involved reduction. In 1904 Kolshorn (402) first prepared the compound by reducing the monoxime of phenylglyoxal with sodium amalgam in aqueous alcohol containing hydrochloric acid. Some ω-aminoacetophenone was obtained as a by-product.

$$C_6H_5COCH{=}NOH \xrightarrow[\substack{H_2O\text{-}C_2H_5OH\\ HCl}]{\text{Na-Hg}}$$

$$C_6H_5CHOHCH_2NH_2 + C_6H_5COCH_2NH_2$$

The reduction of ω-aminoacetophenone to phenylethanolamine has been effected in 71 per cent yield in acetic acid solution, using hydrogen in the presence of a

$$C_6H_5COCH_2NH_2 + H_2 \xrightarrow{Pt} \underset{(71\text{ per cent})}{C_6H_5CHOHCH_2NH_2}$$

platinum catalyst (590). The hydrogenation of its hydrochloride (274, 505, 680) or hydrobromide (475) has been effected in alcohol (302) or aqueous solution (475, 505, 680) in the presence of such catalysts as platinum (274) (63 per cent yield), nickel (505), and palladium (475) (28 per cent yield, 680). Phenylethanolamine has been prepared by the reduction of its *p*-toluenesulfonamide with sodium and amyl alcohol (375). When the hydrochloride of *N*-benzyl-ω-aminoacetophenone was treated with hydrogen in the presence of a palladium on charcoal catalyst, an 88 per cent yield of phenylethanolamine hydrochloride was obtained (674).

$$\underset{\overset{\cdot}{HCl}}{C_6H_5COCH_2NHCH_2C_6H_5} \xrightarrow[Pd]{H_2} C_6H_5CHOHCH_2NH_2\cdot HCl + C_6H_5CH_3$$

Another common preparation of phenylethanolamine is by the reduction of mandelonitrile with sodium amalgam in aqueous alcohol using acetic (83, 494, 785) or hydrochloric (294) acid to keep the mixture neutral. The yields were low, 26 per cent (83) to 35 per cent (785). However, hydrogenation in alcohol solution using a platinum oxide catalyst in the presence of hydrochloric acid gave only β-phenethylamine (130). Recently a somewhat better yield of phenylethanolamine, 48 per cent, has been obtained by reducing mandelonitrile with lithium aluminum hydride (534a). Benzoyl cyanide has been hydrogenated in acetic acid solution in the presence of a palladium catalyst to give phenylethanolamine (381).

$$C_6H_5COCN + H_2 \xrightarrow{Pd} C_6H_5CHOHCH_2NH_2$$

TABLE 23

Hydrogenation of ω-aminoacetophenones

ω-AMINOACETOPHENONE	CATALYST	YIELD	REFERENCE
		per cent	
p-Methoxy (HCl)	Pd on C		(475)
p-Hydroxy	Pd on C	99	(146)
p-Hydroxy (HCl)	Pd on C		(475)
p-Hydroxy (HCl)	Pd		(381)
p-Hydroxy (HCl)	Pd	89	(674)
3,4-Dihydroxy (HCl)	Pd		(381)
3,4-Dimethoxy (HCl)	Pd		(381)
2-Methoxy-5-methyl	Pt		(117)
2-Hydroxy-5-methyl	Pt		(28)
2,5-Dimethoxy (HBr)	PtO_2		(48)

Treatment of styrene bromohydrin with concentrated aqueous ammonia gave phenylethanolamine (597) in 25 per cent yield (598). Styrene oxide reacted with aqueous ammonia at 90–125°C. to give 18 per cent of phenylethanolamine together with some 2,6-diphenylmorpholine (189).

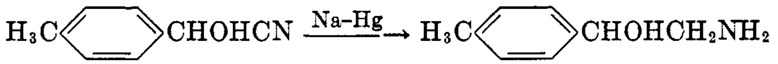
Phenylethanolamine has been prepared by treating β-hydroxycinnamamide with sodium hypobromite and sodium hydroxide according to the Hofmann procedure (2). Reduction of β-nitro-α-hydroxyethylbenzene with sodium amalgam and aqueous alcoholic acetic acid (625, 626) or with iron and sulfuric acid in alcohol (528) also gave phenylethanolamine.

$$C_6H_5CHOHCH_2CONH_2 \xrightarrow[NaOH]{NaOBr} C_6H_5CHOHCH_2NH_2$$

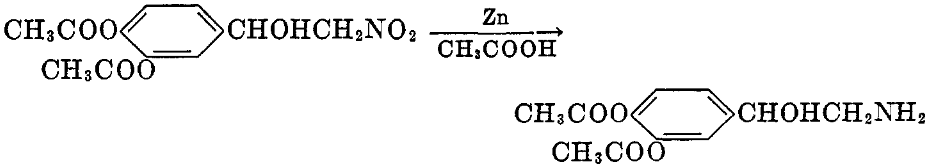
Since the compound is somewhat soluble in water it often has been isolated as a derivative. Those used include the carbonate (83, 475), hydrochloride (2, 597), neutral sulfate (18), picrate (402), and *N*-benzamide (2, 402, 598).

Nuclear-substituted phenylethanolamines have been prepared almost entirely by procedures involving reduction. The ω-aminoacetophenones listed in table 23 have been hydrogenated to phenylethanolamines. The hydrochloride of 3,4-dichloro-ω-aminoacetophenone has been reduced to the hydrochloride of the corresponding phenylethanolamine by means of aluminum amalgam (271). 3,4-Dihydroxyphenylethanolamine has been prepared from 3,4-dihydroxy-ω-aminoacetophenone by reduction with sodium amalgam and aqueous sodium hydroxide (493). Reduction of the hydrochloride of *N*,*N*-dibenzyl-ω-amino-*p*-hydroxyacetophenone with hydrogen in the presence of palladium gave an 86 per cent yield of *p*-hydroxyphenylethanolamine hydrochloride (674).

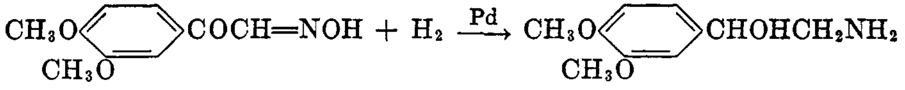
A number of substituted mandelonitriles have been reduced to the corresponding phenylethanolamines by means of sodium amalgam and acetic acid in alcohol solution. These include *p*-methyl- (351), *p*-methoxy- (351), 3,4-methylenedioxy- (83, 485), and 3,4-dihydroxy- (494). Hydrogenation in acetic acid solution in the presence of a palladium catalyst likewise has been used successfully for the 3,4-dimethoxy- (47 per cent yield), 3-methoxy-4-ethoxy- (45 per cent yield), and 3,4-diethoxy- (24 per cent yield) substituted analogs (383). In the first two cases 18 per cent and 16 per cent, respectively, of the corresponding β-phenethylamines also were isolated. Hydrogenation in alcohol solution with a platinum oxide catalyst in the presence of hydrochloric acid was successful only in the case of *o*-methoxy- (59 per cent yield), *o*-chloro- (41 per cent yield), and 2,3-dimethoxy- (23.5 per cent yield) mandelonitriles (130). In the case of *p*-chloro- (130), *p*-methoxy- (130), *p*-dimethylamino- (130), 3,4-dimethoxy- (130), 3-hydroxy- (130a), 4-hydroxy- (130a), 2-hydroxy-3-methoxy- (130a), 3-methoxy-4-hydroxy- (130a) and 3,4-dihydroxy- (130a) mandelonitriles, only the corresponding β-phenethylamine was obtained. The following benzoyl cyanides have been hydrogenated to phenylethanolamines in acetic acid solution in the presence of a palladium catalyst: *p*-methoxy-, 3,4-dimethoxy-, 3,4,5-trimethoxy-, and 3,4-methylenedioxy- (381).



α-Hydroxy-β-nitroethylbenzenes have been reduced to phenylethanolamines. Sodium amalgam and acetic acid in alcohol has been used for the following analogs: *p*-methoxy- (625, 626), 3,4-dimethoxy- (625), and 3,4-dihydroxy- (5 per cent yield) (625). When 3,4-diacetoxy-α-hydroxy-β-nitroethylbenzene was treated with zinc and acetic acid a 49 per cent hield of 3,4-diacetoxyphenylethanolamine was obtained (360).

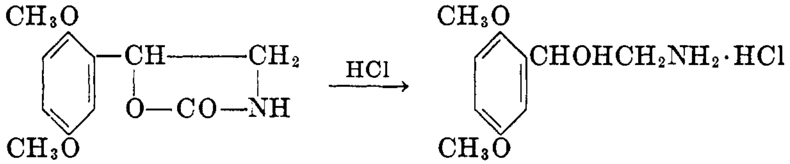


The following ω-nitroacetophenones have been hydrogenated to phenylethanolamines in alcohol solution in the presence of a platinum oxide catalyst: *o*-methoxy (80 per cent yield), 3,4-dimethoxy- (nearly quantitative yield), and 3,4-methylenedioxy- (80 per cent yield) (608). Hydrogenation of 3,4-dimethoxyphenylglyoxal monoxime in acetic acid solution in the presence of a palladium catalyst gave 65 per cent of the corresponding phenylethanolamine (382).



(65 per cent)

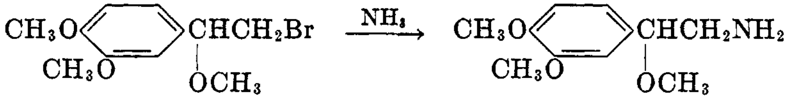
2,5-Dimethoxyphenylethanolamine hydrochloride has been prepared by hydrolyzing the corresponding cyclic urethan with cold concentrated hydrochloric acid (48).



As with phenylethanolamine itself, several derivatives have been utilized for the isolation of substituted phenylethanolamines. These include the neutral sulfate for *p*-methyl-, *p*-methoxy-, 3,4-dimethoxy-, and 3,4-methylenedioxy- (18); the carbonate for *p*-hydroxy- (475); and the oxalate for *o*-methoxy-, 3,4-dimethoxy-, and 3,4-methylenedioxy- (608).

These reductive procedures have been used for the preparation of a number of *O*-ethers of substituted phenylethanolamines. In table 24 are shown the reducing agents used and the products obtained.

Treatment of the ethyl ether of styrene chlorohydrin with alcoholic ammonia at 90–120°C. gave 9.5 per cent of the ethyl ether of phenylethanolamine plus 18 per cent of the corresponding secondary amine as well as some α-ethoxystyrene (315). α,3,4-Trimethoxyphenylethanolamine has been prepared by treating the corresponding bromo compound with ammonia (474).



Besides the salts used to isolate phenylethanolamine, the chloroplatinate and neutral oleate also have been prepared (274). Phenylethanolamine is reported to give a very faint blue to blue-green color with sulfomolybdic acid (595). While it was originally reported that phenylethanolamine gave no color when treated with 4 per cent hydrogen peroxide containing sodium chloride (675), a positive test was later observed (286).

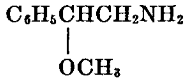
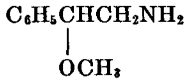
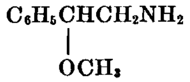
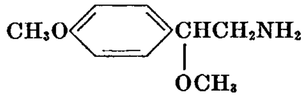
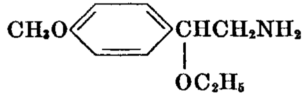
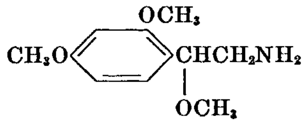
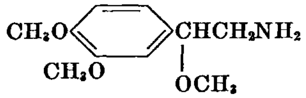
In the acylation of phenylethanolamine with acyl halides the first acyl group becomes affixed to the nitrogen atom. This has been shown to be true in the case of the acetyl (785), chloroacetyl (351), benzoyl (83, 381, 475, 597, 674, 726, 785),

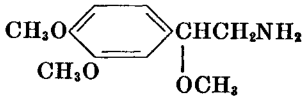
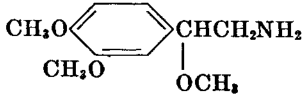
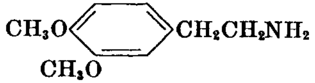
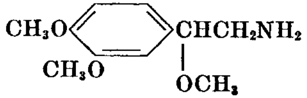
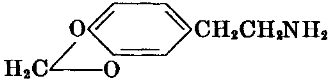
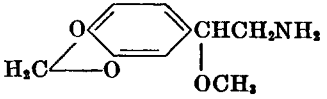
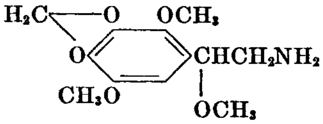
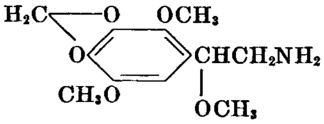
$$C_6H_5CHOHCH_2NH_2 + CH_3COCl \rightarrow C_6H_5CHOHCH_2NHCOCH_3$$

and carbethoxy (from ethyl chloroformate) (294, 475) groups. Many *N*-acyl derivatives also have been prepared by the reduction of the corresponding *N*-acyl-ω-aminoacetophenones, usually by means of sodium amalgam and aqueous alcohol held neutral with acetic acid. These include the *N*-formyl (563), *N*-acetyl (785)

TABLE 24

Reduction of α-hydroxy-β-nitroethylbenzenes

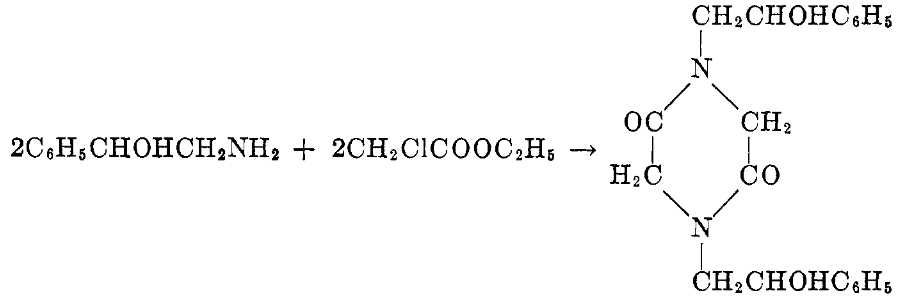
SUBSTITUTED α-HYDROXY-β-NITROETHYLBENZENE	ETHER USED	REDUCING AGENT	PRODUCT	YIELD	REFERENCE
				per cent	
	Methyl	Na–Hg, C_2H_5OH, CH_3COOH	 $C_6H_5\underset{\displaystyle OCH_3}{\underset{|}{CH}}CH_2NH_2$	80	(626)
	Methyl	Electrolysis, Ni cathode	 $C_6H_5\underset{\displaystyle OCH_3}{\underset{|}{CH}}CH_2NH_2$		(626)
	Methyl	Zn, HCOOH	 $C_6H_5\underset{\displaystyle OCH_3}{\underset{|}{CH}}CH_2NH_2$		(476)
p-Methoxy....................	Methyl	Na–Hg, C_2H_5OH, CH_3COOH			(625, 626)
p-Methoxy....................	Ethyl	Na–Hg, C_2H_5OH, CH_3COOH		80	(625)
2,4-Dimethoxy................	Methyl	H_2 + Pt			(471)
3,4-Dimethoxy................	Methyl	Na–Hg, C_2H_5OH, CH_3COOH			(625, 626, 628)

3,4-Dimethoxy................	Methyl	Electrolysis, Ni cathode			(626)
3,4-Dimethoxy................	Methyl	H_2 + Pd, CH_3COOH		57	(382)
3,4-Dimethoxy................	Methyl	H_2 + Pd, CH_3COOH, H_2SO_4		50	(382)
3,4-Dimethoxy................	Methyl	Zn, HCOOH			(476)
3,4-Methylenedioxy...........	Methyl	H_2 + Pd, CH_3COOH, H_2SO_4		50	(382)
3,4-Methylenedioxy...........	Methyl	Zn, HCOOH			(476)
2,5-Dimethoxy-3,4-methylenedioxy.......................	Methyl	H_2 + Pt			(471)
2,5-Dimethoxy-3,4-methylenedioxy.......................	Methyl	Na-Hg, 80% CH_3COOH			(471)

(40 per cent yield) (563), *N*-benzoyl (785) (58 per cent yield) (563), *N*-phenacetyl (621) (44 per cent yield) (563), and *N*-carbethoxy (20 per cent yield) (472). The reduction of *N*-carbethoxy-ω-aminoacetophenone also has been effected in 75 per cent yield in alcohol solution by means of hydrogen and a palladium catalyst. *N*-Dichloroacetyl- and *N*-cyanoacetyl-phenylethanolamines have been

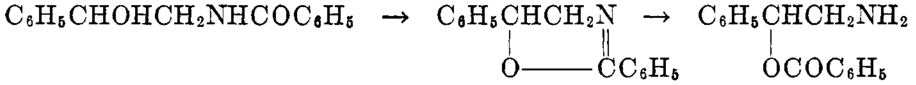
$$C_6H_5COCH_2NHCOOC_2H_5 \xrightarrow[Pd]{H_2} C_6H_5CHOHCH_2NHCOOC_2H_5$$

prepared by treating phenylethanolamine with the ethyl ester of the corresponding acid (475). Phenylethanolamine reacted with ethyl chloroacetate to give a diketopiperazine derivative.



N-Benzoylphenylethanolamine has been acetylated by treatment with acetic anhydride containing sodium acetate (381, 475). When benzoyl chloride and pyridine were used for the benzoylation of phenylethanolamine, instead of benzoyl chloride and sodium hydroxide, the *O*,*N*-dibenzoyl derivative was obtained (83).

Treatment of *N*-benzoylphenylethanolamine with concentrated sulfuric acid, followed by dilution with water and neutralization with potassium carbonate, gave *O*-benzoylphenylethanolamine sulfate (726). By conducting the neutralization in the cold, the intermediate oxazoline was isolated. *O*-Benzoylphenylethanolamine sulfate reverted to *N*-benzoylphenylethanolamine on treatment with sodium or ammonium hydroxide.



$$C_6H_5CHOHCH_2NHCOC_6H_5 \rightarrow \underset{O\text{———}CC_6H_5}{C_6H_5CHCH_2N} \rightarrow \underset{OCOC_6H_5}{C_6H_5CHCH_2NH_2}$$

O-Benzoylphenylethanolamine was obtained along with β-phenethylamine and di(β-phenethyl)amine by the hydrogenation of mandelonitrile benzoate in ethyl acetate solution in the presence of a nickel catalyst (639). Treatment with boiling alcoholic hydrochloric acid gave phenylethanolamine. When *N*-phenacetylphenylethanolamine was treated with concentrated sulfuric acid, no oxazole was obtained and phenylacetaldehyde was isolated from the reaction mixture (621).

Treatment of *N*-benzoylphenylethanolamine with ethylmagnesium bromide at 175°C. gave *N*-benzoylstyrylamine (415).

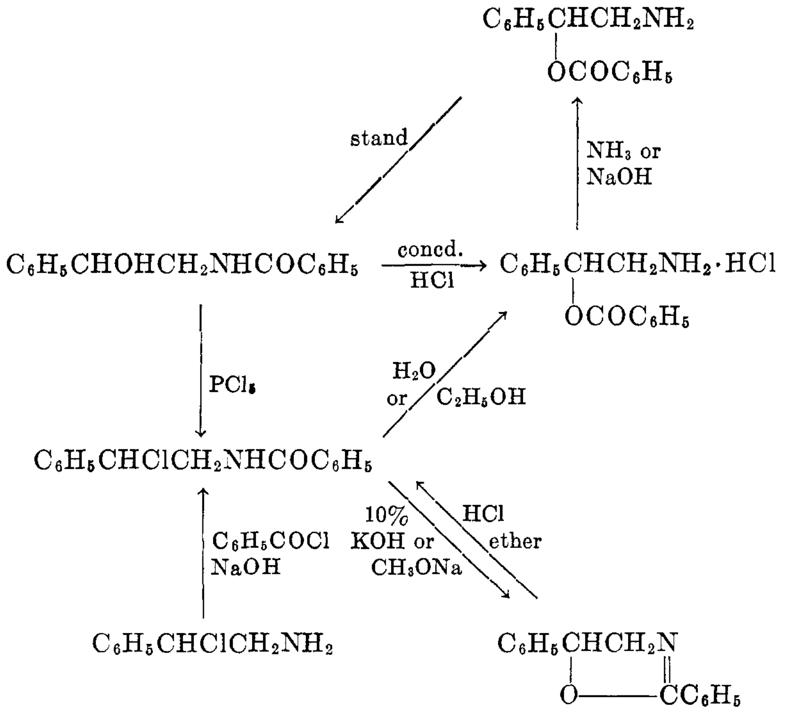
$$C_6H_5CHOHCH_2NHCOC_6H_5 + C_2H_5MgBr \xrightarrow[2\text{ hr.}]{175°\text{C.}} C_6H_5CH{=}CHNHCOC_6H_5$$

N-Chloroacetylphenylethanolamine added hexamethylenetetramine (351). Neither phenylethanolamine nor *N*-carbethoxyphenylethanolamine reacted with acetobromoglucose in the presence of silver carbonate (680).

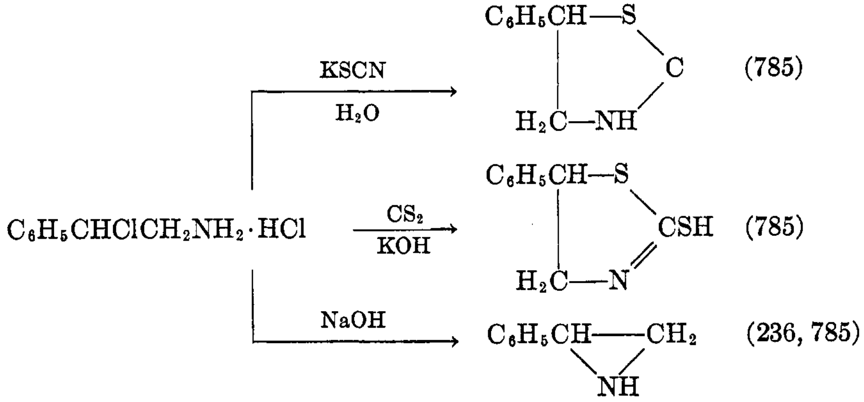
Treatment of *N*-acetylphenylethanolamine with fuming hydrochloric acid at 100°C. or with phosphorus pentachloride gave *N*-acetyl-β-chloro-β-phenethylamine (785).

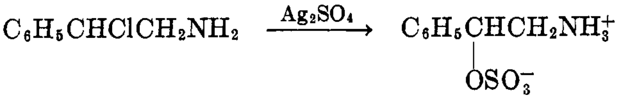
$$C_6H_5CHOHCH_2NHCOCH_3 \xrightarrow[\text{or } PCl_5]{\text{fuming HCl}} C_6H_5CHClCH_2NHCOCH_3$$

With phenylethanolamine itself the same replacement of the hydroxyl group was effected with hot fuming hydrochloric acid or with thionyl chloride. *N*-Benzoyl-β-chloro-β-phenethylamine was prepared by benzoylating β-chloro-β-phenethylamine by the Schotten–Baumann method (785) or by treating diphenyloxazoline with hydrogen chloride in ether (726). The latter transformation was reversed by 10 per cent potassium hydroxide (726) or sodium methoxide (785). *N*-Benzoyl-β-chloro-β-phenethylamine was converted to the hydrochloride of *O*-benzoylphenylethanolamine by treatment with water (726) or hot alcohol (785). This hydrochloride also was obtained by treating *N*-benzoylphenylethanolamine with hot concentrated hydrochloric acid (726). Treatment of *O*-benzoylphenylethanolamine hydrochloride with ammonia or sodium hydroxide gave the free amine, which rearranged on standing to *N*-benzoylphenylethanolamine (785).



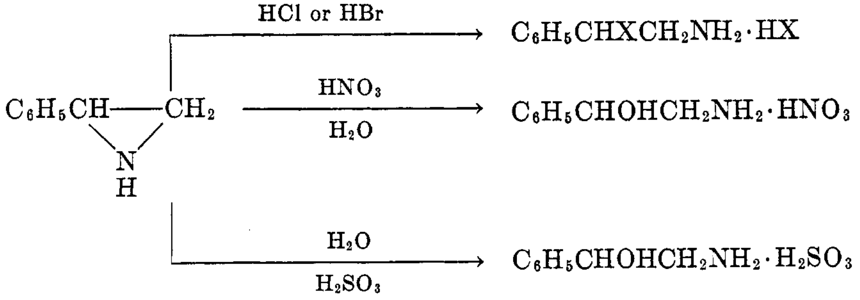
β-Chloro-β-phenethylamine hydrochloride underwent several interesting reactions which are shown by the following equations:





$$C_6H_5CHClCH_2NH_2 \xrightarrow{Ag_2SO_4} C_6H_5\underset{\displaystyle OSO_3^-}{CH}CH_2NH_3^+$$

A few simple reactions of phenylethylenimine were examined and are also summarized in equation form (785).

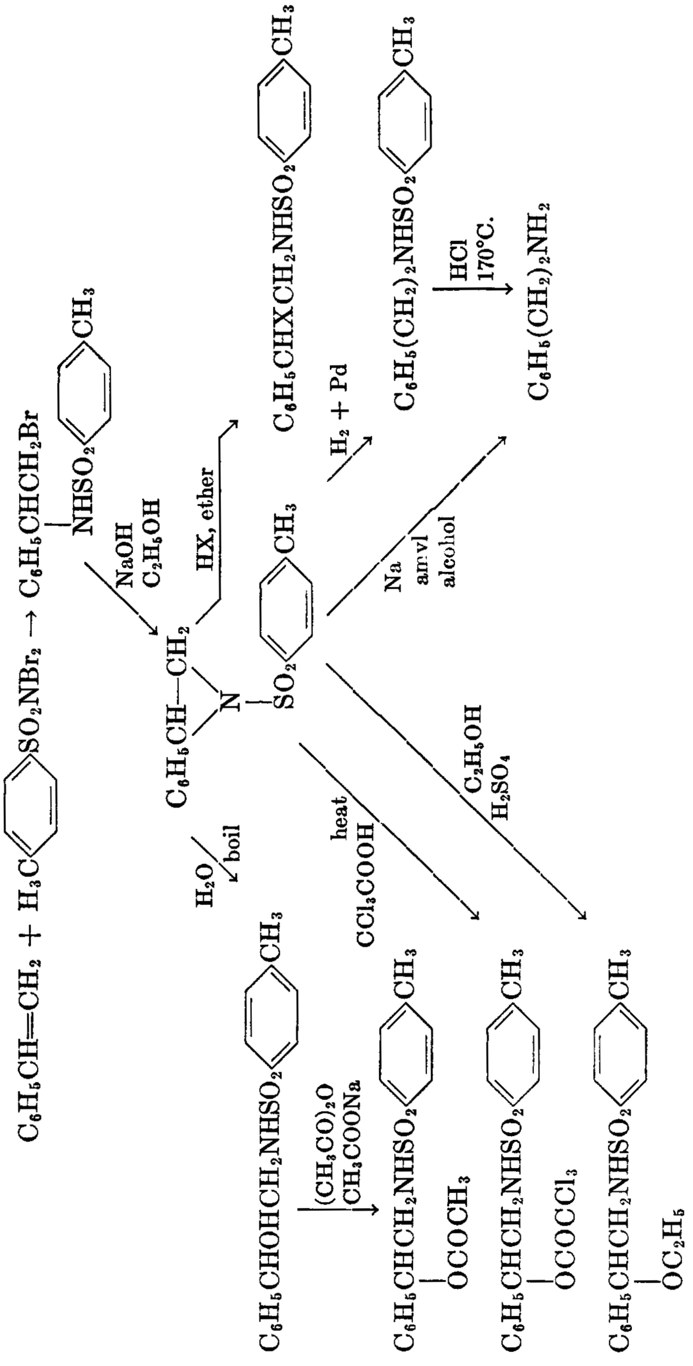


The p-toluenesulfonamide of phenylethylenimine, prepared as shown on page 267, underwent a wide variety of reactions. For convenience these are summarized in equation form (375).

Phenylethanolamine has shown a number of miscellaneous reactions similar to those observed with β-chloro-β-phenethylamine. For convenience they are summarized in equation form (see page 268).

Salts of phenylethanolamine have been prepared with d-camphor-10-sulfonic acid and with d-methylenecamphor, and the d-tartrate has been resolved (597). The d-phenylethanolamine thus formed reacted with methyl iodide and sodium methoxide to give 80 per cent of the d-quaternary iodide (597).

$$C_6H_5CHOHCH_2NH_2 + CH_3I + CH_3ONa \xrightarrow{CH_3OH} C_6H_5CHOHCH_2N(CH_3)_3I$$


$C_6H_5CH{=}CH_2$ + H_3C
SO_2NBr_2 → $C_6H_5CHCH_2Br$
$NHSO_2$
CH_3
NaOH
C_2H_5OH
HX, ether
C_6H_5CH—CH_2
N
SO_2
CH_3
$C_6H_5CHXCH_2NHSO_2$
CH_3
H_2 + Pd
$C_6H_5(CH_2)_2NHSO_2$
CH_3
HCl
170°C.
$C_6H_5(CH_2)_2NH_2$
Na
amyl
alcohol
C_2H_5OH
H_2SO_4
heat
CCl_3COOH
H_2O
boil
$C_6H_5CHOHCH_2NHSO_2$
CH_3
$(CH_3CO)_2O$
CH_3COONa
$C_6H_5CHCH_2NHSO_2$
$OCOCH_3$
CH_3
$C_6H_5CHCH_2NHSO_2$
$OCOCCl_3$
CH_3
$C_6H_5CHCH_2NHSO_2$
OC_2H_5
CH_3

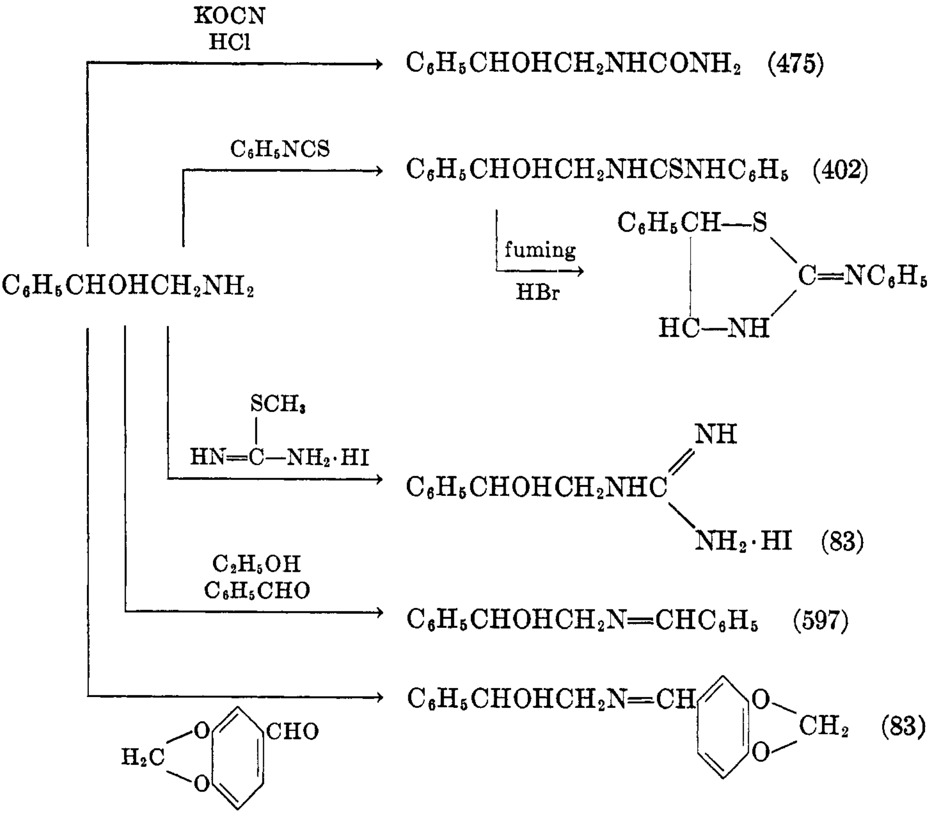


TABLE 25

N-Acylphenylethanolamines

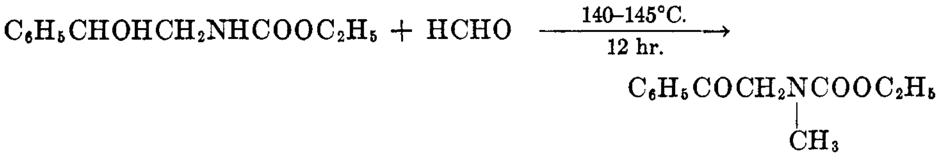
PHENYLETHANOLAMINE	*N*-SUBSTITUTED DERIVATIVES	REFERENCES
p-Methyl	Chloroacetyl	(351)
p-Methoxy	Benzoyl Carbethoxy	(381, 475) (475)
3,4-Dimethoxy	Homoveratroyl	(381, 562*)
3,4-Methylenedioxy	Formyl Benzoyl *p*-Nitrobenzoyl Veratroyl	(485) (381, 485) (485) (485)
p-Benzoxy	Benzoyl	(475, 674, 758)

* By reduction of the acylaminoacetophenone with sodium amalgam and acetic acid in alcohol.

A number of nuclear-substituted phenylethanolamines have been acylated by standard methods to give *N*-substituted derivatives. These compounds are listed in table 25, together with one prepared by another method.

Certain of the above listed *N*-acyl compounds have been further acylated to give *N*-acyl-*O*-acyl derivatives. These are listed in table 26.

N-Carbethoxyphenylethanolamine reacted with formaldehyde at 140–145°C. to give 55 per cent of ω-(*N*-methyl-*N*-carbethoxyamino)acetophenone (294).



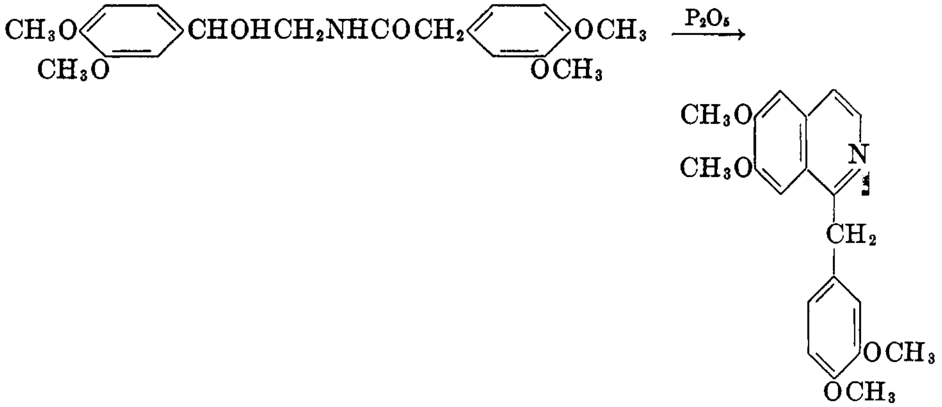
$$C_6H_5CHOHCH_2NHCOOC_2H_5 + HCHO \xrightarrow[12\ hr.]{140\text{–}145°C.} C_6H_5COCH_2N(CH_3)COOC_2H_5$$

TABLE 26

N-Acyl-O-acylphenylethanolamines

PHENYLETHANOLAMINE	*N*-GROUP	*O*-GROUP	REFERENCES
p-Methoxy	Benzoyl	Acetyl	(381, 475)
3,4-Dimethoxy	Benzoyl	Benzoyl	(381)
3,4,5-Trimethoxy	Benzoyl	Benzoyl	(381)
3,4-Methylenedioxy	Benzoyl	Acetyl	(381)
	p-Nitrobenzoyl	*p*-Nitrobenzoyl	(485)
p-Benzoxy	Benzoyl	Acetyl	(475)
	Benzoyl	Benzoyl	(758)

Treatment of *N*-homoveratroyl-3,4-dimethoxyphenylethanolamine for 5 min. with phosphorus pentoxide in boiling xylene gave a 30 per cent yield of papaverine (562).



This type of ring closure to give compounds related to papaverine has been applied to a number of *O*-methyl ethers of *N*-acylated phenylethanolamines.

The ring closure has been effected with both phosphorus pentoxide in toluene and phosphorus oxychloride in xylene. These preparations are summarized in table 27.

Table 28 lists the *N*-acyl derivatives of *O*-methyl ethers of phenylethanolamines which have been prepared but not cyclized.

TABLE 27

Papaverine derivatives

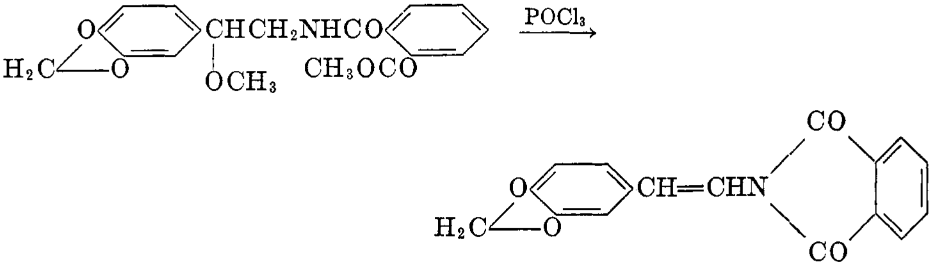
PHENYLETHANOLAMINE *O*-METHYL ETHER	*N*-ACYL GROUP	RING-CLOSING AGENT	REFERENCE
3,4-Dimethoxy	Benzoyl	P_2O_5	(628)
	Benzoyl	$POCl_3$	(476)
	Phenacetyl	$POCl_3$	(476)
	Homopiperonyl	$POCl_3$	(476)
	Homoveratroyl	$POCl_3$	(476)
	Homoveratroyl	P_2O_5	(628)
3,4-Methylenedioxy	Benzoyl	$POCl_3$	(476)
	Phenacetyl	$POCl_3$	(476)
	Homopiperonyl	$POCl_3$	(476)
	Homoveratroyl	$POCl_3$	(476)
2,5-Dimethoxy-3,4-methylenedioxy	Benzoyl	$POCl_3$	(471)
	Homopiperonyl	$POCl_3$	(471)
	Homoveratroyl	$POCl_3$	(471)

TABLE 28

Acylated phenylethanolamine ethers

PHENYLETHANOLAMINE *O*-METHYL ETHER	*N*-ACYL GROUP	REFERENCE
2,4-Dimethoxy	Phenacetyl	(471)
	Homopiperonyl	(471)
	Homoveratroyl	(471)
2,5-Dimethoxy-3,4-methylenedioxy	Phenacetyl	(471)

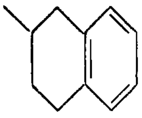
Treatment of *N*-(*o*-carbomethoxybenzoyl)-3,4-methylenedioxyphenylethanolamine-*O*-methyl ether with phosphorus oxychloride in boiling xylene gave the styrylimide (477).



The same results were obtained by treating the *N*-(*o*-carboxybenzoyl) derivative of phenylethanolamine-*O*-methyl ether with phosphorus pentoxide. With phosphorus oxychloride the imide was obtained without the loss of methanol.

TABLE 29

Reductions of ω-(N-alkyl)aminoacetophenones

ω-(*N*-ALKYL)-AMINOACETOPHENONE	RING SUBSTITUENTS	REDUCING AGENT	YIELD	REFERENCE
			per cent	
Methyl		H_2 + Ni		(505)
		H_2 + PtO_2	90	(3)
		H_2 + Pd		(506)
	m-Hydroxy	H_2 + Pd		(443)
	p-Hydroxy	H_2 + Pd	90	(443)
	p-Hydroxy	H_2 + Pd	89	(146)
	p-Hydroxy	H_2 + Pd		(381)
	3,4-Dihydroxy	H_2 + Pd		(381)
	3,4-Dihydroxy	Al-Hg + aqueous H_2SO_4		(493)
	2-Hydroxy-3-methyl	H_2 + Pt		(28)
	3-Amino-4-hydroxy	H_2 + PtO_2		(657)
	3-Acetamino-4-hydroxy	H_2 + PtO_2		(657)
Ethyl	4-Hydroxy	H_2 + Pd	71	(146)
	3,4-Dihydroxy	Electrolysis		(493)
n-Propyl	*p*-Hydroxy	H_2 + Pd	68	(146)
Isopropyl	*p*-Hydroxy	H_2 + Pd	86	(146)
n-Butyl		H_2 + PtO_2	90	(3)
	p-Hydroxy	H_2 + Pd	83	(146)
Isobutyl	*p*-Hydroxy	H_2 + Pd	87	(146)
sec-Butyl	*p*-Hydroxy	H_2 + Pd	91	(146)
tert-Butyl	*p*-Hydroxy	H_2 + Pd	78	(146)
β-Phenethyl		H_2 + Pd		(20)
		H_2 + Pd	90	(20)

Besides the above amide chemistry *p*-hydroxyphenylethanolamine has been reported to give a blue color with sulfomolybdic acid (595). 3,4-Methylenedioxyphenylethanolamine gave a quaternary iodide when treated with methyl iodide (83).

Both *N*-*n*-butyl- and *N*-isobutyl-phenylethanolamines have been prepared by alkylating phenylethanolamine with *n*-butyl and isobutyl iodides, respectively (361). *N*-Methyl-3,4-methylenedioxyphenylethanolamine has been prepared by alkylating *N*-benzoyl-3,4-methylenedioxyphenylethanolamine with methyl iodide and then removing the benzoyl group by hydrolysis (83). Similar alkylation of piperonalphenylethanolamine followed by hydrolysis gave *N*-methylphenylethanolamine.

In general the other preparations of *N*-alkylphenylethanolamines parallel those used for the unsubstituted compounds. Probably the most widely used is the reduction of the corresponding ω-(*N*-alkylamino)acetophenone. For convenience the numerous compounds prepared in this way are summarized in table 29.

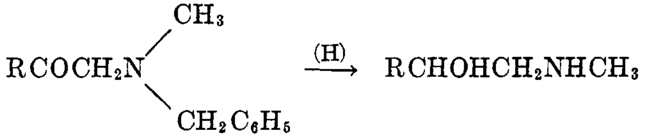
In addition, 3-acetamino-4-hydroxy-ω-(*N*-methyl-*N*-acetylamino)acetophenone has been reduced to the corresponding phenylethanolamine by means of hydrogen and a platinum oxide catalyst (657).

TABLE 30

Reductive debenzylations

SUBSTITUTED ω-(*N*-METHYL-*N*-BENZYL)-AMINOACETOPHENONE	REDUCING AGENT	YIELD	REFERENCE
		per cent	
	$H_2 + Ni$		(335)
p-Hydroxy	$H_2 + Ni$		(335)
2,5-Dimethoxy	$H_2 + PtO_2$		(48)
2-Methoxy-5-methyl	$H_2 + Pt$		(28)
3-Chloro-4-hydroxy	$H_2 + Pt$	95	(229)
3-Chloro-4-acetoxy	$H_2 + Pt$	97	(229)
3-Fluoro-4-hydroxy	$H_2 + Pt$	85	(229)
3-Chloro-4-hydroxy (*N*-ethyl)	$H_2 + Pt$	90	(229)

Certain ω-(*N*-methyl-*N*-benzylamino)acetophenones have been simultaneously reduced and debenzylated to give the corresponding *N*-methylphenylethanolamines. These preparations are summarized in table 30.



$$RCOCH_2N\begin{matrix} CH_3 \\ CH_2C_6H_5 \end{matrix} \xrightarrow{(H)} RCHOHCH_2NHCH_3$$

A number of *N*-alkylphenylethanolamines have been prepared by the reductive alkylation of the corresponding β-nitro-α-phenethyl alcohol by means of an aldehyde and zinc and acetic acid as the reducing agent. These preparations are summarized in table 31.

$$RCHOHCH_2NO_2 + R'CHO \xrightarrow{(H)} RCHOHCH_2NHCH_2R'$$

Another very common method for preparing *N*-alkylphenylethanolamines is to treat a styrene halohydrin with the appropriate primary amine. These preparations are summarized in table 32.

$$RCHOHCH_2X + R'NH_2 \rightarrow RCHOHCH_2NHR'$$

When the methyl ether of styrene bromohydrin was treated with methylamine, a 33 per cent yield of the methyl ether of phenylethanolamine was obtained (465). This same reaction has been utilized successfully with the methyl ethers of 3,4-dimethoxystyrene bromohydrin and 3,4-methylenedioxystyrene bromohydrin.

TABLE 31

Reductive alkylations

β-NITRO-α-PHENETHYL ALCOHOL	ALDEHYDE	YIELD	REFERENCE
		per cent	
	Formaldehyde		(528)
3,4-Diacetoxy...........	Formaldehyde		(527)
	Formaldehyde		(360)
	n-Heptaldehyde	30	(360)
	Benzaldehyde	17	(360)
	Piperonal	32	(360)
	3,4-Diacetoxybenzaldehyde	51	(360)
	3-Methoxy-4-acetoxybenzaldehyde	22	(360)
	Furfural	28	(360)

TABLE 32

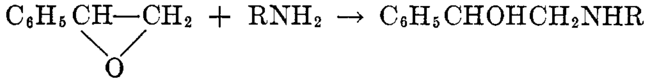
N-Alkylphenylethanolamines from styrene halohydrins

SUBSTITUTED STYRENE	HALOGEN IN HALOHYDRIN	AMINE	REFERENCE
	I	Aniline	(361)
3,4-Dimethoxy..............................	Br	Methylamine	(54)
3,4-Dimethoxy*.............................	Br	Methylamine	(474)
3,4-Methylenedioxy.........................	Cl	Methylamine	(549)
3,4-Methylenedioxy.........................	Br	Methylamine	(54)
3,4-Methylenedioxy†........................	Br	Methylamine	(474)
3,4-Dihydroxy..............................	Cl	Methylamine	(100, 472)
3,4-Dihydroxy..............................	Br	Methylamine	(100, 497)
Bromo-3,4-dihydroxy........................	Br	Methylamine	(100)

* In this case the α-methylamino-β-phenethylalcohol also was isolated in the ratio of one to four of the β-methylamino-α-phenethylalcohol.

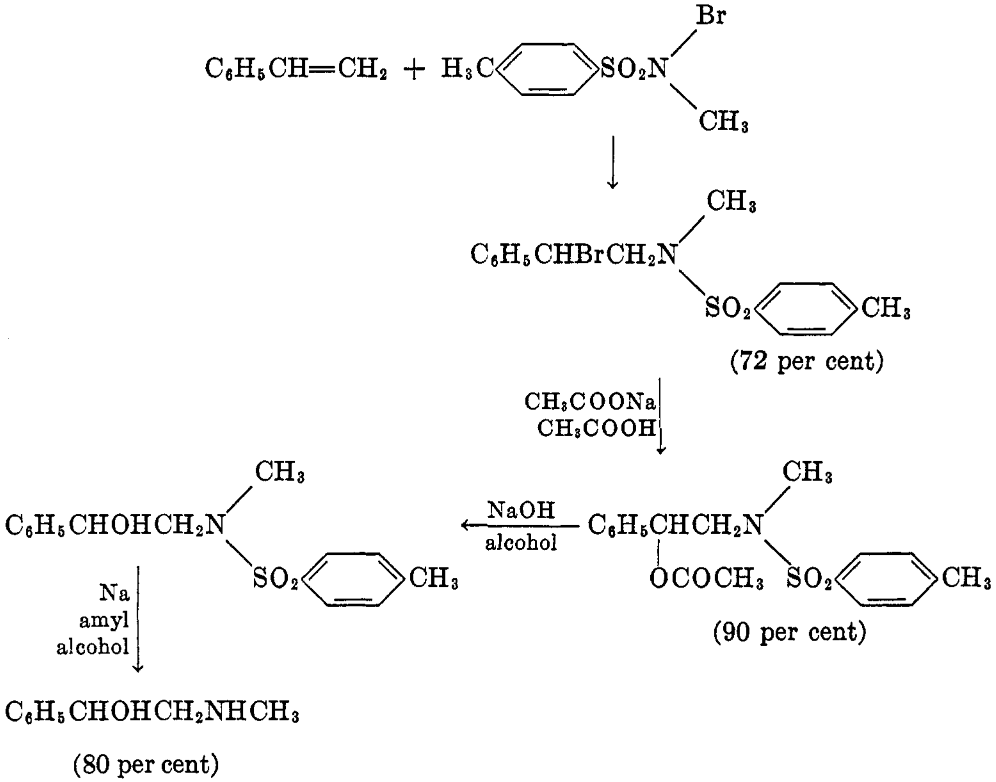
† Here the two isomers occurred in equal quantities.

A closely related method is the reaction of styrene oxide with a primary amine to give an *N*-alkylphenylethanolamine (189). Phenylethanolamines prepared successfully in this way include *N*-ethyl- (56 per cent yield), *N*-*n*-butyl- (64 per cent yield), *N*-*n*-dodecyl- (70 per cent yield), and *N*-β-hydroxyethyl- (63 per cent yield). In the case of the *n*-butyl compound some 2,6-diphenyl-4-*n*-butylmorpholine was isolated as a by-product.



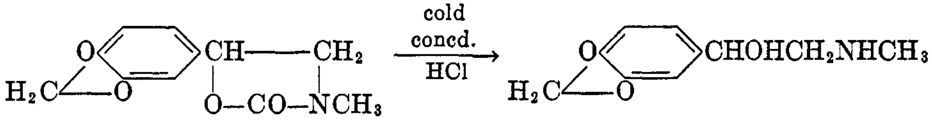
$$C_6H_5\underbrace{CH{-}CH_2}_{O} + RNH_2 \rightarrow C_6H_5CHOHCH_2NHR$$

An interesting synthesis of *N*-methylphenylethanolamine is outlined below (375):

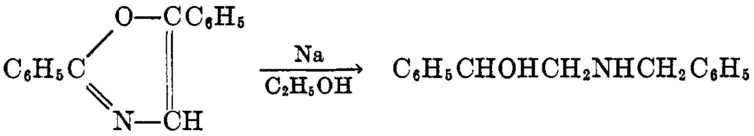


When this method was applied to *N*-methyl-*p*-fluorophenylethanolamine, the overall yield from *p*-fluorostyrene was 56 per cent (229).

N-Methyl-3,4-methylenedioxyphenylethanolamine has been prepared by the hydrolysis reaction shown below (664).

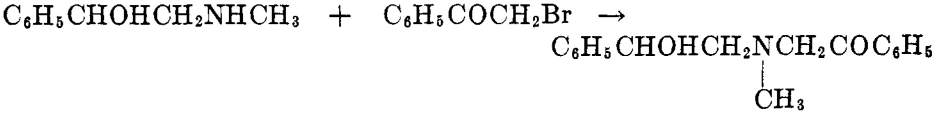


N-Benzylphenylethanolamine has been prepared by the reduction of diphenyloxazole (219).



Recently a number of *N*-alkylphenylethanolamines have been prepared by the reductive amination of the corresponding phenylglyoxals (225a).

N-Methylphenylethanolamine has been alkylated with phenacyl bromide and with α-bromopropiophenone (770).

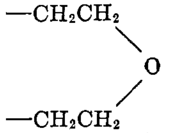
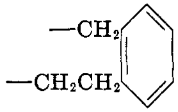


$$C_6H_5CHOHCH_2NHCH_3 + C_6H_5COCH_2Br \rightarrow C_6H_5CHOHCH_2\underset{\displaystyle CH_3}{\underset{|}{N}}CH_2COC_6H_5$$

Other N,N-dialkylphenylethanolamines generally have been prepared by the same methods previously described for the less highly substituted compounds.

TABLE 33

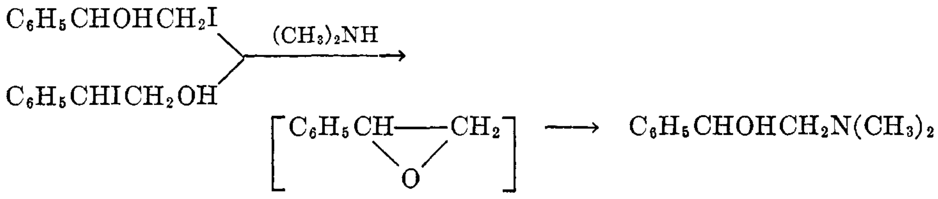
N,N-Dialkylphenylethanolamines from ω-aminoacetophenones

NUCLEAR-SUBSTITUTED ω-AMINOACETOPHENONE	SUBSTITUENTS ON NITROGEN ATOM	REDUCING AGENT	YIELD	REFERENCE
			per cent	
	Dimethyl			(742)
	Diethyl	$H_2 + PtO_2$	73–75	(484)
	Di-*n*-butyl	$(i\text{-}C_3H_7O)_3Al$	69	(272)
		$H_2 + Pd$	87.5	(630)
		$H_2 + Pd$	91	(20)
p-Bromo	Diethyl	$(i\text{-}C_3H_7O)_3Al$	70	(165)
	Di-*n*-propyl	$(i\text{-}C_3H_7O)_3Al$	70	(165)
	Di-*n*-butyl	$(i\text{-}C_3H_7O)_3Al$	93	(165)
	Pentamethylene	$(i\text{-}C_3H_7O)_3Al$	81	(165)
p-Hydroxy	Dimethyl	$H_2 + Pd$	75	(146)
3,4-Dihydroxy	Dimethyl	Electrolysis		(493)
2,5-Dimethoxy	Dimethyl	$H_2 + PtO_2$		(48)

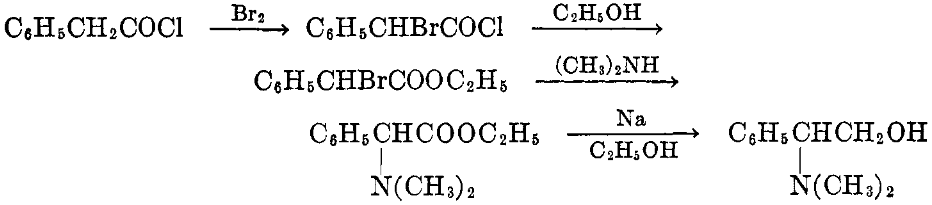
In table 33 are listed those N,N-dialkylphenylethanolamines which have been prepared by the reduction of the corresponding ω-(N,N-dialkylamino)acetophenone.

A number of N,N-dialkylphenylethanolamines have been prepared from the corresponding styrene halohydrin and a secondary amine. These preparations are summarized in table 34.

It is of interest that N,N-dimethylphenylethanolamine was obtained from β-iodo-β-phenethyl alcohol as well as from styrene iodohydrin (744). This suggests a common intermediate, probably styrene oxide.

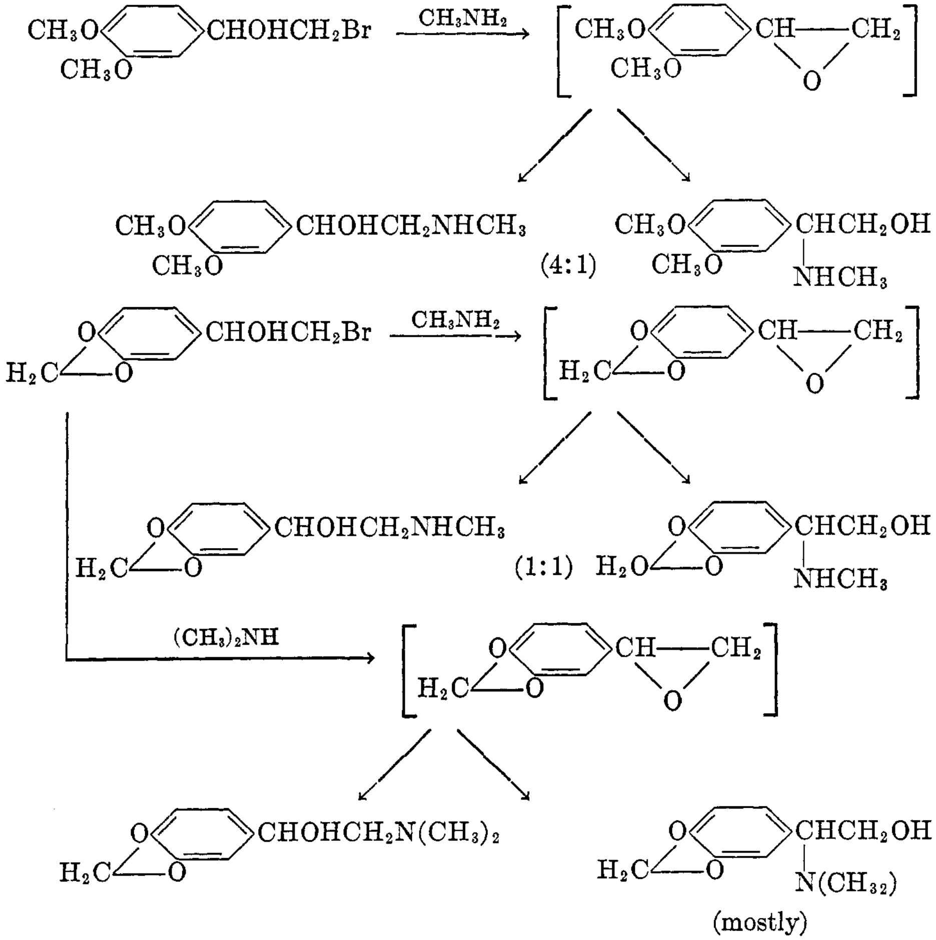


The isomeric β-dimethylamino-β-phenethyl alcohol was synthesized by the following method and its derivatives were shown to have different properties from those of *N*,*N*-dimethylphenylethanolamine (744).

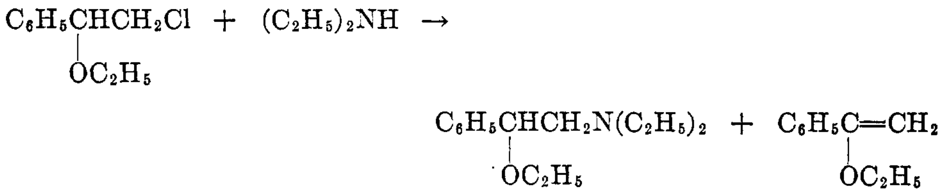


$$C_6H_5CH_2COCl \xrightarrow{Br_2} C_6H_5CHBrCOCl \xrightarrow{C_2H_5OH} C_6H_5CHBrCOOC_2H_5 \xrightarrow{(CH_3)_2NH} \underset{\displaystyle N(CH_3)_2}{\underset{|}{C_6H_5CHCOOC_2H_5}} \xrightarrow[C_2H_5OH]{Na} \underset{\displaystyle N(CH_3)_2}{\underset{|}{C_6H_5CHCH_2OH}}$$

Additional evidence for an oxide intermediate is found in the cases of 3,4-dimethoxy- and 3,4-methylenedioxy-styrene bromohydrins, where two different products are obtained on treatment with amines (474).



The ethyl ether of styrene chlorohydrin reacted with diethylamine at 90–128°C. to give 69 per cent of *O*,*N*,*N*-triethylphenylethanolamine together with a little α-ethoxystyrene (315). The same reaction occurred with dimethylamine (744).



$$C_6H_5\underset{OC_2H_5}{\underset{|}{C}}HCH_2Cl + (C_2H_5)_2NH \rightarrow C_6H_5\underset{OC_2H_5}{\underset{|}{C}}HCH_2N(C_2H_5)_2 + C_6H_5\underset{OC_2H_5}{\underset{|}{C}}{=}CH_2$$

The methyl ethers of both 3,4-dimethoxy- and 3,4-methylenedioxy-styrene bromohydrins reacted with dimethylamine to give the corresponding *N*,*N*-dimethylphenylethanolamines, the former in quantitative yield (474).

TABLE 34

N,N-Dialkylphenylethanolamines from styrene halohydrins

SUBSTITUTED STYRENE HALOHYDRIN	SECONDARY AMINE	HALOGEN IN HALOHYDRIN	YIELD	REFERENCE
			per cent	
	Diethyl	Cl	66	(189)
	Diamyl	Cl	63	(189)
	Diethanol	Cl	63	(189)
	Dimethyl	I		(742, 744)
3,4-Methylenedioxy	Dimethyl	Br	90	(577)
	Dimethyl	Br		(474)

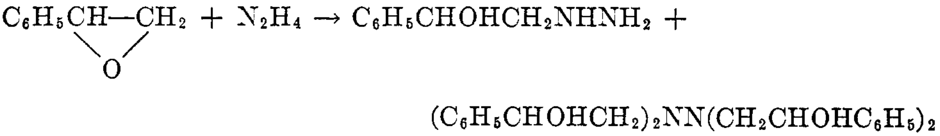
TABLE 35

N,N-Dialkylphenylethanolamines from styrene oxide

SECONDARY AMINE	YIELD	REFERENCE
	per cent	
Dimethyl	Quantitative	(742, 743)
Di-*n*-propyl	91	(189)
Di-*n*-butyl	92	(189)
Diethanol	89	(189)
Morpholine	80	(189)

Several *N*,*N*-dialkylphenylethanolamines have been prepared by treating styrene oxide with the appropriate secondary amine. These preparations are summarized in table 35.

Styrene oxide reacted with hydrazine, *N*,*N*-dimethylhydrazine, and *N*,*N*-diethylhydrazine in xylene solution at 120–140°C. to give the corresponding phenylethanolhydrazines in 29, 22, and 37 per cent yields, respectively (62). In the first case some completely alkylated hydrazine appeared as a by-product.



$$C_6H_5\overbrace{CH{-}CH_2}^{}\!\!\underset{O}{} + N_2H_4 \rightarrow C_6H_5CHOHCH_2NHNH_2 + (C_6H_5CHOHCH_2)_2NN(CH_2CHOHC_6H_5)_2$$

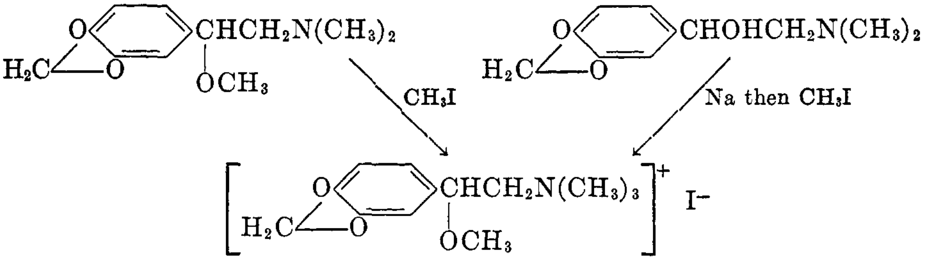
Quaternary salts in this series have been prepared by treating a styrene halohydrin with the appropriate tertiary amine. Styrene bromohydrin reacted with pyridine to give 59 per cent of the quaternary bromide (618).

$$C_6H_5CHOHCH_2Br + C_6H_5N \rightarrow C_6H_5CHOHCH_2NC_5H_5^+Br^-$$

Styrene iodohydrin gave small amounts of quaternary iodides with trimethylamine and dimethylbenzylamine, together with larger amounts of acetophenone (80 per cent in the trimethylamine reaction) (745).

Quaternary pyridinium bromides also have been prepared by hydrogenating in the presence of a platinum oxide catalyst the corresponding derivatives of ω-aminoacetophenone (30 per cent yield) (618) and of 3-methoxy-4-acetoxy-ω-aminoacetophenone (20 per cent yield) (619). In the latter case some material in which the pyridine ring also was reduced likewise was isolated. 3-Methoxy-4-hydroxyphenacylpyridinium bromide was too insoluble for catalytic hydrogenation.

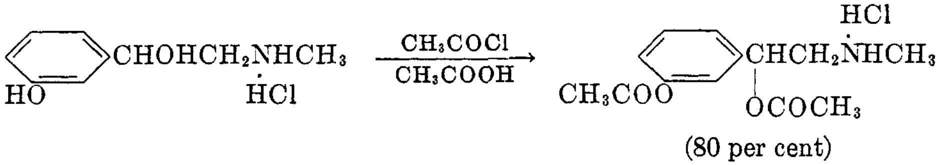
d-Phenylethanolamine has been alkylated with methyl iodide and sodium methoxide to give 80 per cent of the quaternary iodide (597). *N*,*N*-Dimethylphenylethanolamine yielded quaternary salts with both methyl iodide and methyl chloride (744). A quaternary iodide was obtained by treating *N*,*N*-dimethyl-2,5-dimethoxyphenylethanolamine with methyl iodide (48). Treatment with silver chloride gave the corresponding quaternary chloride. The methyl and ethyl ethers of *N*,*N*-dimethylphenylethanolamine (744) and the methyl ether of *N*,*N*-dimethyl-3,4-methylenedioxyphenylethanolamine (474) added methyl iodide to give quaternary iodides. The same compound was prepared by treating *N*,*N*-dimethyl-3,4-methylenedioxyphenylethanolamine with sodium and then with methyl iodide.



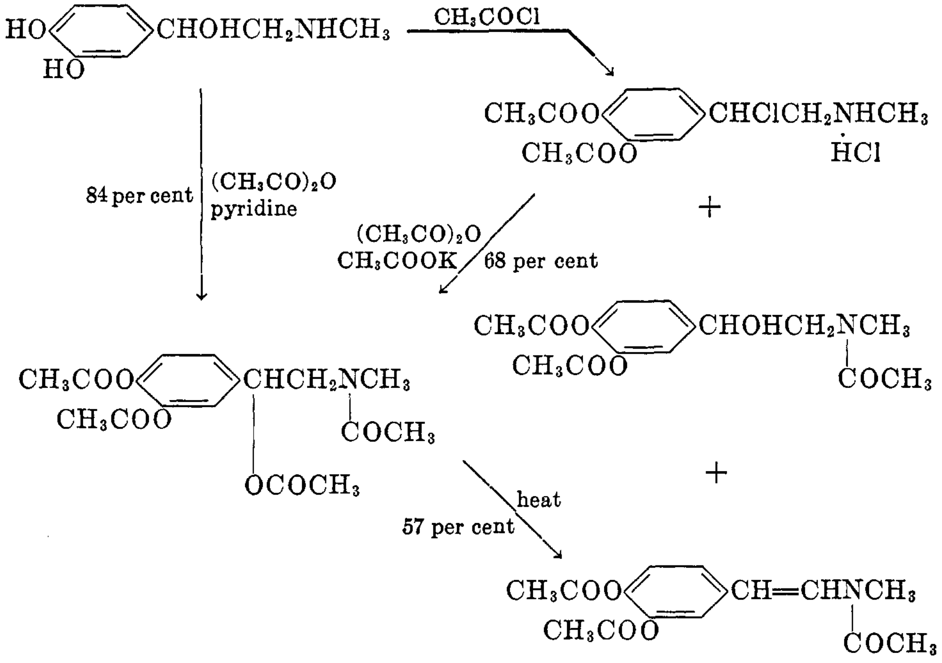
N-Methylphenylethanolamine gave an orange-yellow color when warmed with 4 per cent hydrogen peroxide containing sodium chloride (675). The hydrochloride of *N*-methyl-*p*-hydroxyphenylethanolamine gave a blue color with sulfomolybdic acid (595).

Treatment of *N*-β-phenethylphenylethanolamine with benzoyl chloride gave 88 per cent of the *O*-benzoate (20). With *N*-β-tetrahydronaphthylphenylethanolamine the yield was 67 per cent.

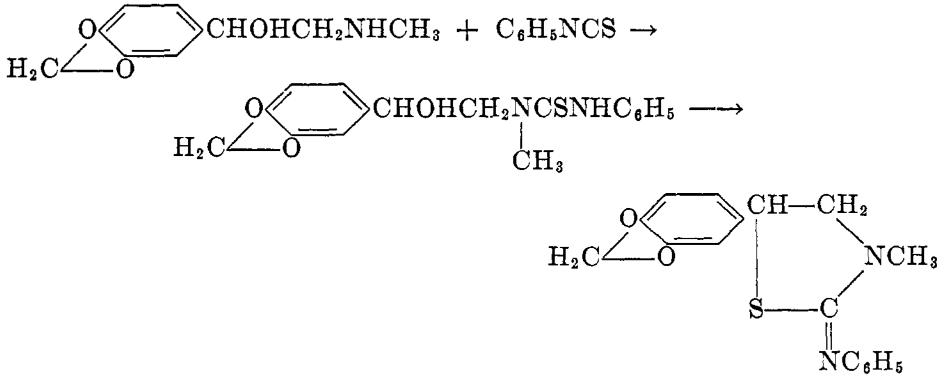
N-Methyl-*m*-hydroxyphenylethanolamine hydrochloride reacted with acetyl chloride in glacial acetic acid to give 80 per cent of *N*-methyl-*O*,*m*-diacetoxyphenylethanolamine hydrochloride (119). The analogous dipropionyl derivative was prepared by the same method in 83 per cent yield.



Some of the acetylation reactions of *N*-methyl-3,4-dihydroxyphenylethanolamine (adrenaline) are summarized in equation form below (118):

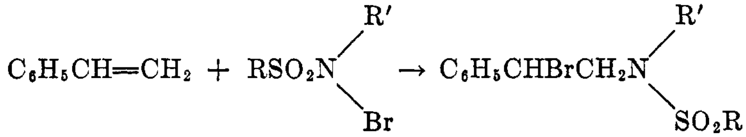


N-Methyl-3,4-methylenedioxyphenylethanolamine formed a picrate and reacted with phenyl isothiocyanate to give a thiourea (549). The latter compound lost water to give a substituted tetrahydrothiazole.



N-Benzylphenylethanolamine reacted with nitrous acid to give an *N*-nitroso derivative and with hydriodic acid to give benzyl β-phenethylamine (219).

A number of sulfonamides of *N*-alkyl-β-bromo-β-phenethylamines have been prepared by adding *N*-alkyl-*N*-bromosulfonamides to styrene (375). These



$$C_6H_5CH{=}CH_2 + RSO_2N(R')Br \rightarrow C_6H_5CHBrCH_2N(R')SO_2R$$

preparations are summarized in table 36.

The *N*-methyl-*N*-*p*-toluenesulfonyl compound was dehydrobrominated by means of both quinoline and alcoholic sodium ethoxide. Treatment with sodium in amyl alcohol gave methyl-β-phenethylamine. The *N*-benzyl-*N*-*p*-toluenesulfonyl compound also was dehydrobrominated with alcoholic sodium ethoxide.

TABLE 36

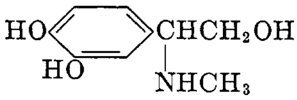
Styrene and N-bromosulfonamides

N-ALKYL GROUP	SULFONAMIDE	YIELD
		per cent
Methyl	*p*-Toluene	72
Benzyl	*p*-Toluene	
Benzyl	Benzene	
β-Bromo-α-phenethyl	*p*-Toluene	
β-Phenethyl	*p*-Toluene	

The numerous esters of the *N*,*N*-dialkylphenylethanolamines are summarized in table 37, together with their methods of preparation.

The benzoate of *N*,*N*-dimethyl-3,4-methylenedioxyphenylethanolamine also was prepared in 78 per cent yield by the acid chloride method (577). The above-mentioned *N*,*N*-dimethyl-*O*-acetylphenylethanolamine added methyl iodide to give a quaternary salt (746).

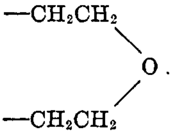
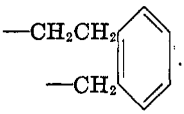
No discussion of the reactions of phenylethanolamines would be complete without mentioning the elucidation of the structure of adrenaline. In 1903 Abel (1), who prepared and saponified the monobenzoyl derivative, suggested the empirical formula $C_{10}H_{13}NO_3$. Pauly (546) showed the correct formula to be $C_9H_{13}NO_3$, recalled the previous evidence for a catechol nucleus, and postulated the five possible side chains. On the basis of a tribenzenesulfonyl derivative with benzenesulfonyl chloride, a tribenzoyl derivative with benzoic anhydride, an addition product with methyl iodide, and oxalic acid from treatment with hydrogen peroxide or potassium permanganate, v. Furth (250) suggested the structural formula $CH_3NC_2HOHC_6H_6(OH)_2$. In 1904 Pauly (547) prepared a dibenzoyl derivative, using benzoyl chloride and sodium bicarbonate so as not to touch the phenolic hydroxyl groups. From this reaction and the fact that methylamine was obtained on degradation, the presence of a methylamino group was indicated. Pauly favored the formula:



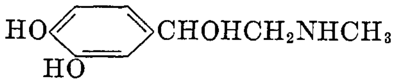
$$HO(HO)C_6H_3CH(NHCH_3)CH_2OH$$

TABLE 37

N,N-Dialkylphenylethanolamine esters

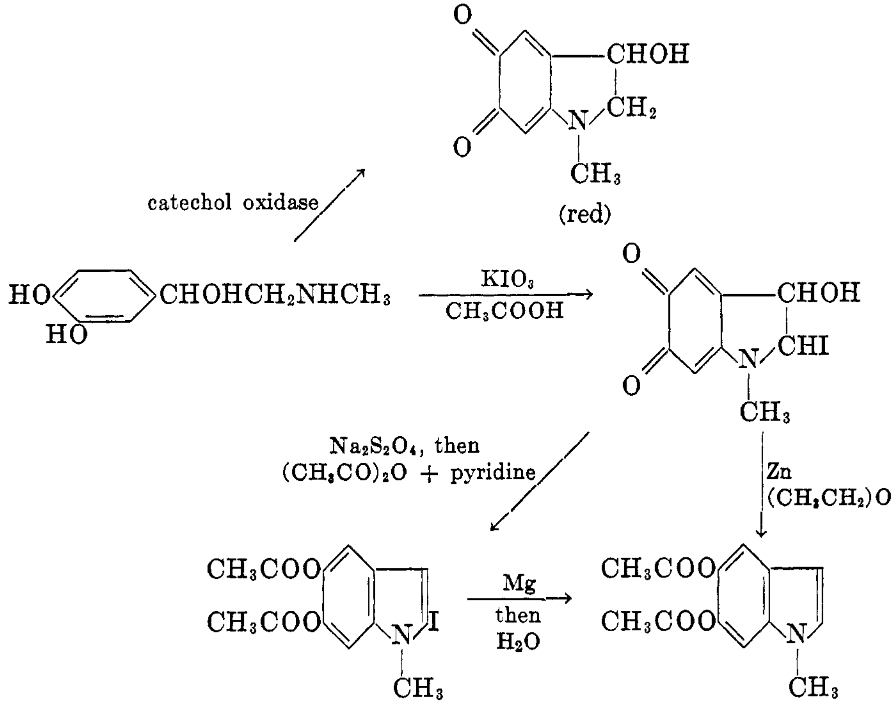
SUBSTITUENTS ON NITROGEN ATOM	ESTER	METHOD OF PREPARATION	YIELD	REFERENCE
			per cent	
Dimethyl	Acetate	Anhydride		(746)
	Acetate	Acid chloride	96	(119)
	Benzoate	Acid chloride		(742, 744)
Diethyl	*p*-Nitrobenzoate	Acid chloride	89–91	(484)
	p-Aminobenzoate	Reduction of nitro	77–81	(484)
	2-Ethylhexoate	Acid	53	(189)
Di-*n*-propyl	Butyrate	Acid	72	(189)
Di-*n*-butyl	Acetate	Anhydride	63	(189)
	3,5-Dinitrobenzoate	Acid chloride		(272)
Diamyl	Butyrate	Acid	54	(189)
Diethanol	Triacetate	Anhydride	75	(189, 196)
	Propionate	Acid	77	(189)
	Benzoate	Acid chloride	60–65	(630)
	Cinnamate	Acid chloride	88	(630)
	Benzoate	Acid chloride	88	(20)

In the same year Jowett (357) favored the correct structure for adrenaline, although Pauly had suggested it as a possibility:



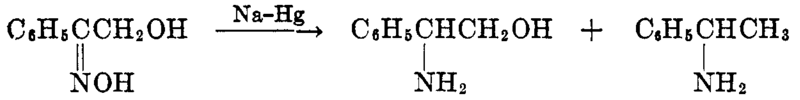
Jowett's evidence was that oxidation with potassium permanganate gave methylamine, formic acid, and oxalic acid; the fusion product with potassium hydroxide gave the color reactions of catechol; and methylation with methyl iodide followed by oxidation with potassium permanganate gave veratric acid and trimethylamine. Aldrich (11) summarized the known chemistry of adrenaline and also favored the correct structure. In 1906 Friedman (245) obtained a tribenzenesulfonyl derivative by treating adrenaline with benzenesulfonyl chloride and sodium hydroxide. Oxidation with chromic acid in acetic acid yielded a ketone, tribenzenesulfonyl adrenalone, which Friedman synthesized. This reaction differentiated between the two structures suggested by Pauly and showed the one favored by Jowett and Aldrich to be correct.

Treatment of adrenaline with catechol oxidase yielded a red indole quinone (275). A similar compound containing iodine was obtained with potassium iodate in acetic acid (64, 617). Some of its chemistry is shown below (64):



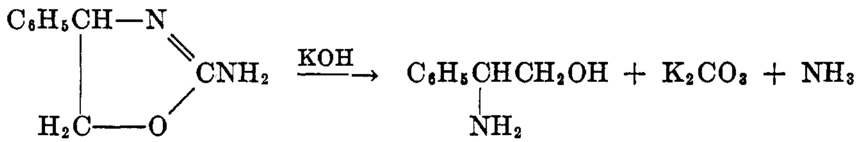
Treatment of adrenaline with lead dioxide in aqueous acetic acid gave a compound which has been postulated as an isomer of that obtained with catechol oxidase (593). In this case the ring closure was postulated as taking place ortho rather than para to the 3-hydroxyl group.

β-Amino-β-phenethyl alcohol usually has been prepared by the reduction of ω-hydroxyacetophenone oxime by means of sodium amalgam (414, 611, 727) in 44 per cent yield (251). α-Phenethylamine has appeared as a by-product (414) to the extent of 27 per cent (251).

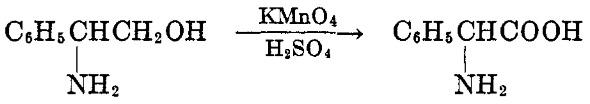


$$C_6H_5\underset{\underset{NOH}{\|}}{C}CH_2OH \xrightarrow{Na\text{-}Hg} C_6H_5\underset{\underset{NH_2}{|}}{C}HCH_2OH + C_6H_5\underset{\underset{NH_2}{|}}{C}HCH_3$$

An alternative route is the reduction of ethyl phenylglycinate by means of sodium and ethanol (27 per cent yield) (442) or hydrogen and Raney nickel in methanol solution at 40°C. for 9 hr. (59 per cent yield) (540). With longer times the benzene ring was saturated and at higher temperatures the amino group was methylated. At 100°C. no reduction occurred in the presence of copper chromite. β-Amino-β-phenethyl alcohol has been prepared by treating 2-amino-4-phenyloxazoline with alcoholic potassium hydroxide (727).

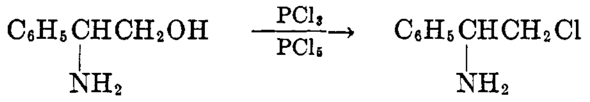


Treatment with benzoyl chloride gave the *N*-benzoyl derivative (414, 442, 611). This compound has been acylated further with acetic anhydride and sodium acetate (414) or pyridine (611) to give the *N*-benzoyl-*O*-acetyl derivative and with benzoyl chloride and pyridine to give the dibenzoyl derivative (611, 727) and the tribenzoyl derivative (611). Treatment of β-amino-β-phenethyl alcohol with acetic anhydride in pyridine gave the diacetyl derivative (611). The *N*-dichloroacetate and the urea also have been prepared (414), and β-amino-β-phenethyl alcohol has been resolved as the tartrate (611). Oxidation with dilute acid potassium permanganate gave phenylglycine (611). Distillation gave diphenylpyrazine (611).



$$C_6H_5\underset{\underset{NH_2}{|}}{C}HCH_2OH \xrightarrow[H_2SO_4]{KMnO_4} C_6H_5\underset{\underset{NH_2}{|}}{C}HCOOH$$

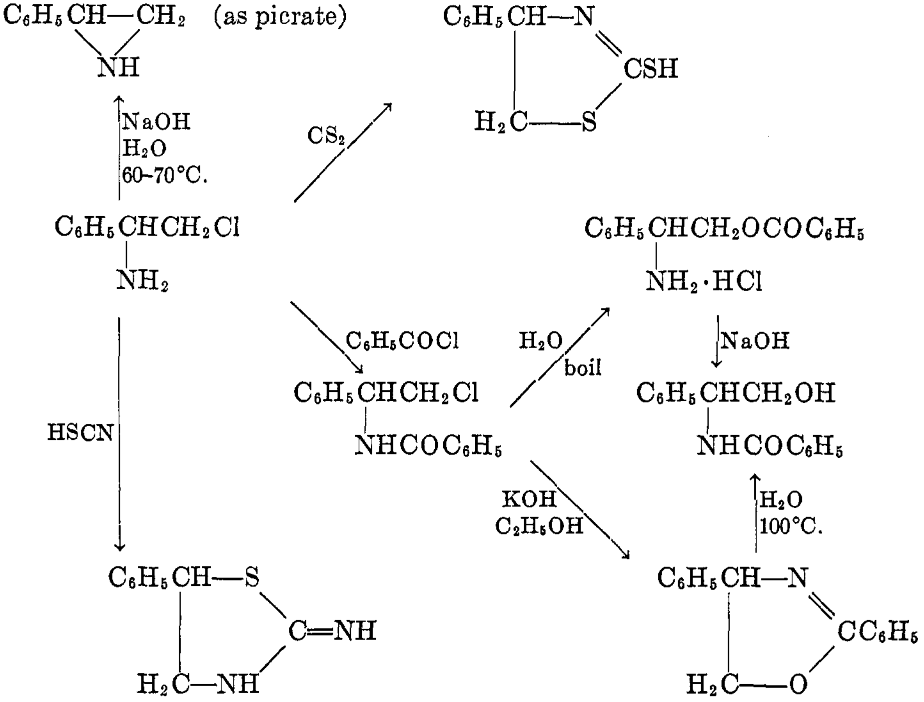
β-Amino-β-phenethyl alcohol reacted with a mixture of phosphorus trichloride and phosphorus pentachloride to give β-chloro-α-phenethylamine (611) in 76 per cent yield (442) and 56 per cent yield (251). Neither hydrochloric acid



$$C_6H_5\underset{\underset{NH_2}{|}}{C}HCH_2OH \xrightarrow[PCl_5]{PCl_3} C_6H_5\underset{\underset{NH_2}{|}}{C}HCH_2Cl$$

at 100°C. nor thionyl chloride was effective (251). β-Chloro-α-phenethylamine has also been prepared by treating the nitrogen trichloride adduct of styrene with hydrogen chloride (142, 143). β-Chloro-α-phenethylamine has been benzoylated (142) and acetylated by standard means and also resolved as the tartrate

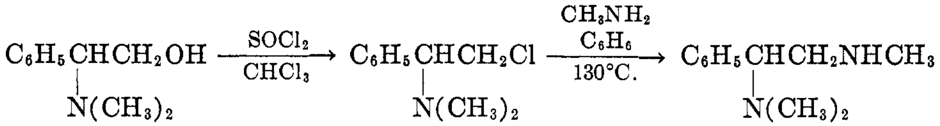
(611). Certain other reactions are shown below (251):



The *N*-*p*-nitrobenzoyl derivative has been prepared by the Schotten–Baumann reaction in 92 per cent yield and cyclized to the oxazoline in 86 per cent yield by heating with alcoholic potassium hydroxide at 70–75°C. for 1 min. (442).

β-Amino-β-phenethyl alcohol reacted with a mixture of phosphorus tribromide and phosphorus pentabromide to give β-bromo-α-phenethylamine (611). Fuming hydrobromic acid at 100°C. was ineffective (251). The last-named compound was resolved as the malate and the active *N*-acetyl compound prepared by treating this salt with acetic anhydride (611). The malate also was reduced to α-phenethylamine by means of hydrogen in the presence of a palladium catalyst.

The preparation of β-*N*-methylamino-β-3,4-dimethoxyphenethyl alcohol, β-*N*-methylamino-β-3,4-methylenedioxyphenethyl alcohol and β-*N*,*N*-dimethylamino-β-3,4-methylenedioxyphenethyl alcohol along with the isomeric phenylethanolamines from the corresponding styrene bromohydrins has been mentioned previously (474). The β-*N*,*N*-dimethylamino-β-3,4-methylenedioxyphenethyl alcohol added methyl iodide to form a quaternary salt. β-*N*,*N*-Dimethylamino-β-phenethyl alcohol has been prepared in 32 per cent yield by reducing ethyl *N*,*N*-dimethylphenylglycinate with sodium in alcohol (744). It has been characterized as the hydrochloride, picrate, gold chloride, *o*-benzoyl hydrochloride, morpholone, methiodide, and methyl chloride. Treatment with thionyl chloride in chloroform replaced the hydroxyl group with chlorine and further treatment with methylamine in benzene at 130°C. gave a 60 per cent overall yield of the substituted phenylethylenediamine (63).



$$C_6H_5\underset{\substack{|\\N(CH_3)_2}}{C}HCH_2OH \xrightarrow[CHCl_3]{SOCl_2} C_6H_5\underset{\substack{|\\N(CH_3)_2}}{C}HCH_2Cl \xrightarrow[130°C.]{\substack{CH_3NH_2\\C_6H_6}} C_6H_5\underset{\substack{|\\N(CH_3)_2}}{C}HCH_2NHCH_3$$

Treatment of β-iodo-β-phenethyl alcohol with trimethylamine in benzene gave mostly phenylacetaldehyde and its polymers, together with some of the expected quaternary iodide (745). With dimethylbenzylamine the expected quaternary iodide also was obtained, along with a trace of acetophenone in this case.

Since the completion of this manuscript a long paper has appeared describing the preparation of a large number of *N*,*N*-dialkylphenylethanolamines (463).

E. β-Alkoxy- and β-acyloxystyrenes

The commonest preparation of β-alkoxystyrenes is the addition of alcohols to phenylacetylene in the presence of a basic catalyst at around 135°C. Potassium hydroxide (33, 448) has served for the methoxy- and ethoxy-styrenes (77 per cent yield) (531) and the sodium alkoxide (519) for the methoxy- (68 per cent yield) (521), ethoxy- (531) (69 per cent yield) (521), *n*-propoxy- (69 per cent yield) (521), and isobutoxy-styrenes (75 per cent yield) (521). ω-Chlorophenylacetylene also added ethanol in the presence of potassium hydroxide or sodium ethoxide (531).

$$C_6H_5C{\equiv}CH + ROH \rightarrow C_6H_5CH{=}CHOR$$

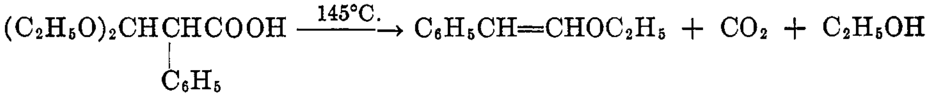
Closely related to this method is the reaction of a β-chloro- or β-bromo-styrene with a sodium alkoxide or alcoholic alkali, with phenylacetylene as a possible intermediate. Treatment of β-chlorostyrene with potassium hydroxide (207, 227) or sodium ethoxide (207) at 180°C. gave β-ethoxystyrene in 67 per cent yield (197). β-Bromostyrene reacted with sodium methoxide to give 12 per cent of β-methoxystyrene, 28 per cent of phenylacetylene, and a 55 per cent recovery of the β-bromostyrene (456). Similarly β-bromostyrene reacted with potassium hydroxide in ethanol (448) to give 60 per cent of phenylacetylene and 17 per cent of β-ethoxystyrene (531), although a later report states the yield of β-ethoxystyrene to be almost quantitative (292).

Over porous plate at 200°C. phenylacetaldehyde dimethylacetal gave 36 per cent of β-methoxystyrene (672). At 250°C. the di-*n*-propylacetal gave 70 per cent of β-*n*-propoxystyrene.

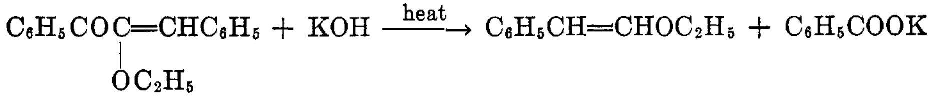
$$C_6H_5CH_2CH(OCH_3)_2 \xrightarrow{200°C.} C_6H_5CH{=}CHOCH_3$$

Treatment of phenylmagnesium bromide with ethoxyacetal gave a mixture of β-ethoxystyrene and styrene glycol diethyl ether (292, 695, 697). The analogous mixture was obtained from *o*-tolyl-, *m*-tolyl-, and 2,4-dimethylphenyl-magnesium iodides and *p*-tolyl- and *p*-chlorophenyl-magnesium bromides (697).

Pyrolysis (145°C.) of β,β-diethoxy-α-phenylpropionic acid gave β-ethoxystyrene (780). The same compound was obtained by heating benzal-ω-ethoxyacetophenone with potassium hydroxide (172).

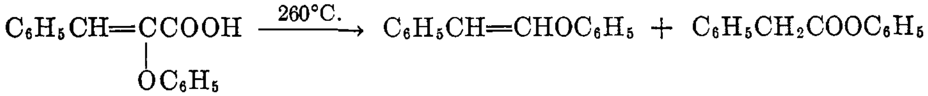


$$(C_2H_5O)_2CH\underset{\displaystyle C_6H_5}{\underset{|}{C}}HCOOH \xrightarrow{145°C.} C_6H_5CH{=}CHOC_2H_5 + CO_2 + C_2H_5OH$$



$$C_6H_5CO\underset{\displaystyle OC_2H_5}{\underset{|}{C}}{=}CHC_6H_5 + KOH \xrightarrow{heat} C_6H_5CH{=}CHOC_2H_5 + C_6H_5COOK$$

Pyrolysis (260°C.) of α-phenoxycinnamic acid gave 13–14 per cent of phenyl phenylacetate and the remainder of the product was β-phenoxystyrene (710). A yield of 63–64 per cent has been reported (711).



$$C_6H_5CH{=}\underset{\displaystyle OC_6H_5}{\underset{|}{C}}COOH \xrightarrow{260°C.} C_6H_5CH{=}CHOC_6H_5 + C_6H_5CH_2COOC_6H_5$$

At 260–270°C. α-p-tolyloxycinnamic acid underwent the same reaction.

β-Phenoxystyrene reacted with ethyl alcohol in the presence of potassium hydroxide at 200°C. to give β-ethoxystyrene and a little styrene (710). β-Methoxystyrene has been postulated as an intermediate in the preparation of phenylacetaldehyde by treating styrene iodohydrin methyl ether with silver nitrate (741).

Phenylacetaldehyde was produced when β-methoxystyrene (672), β-ethoxystyrene (419, 521, 531, 710), β-n-propoxystyrene (672), β-isobutoxystyrene (519), and β-phenoxystyrene (710) were boiled with dilute sulfuric acid. β-Ethoxystyrene yielded phenylacetaldehyde merely on steam distillation (207, 227). A 74 per cent yield of phenylacetaldehyde was obtained by passing the vapors of β-ethoxystyrene together with steam over a silica catalyst held at 215–225°C. (191, 197).

$$C_6H_5CH{=}CHOC_2H_5 \xrightarrow[215\text{–}225°C.]{H_2O,\ SiO_2} \underset{\text{(74 per cent)}}{C_6H_5CH_2CHO}$$

Phenylacetaldehyde also was obtained by passing, together with steam, β-ethoxystyrene and phenylacetaldehyde acetal at 180–210°C. over silica impregnated with sodium bisulfate, and β-methoxystyrene and phenylacetaldehyde dimethylacetal at 210–235°C. over pumice impregnated with phosphoric acid (191). Phenylacetaldehyde (292, 695, 697) and the following analogs were obtained by boiling a mixture of the corresponding β-ethoxystyrene and styrene glycol diethyl ether with dilute sulfuric acid: o-methyl-, m-methyl-, p-methyl-, 2,4-dimethyl-, and p-chloro- (697).

β-Phenoxystyrene was unaffected by boiling alcoholic potassium hydroxide (710).

β-Acetoxystyrene has been prepared by treating phenylacetaldehyde with acetic anhydride in the presence of pyridine (95, 96) or sodium acetate (36, 226) in 80 per cent yield (292, 665). While the above method gave the *trans* isomer,

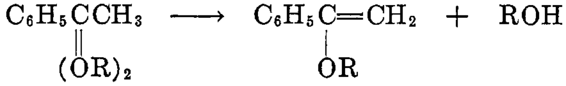
$$C_6H_5CH_2CHO + (CH_3CO)_2O \rightarrow C_6H_5CH{=}CHOCOCH_3 + CH_3COOH$$

the *cis* isomer was produced by treating benzalacetone with peracetic or perbenzoic acid (95, 96).

Hydrogenation of β-acetoxystyrene in the presence of a palladium catalyst gave 82.5 per cent of β-phenethyl acetate (678). Oxidation with ozone gave benzaldehyde and benzoic acid (665) and with peracetic acid gave benzoic and formic acids (96). Hydrolysis with water at 100–110°C. (both isomers) (95) gave phenylacetaldehyde and acetic acid (665).

F. α-Alkoxy- and α-acyloxystyrenes

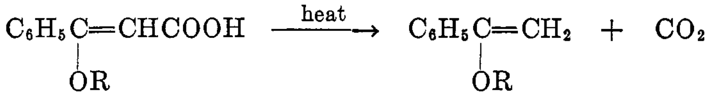
One of the commonest preparations of α-alkoxystyrenes has been to distil or pyrolyze the corresponding ketal of acetophenone. This method has been ap-



$$C_6H_5\underset{(OR)_2}{\underset{\|}{C}}CH_3 \longrightarrow C_6H_5\underset{OR}{\underset{|}{C}}{=}CH_2 + ROH$$

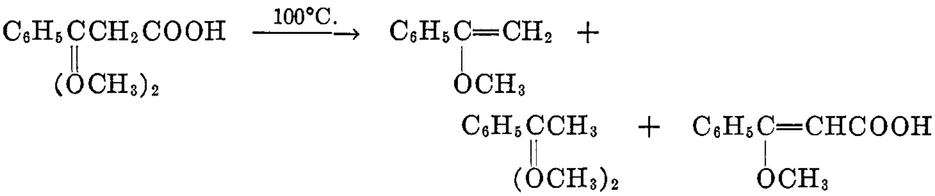
plied successfully to obtain the following styrenes: α-methoxy- (140) (86 per cent yield, 672), α-ethoxy- (140, 141) (85 per cent yield, 334), and α-*n*-propoxy- (140) (97 per cent yield, 672). Treatment of acetophenone ketal with acetyl chloride and pyridine gave α-ethoxystyrene, while acetyl chloride alone gave 1,3,5-triphenylbenzene (141).

Decarboxylation of a β-alkoxycinnamic acid gives an α-alkoxystyrene.



$$C_6H_5\underset{OR}{\underset{|}{C}}{=}CHCOOH \xrightarrow{\text{heat}} C_6H_5\underset{OR}{\underset{|}{C}}{=}CH_2 + CO_2$$

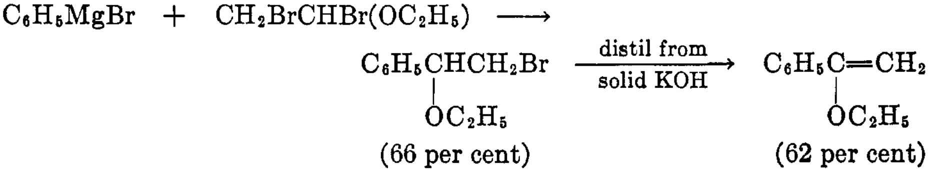
The styrenes listed in table 38 have been prepared in this way. Closely related to this method is the pyrolysis of a β-phenyl-β,β-dialkoxypropionic acid. This has been used for the preparation of α-methoxy- (33, 518, 520) and α-ethoxystyrenes (33). The by-products are the acetophenone ketal (518, 520) and the β-alkoxycinnamic acid (520).



$$C_6H_5\underset{(OCH_3)_2}{\underset{\|}{C}}CH_2COOH \xrightarrow{100°C.} C_6H_5\underset{OCH_3}{\underset{|}{C}}{=}CH_2 + C_6H_5\underset{(OCH_3)_2}{\underset{\|}{C}}CH_3 + C_6H_5\underset{OCH_3}{\underset{|}{C}}{=}CHCOOH$$

The third general method for preparing α-alkoxystyrenes is to dehydrohalogenate the appropriate ether of a styrene halohydrin. Treatment of styrene chlorohydrin ethyl ether with sodium hydroxide in methanol gave α-ethoxystyrene (314) in 70 per cent yield (302). The same result was effected in the case of *p*-methoxystyrene chlorohydrin ethyl ether by means of alcoholic sodium ethoxide (583).

A convenient synthesis is that shown below for α-ethoxystyrene (433).



$$C_6H_5MgBr + CH_2BrCHBr(OC_2H_5) \longrightarrow \underset{\text{(66 per cent)}}{C_6H_5\underset{\substack{|\\OC_2H_5}}{C}HCH_2Br} \xrightarrow[\text{solid KOH}]{\text{distil from}} \underset{\text{(62 per cent)}}{C_6H_5\underset{\substack{|\\OC_2H_5}}{C}{=}CH_2}$$

TABLE 38

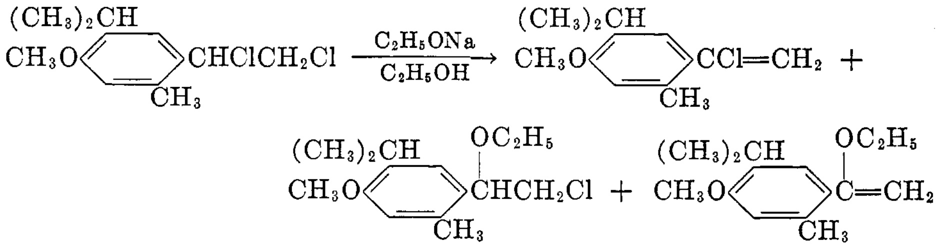
α-Alkoxystyrenes from β-alkoxycinnamic acids

STYRENE PREPARED	YIELD	REFERENCES
α-Methoxy	Nearly quantitative	(518, 519, 520)
α-Ethoxy		(139, 448, 519)
α-Phenoxy		(635)
α-(*o*-Tolyloxy)		(635)
α-(*m*-Tolyloxy)		(636)
α-(*p*-Tolyloxy)		(635)
α-(2,4-Dimethylphenoxy)		(638)
α-(2-Isopropyl-5-methylphenoxy)		(633)
α-(*p*-Methoxyphenoxy)		(637)
α-(α-Naphthoxy)		(635)

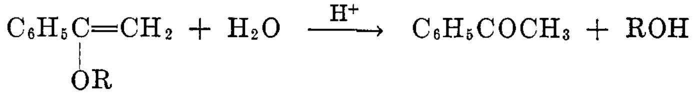
The method has been applied successfully for the preparation of the following styrenes (434): α-methoxy- (65 per cent, –), α-*n*-propoxy- (66 per cent, –), α-*n*-butoxy- (57 per cent, 70 per cent), α-isoamoxy (81 per cent, –), and *p*-chloro-α-methoxy- (51 per cent, 59 per cent). The yields in parentheses are for the two successive steps in the synthesis. Styrene bromohydrin methyl ether has been dehydrohalogenated with sodium methoxide in methanol to give 45 per cent of α-methoxystyrene (796).

α-Methoxy-, α-ethoxy-, and α-amoxy-styrenes have been prepared by treating the corresponding ether of styrene iodohydrin with alcoholic potassium hydroxide (741).

α-Ethoxystyrene was a by-product in the reaction between styrene chlorohydrin ethyl ether and ammonia or diethylamine (315). When 2-methyl-4-methoxy-5-isopropylstyrene dichloride was treated with alcoholic sodium ethoxide, the three products shown below were obtained (583).



α-Alkoxystyrenes react readily with dilute acids to give acetophenone. This has been shown to be true with the following styrenes: α-methoxy- (518, 519,

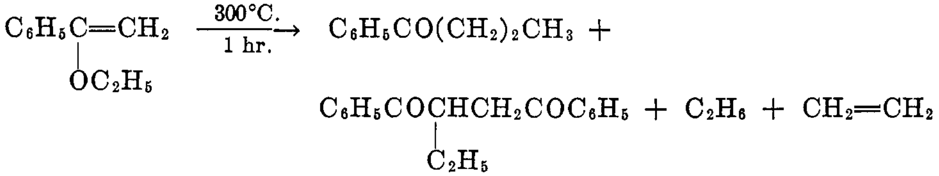


$$\underset{\text{OR}}{C_6H_5\overset{}{C}}{=}CH_2 + H_2O \xrightarrow{H^+} C_6H_5COCH_3 + ROH$$

796), α-ethoxy- (302, 314, 519), α-phenoxy- (635), α-(*o*-tolyloxy)- (635), α-(*m*-tolyloxy)- (636), α-(*p*-tolyloxy)- (635), and α-(α-naphthoxy)- (635). Houben and Führer reported that α-ethoxystyrene also could be hydrolyzed to acetophenone by means of alcoholic alkali (312, 314). Hoering maintained that this was not true (301), and the controversy went on for some time (302, 313). No one since has reported the alkaline hydrolysis of an α-alkoxystyrene.

α-Ethoxystyrene has been reported to react instantly with bromine, nitrous acid, and phenyldiazonium acetate in acetic acid (508).

Claisen (140) showed that when α-methoxystyrene was heated, propiophenone was produced. Similarly α-ethoxystyrene gave butyrophenone and α-*n*-propoxystyrene gave valerophenone. This reaction has been studied in detail and at 300°C. the following yields were obtained: propiophenone, 65 per cent; butyrophenone, 58 per cent; valerophenone, 30 per cent; caprophenone, 74 per cent; *p*-chloropropiophenone, 68 per cent; isoenanthylophenone, not given (434). In the pyrolysis of α-methoxystyrene to give propiophenone some methane also was isolated as well as 11 per cent of 1,2-dibenzoylpropane. From α-ethoxystyrene there was obtained, besides butyrophenone, 7 per cent of 1,2-dibenzoylbutane and ethane containing 6 per cent of ethylene. Propane containing 16

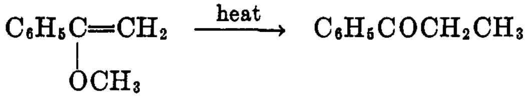


$$\underset{OC_2H_5}{C_6H_5C}{=}CH_2 \xrightarrow[\text{1 hr.}]{\text{300°C.}} C_6H_5CO(CH_2)_2CH_3 + \underset{C_2H_5}{C_6H_5COCH}CH_2COC_6H_5 + C_2H_6 + CH_2{=}CH_2$$

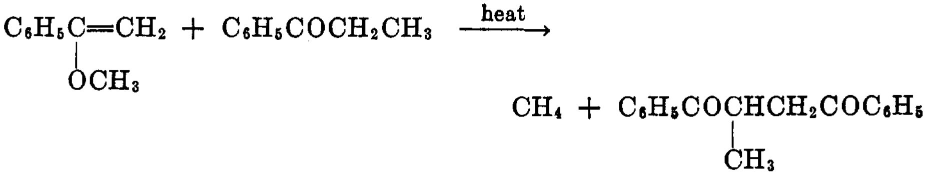
per cent of propylene was isolated from the α-*n*-propoxystyrene pyrolysis and 4 per cent of 1,2-di(*p*-chlorobenzoyl)propane was the by-product in the *p*-chloro-α-methoxystyrene pyrolysis. Besides the isoenanthylophenone obtained in the α-isoamoxystyrene pyrolysis, 2-methylbutane, acetophenone, and dibenzoylethane were produced. The copyrolysis of α-*n*-butoxystyrene and *p*-

chloro-α-methoxystyrene gave acetophenone and propiophenone besides a variety of other products. .

These reactions have been considered from a theoretical angle (434) and have been shown to proceed in two stages, both of which kinetic studies have shown to be of the second order (464).

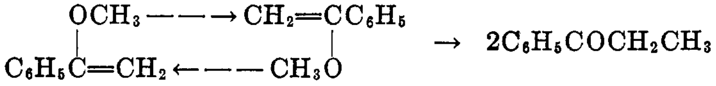


$$C_6H_5\underset{OCH_3}{\underset{|}{C}}{=}CH_2 \xrightarrow{\text{heat}} C_6H_5COCH_2CH_3$$



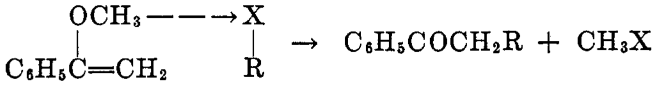
$$C_6H_5\underset{OCH_3}{\underset{|}{C}}{=}CH_2 + C_6H_5COCH_2CH_3 \xrightarrow{\text{heat}} CH_4 + C_6H_5CO\underset{CH_3}{\underset{|}{C}}HCH_2COC_6H_5$$

A bimolecular mechanism has been suggested for the first of the above reactions (517).



$$\begin{array}{lcl} OCH_3 & \dashrightarrow & CH_2{=}CC_6H_5 \\ \;| & & \qquad\;\, | \\ C_6H_5C{=}CH_2 & \dashleftarrow & CH_3O \end{array} \rightarrow 2C_6H_5COCH_2CH_3$$

α-Methoxystyrene also reacts with halogen-containing compounds by a similar mechanism.

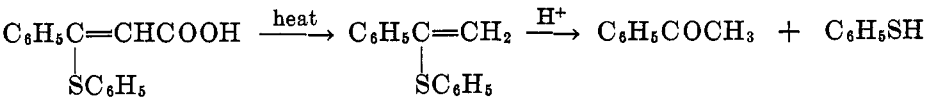


$$\begin{array}{lcl} OCH_3 & \dashrightarrow & X \\ \;| & & | \\ C_6H_5C{=}CH_2 & & R \end{array} \rightarrow C_6H_5COCH_2R + CH_3X$$

Examples are shown by the equations on page 291. In all cases a large excess of the halogen compound was employed.

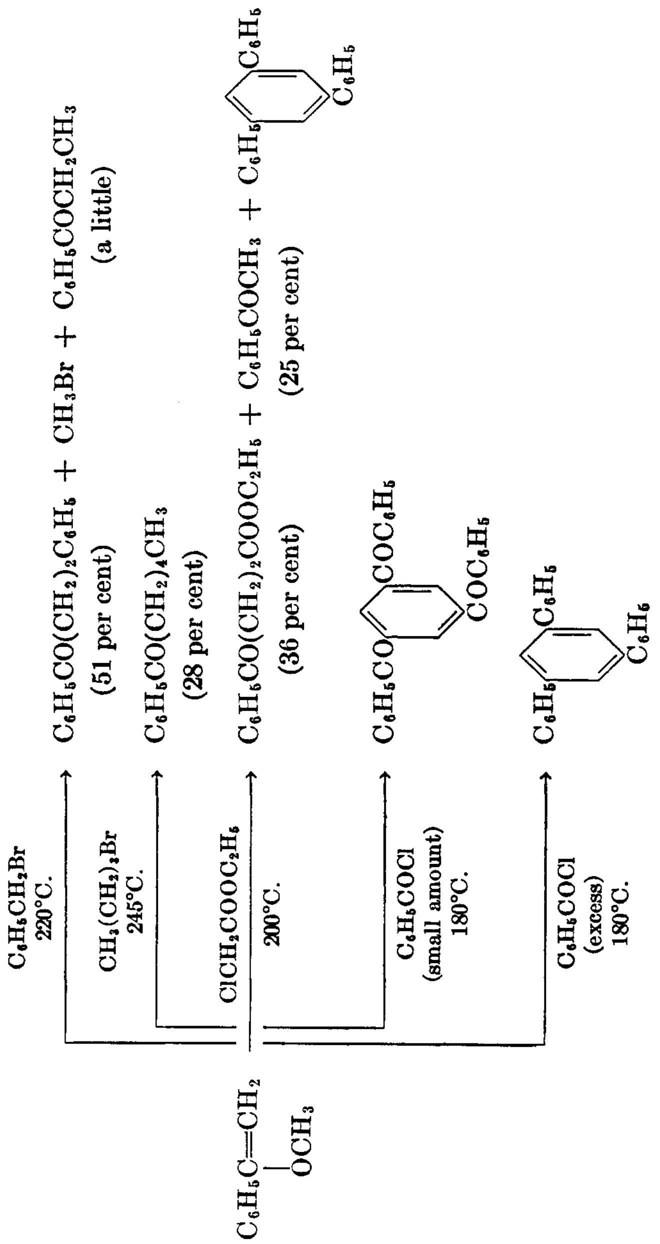
Just as α-alkoxystyrenes react with aralkyl ketones as shown in the previous section, so do they react with other compounds containing activated hydrogen atoms (701). In the equations on page 292 are shown a number of such reactions for α-methoxystyrene. A large excess of the second reactant always was employed.

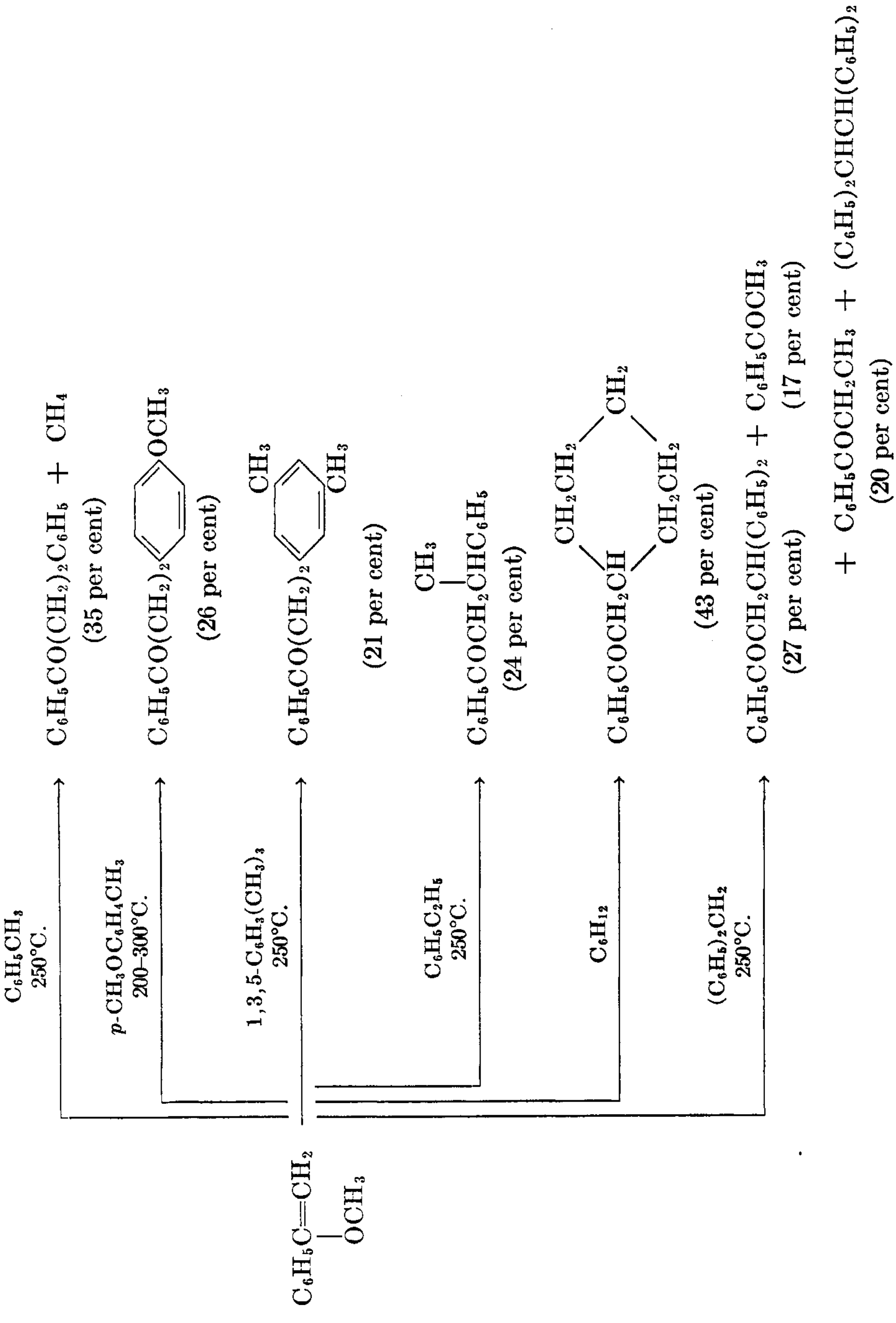
The preparation of α-styrylthioethers by decarboxylating the appropriate cinnamic acid has been utilized in the case of the phenyl (637), *o*-tolyl (634), and 2,4-dimethylphenyl (634) derivatives. Both the phenyl (637) and *o*-tolyl (634) compounds were converted to acetophenone and the corresponding mercaptan by treatment with dilute aqueous acids.



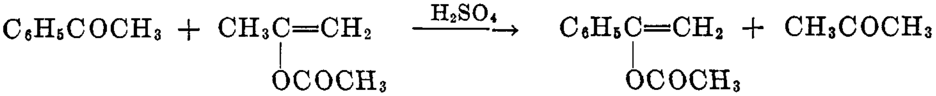
$$C_6H_5\underset{SC_6H_5}{\underset{|}{C}}{=}CHCOOH \xrightarrow{\text{heat}} C_6H_5\underset{SC_6H_5}{\underset{|}{C}}{=}CH_2 \xrightarrow{H^+} C_6H_5COCH_3 + C_6H_5SH$$

α-Acetoxystyrene has been prepared in 34 per cent yield by treating styrene bromohydrin acetate with quinoline in the presence of hydroquinone (479) and in 19 per cent conversion by treating acetophenone with ketene in the presence of


C6H5C(OCH3)=CH2
C6H5CH2Br
220°C.
C6H5CO(CH2)2C6H5 + CH3Br + C6H5COCH2CH3
(51 per cent)
(a little)
CH3(CH2)3Br
245°C.
C6H5CO(CH2)4CH3
(28 per cent)
ClCH2COOC2H5
200°C.
C6H5CO(CH2)2COOC2H5 + C6H5COCH3 + C6H5 C6H5 C6H5
(36 per cent)
(25 per cent)
C6H5COCl
(small amount)
180°C.
C6H5CO COC6H5 COC6H5
C6H5COCl
(excess)
180°C.
C6H5 C6H5 C6H5

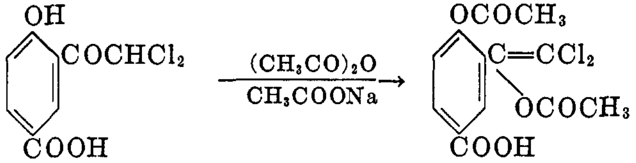

$C_6H_5C(OCH_3)=CH_2$
$C_6H_5CH_3$ 250°C.
$C_6H_5CO(CH_2)_2C_6H_5 + CH_4$
(35 per cent)
p-$CH_3OC_6H_4CH_3$ 200–300°C.
$C_6H_5CO(CH_2)_2$ OCH$_3$
(26 per cent)
1,3,5-$C_6H_3(CH_3)_3$ 250°C.
$C_6H_5CO(CH_2)_2$ CH$_3$ CH$_3$
(21 per cent)
$C_6H_5C_2H_5$ 250°C.
$C_6H_5COCH_2CH(CH_3)C_6H_5$
(24 per cent)
C_6H_{12}
$C_6H_5COCH_2CH$ CH$_2$CH$_2$ CH$_2$ CH$_2$CH$_2$
(43 per cent)
$(C_6H_5)_2CH_2$ 250°C.
$C_6H_5COCH_2CH(C_6H_5)_2 + C_6H_5COCH_3$
(27 per cent) (17 per cent)
$+ C_6H_5COCH_2CH_3 + (C_6H_5)_2CHCH(C_6H_5)_2$
(20 per cent)

sulfuric acid (157a, 278). Acetophenone reacted with isopropenyl acetate in the presence of sulfuric acid to give 52 per cent of α-acetoxystyrene (577a).



$$C_6H_5COCH_3 + \underset{\displaystyle OCOCH_3}{CH_3C}{=}CH_2 \xrightarrow{H_2SO_4} \underset{\displaystyle OCOCH_3}{C_6H_5C}{=}CH_2 + CH_3COCH_3$$

The compound added bromine to form a dibromide (278). With ethyl methyl ketone in the presence of sulfuric acid α-acetoxystyrene yielded 67 per cent of acetoxybutene (577b). Treatment of 2-hydroxy-5-carboxy-ω,ω-dichloroacetophenone with acetic anhydride and sodium acetate gave α,2-diacetoxy-5-carboxy-β,β-dichlorostyrene (138).



VII. ADDITION OF HYDROGEN HALIDES

In 1865 Erlenmeyer (202) reported that treatment of styrene with hydrochloric acid at 170°C. gave distyrene. Two years later Berthelot (75, 76, 77) listed the addition of hydrogen chloride as one of the characteristic reactions of styrene. Schramm (663) first formulated the product as α-chloroethylbenzene. This reaction has been patented (325, 328, 331, 339). Most of the examples employ hydrogen chloride gas under pressure with xylene as a solvent, and yields up to 99 per cent (325, 328, 339) have been claimed.

$$C_6H_5CH{=}CH_2 + HCl \rightarrow C_6H_5CHClCH_3$$

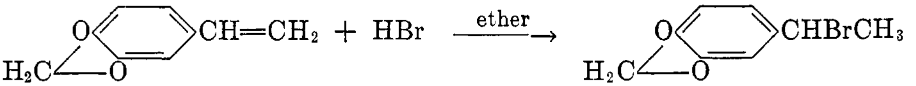
The addition of hydrogen bromide to styrene was first reported by Bernthsen and Bender (71), who formulated the reaction as giving principally β-bromoethylbenzene and a little α-bromoethylbenzene. Subsequent investigators (31, 256a, 373, 565, 663) formulated the product correctly as α-bromoethylbenzene. The heat of this addition has been measured (460), and yields of 74 per cent (629) and 84 per cent (733, 768) have been reported.

At 125°C. in ethylbenzene as a solvent the product consisted of 63 per cent α-bromoethylbenzene and 30 per cent β-bromoethylbenzene (688). At 95°C. in the presence of benzoyl peroxide the product contained 92 per cent β-bromoethylbenzene and 7 per cent of the α-isomer. In chlorobenzene the ratio was 79 per cent β and 21 per cent α. With lauroyl peroxide and no solvent 80 per cent of product was obtained, of which 93 per cent was the α-isomer (768). When the mixture was diluted with pentane 75 per cent of product was isolated, of which 80 per cent was the β-isomer. With no peroxide present the addition gave primarily the α-isomer in the absence of a solvent or in carbon tetrachloride solution (724). Somewhat more β-isomer was obtained in benzene solution and still more in ligroin. Nickelous bromide accelerated the formation of the α-isomer and disturbed the effect of oxygen.

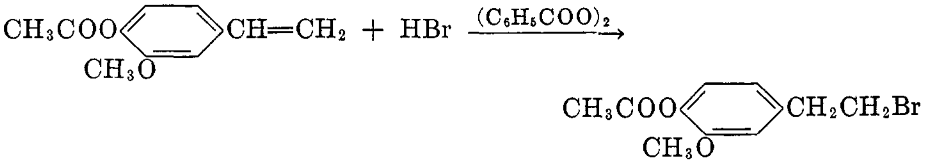
Styrene has been reported to add thiocyanic acid (372). No reaction occurred with hydrogen cyanide alone (401); in the presence of aluminum chloride and hydrogen chloride the product was polystyrene (776).

p-Divinylbenzene added hydrogen bromide in acetic acid solution to give *p*-bis(α-bromoethyl)benzene (342).

o-(β-Dimethylaminoethyl)styrene added both hydrogen chloride and hydrogen bromide (116). *o*-α-Bromoethylbenzyl bromide was obtained by treating *o*-bromomethylstyrene with fuming hydrobromic acid (110). In ether solution 3,4-methylenedioxystyrene added hydrogen bromide in normal fashion (466).

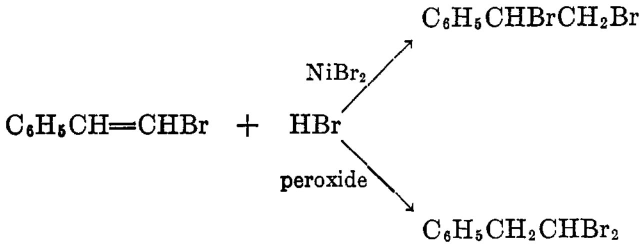


In benzene–pentane solution in the presence of benzoyl peroxide a low yield of the β-adduct was obtained from 3-methoxy-4-acetoxystyrene (619).

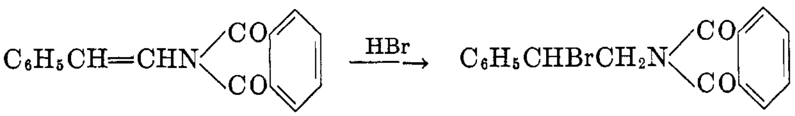


Normal addition of hydrogen bromide with the bromine atom going into the α-position also has been observed with 3,5-dibromo-4-hydroxystyrene (814), β,3,5-tribromo-4-hydroxystyrene (814), and 2,3,4-tribromo-4-hydroxystyrene (816). The quinoid forms of *p*-hydroxystyrenes add hydrogen bromide with the bromine going into the α-position (816).

α-Bromostyrene added hydrogen bromide very rapidly to give α,α-dibromoethylbenzene (725). With β-bromostyrene the addition was very slow. In the presence of nickelous bromide the product was styrene dibromide and in the presence of peroxide β,β-dibromoethylbenzene.



β-Phthalimidostyrene added hydrogen bromide in the normal fashion (628).

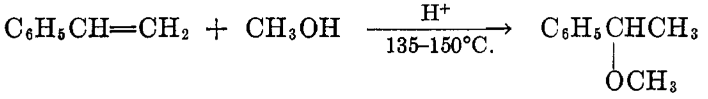


β-Nitrostyrene did not react with hydrogen bromide (571), and α-methoxystyrene gave 1,3,5-triphenylbenzene on treatment with hydrogen chloride (517). When treated with hydriodic acid, β-phenoxystyrene yielded phenol and β-phenylnaphthalene, with styrene diiodide as the postulated intermediate in the formation of the latter compound (711).

VIII. ADDITION OF WATER AND ALCOHOLS

The hydration of styrene has been mentioned in a patent but no experimental details were given (126). When styrene and deuterium oxide were heated for 100 hr. at 110°C., some exchange was noted (124). The exchange was catalyzed by both sodium hydroxide and sulfuric acid.

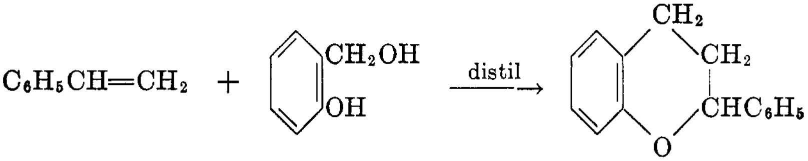
The sulfuric acid-catalyzed addition of alcohols to styrene at 135–150°C. has been reported in the case of methanol (90 per cent yield), ethanol (59 per cent yield), and 1-butanol (80 per cent yield) (704) to give the corresponding α-alkoxyethylbenzenes. With 2-propanol 50 per cent of the styrene reacted and the product was 23 per cent polymer and 77 per cent isopropyl ether. Some methanol addition has been observed in the titration of styrene with bromine and calcium bromide in methanol solution (490).



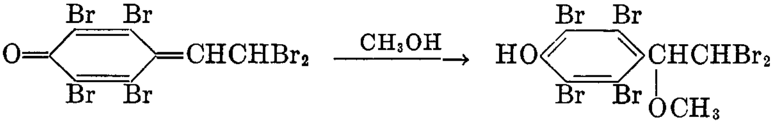
$$C_6H_5CH{=}CH_2 + CH_3OH \xrightarrow[135\text{–}150^\circ C.]{H^+} C_6H_5\underset{\underset{OCH_3}{|}}{CH}CH_3$$

(90 per cent)

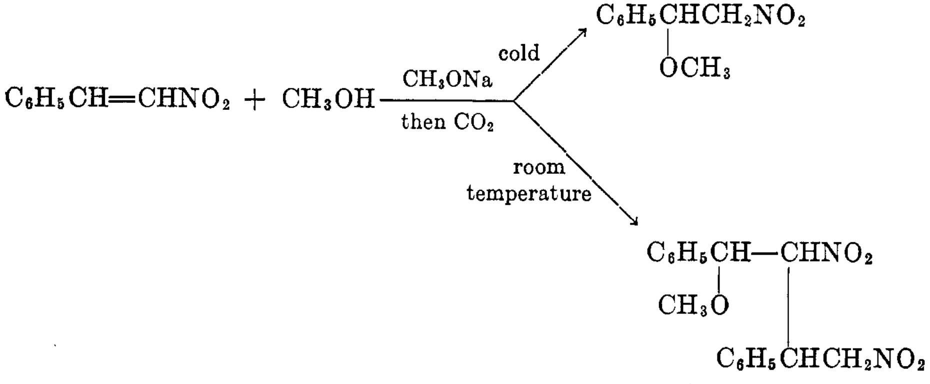
Styrene added saligenin (57 per cent yield) and 3,5-dimethyl-2-hydroxybenzyl alcohol (74 per cent yield) to give cyclic products (318).



Methanol has been added to the quinoid forms of the following substituted styrenes: β,2,3,5-tetrabromo-4-hydroxy-, β,β,2,3,5-pentabromo-4-hydroxy-, and β,β,2,3,5,6-hexabromo-4-hydroxy- (816).



Meisenheimer and Heim (491) were the first to add methanol and ethanol to β-nitrostyrene. In the case of methanol their yield was 62 per cent. The reactions were conducted in the cold with the sodium alkoxide as the catalyst. When the reactants were allowed to stand 40 hr. at room temperature, bimolecular products were obtained in 15–35 per cent and 20 per cent yields, respectively (491, 492).



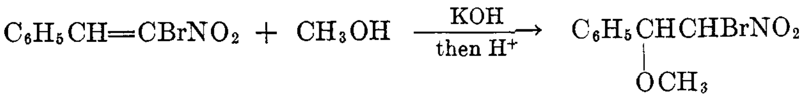
(15–35 per cent)

TABLE 39

β-Nitrostyrenes and alcohols

SUBSTITUTED β-NITROSTYRENE	ALCOHOL	CATALYST	YIELD	REFERENCE
			per cent	
	C_2H_5OH	None	0	(225)
	CH_3OH	CH_3ONa		(476)
β-Bromo	C_2H_5OH	None	14	(225)
o-Nitro-β-bromo	C_2H_5OH	None		(224)
m-Nitro	CH_3OH	NaOH		(441)
	C_2H_5OH	NaOH		(441)
p-Nitro	CH_3OH	KOH		(441)
	C_2H_5OH	KOH		(244)
p-Nitro-β-bromo	C_2H_5OH	None	100	(225)
	C_2H_5OH	None		(224)
o-Methoxy-β-bromo	CH_3OH	KOH		(608)
p-Methoxy-β-bromo	CH_3OH	KOH		(608)
2,4-Dimethoxy	CH_3OH	KOH		(471)
3,4-Dimethoxy	CH_3OH	CH_3ONa	67–72	(628)
	CH_3OH	CH_3ONa		(622)
	CH_3OH	CH_3ONa		(487)
	CH_3OH	CH_3ONa		(476)
3,4-Methylenedioxy	CH_3OH	CH_3ONa		(476)
	CH_3OH	CH_3ONa		(628)
3,4-Methylenedioxy-β-bromo	CH_3OH	KOH		(530)
2,5-Dimethoxy-3,4-methylenedioxy	CH_3OH	KOH		(471)

A little before the work of Meisenheimer and Heim, Thiele and Haeckel (737) had added methanol to β-bromo-β-nitrostyrene (97 per cent yield) and to β-bromo-β,*p*-dinitrostyrene in the presence of potassium hydroxide as a catalyst.

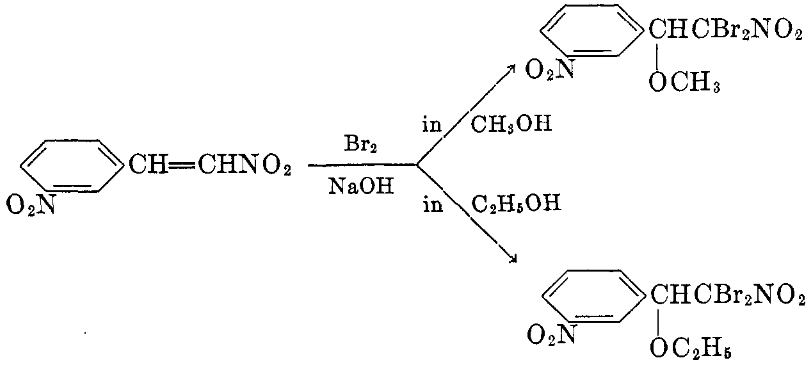


$$C_6H_5CH{=}CBrNO_2 + CH_3OH \xrightarrow[\text{then } H^+]{KOH} \underset{\displaystyle OCH_3}{C_6H_5\underset{|}{C}HCHBrNO_2}$$

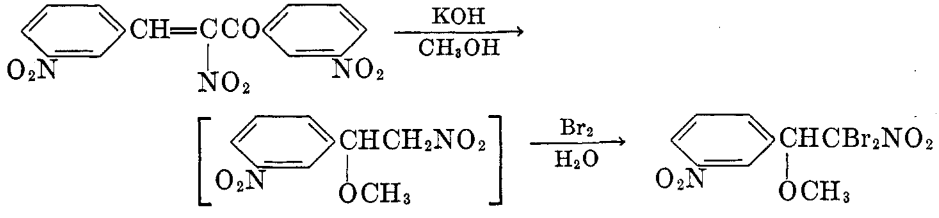
(97 per cent)

Since this early work a great many investigators have added alcohols to β-nitrostyrenes in the presence of alkaline catalysts. These reactions are summarized in table 39.

There have been a few examples of simultaneous bromination and alcohol addition as in the case of β,*m*-dinitrostyrene (243).



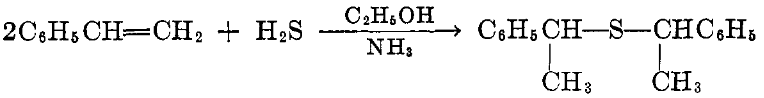
The same reaction has been carried out with β,*p*-dinitrostyrene in ethanol solution (224). An interesting alternate synthesis of β,*m*-dinitro-β,β-dibromo-α-methoxyethylbenzene, which also was applied to the α-ethoxy compound, is shown below (441).



(not isolated)

IX. ADDITION OF HYDROGEN SULFIDE, MERCAPTANS, SULFUR, THIOCYANOGEN, ETC.

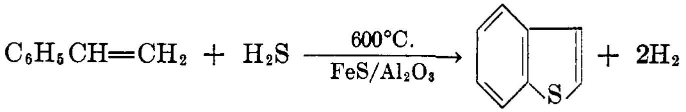
Originally it was reported that no reaction occurred between styrene and liquid hydrogen sulfide (386). More recently it has been shown that bimolecular products are formed when styrene or *p*-methoxystyrene and hydrogen sulfide are heated in ethanol or 1-butanol solution in the presence of ammonia or the sodium alkoxide (340). Yields run as high as 80 per cent.



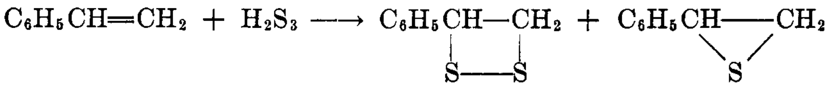
$$2C_6H_5CH{=}CH_2 + H_2S \xrightarrow[NH_3]{C_2H_5OH} C_6H_5\underset{\displaystyle CH_3}{\underset{|}{C}H}{-}S{-}\underset{\displaystyle CH_3}{\underset{|}{C}H}C_6H_5$$

(80 per cent)

At 600°C. in the presence of a ferrous sulfide–alumina catalyst styrene reacted with hydrogen sulfide to give 60 per cent of benzothiophene (515).



When treated with H_2S_2, styrene yielded metastyrene and a compound having the formula $C_8H_8S_2$ (304). With H_2S_3 the products were mono- and di-sulfides of styrene (386).



$$C_6H_5CH{=}CH_2 + H_2S_3 \longrightarrow \underset{S-\!\!-S}{C_6H_5CH{-}CH_2} + \underset{S}{C_6H_5CH{-\!\!-}CH_2}$$

Styrene has been reported to give an addition product with ethyl mercaptan (420). The addition of thiophenol proceeded contrary to Markownikoff's rule to give phenyl β-phenethyl thioether (565) in 90 per cent (31) to 100 per cent yield (658). It has been suggested that the reaction proceeds by a free-radical mechanism (658). It is accelerated by light and stopped by bases.

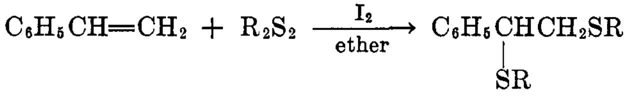
Styrene also adds thioglycolic acid contrary to Markownikoff's rule (307).

$$C_6H_5CH{=}CH_2 + HSCH_2COOH \rightarrow C_6H_5(CH_2)_2SCH_2COOH$$

This reaction is catalyzed by ascaridole (373, 376) and by peroxides in general, since no reaction occurs *in vacuo* over hydroquinone (376). The addition of thioacetic acid to styrene likewise is abnormal (309).

$$C_6H_5CH{=}CH_2 + CH_3COSH \rightarrow C_6H_5(CH_2)_2SCOCH_3$$

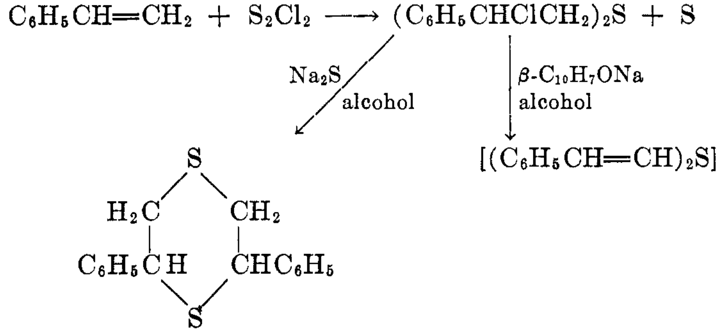
In the presence of iodine in anhydrous ether styrene added the following disulfides: dimethyl (75 per cent yield) (311), diethyl (72 per cent yield) (311),



$$C_6H_5CH{=}CH_2 + R_2S_2 \xrightarrow[\text{ether}]{I_2} C_6H_5\underset{SR}{CH}CH_2SR$$

diphenyl (75 per cent yield) (311), dithiodiglycolic acid (310) (69 per cent yield, 311), and ethyl dithioglycolate (73 per cent yield) (311). Tri- and tetrathiodiglycolic acids gave tarry products and diacetyl disulfide did not react (311).

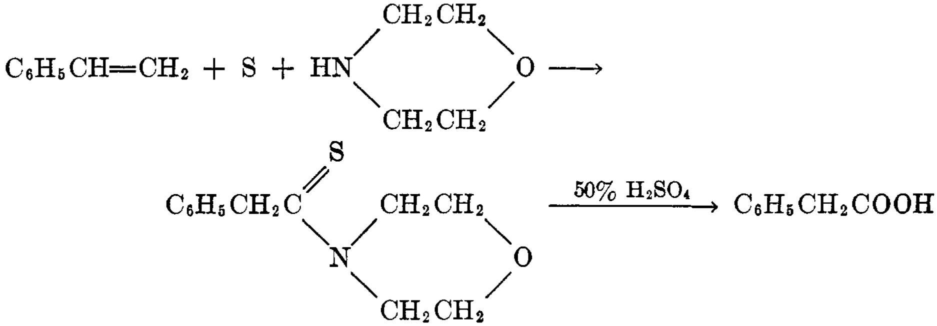
Styrene reacted with sulfur monochloride to give di(β-phenyl-β-chloro)ethyl sulfide and sulfur (564). Treatment of this compound with sodium sulfide in alcohol gave diphenyl dithiane (270). With sodium β-naphthoxide in alcohol the product was distyryl sulfide, which decomposed before distillation (564).



$$C_6H_5CH{=}CH_2 + S_2Cl_2 \longrightarrow (C_6H_5CHClCH_2)_2S + S \xrightarrow[\text{alcohol}]{\beta\text{-}C_{10}H_7ONa} [(C_6H_5CH{=}CH)_2S]$$

When the two were heated together, styrene and sulfur reacted to form an addition product (510). This was shown to be primarily 2,4-diphenylthiophene (57, 507) plus a little 2,5-diphenylthiophene and ethylbenzene (57).

Recently it has been found that styrene will undergo the Willgerodt reaction. With ammonium polysulfide at 210°C. the yield of phenylacetamide was 49 per cent (384), while the addition of pyridine (using sulfur and ammonium hydroxide) at the lower temperature of 165°C. raised this figure to 64 per cent (134). In a careful study of the reaction (385) the styrene and sulfur were boiled 2 hr. with different amines and then the resulting phenylthioacetamide hydrolyzed with 50 per cent sulfuric acid. The yields of phenylacetic acid obtained are listed after each amine: morpholine, 84 per cent; *n*-heptylamine, 59 per cent; piperidine, 58 per cent; 2-ethylcyclohexylamine, 49 per cent; cyclohexylamine, 47 per cent; benzylamine, 34 per cent; aniline, 23 per cent; *n*-butylamine, 12.5 per cent; diethanolamine, 10.3 per cent; ethanolamine, 3.5 per cent. The morpholine modification was applied to substituted styrenes to obtain the following yields of substituted phenylacetic acids: *o*-chloro-, 63 per cent; *p*-chloro-, 59 per cent; 2,5-dichloro-, 61 per cent. When 2,5-dichlorostyrene was heated with sulfur and ammonium hydroxide 11 per cent of 2,5-dichlorophenylacetamide was obtained. Finally, the treatment of styrene with sulfur and ammonium hydroxide was found to give 61 per cent of phenylacetamide and 32 per cent of phenylacetic acid.



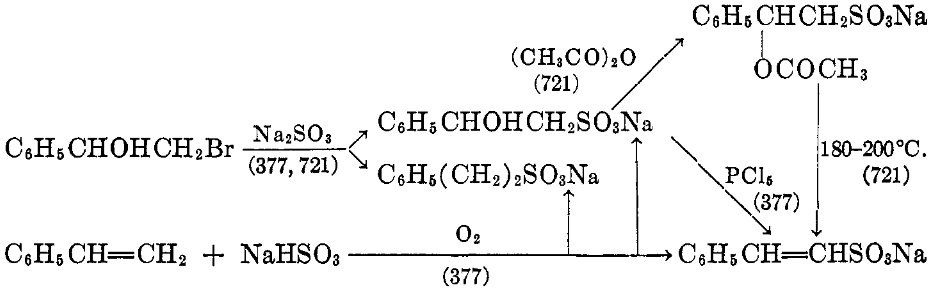
Several investigators have added thiocyanogen to styrene to give styrene dithiocyanate (316, 364, 365, 690) and the reaction has been the subject of a number of patents (327, 333, 363). When the reaction was run in acetic acid solution and the thiocyanogen generated from sodium thiocyanate and bromine in the presence of the styrene, the yield was 65 per cent (365). A much better procedure was to generate the thiocyanogen from lead thiocyanate and bromine in benzene (690) or carbon tetrachloride (364) and then add the styrene. The yields were 80 and 87 per cent, respectively.

Styrene dithiocyanate also has been prepared by boiling an alcoholic solution of styrene dibromide and potassium thiocyanate (529). It can be nitrated in the para position.

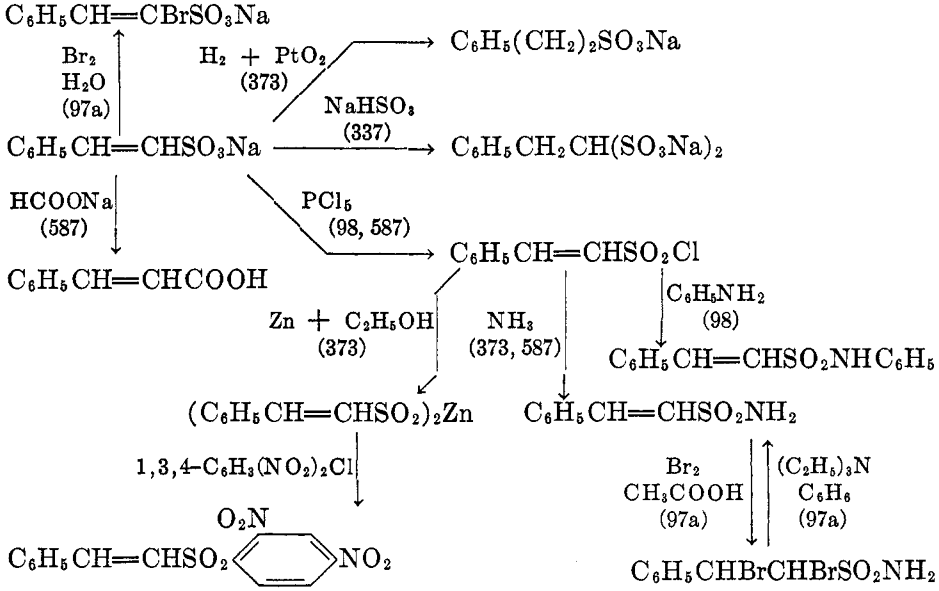
X. REACTIONS WITH OXYGENATED SULFUR COMPOUNDS

Styrene reacts with sulfur dioxide in the presence of ascaridole to give a polymer (270, 643).

Treatment of styrene with sodium bisulfite at 100–140°C. gave mostly polystyrene (288) plus a trace of addition (429, 512). With ammonium bisulfite at 25°C. the product, obtained in 16 per cent yield, was formulated first as ethylbenzene-α-sulfonic acid (31). Subsequently it was shown that, in the addition of sulfites, the sulfur becomes attached to the β-carbon atom (373). That this addition is catalyzed by oxygen was shown by treating styrene with ammonium sulfite at 25°C. and 1 mm. pressure and also at 25°C. with air bubbled into the mixture (374). In the first case there was 2 per cent of addition, in the second 50 per cent. With sodium bisulfite in the presence of oxygen the principal product was shown to be sodium β-phenyl-β-hydroxyethanesulfonate plus smaller quantities of sodium β-styrylsulfonate and sodium β-phenylethanesulfonate (377). Sodium β-phenyl-β-hydroxyethanesulfonate also has been prepared by treating styrene bromohydrin (377, 721) or iodohydrin (377) with sodium sulfite. Some of its chemistry is illustrated by the following equations:



Styrene has been reported to add chlorosulfonic acid (322, 338). Sulfonation in the β-position has been effected by means of sulfamic acid (587) and by means of dioxane–sulfur trioxide (98, 720). At 2°C. the products isolated after neutralization were 19–26 per cent of sodium β-styrylsulfonate, 66–76 per cent of sodium β-phenyl-β-hydroxyethanesulfonate, and 6–10 per cent of distyrene sultone; whereas at 54.4°C. 74–75 per cent of sodium β-styrylsulfonate, 22–24 per cent of sodium β-phenyl-β-hydroxyethanesulfonate, and 3–5 per cent of distyrene sultone were obtained (97a). In the following equations are shown some of the reactions of sodium β-styrylsulfonate:

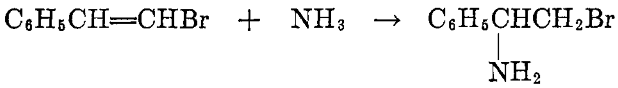


β-Bromostyrene also sulfonated in the β-position on treatment with the dioxane–sulfur trioxide complex (757a). The resulting sulfonic acid was converted to the amide by means of phosphorus pentachloride followed by ammonia.

XI. REACTIONS WITH NITROGEN COMPOUNDS

In the presence of sodium, styrene added di-*n*-butylamine to give 21 per cent of di-*n*-butyl-α-phenethylamine (149a).

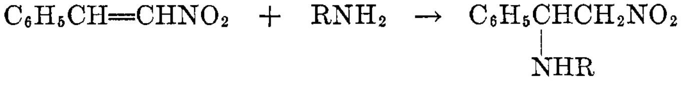
β-Bromostyrene added ammonia (24 per cent yield) and piperidine (33 per cent yield) in ether solution at room temperature (456). An aniline addition of 5 per cent was obtained by boiling the two compounds for several days.



$$C_6H_5CH{=}CHBr + NH_3 \rightarrow C_6H_5\underset{\displaystyle NH_2}{\underset{|}{C}}HCH_2Br$$

Neither styrene, β-bromostyrene, nor β-chlorostyrene added hydroxylamine (566).

The addition of amines to β-nitrostyrenes proceeds similarly to the addition of ammonia to β-bromostyrene. This reaction has been studied very extensively



$$C_6H_5CH{=}CHNO_2 + RNH_2 \rightarrow C_6H_5\underset{\displaystyle NHR}{\underset{|}{C}}HCH_2NO_2$$

by Worrall and the results of his many investigations are summarized in table 40. Included therein are hydrazines and other similar nitrogen compounds which also were examined.

TABLE 40

β-Nitrostyrenes and amines

SUBSTITUTED β-NITROSTYRENE	AMINE	ADDITION	REFERENCE
	Ammonia in alcohol	Polymerization	(789)
	Ammonia in benzene	2 moles	(789)
	Hydroxylamine	+	(566)
	Aniline	+	(789)
	p-Toluidine	+	(789)
	Phenylhydrazine	+	(526, 789)
	N,N-Diphenylhydrazine	+	(789)
	β-Naphthylhydrazine	+	(789)
	p-Tolylhydrazine	+	(789)
	Semicarbazide	+	(789)
	Thiosemicarbazide	+	(789)
	Piperidine	+	(789)
	Acetanilide	−	(789)
	N-Methylaniline	−	(789)
	N,N-Dimethylaniline	−	(789)
	o-Nitroaniline	−	(789)
	m-Nitroaniline	−	(789)
	p-Nitroaniline	−	(789)
	p-Chloroaniline	−	(789)
	p-Aminobiphenyl	−	(789)
	p-Aminophenol	−	(789)
	p-Phenetidine	−	(789)
	Ethyl *p*-aminobenzoate	−	(789)
	p-Aminoacetophenone	−	(789)
	p-Aminoacetophenone oxime	−	(789)
	Rosaniline	Polymerization	(789)
	o-Toluidine	−	(789)
	m-Toluidine	−	(789)
	α-Naphthylamine	−	(789)
	β-Naphthylamine	−	(789)
	p-Aminoazobenzene	−	(789)
	N-Methyl-*p*-aminoazobenzene	−	(789)
	N-Acetyl-*p*-phenylenediamine	−	(789)
	p-Bromophenylhydrazine	−	(789)
	p-Nitrophenylhydrazine	−	(789)
	α-Naphthylhydrazine	−	(789)
	Urea	−	(789)
	Thiourea	−	(789)
	o-Phenylenediamine	−	(789)
	m-Phenylenediamine	−	(789)
	Benzylamine	Polymerization	(789)
	N,N-Dimethyl-*p*-phenylenediamine	Polymerization	(789)
	N-Methyl-*N*-phenylhydrazine	Polymerization	(789)
	Guanidine	Polymerization	(789)

TABLE 40—*Continued*

SUBSTITUTED β-NITROSTYRENE	AMINE	ADDITION	REFERENCE
	Aminoguanidine	Polymerization	(789)
	Hydrazine	Polymerization	(789)
	p-Phenylenediamine	2 moles	(789)
	Benzidine	2 moles	(789)
β-Bromo	Aniline	Decomposition	(788)
	o-Toluidine	+	(788)
	m-Toluidine	+	(788)
	p-Toluidine	+	(788)
	Phenylhydrazine	+	(788)
	β-Naphthylamine	Decomposition	(788)
	Diphenylamine	−	(788)
	m-Nitroaniline	−	(788)
	N,*N*-Dimethylaniline	−	(788)
p-Methyl	Ammonia in alcohol	Polymerization	(790)
	Aniline	−	(790)
	p-Toluidine	−	(790)
	Phenylhydrazine	−	(790)
p-Methyl-β-chloro	Ammonia	−	(790)
	p-Toluidine	−	(790)
	p-Phenylenediamine	−	(790)
p-Methyl-β-bromo	Ammonia	−	(790)
	p-Toluidine	−	(790)
	p-Phenylenediamine	−	(790)
3-Nitro-4-methyl	Ammonia in benzene	2 moles	(790)
	Aniline	+	(790)
	p-Toluidine	+	(790)
	p-Phenylenediamine	2 moles	(790)
3-Nitro-4-methyl-β-chloro	Ammonia	−	(790)
	Aromatic amines	−	(790)
3-Nitro-4-methyl-β-bromo	Ammonia	−	(790)
	Aromatic amines	−	(790)
o-Fluoro-β-bromo	*p*-Phenylenediamine	2 moles	(795)
	Benzidine	2 moles	(795)
2-Fluoro-5-nitro	Aniline	+	(795)
	m-Toluidine	+	(795)
	p-Toluidine	+	(795)
	Phenylhydrazine	+	(795)
	Benzidine	2 moles	(795)
	o-Toluidine	−	(795)
	Hydroxylamine	−	(795)
	p-Tolylhydrazine	−	(795)

TABLE 40—*Continued*

SUBSTITUTED β-NITROSTYRENE	AMINE	ADDITION	REFERENCE
2-Fluoro-5-nitro—*Continued.*	Ammonia	−	(795)
	o-Anisidine	−	(795)
	m-Anisidine	−	(795)
	p-Anisidine	−	(795)
o-Chloro	*p*-Toluidine	−	(791)
	p-Phenylenediamine	2 moles	(791)
2-Chloro-5-nitro	*o*-Toluidine	+	(791)
	m-Toluidine	+	(791)
	p-Toluidine	+	(791)
	p-Anisidine	+	(791)
	Phenylhydrazine	+	(791)
	p-Tolylhydrazine	+	(791)
	Ammonia	2 moles	(791)
	p-Phenylenediamine	2 moles	(791)
	Benzidine	2 moles	(791)
	Aniline	−	(791)
	m-Anisidine	−	(791)
	β-Naphthylamine	−	(791)
	β-Naphthylhydrazine	−	(791)
	m-Tolylhydrazine	−	(791)
	m-Phenylenediamine	−	(791)
	Hydroxylamine	Decomposition	(791)
	Hydrazine	Decomposition	(791)
	Piperidine	Decomposition	(791)
2-Chloro-5-nitro-β-bromo	Aniline	−	(791)
	m-Toluidine	−	(791)
	p-Toluidine	+	(791)
	p-Phenylenediamine	2 moles	(791)
o-Bromo	*p*-Toluidine	−	(794)
	p-Phenylenediamine	2 moles	(794)
2-Bromo-5-nitro	*o*-Toluidine	+	(794)
	m-Toluidine	+	(794)
	p-Toluidine	+	(794)
	o-Anisidine	+	(794)
	m-Anisidine	+	(794)
	p-Anisidine	+	(794)
	p-Phenetidine	+	(794)
	N,*N*-Dimethyl-*p*-phenylenediamine	+	(794)
	Phenylhydrazine	+	(794)
	Ammonia	2 moles	(794)
	p-Phenylenediamine	2 moles	(794)
	Benzidine	2 moles	(794)

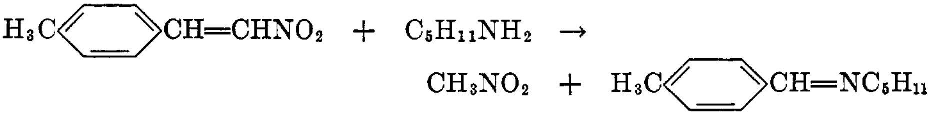
TABLE 40—*Continued*

SUBSTITUTED β-NITROSTYRENE	AMINE	ADDITION	REFERENCE
β,2-Dibromo-5-nitro	*p*-Toluidine	+	(794)
	p-Phenylenediamine	2 moles	(794)
2-Iodo-5-nitro	Aniline	+	(793)
	o-Toluidine	+	(793)
	m-Toluidine	+	(793)
	p-Toluidine	+	(793)
	o-Anisidine	+	(793)
	m-Anisidine	+	(793)
	p-Anisidine	+	(793)
	Phenylhydrazine	+	(793)
	β-Naphthylhydrazine	+	(793)
	Hydroxylamine	+	(793)
	Semicarbazide	+	(793)
	Ammonia	2 moles	(793)
2-Iodo-5-nitro-β-bromo	*p*-Toluidine	+	(793)
o-Nitro	*p*-Toluidine	−	(792)
	p-Phenylenediamine	2 moles	(792)
m-Nitro	*p*-Toluidine	−	(792)
	p-Phenylenediamine	2 moles	(792)
p-Nitro	*p*-Toluidine	−	(792)
	p-Phenylenediamine	2 moles	(792)
	Phenylhydrazine	+	(526)
2-Methoxy-4-nitro	*p*-Toluidine	−	(792)
	p-Phenylenediamine	2 moles	(792)
2-Nitro-4-chloro	*p*-Toluidine	+	(792)
	p-Phenylenediamine	2 moles	(792)
p-Chloro	*p*-Toluidine	−	(792)
	p-Phenylenediamine	−	(792)
o-Methoxy	*p*-Toluidine	−	(792)
	p-Phenylenediamine	−	(792)
p-Methoxy	*p*-Toluidine	−	(792)
	p-Phenylenediamine	−	(792)
	Phenylhydrazine	+	(526)
2,4-Dimethoxy	*p*-Toluidine	−	(792)
	p-Phenylenediamine	−	(792)
3,4-Dimethoxy	Phenylhydrazine	+	(526)
2-Nitro-4-methoxy	*p*-Toluidine	−	(792)
	p-Phenylenediamine	−	(792)

TABLE 40—*Concluded*

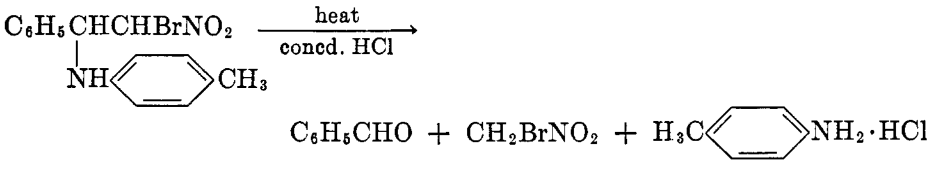
SUBSTITUTED β-NITROSTYRENE	AMINE	ADDITION	REFERENCE
2,4-Dimethoxy-6-nitro.	*p*-Toluidine	–	(792)
	p-Phenylenediamine	–	(792)
3-Methoxy-4-hydroxy.	*p*-Toluidine	–	(792)
	p-Phenylenediamine	–	(792)
3,4-Methylenedioxy.	*p*-Toluidine	–	(792)
	p-Phenylenediamine	–	(792)
	Phenylhydrazine	+	(526)

p-Methyl-β-nitrostyrene was decomposed by amylamine and by *p*-phenylenediamine to nitromethane and the Schiff's base corresponding to the amine (790).

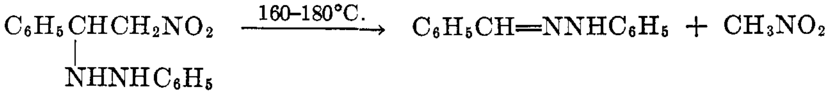


This same reaction was observed between β-nitrostyrene and *p*-methoxy-β-nitrostyrene and hydrazine (526). β-Bromo-β-nitrostyrene behaved similarly with *p*-phenylenediamine, benzidine, and *N*,*N*-diphenylhydrazine and with phenylhydrazine in boiling ethanol (788). The same reaction occurred between phenylhydrazine and *p*-methoxy-β-bromo-β-nitrostyrene and 3-methoxy-4-hydroxy-β-nitrostyrene (526).

The addition product of β-bromo-β-nitrostyrene and *p*-toluidine was decomposed by hot concentrated hydrochloric acid as follows (788):



Pyrolysis of the phenylhydrazine addition products of β-nitrostyrene, *p*-methoxy-β-nitrostyrene, 3,4-dimethoxy-β-nitrostyrene, 3,4-methylenedioxy-β-nitrostyrene, and β,*p*-dinitrostyrene gave nitromethane and the phenylhydrazone of the corresponding aromatic aldehyde (526).

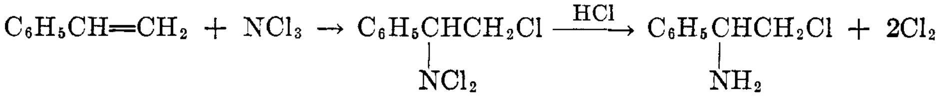


$$\underset{\displaystyle \text{NHNHC}_6\text{H}_5}{\text{C}_6\text{H}_5\text{CHCH}_2\text{NO}_2} \xrightarrow{160\text{–}180°\text{C.}} \text{C}_6\text{H}_5\text{CH}{=}\text{NNHC}_6\text{H}_5 + \text{CH}_3\text{NO}_2$$

Selenium dioxide oxidation of the phenylhydrazine addition product of β,*p*-dinitrostyrene gave the phenylhydrazone of β,*p*-dinitroacetophenone.

When styrene was heated with phenylhydrazine some benzaldehyde phenylhydrazone was isolated (545). The yields of quaternary salts from β-bromostyrene and pyridine or quinoline were too low for the reactions to be of preparative value (287).

Styrene added trichloroamine and the addition product reacted with hydrogen chloride in carbon tetrachloride to give a 28 per cent yield based on styrene of β-chloro-α-phenethylamine (142, 143).



$$C_6H_5CH{=}CH_2 + NCl_3 \rightarrow \underset{\displaystyle NCl_2}{C_6H_5CHCH_2Cl} \xrightarrow{HCl} \underset{\displaystyle NH_2}{C_6H_5CHCH_2Cl} + 2Cl_2$$

The addition of *N*,*N*-dibromo-*p*-toluenesulfonamide proceeded similarly (375). With *N*-alkyl-*N*-bromosulfonamides the mode of addition was reversed, so that the nitrogen became attached to the β-carbon atom. This was true for the addition of the following *N*-bromosulfonamides to styrene (375): *N*-methylbenzene, *N*-methyl-*p*-toluene, *N*-benzyl-*p*-toluene, *N*-benzylbenzene, *N*,β-phenethyl-*p*-toluene, and *N*-(α-phenyl-β-bromoethyl)-*p*-toluene; and for the addition of *N*-methyl-*N*-bromo-*p*-toluenesulfonamide to *p*-fluorostyrene (229).

β-Aminosytrenes have been prepared by distilling the corresponding diamines derived from phenylacetaldehyde (470). This method has been applied to β-diethylamino-, β-piperidino-, β-methylbenzylamino-, and β-dibenzylamino-styrenes.

$$C_6H_5CH_2CH[N(C_2H_5)_2]_2 \xrightarrow{distil} C_6H_5CH{=}CHN(C_2H_5)_2 + (C_2H_5)_2NH$$

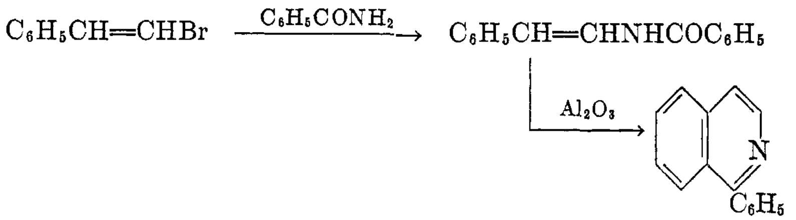
Both β-methylphenylamino- and β-methyl-*p*-tolylamino-styrene have been prepared by heating phenylacetaldehyde acetal with the appropriate amine (500). The *p*-toluenesulfonamides of β-(*N*-methylamino)styrene and β-(*N*-benzylamino)styrene were prepared by dehydrohalogenating the *p*-toluenesulfonamides of the corresponding β-phenyl-β-bromoethylamines (375).

Both acetophenone ketal and *p*-methylacetophenone ketal were treated with methylaniline, ethylaniline, methyl-*p*-toluidine, and methyl-*p*-anisidine at 140–240°C. to give 50–85 per cent of the corresponding α-aminostyrenes (300).

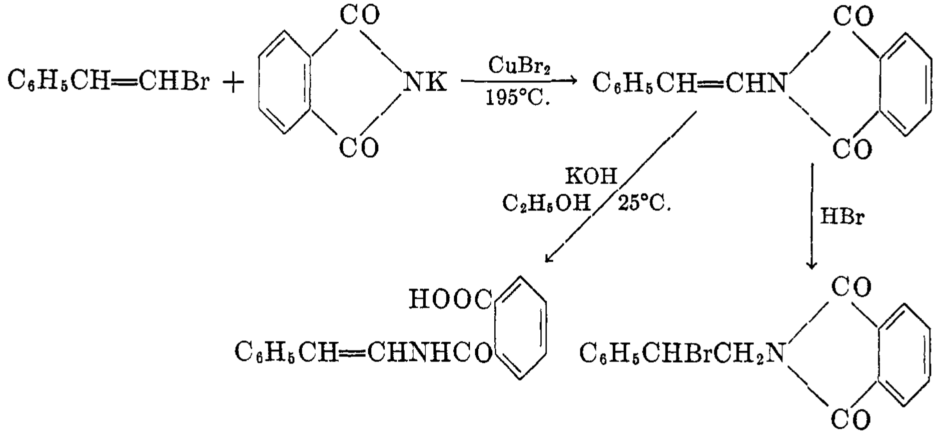
$$\underset{\displaystyle (OC_2H_5)_2}{C_6H_5CCH_3} + C_6H_5NHCH_3 \rightarrow \underset{\displaystyle CH_3NC_6H_5}{C_6H_5C{=}CH_2}$$

The hydrogenation of these compounds has been mentioned previously. β-Methylaminostyrene has been postulated as an intermediate in the formation of 1,3,5-triphenylbenzene from phenylacetylene and methylamine at 260°C. (419).

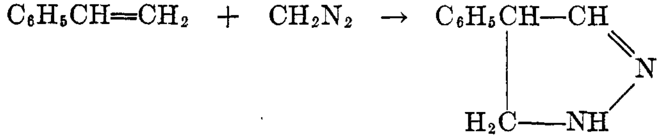
Benzamide reacted with β-bromostyrene, *p*-methoxy-β-bromostyrene, and 3,4-methylenedioxy-β-bromostyrene in the presence of copper acetate and potassium carbonate in boiling cymene to give the corresponding β-benzaminostyrene (628). That from β-bromostyrene was converted to the corresponding isoquinoline by boiling in decalin in the presence of alumina.



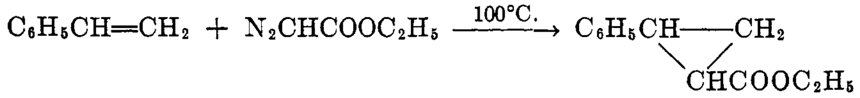
β-Bromostyrene also reacted with potassium phthalimide to give a 60 per cent yield of β-phthalimidostyrene. This compound added hydrogen bromide and was partly hydrolyzed by cold alcoholic potassium hydroxide.



Styrene first was reported to have coupled with diazotized *p*-nitroaniline (735), but a later paper stated that neither styrene nor dimethylstyrene coupled with either diazotized *p*-nitroaniline or diazotized 2,4-dinitroaniline (734). In alcohol solution 2,4-dinitrobenzenediazonium sulfate reacted with *p*-methoxystyrene to give anisaldehyde 2,4-dinitrophenylhydrazone and with styrene to give a small amount of unidentified product (7). α-Ethoxystyrene was reported to react instantly with benzenediazonium acetate in acetic acid (508). Styrene added diazomethane to give a dihydropyrazole (537). At low temperatures



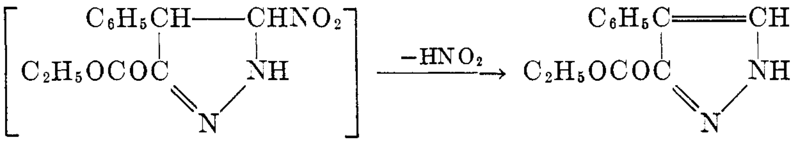
styrene did not react with ethyl diazoacetate to give a pyrazole (128). At 100°C. 33 per cent of the substituted cyclopropane was obtained (129). With *p*-nitro-



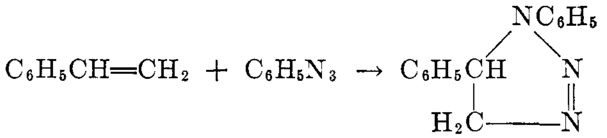
styrene the yield was 83.5 per cent (477a).

β-Nitrostyrene reacted with ethyl diazoacetate to give an unstable dihydropyrazole which lost nitrous acid (400).

$C_6H_5CH{=}CHNO_2 + N_2CHCOOC_2H_5 \rightarrow$



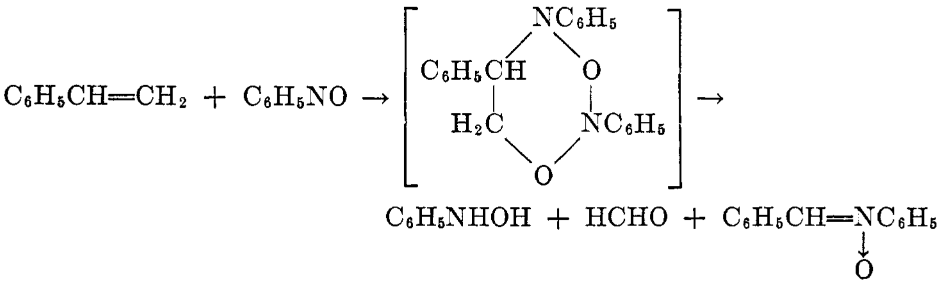
With phenylazide styrene gave a dihydrotriazole (784).



Styrene reacted with nitrosyl chloride to give a nitrosochloride, which decomposed on heating or treatment with alcoholic potassium hydroxide (748). By-products of the reaction were styrene dichloride and β-nitrostyrene (555). When the reaction was conducted at −30°C., the yield of nitrosochloride was 30 per cent (556). It reacted with piperidine to give a nitrolpiperidine. Early attempts to prepare nitrosochlorides from *p*-methylstyrene, *p*-ethylstyrene, and 2,4,6-trimethylstyrene were unsuccessful (389). Later, at 25°C., only *p*-methyl-β-chlorostyrene was obtained from the reaction between *p*-methylstyrene and nitrosyl chloride (555). At −60°C. an 80 per cent yield of nitrosochloride was obtained, from which a nitrolpiperidine was prepared (556). At −10°C. β-bromostyrene reacted with nitrosyl chloride to give a nitrosochloride from which a nitrolpiperidine was prepared. Heating of this nitrosochloride with alcoholic hydrogen chloride gave hydroxylamine hydrochloride. All six of these nitrosochlorides and nitrolpiperidines were believed to be partly dimeric (556). When treated with nitrosyl chloride, β-chlorostyrene and β-nitrostyrene gave difficultly separable mixtures (555). α-Chlorostyrene reacted to give trichlorostyrene and β-nitrodichlorostyrene.

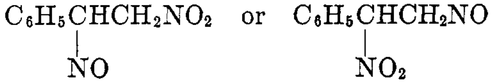
$$C_6H_5CCl{=}CH_2 + NOCl_2 \rightarrow C_6H_5CCl{=}CCl_2 + C_6H_5CCl{=}CClNO_2$$

Styrene added nitrosobenzene to give an unstable adduct which decomposed to give phenylhydroxylamine, formaldehyde, and diphenylnitrone (347).



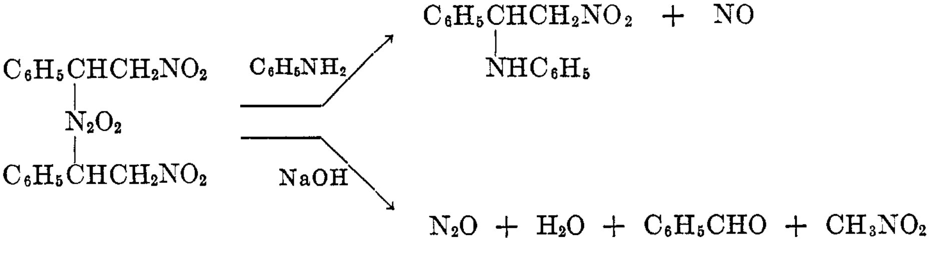
Phenyl-*p*-chlorophenylnitrone was isolated from the reaction between styrene and *p*-chloronitrosobenzene. Styrene reacted with nitrobenzene to give diphenylnitrone, azobenzene, formic acid, benzaldehyde, and benzoic acid (12).

Tönnies (754, 755) first effected the addition of N_2O_2 to styrene by treating the compound with potassium nitrite in acetic acid. The product gave β-nitrostyrene on treatment with sulfuric acid, was reduced to a compound having the empirical formula of phenylethanolamine, and reacted with aniline, ammonia, or methylamine (756). Sommer (691) treated styrene with nitrogen trioxide in ether to obtain β-nitrostyrene and an N_2O_3 addition product which he called α-styrene nitrosite. Heating in ethanol converted α-styrene nitrosite to an isomeric β-styrene nitrosite. When the α-styrene nitrosite was heated dry, the products were β-nitrostyrene, benzonitrile, nitric oxide, carbon dioxide, and water (692). The β-styrene nitrosite gave all but the β-nitrostyrene under the same conditions. When β-styrene nitrosite was treated with concentrated hydrochloric acid, a compound was formed which Sommer postulated as α-nitrophenylacetaldehyde. The aniline reaction product of α-styrene nitrosite was formulated as β,*N*-diphenyl-β-nitroethylamine. Sommer believed that β-styrene nitrosite had one of the two alternate formulas shown below and that α-styrene nitrosite was a dimer of the β-isomer.



$$C_6H_5\underset{\substack{|\\ NO}}{C}HCH_2NO_2 \quad \text{or} \quad C_6H_5\underset{\substack{|\\ NO_2}}{C}HCH_2NO$$

Wieland (775) raised the yield of α-styrene nitrosite to 70–80 per cent by using nitrogen trioxide in ether. The conversion of the α-form to the β-form was quantitative. Wieland believed β-styrene nitrosite to be ω-nitroacetophenone oxime, since it gave ω-nitroacetophenone with concentrated hydrochloric acid in the cold (Sommer had postulated the nitroaldehyde) and benzonitrile, carbon dioxide, and hydroxylamine with hot concentrated hydrochloric acid. The α-styrene nitrosite was postulated as a dimer which underwent the following reactions:

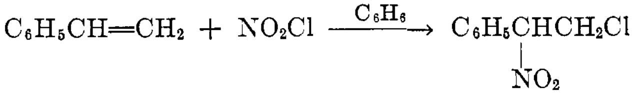


$$\begin{array}{l} C_6H_5\underset{\substack{|}}{C}HCH_2NO_2 \\ \qquad N_2O_2 \\ C_6H_5\overset{\substack{|}}{C}HCH_2NO_2 \end{array} \quad \begin{array}{l} \xrightarrow{C_6H_5NH_2} C_6H_5\underset{\substack{|\\ NHC_6H_5}}{C}HCH_2NO_2 + NO \\[2ex] \xrightarrow[NaOH]{} N_2O + H_2O + C_6H_5CHO + CH_3NO_2 \end{array}$$

The corresponding structures were given for the nitrosites from *p*-methoxystyrene and nitrogen trioxide (778). In this case the α-nitrosite gave β-nitro-*p*-methoxystyrene on heating with alcoholic potassium hydroxide.

α-Ethoxystyrene reacted instantly with nitrous acid (508).

In benzene solution styrene added NO_2Cl in low yield (707).

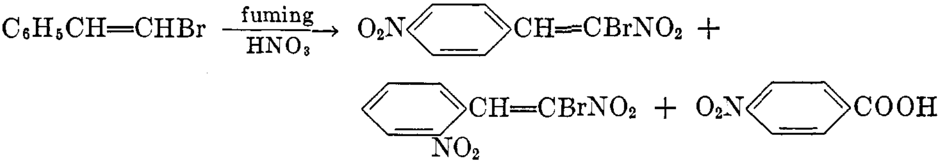


$$C_6H_5CH{=}CH_2 + NO_2Cl \xrightarrow{C_6H_6} C_6H_5\underset{\substack{|\\ NO_2}}{C}HCH_2Cl$$

In ether the pseudonitrosite was obtained. In ether solution phenylacetylene gave β-chloro-α-nitrostyrene.

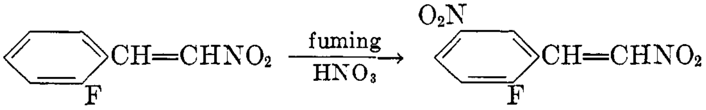
As early as 1839 Simon (673) obtained β-nitrostyrene in low yield by distilling styrene with nitric acid. Kopp (411) and Blyth and Hofmann (87) repeated the experiment shortly thereafter. Boiling styrene with concentrated nitric acid gave nitrobenzoic acid (87, 411) as well as benzaldehyde and benzoic acid (87). When Sommer (691) treated styrene with potassium nitrate in acetic acid, α-styrene nitrosite and a variety of other nitration products were obtained. Treatment of styrene with nitrogen pentoxide in ether gave a 28 per cent yield of β-nitrostyrene (571).

Isopropylstyrene reacted vigorously with fuming nitric acid to give a tar (551). Treatment of β-bromostyrene with fuming nitric acid gave 37 per cent of β,*p*-dinitro-β-bromostyrene, 20 per cent of β,*o*-dinitro-β-bromostyrene, and a little *p*-nitrobenzoic acid (224).



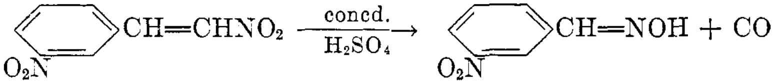
Early investigators reported the nitration of β-nitrostyrene with fuming nitric acid as giving mostly β,*p*-dinitrostyrene and some β,*o*-dinitrostyrene (571, 737). At −15° to −10°C. a 95.3 per cent yield of dinitro compounds was obtained (46). By oxidation with potassium permanganate to the corresponding nitrobenzoic acids, the mixture was shown to be 67 per cent para, 30 per cent ortho, and <2 per cent meta.

When the 2-position in β-nitrostyrene is substituted by halogen, treatment with fuming nitric acid places the second nitro group in the 5-position. This has been shown to be true for 2-fluoro- (795), 2-chloro- (791, 794), 2-bromo- (794), and 2-iodo-β-nitrostyrenes (793). Nitration of *o*-methoxy-β-nitrostyrene has been reported to give 2-methoxy-β,4-dinitrostyrene, and nitration of *p*-methoxy-β-nitrostyrene gave 4-methoxy-β,2-dinitrostyrene (792).



Treatment of styrene with silver nitrate, pyridine, and chlorine in chloroform gave a product containing 22.9 per cent chlorine (760). $ClNO_3$ was believed to be an intermediate in this reaction.

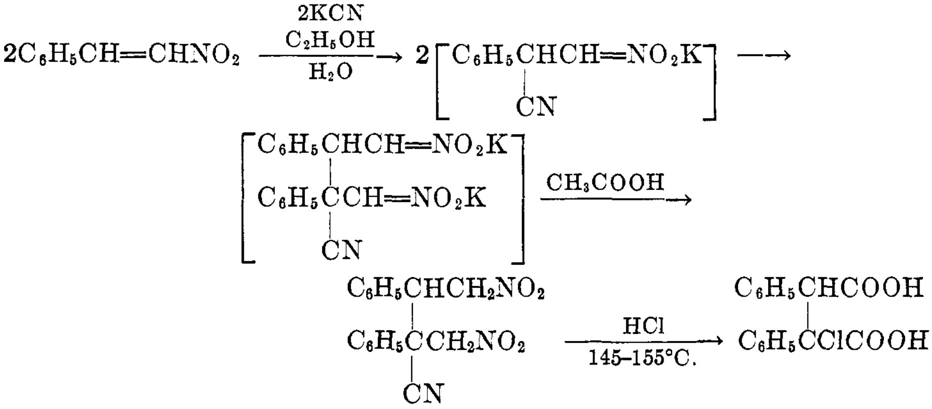
Treatment of *m*,β-dinitrostyrene (243) or *p*,β-dinitrostyrene (244) with concentrated sulfuric acid gave the corresponding aldoxime and carbon monoxide.



4-Amino-β,2-dinitrostyrene gave off carbon monoxide on heating with concentrated sulfuric acid (243). When β-nitrostyrene was heated with more dilute sulfuric acid, benzaldehyde, hydroxylamine, and carbon monoxide were obtained (571). With saturated hydrochloric acid β-nitrostyrene yielded α-chlorophenylacetic acid and hydroxylamine.

$$C_6H_5CH{=}CHNO_2 \xrightarrow{HCl} C_6H_5CHClCOOH + NH_2OH$$

β-Nitrostyrene reacted with potassium cyanide to give α- and β-forms of a dimeric product (306). Treatment of the α-form with hydrochloric acid at 145–155°C. gave diphenylchlorosuccinic acid.



$$2C_6H_5CH{=}CHNO_2 \xrightarrow[H_2O]{\begin{array}{c}2KCN\\ C_2H_5OH\end{array}} 2\left[\begin{array}{l} C_6H_5CHCH{=}NO_2K \\ \qquad\ | \\ \qquad CN \end{array}\right] \longrightarrow$$

$$\left[\begin{array}{l} C_6H_5CHCH{=}NO_2K \\ \qquad\ | \\ C_6H_5CCH{=}NO_2K \\ \qquad\ | \\ \qquad CN \end{array}\right] \xrightarrow{CH_3COOH}$$

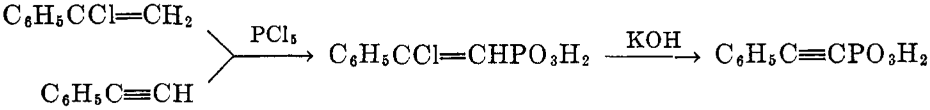
$$\begin{array}{l} C_6H_5CHCH_2NO_2 \\ \qquad\ | \\ C_6H_5CCH_2NO_2 \\ \qquad\ | \\ \qquad CN \end{array} \xrightarrow[145\text{–}155^\circ C.]{HCl} \begin{array}{l} C_6H_5CHCOOH \\ \qquad\ | \\ C_6H_5CClCOOH \end{array}$$

XII. PHOSPHORUS AND ARSENIC DERIVATIVES

Treatment of styrene with phosphorus pentachloride gave an addition product which reacted with water to produce styrenephosphonic acid (66, 285, 736).

$$C_6H_5CH{=}CH_2 + PCl_5 \rightarrow C_6H_5CHClCH_2PCl_4 \xrightarrow{H_2O} C_6H_5CH{=}CHPO_3H_2$$

This general method has been used to synthesize the substituted β-styrenephosphonic acids (412) listed in table 41. Under similar conditions α-chlorostyrene gave α-chlorostyrenephosphonic acid as well as considerable benzoic acid (67). α-Chlorostyrenephosphonic acid was obtained in 34 per cent yield by treating phenylacetylene with phosphorus pentachloride, followed by hydrolysis of the addition compound. Treatment with boiling aqueous potassium hydroxide gave phenylacetylenephosphonic acid.



$$\left.\begin{array}{l} C_6H_5CCl{=}CH_2 \\ \\ C_6H_5C{\equiv}CH \end{array}\right\rangle \xrightarrow{PCl_5} C_6H_5CCl{=}CHPO_3H_2 \xrightarrow{KOH} C_6H_5C{\equiv}CPO_3H_2$$

The following phenylacetylenes similarly were converted to α-chlorostyrenephosphonic acids; o-methoxy- (quantitative yield), *p*-methoxy- (64 per cent yield), and *o*-chloro- (49 per cent yield). The last two named were converted to the corresponding phenylacetylenephosphonic acids in 70 and 70 per cent yields, respectively.

Phosphorus pentabromide reacted differently from phosphorus pentachloride (68). With phenylacetylene 34 per cent of α,β-dibromostyrene was obtained, and with β-bromostyrene no reaction occurred.

Phenylacetylene reacted with arsenic trichloride to give 55 per cent of β-(α-chlorostyryl)dichloroarsine (350) as well as some bis-β-(α-chlorostyryl)chloroarsine (319). Treatment of the dichloroarsine with hot aqueous alcoholic sodium hydroxide gave the arsenious oxide (350). With aqueous alcoholic hydrogen peroxide an almost quantitative yield of the arsonic acid was obtained.

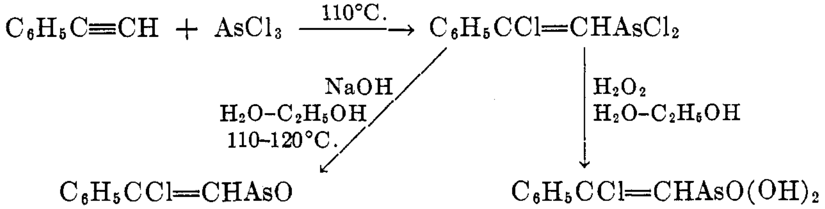
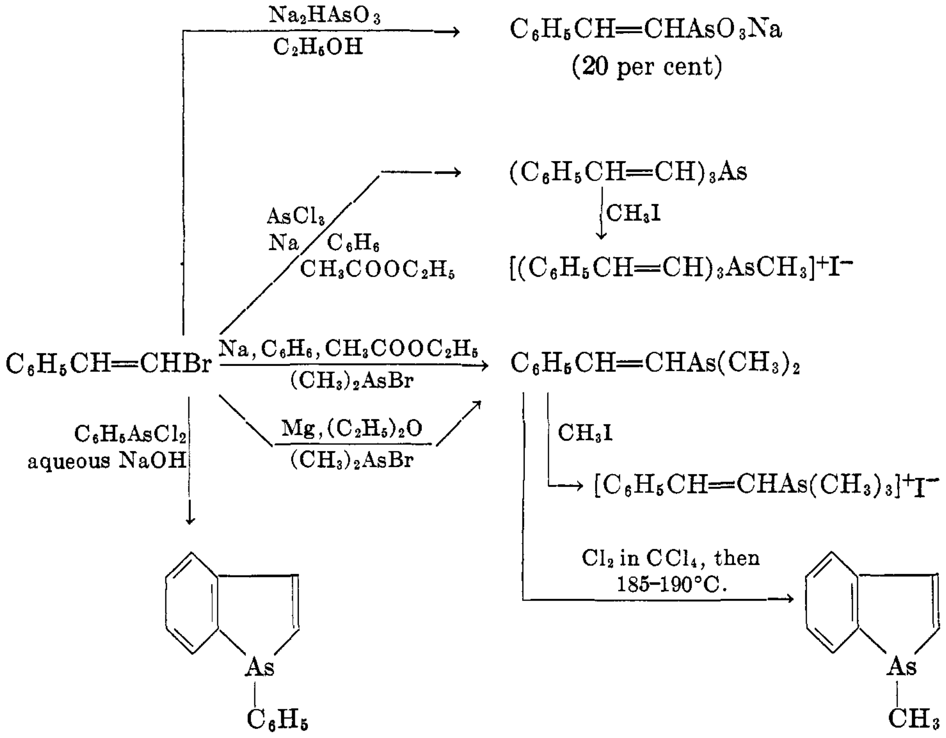


TABLE 41

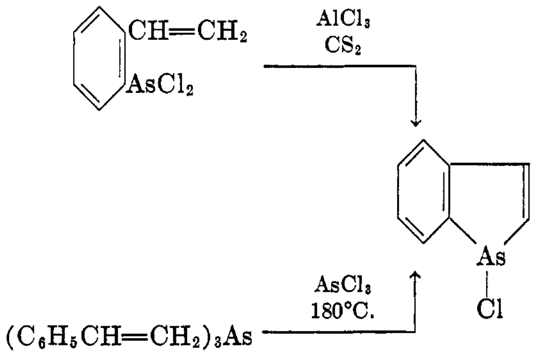
β-Styrenephosphonic acids

β-STYRENEPHOSPHONIC ACID	YIELD
	per cent
2,4-Dimethyl	47
2,4,6-Trimethyl	55
p-Ethyl	39
o-*tert*-Butyl	33
p-*tert*-Butyl	47

β-Bromostyrene served as a source of arsenic derivatives, as shown by the following equations (153):



o-Vinylphenyldichloroarsine was cyclized by treatment with aluminum chloride in carbon disulfide (151, 152). The same product was obtained by treating tristyrylarsine with arsenic trichloride at 180°C. (153).

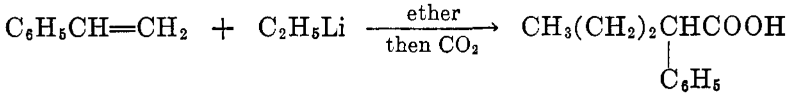


While β-bromostyrene gave a color with antimony trichloride in chloroform, styrene itself did not (646).

XIII. CHEMISTRY INVOLVING METALS

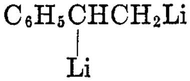
A. Alkali metals

When styrene was treated with ethyllithium in anhydrous ether followed by carbonation, a 1.7 per cent yield of α-phenylvaleric acid was obtained (261).



$$C_6H_5CH{=}CH_2 + C_2H_5Li \xrightarrow[\text{then } CO_2]{\text{ether}} CH_3(CH_2)_2\underset{\displaystyle C_6H_5}{\underset{|}{C}}HCOOH$$

A metal adduct has been postulated as the intermediate in the reduction of styrene by lithium or sodium and secondary amines in ether solution (806a).



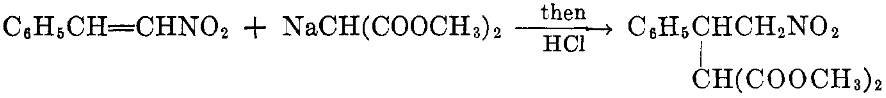
$$C_6H_5\underset{\displaystyle Li}{\underset{|}{C}}HCH_2Li$$

The reactions of β-chlorostyrene and β-bromostyrene with phenyllithium and with butyllithium have been considered in connection with those compounds.

β-Styryllithium, from β-bromostyrene and lithium, has been discussed in the section on β-bromostyrene chemistry.

In ether styrene was polymerized almost entirely by sodium (654). In liquid ammonia about 50 per cent of ethylbenzene was isolated along with polystyrene (787). The reactions of β-bromostyrene, styrene dibromide, α-chlorostyrene, and *p*-methyl-α-chlorostyrene with sodium in liquid ammonia have been discussed in connection with those compounds. Carbonation of the reaction product between α-bromostyrene and sodium gave a mixture of cinnamic and β-phenylpropionic acids (722).

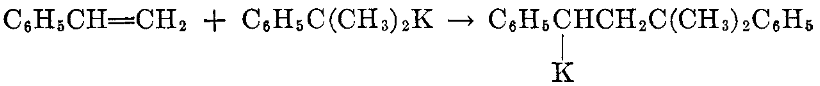
Early investigators reported that sodiomalonic ester polymerized both styrene (293, 767) and β-nitrostyrene (293). Later, an 80 per cent yield of addition product was obtained with β-nitrostyrene (399).



$$C_6H_5CH{=}CHNO_2 + NaCH(COOCH_3)_2 \xrightarrow[HCl]{then} C_6H_5\underset{\substack{|\\ CH(COOCH_3)_2}}{C}HCH_2NO_2$$

β-Bromostyrene did not react with the sodium derivatives of ethyl malonate, ethyl acetoacetate, or ethyl cyanoacetate (452).

Styrene reacted with potassium cumene to give the addition product shown below (805). This in turn added more styrene, depending on the ratio of the reactants in the reaction mixture.



$$C_6H_5CH{=}CH_2 + C_6H_5C(CH_3)_2K \rightarrow C_6H_5\underset{\substack{|\\ K}}{C}HCH_2C(CH_3)_2C_6H_5$$

B. Magnesium

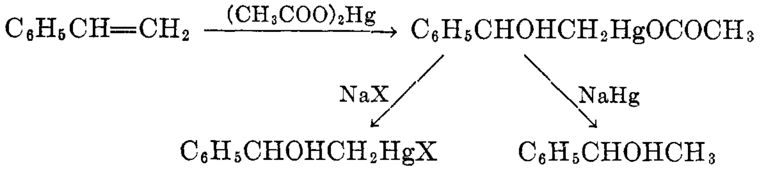
While it was reported originally that styrene reacted with phenylmagnesium bromide (144), it has been shown since that no reaction occurs with this reagent (536) even in boiling xylene (387). Ethylmagnesium iodide (536), methylmagnesium iodide (536), benzylmagnesium chloride (264), and triphenylmethylmagnesium chloride (264) likewise do not react with styrene.

The preparation and reactions of styrylmagnesium bromide have been discussed in detail in connection with the source material, β-bromostyrene.

While styrene did not react with ethylstrontium, with ethylbarium there was obtained upon carbonation a 0.6 per cent yield of α-phenylvaleric acid (261).

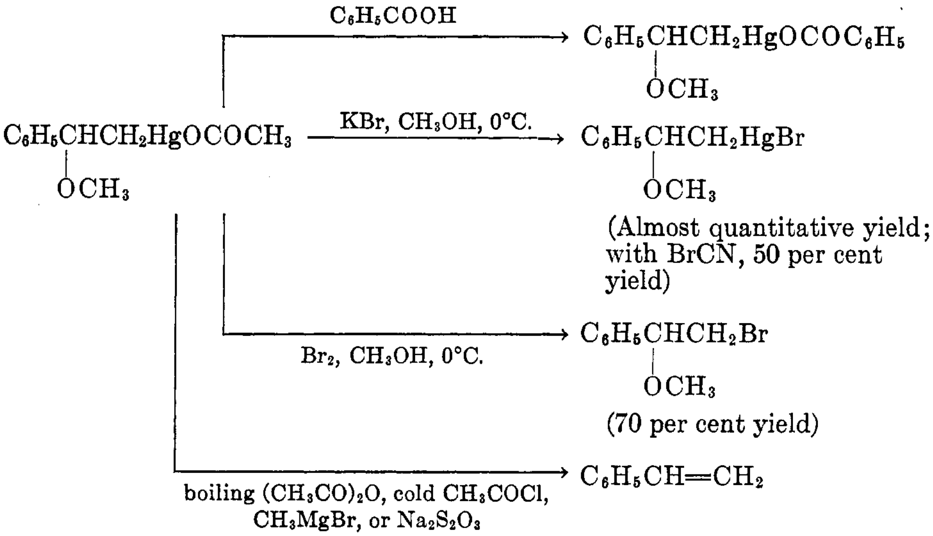
C. Mercury

The addition of mercuric acetate to styrene from aqueous solution was reported long before the structure of the product was established (468, 731). The compound proved to be β-hydroxy-β-phenethylmercuric acetate (534). With sodium chloride or sodium bromide the acetate group was replaced by the halogen in question. Treatment with sodium amalgam gave α-phenethyl alcohol.



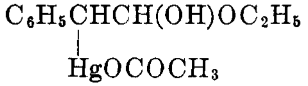
$$\begin{tikzcd} C_6H_5CH{=}CH_2 \arrow[rr, "(CH_3COO)_2Hg"] & & C_6H_5CHOHCH_2HgOCOCH_3 \arrow[dl, "NaX"'] \arrow[dr, "NaHg"] & \\ & C_6H_5CHOHCH_2HgX & & C_6H_5CHOHCH_3 \end{tikzcd}$$

In acetic acid solution styrene reacted with mercuric acetate to give β-acetoxy-β-phenethylmercuric acetate (572). In methanol solution a 60 per cent yield of β-methoxy-β-phenethylmercuric acetate was obtained (796). Some of the reactions of this compound are shown in the following equations:



2,6-Dimethoxystyrene also added mercuric acetate from aqueous solution (667). The product was converted to β-(2,6-dimethoxyphenyl)-β-hydroxyethylmercuric chloride by means of aqueous potassium chloride and then the latter compound was reduced to α-(2,6-dimethoxyphenyl)ethyl alcohol by means of sodium amalgam and water.

β-Ethoxystyrene added mercuric acetate from aqueous solution (467) to give a compound of the following probable structure (534):



$$\underset{\displaystyle \text{HgOCOCH}_3}{C_6H_5\text{CH}}\text{CH(OH)OC}_2H_5$$

Treatment with dilute hydrochloric acid gave phenylacetaldehyde (467).

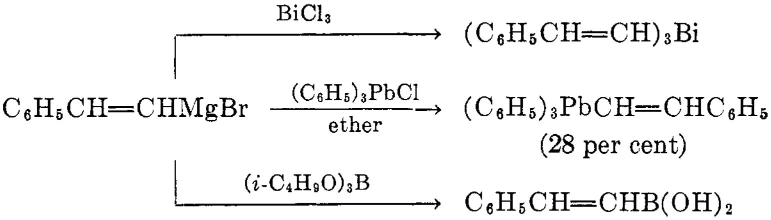
p-Methoxystyrene reacted with mercuric oxide and iodine in moist ether to give p-methoxyphenylacetaldehyde without the appearance of any intermediate iodohydrin or mercury compound (473).

Styrylmercuric chloride has been prepared by treating zinc styrylsulfinate with alcoholic mercuric chloride (373). The bromide was obtained in 36 per cent yield from the reaction between styrylmagnesium bromide and mercuric bromide in ether (797). The compound also was obtained, along with distyrylmercury, from β-bromostyrene and sodium amalgam in a mixture of xylene and ethyl acetate at 140°C. or from β-bromostyrene, mercuric chloride, and sodium in boiling benzene (153). Styrylmercuric bromide reacted with bromine and with iodine in chloroform to give 74 and 79 per cent yields of β-bromostyrene and of β-iodostyrene, respectively (797).

D. Miscellaneous

Styrene formed an addition compound with aluminum chloride (255).

Tristyrylbismuth (216), triphenylstyryllead (265), and styrylboric acid (504) have been prepared from styrylmagnesium bromide. As usual, diphenylbutadiene also was isolated from the reaction mixture (216, 265).

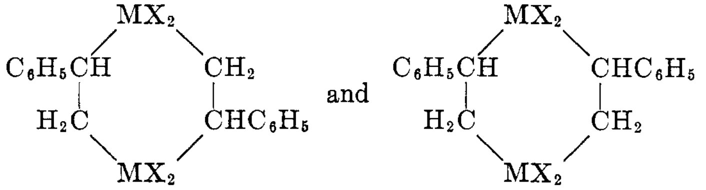


$$C_6H_5CH{=}CHMgBr \xrightarrow{BiCl_3} (C_6H_5CH{=}CH)_3Bi$$

$$C_6H_5CH{=}CHMgBr \xrightarrow[\text{ether}]{(C_6H_5)_3PbCl} (C_6H_5)_3PbCH{=}CHC_6H_5 \quad \text{(28 per cent)}$$

$$C_6H_5CH{=}CHMgBr \xrightarrow{(i\text{-}C_4H_9O)_3B} C_6H_5CH{=}CHB(OH)_2$$

Styrene reacted with the addition compound of benzonitrile and palladous chloride in benzene to give a rather unstable compound $(C_6H_5CH{=}CH_2 \cdot PdCl_2)_2$ (378). Treatment of styrene with platinum tetrachloride or tetrabromide in glacial acetic acid gave similar compounds containing platinous chloride and platinous bromide, respectively (368). It has been suggested that all three of these products are a mixture of the two possible cyclic isomers (368, 378):



The platinous chloride compound also has been prepared by treating the corresponding ethylene adduct with styrene (23).

Styrene replaced ethylene, propylene, and butylene in their complexes with ammonium chloroplatinite (258).

$$NH_4(C_2H_4PtCl_3) + C_8H_8 \rightarrow NH_4(C_8H_8PtCl_3) + C_2H_4$$

Styrene also reacted with metal chloroplatinites to give complexes (257) of the type $K(PtCl_3C_8H_8)$ (23). *Cis* and *trans* forms of the compound $PtC_8H_8NH_3Cl_2$ have been reported (257). While the *cis* form is insoluble in hydrochloric acid, the *trans* form dissolves to give the $NH_4(C_8H_8PtCl_3)$ mentioned above. Thiourea removed the styrene from either form. With ethylene adducts of metallic compounds somewhat more complicated products were obtained (23).

$$C_8H_8 + K[PtCl_3C_2H_4]H_2O \xrightarrow[C_2H_5OH]{\text{heat}} [Pt(NH_3)_4][PtCl_3C_8H_8]$$

XIV. REACTIONS WITH ACID CHLORIDES, ETC.

In the presence of aluminum chloride in toluene solution styrene reacted with phosgene to give β-chlorophenylpropionyl chloride (541).

$$C_6H_5CH{=}CH_2 + COCl_2 \xrightarrow{AlCl_3} C_6H_5CHClCH_2COCl$$

When refluxed for 24 hr. with oxalyl chloride, styrene yielded 9 per cent of cinnamoyl chloride (371).

Both acetyl chloride (432) and malonyl chloride (766) in the presence of stannic chloride gave the same type of addition product as was obtained with phosgene. Both adducts were dehydrohalogenated to the corresponding unsaturated ketones by heating with diethylaniline.

$$2C_6H_5CH{=}CH_2 + CH_2(COCl)_2 \xrightarrow[CS_2]{SnCl_4}$$

$$C_6H_5CHClCH_2COCH_2COCH_2CHClC_6H_5$$

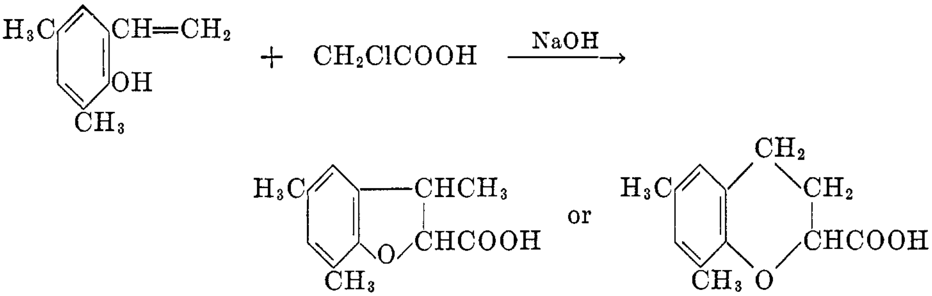
(not isolated)

$$\xrightarrow[180°C.]{C_6H_5N(C_2H_5)_2} C_6H_5CH{=}CHCOCH_2COCH{=}CHC_6H_5$$

With such higher acid chlorides as stearoyl (89 per cent yield), lauroyl, oleoyl, linoleoyl, and linolenoyl in the presence of aluminum chloride, the nucleus was acylated without affecting the vinyl group (591, 592).

In the presence of mercuric chloride methyl α-chlorobenzyl ether added to styrene, but the structure of the product was not determined (715).

3,5-Dimethyl-2-hydroxystyrene reacted with chloroacetic acid in the presence of sodium hydroxide to give a product of undetermined structure (6).



The reactions of α-methoxystyrene with acid chlorides and other halogen compounds have been discussed in connection with the chemistry of α-alkoxystyrenes.

When a carbon tetrachloride solution of styrene and carbon tetrabromide was irradiated with white light, a nearly quantitative yield of 1,1,1,3-tetrabromo-3-phenylpropane was obtained (370).

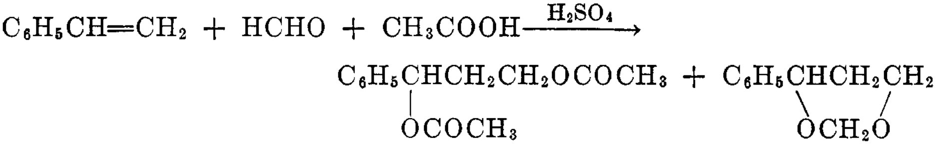
$$C_6H_5CH{=}CH_2 + CBr_4 \xrightarrow[CCl_4]{light} C_6H_5CHBrCH_2CBr_3$$

Styrene added bromotrichloromethane under similar conditions (369a).

At 295–305°C. and 33 atm. pressure in the presence of a zinc–copper–chromium oxide catalyst styrene reacted with carbon dioxide to give 0.28 per cent of cinnamic acid (388).

XV. REACTIONS WITH ALDEHYDES

Prins (573, 574, 575, 576) first condensed styrene with formaldehyde by means of a sulfuric acid catalyst in glacial acetic acid solution. The products were 40 per cent of 1-phenyltrimethylene glycol diacetate and some 4-phenyl-1,3-dioxane. Prins and subsequent workers (514) formulated these compounds incorrectly as derivatives of 2-phenyltrimethylene glycol. It was finally shown that the products



$$C_6H_5CH{=}CH_2 + HCHO + CH_3COOH \xrightarrow{H_2SO_4} C_6H_5\underset{\underset{\displaystyle OCOCH_3}{|}}{C}HCH_2CH_2OCOCH_3 + C_6H_5\underbrace{CHCH_2CH_2}_{\diagdown\ OCH_2O\ \diagup}$$

were really derivatives of 1-phenyltrimethylene glycol (230, 231), and the yields were raised to 48 per cent for the glycol diacetate and 30 per cent for the dioxane. The proof of structure consisted in preparing the dibenzoate of the glycol and showing it to be identical with that of the glycol obtained by the reduction of methylolacetophenone.

TABLE 42

Styrene and aldehydes

ALDEHYDE USED	R	R′	STYRENE RECOVERED	$C_6H_5CH{=}CHCH{=}CRR'$	$C_6H_5CHCH_2CHCHRR'$ O—CH—O CHRR′	GLYCOL MONOACETATE
			per cent	*per cent*	*per cent*	*per cent*
Acetaldehyde.....	H	H	5	32	18	12 (di)
Propionaldehyde .	H	CH_3	18	8	10	26
n-Butyraldehyde .	H	C_2H_5	23	14	0	39
Isobutyraldehyde.	CH_3	CH_3	14	23	13	13

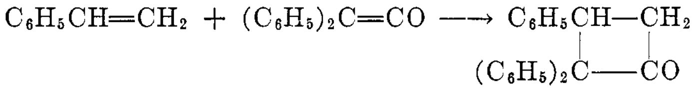
With higher aldehydes the products were the dioxane, the substituted trimethylene glycol monoacetate (with acetaldehyde mostly the diacetate), and the substituted phenylbutadiene corresponding to the loss of two moles of water from the glycol (190). These products are summarized in table 42.

In the presence of hydrochloric acid styrene reacted with formaldehyde to give only 4-phenyl-1,3-dioxane (198). Styrene polymerized when an aldehyde condensation was attempted in the presence of light or peroxides (369a).

XVI. ADDITION REACTIONS

When the vapors of styrene and ethylene or acetylene were passed through a hot tube, benzene and naphthalene were produced (75, 79). Similarly from styrene and benzene, anthracene and some naphthalene were obtained. With tetrafluoroethylene styrene yielded 85 per cent of 1-phenyl-2,2,3,3-tetrafluorocyclobutane (141a).

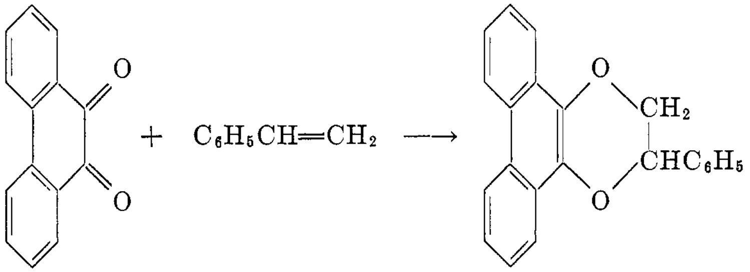
Styrene added diphenylketene to give a 93 per cent yield (706) of a triphenylcyclobutanone (65, 705).



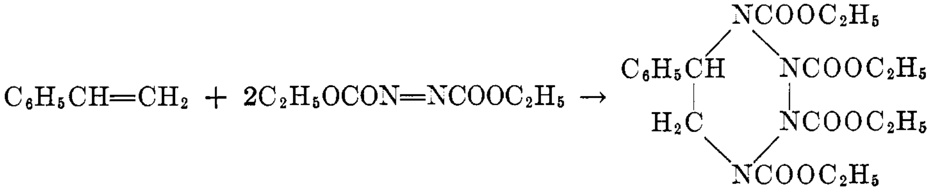
$$C_6H_5CH{=}CH_2 + (C_6H_5)_2C{=}CO \longrightarrow \begin{array}{rcl} C_6H_5CH & - & CH_2 \\ | & & | \\ (C_6H_5)_2C & - & CO \end{array}$$

The reaction was postulated originally as proceeding in the reverse fashion (706), but subsequent work showed the phenyl groups to be on adjacent carbon atoms (705). The addition of diphenylketene also was observed in the case of the following styrenes: *p*-methyl- (81 per cent yield), *p*-chloro- (82 per cent yield), and *p*-methoxy- (84 per cent yield) (706).

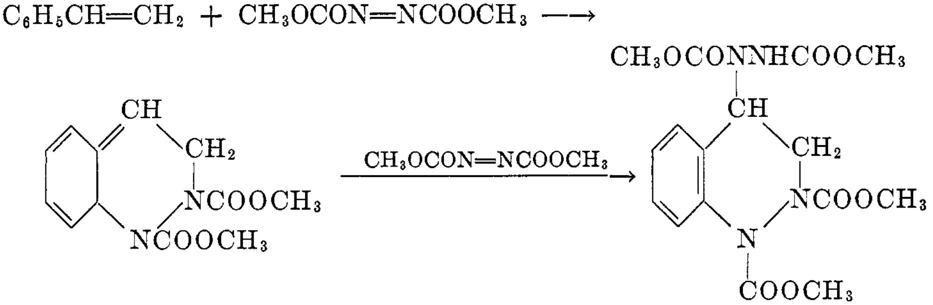
When exposed to sunlight in thiophene-free benzene solution, styrene added phenanthrenequinone (659, 660).



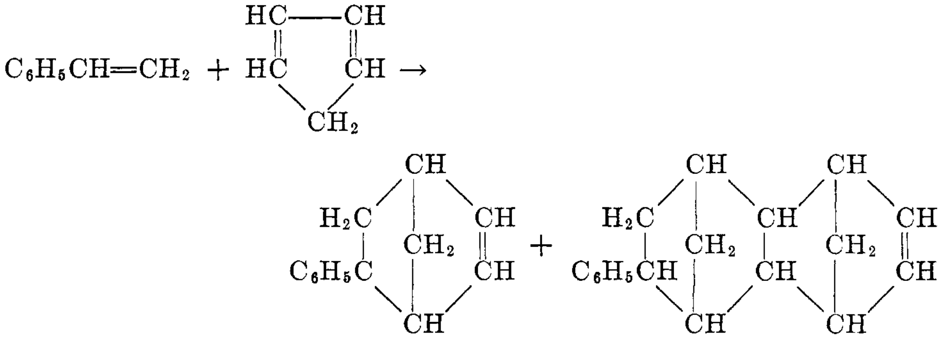
Styrene reacted with methyl acetylenedicarboxylate to give a compound of unknown structure (9). The product with ethyl azodicarboxylate was formulated as a ring compound containing four nitrogen atoms (348).



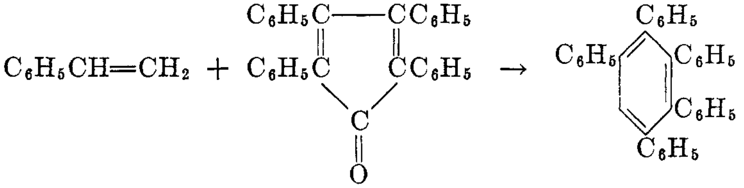
With the methyl ester the product, obtained in quantitative yield, was formulated as involving condensation with the benzene ring (162).



Styrene readily serves as the olefinic component in the Diels–Alder reaction. Such diolefins were added as butadiene (33 per cent yield), 2,3-dimethylbutadiene (38 per cent yield), cyclopentadiene (10 per cent yield) (10), 2,5-diphenylisobenzofuran, and 2,5-diphenyliso(3′,4′-dimethyl)benzofuran (16). In the case of cyclopentadiene 12 per cent of the product containing two moles of cyclopentadiene also was obtained.



With tetraphenylcyclopentadienone (1a) and 2,5-diphenyl-3,4-bis(3′,4′-methylenedioxy)phenylcyclopentadienone (27) the carbonyl bridge was lost.



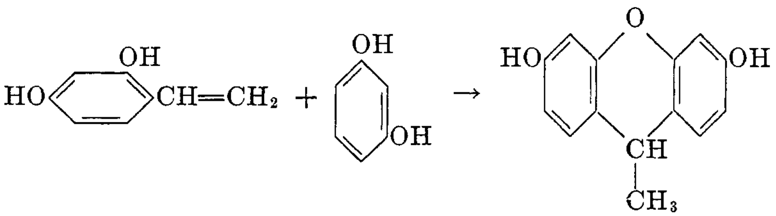
Styrene did not react with quinone (751).

The diene addition reactions of β-nitrostyrene are summarized in table 43.

XVII. CONDENSATION REACTIONS

In the presence of acid catalysts styrene reacts with aromatic compounds, particularly with those possessing reactive nuclei, to give products of the type $C_6H_5CHRCH_3$, where R is the aryl nucleus in question. These reactions are summarized in table 44.

2,4-Dihydroxystyrene reacted with resorcinol to give 10 per cent of an adduct which also had lost water (223).



The reactions of α-methoxystyrene with various hydrocarbons have been discussed in connection with α-alkoxystyrenes.

XVIII. REACTIONS NOT INVOLVING THE VINYL GROUP

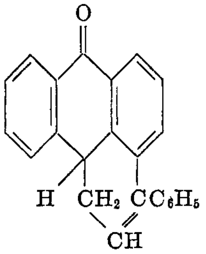
The preceding seventeen sections have been devoted to reactions occurring at the double bonds in the various styrenes considered. Section XVIII is concerned with reactions of other parts of the molecule during the course of which the double bond remains intact.

TABLE 43

β-Nitrostyrene and dienes

DIENE ADDED	YIELD	REFERENCE
	per cent	
Butadiene	70	(16)
Isoprene	58	(16)
2,3-Dimethylbutadiene	82	(15, 16)
2,3-Diphenylbutadiene	9	(15, 16)
1,4-Diphenylbutadiene	80	(16)
Cyclopentadiene	95	(15, 16)
Cyclohexadiene	20–25	(15, 16)
Phellandrene	45	(15, 16)
1,1′-Bicyclohexenyl	95	(69)
Methyleneanthrone*	3	(15, 16)
2,5-Diphenylisobenzofuran	Quantitative	(16)
2,5-Diphenyliso(3′,4′-dimethyl)benzofuran	Quantitative	(16)
Furan	0	(16)
Sylvan	0	(16)
2,5-Dimethylfuran	0	(16)

* In this reaction the principal product (25 per cent yield) was that in which nitrous acid had been lost:



Similarly with tetraphenylcyclopentadienone only pentaphenylbenzene was isolated (15, 16).

Phenolic hydroxyl groups undergo a variety of reactions which do not affect vinyl groups in the same molecule. The following styrenes have been acetylated by means of acetic anhydride: 3-methoxy-4-hydroxy- (249), 2,4-dihydroxy- (223), 2-hydroxy-3,5-dibromo- (248), 2-hydroxy-β,3,5-tribromo- (248), 4-hy-

TABLE 44

Condensation reactions of styrene

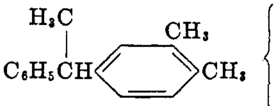
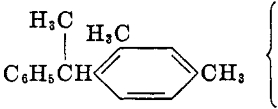
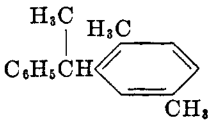
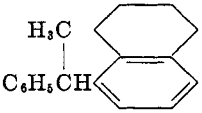
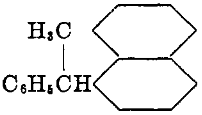
AROMATIC COMPOUND	CATALYST	TEMPERATURE	PRODUCT	YIELD	REFERENCE
		°C.		per cent	
Benzene	$AlCl_3$	25	$(C_6H_5)_2CHCH_3$	5	(533)
	93% H_2SO_4	30–35	$(C_6H_5)_2CHCH_3$	25	(702)
Toluene	H_2SO_4		Structure not given	46	(417, 418)
	93% H_2SO_4		Structure not given		(702)
o-Xylene	H_2SO_4			66	(417, 418)
	93% H_2SO_4				(702)
m-Xylene	H_2SO_4			63	(417, 418)
	93% H_2SO_4				(702)
p-Xylene	H_2SO_4				(417, 418)
	93% H_2SO_4				(702)
Pseudocumene	H_2SO_4		Structure not given	65	(417, 418)
Xylene	H_2SO_4		Structure not given		(416)
Naphthalene	Cerium metaphosphate	380	Reddish oil		(323)
Tetralin	H_2SO_4				(114)
	93% H_2SO_4		Structure not given		(702)
Decalin	93% H_2SO_4	30–35		52	(702)
Hydrindene	93% H_2SO_4		Structure not given		(702)
Anisole	Bleaching earth		Resin and oil		(326)
Glycol monophenyl ether	Bleaching earth		Resin and oil		(326)
Diphenyl ether	Retrol	270	Monocondensation product	26	(685)
			Polycondensation product		

TABLE 44—*Continued*

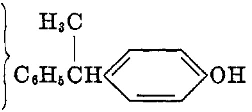
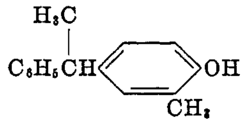
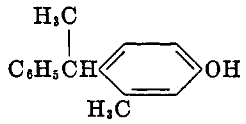
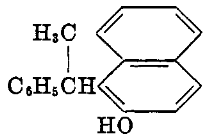
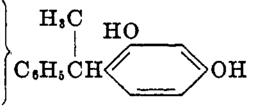
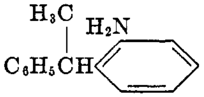
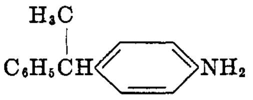
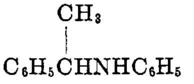
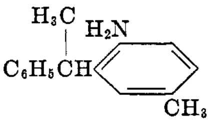
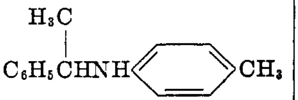
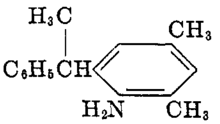
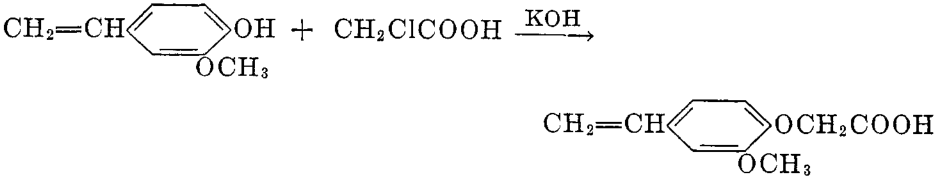
AROMATIC COMPOUND	CATALYST	TEMPERATURE	PRODUCT	YIELD	REFERENCE
		°C.		*per cent*	
o-Phenoxybiphenyl	Retrol	270	Monocondensation product Polycondensation product	26	(685)
Phenol	H_2SO_4		Mono-, di-, and poly-condensation products		(769)
	Bleaching earth	90	Resin and oil		(326)
	H_2SO_4, CH_3COOH			40	(396, 397)
	HCl			65	(544)
	HI				(711)
o-Cresol	HI				(397)
m-Cresol	HI			32	(397)
	Bleaching earth		Resin and oil		(326)
p-Cresol	H_2SO_4, CH_3COOH		None		(397)
α-Naphthol	H_2SO_4, CH_3COOH		None		(397)
β-Naphthol	H_2SO_4, CH_3COOH				(397)
Resorcinol	H_2SO_4, CH_3COOH				(396)
	$HClO_4$, CH_3COOH			51	(653)

TABLE 44—*Concluded*

AROMATIC COMPOUND	CATALYST	TEMPERATURE	PRODUCT	YIELD	REFERENCE
		°C.		*per cent*	
Aniline	Aniline hydrochloride	200–240		8	(299)
				18	
			 $C_6H_5\overset{\overset{CH_3}{\vert}}{C}HNHC_6H_5$	3	
p-Toluidine	*p*-Toluidine hydrochloride	260–270		14	(299)
				3	
2,4-Xylidine	2,4-Xylidine hydrochloride	255–290		4	(299)

droxy-2,3,5-tribromo- (816), 4-hydroxy-β,2,3,5-tetrabromo- (816), and 4-hydroxy-β,2,3,5,6-pentabromo- (816). 3-Methoxy-4-hydroxystyrene also yielded a carbonate on treatment with phosgene (249, 610), a benzoate by the Schotten–Baumann procedure (249, 610), a *p*-nitrobenzoate (610), and a 3,5-dinitrobenzoate (561). *m*-Hydroxystyrene was benzoylated by the Schotten–Baumann procedure (404).

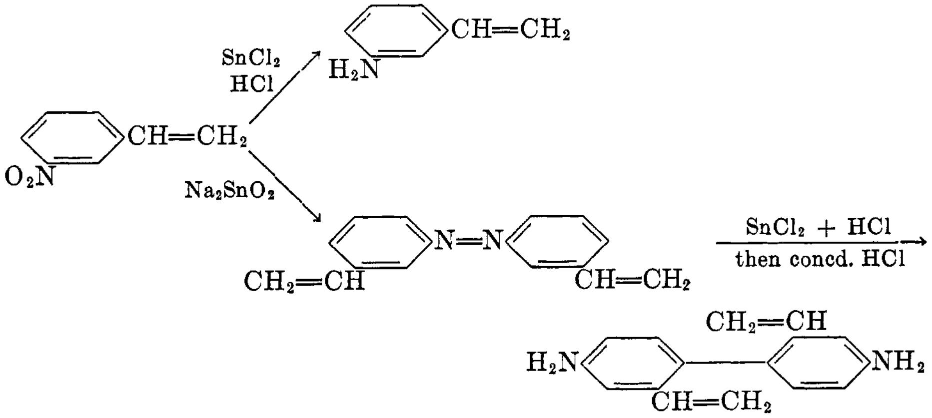
Phenoxyacetic acids have been prepared from the following substituted styrenes by treatment with chloro- or bromo-acetic acids in the presence of alkali: *o*-hydroxy- (686), 2-hydroxy-5-methyl- (6), and 3-methoxy-4-hydroxy- (249, 610).



Treatment of 3-methoxy-4-hydroxystyrene with methyl iodide and sodium hydroxide gave the methyl ether (249, 610).

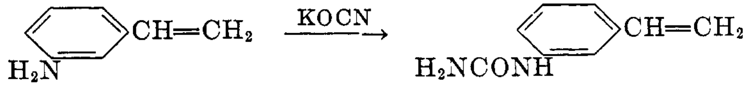
The phenylurethan of 3-hydroxy-4-ethoxystyrene has been prepared (359). Hydrolysis of *p*-vinylbenzyl acetate with alcoholic potassium hydroxide yielded 38 per cent of *p*-vinylbenzyl alcohol (197a).

The *o*-, *m*-, and *p*-aminostyrenes (404, 557) as well as *o*-amino-β-chloro- (404, 405, 453, 504) and *o*-amino-β-bromo-styrenes (404) have all been prepared by reducing the corresponding nitrostyrene with stannous chloride and hydrochloric acid. *m*-Nitrostyrene was reduced to 3,3′-divinylazobenzene in 69 per cent yield by means of sodium stannite and the latter compound converted to 2,2′-divinylbenzidine in 25 per cent yield by means of stannous chloride and hydrochloric acid followed by concentrated hydrochloric acid (404).

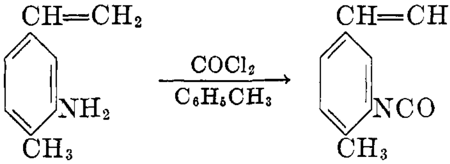


In a more recent investigation (778c) only polymer could be obtained when *m*-nitrostyrene was treated with zinc and hydrochloric acid or with stannous chloride. With sodium methoxide or zinc and ammonium chloride *m*-nitrostyrene yielded 3,3′-divinylazoxybenzene. Reduction of *m*-nitrostyrene with zinc and alcoholic sodium hydroxide gave 3,3′-divinylhydrazobenzene. This latter compound was oxidized to 3,3′-divinylazobenzene by means of alcoholic ferric chloride, sodium hypobromite, or air and sodium hydroxide. With concentrated hydrochloric acid in ether 3,3′-divinylhydrazobenzene yielded 30 per cent of 2,2′-divinylbenzidine.

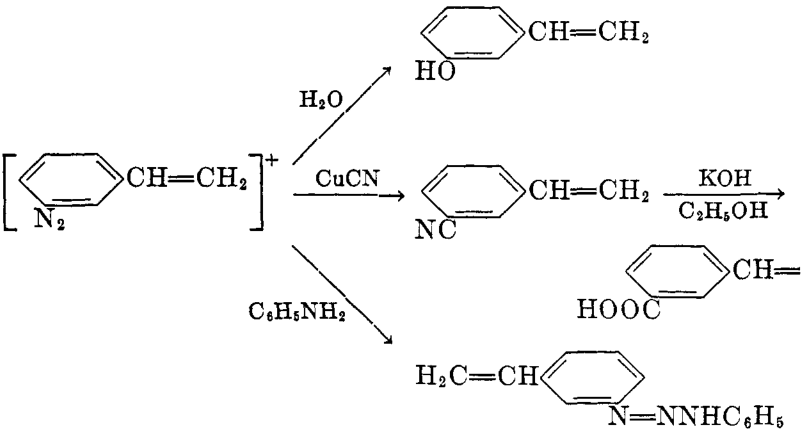
Acetamides have been prepared from the following styrenes by treatment with acetic anhydride: *o*-amino- (404), *m*-amino- (75 per cent yield) (404), *p*-amino- (404), and *o*-amino-β-chloro- (404, 405). Benzamides have been prepared from the following styrenes by treatment with benzoyl chloride in the presence of alkali: *m*-amino- (404, 758) and *p*-amino- (404). *m*-Aminostyrene also reacted with potassium cyanate to give a substituted urea (404).



Treatment of a mixture of *m*- and *p*-aminostyrenes with phosgene in toluene yielded 71 per cent of the corresponding isocyanates (419a). 2-Methyl-5-vinylphenylisocyanate was prepared by the same method in 31 per cent yield.

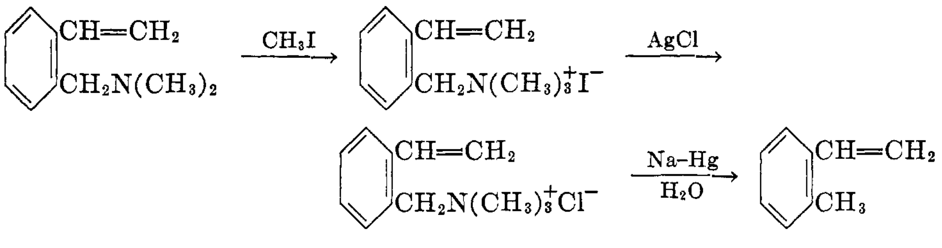


While the diazotization of *o*-aminostyrene gave impure *o*-hydroxystyrene (557), a 39 per cent yield of *o*-hydroxy-β-chlorostyrene was obtained from the diazotization of *o*-amino-β-chlorostyrene (404, 405). The diazotization of *p*-aminostyrene gave only tar (71, 404, 557). On the other hand *m*-aminostyrene gave a stable diazonium salt (404). Treatment with steam gave a 69 per cent yield of *m*-hydroxystyrene, with cuprous cyanide *m*-cyanostyrene, and with aniline *m*-vinyldiazoaminobenzene. The *m*-cyanostyrene was hydrolyzed to *m*-carboxystyrene by boiling with alcoholic potassium hydroxide.

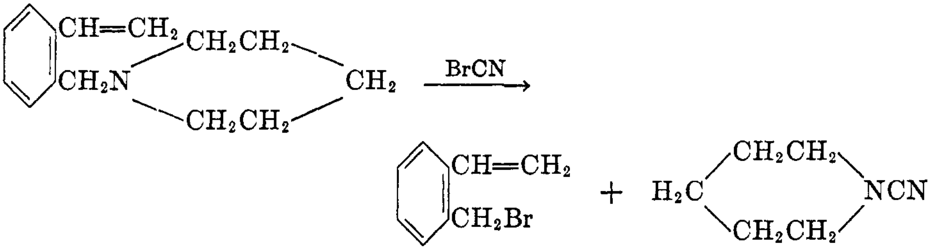


2,2′-Divinylbenzidine also has been diazotized and coupled.

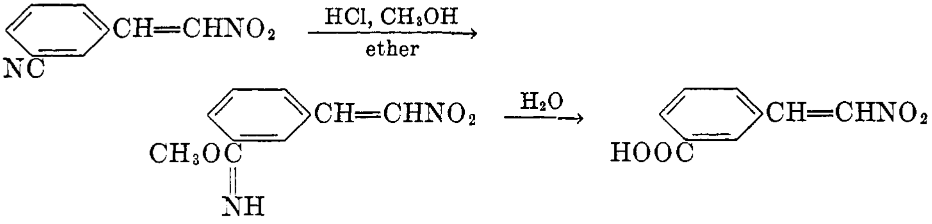
Both *o*-dimethylaminomethyl- (109, 188) and *o*-(β-dimethylaminoethyl)-styrenes (116) readily add methyl iodide to give quaternary salts. The iodide from dimethylaminomethylstyrene was converted to the chloride with silver chloride and this latter compound was reduced to *o*-methylstyrene by means of sodium amalgam and water (188).



Treatment of *o*-dimethylaminomethyl- (50 per cent yield) (110), *o*-piperidinomethyl- (109), and *o*-pyrrolidinomethyl-styrenes (109) with cyanogen bromide gave *o*-bromomethylstyrene and the corresponding cyanamide.

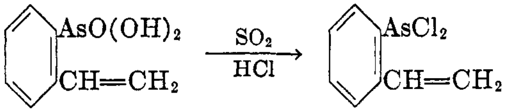


m-Cyano-β-nitrostyrene was converted to the imino methyl ether in 28 per cent yield by means of hydrogen chloride and methanol in ether (682). This compound was hydrolyzed with water to give a small amount of *m*-carboxy-β-nitrostyrene.



p-Vinylbenzaldehyde formed a phenylhydrazone and was oxidized by means of silver oxide to a 75 per cent yield of *p*-vinylbenzoic acid (778a).

o-Vinylphenylarsonic acid was converted to *o*-vinylphenyldichloroarsine by treatment with sulfur dioxide and hydrogen chloride (151, 152).



XIX. REFERENCES[2]

(1) Abel: Ber. **36,** 1839 (1903).
(1a) Abramov and Mitropolitanskaya: J. Gen. Chem. (U.S.S.R.) **10,** 207 (1940); Chem. Abstracts **34,** 7284 (1940).
(2) Abrams and Kipping: J. Chem. Soc. **1934,** 1988.
(3) Adams, Hyde, and Browning: J. Am. Chem. Soc. **50,** 2287 (1928).
(4) Adams and Theobald: J. Am. Chem. Soc. **65,** 2208 (1943).
(5) Adams and Theobald: J. Am. Chem. Soc. **65,** 2383 (1943).
(6) Adler, Euler, and Gie: Arkiv Kemi, Mineral. Geol. **16A,** No. 12 (1942).
(7) Ainley and Robinson: J. Chem. Soc. **1937,** 369.
(8) Alberts and Bachman: J. Am. Chem. Soc. **57,** 1284 (1935).
(9) Alder, Pascher, and Vagt: Ber. **75,** 1501 (1942).

---

[2] The abstract reference is included for all patents and for all articles which were read in abstract instead of in the original.

(10) ALDER AND RICKERT: Ber. **71,** 379 (1938).
(11) ALDRICH: J. Am. Chem. Soc. **27,** 1074 (1905).
(12) ALESSANDRI: Gazz. chim. ital. **54,** 426 (1924); Chem. Zentr. **1924, II,** 1082.
(13) ALEXEYEV: Ber. **6,** 1209 (1873).
(14) ALIMCHANDANI AND MELDRUM: J. Chem. Soc. **119,** 201 (1921).
(15) ALLEN AND BELL: J. Am. Chem. Soc. **61,** 521 (1939).
(16) ALLEN, BELL, AND GATES: J. Org. Chem. **8,** 373 (1943).
(17) ALLEN AND WILSON: J. Org. Chem. **5,** 146 (1940).
(18) ALLES: U.S. patent 1,931,123; Chem. Abstracts **28,** 180 (1934).
(19) ALLES AND KNOEFEL: Arch. intern. pharmacodynamie **47,** 96 (1934).
(20) ALLEWELT AND DAY: J. Org. Chem. **6,** 384 (1941).
(21) ALQUIST AND GUSS: U.S. patent 2,237,284; Chem. Abstracts **35,** 4398 (1941).
(22) ANANTAKRISHNAN AND INGOLD: J. Chem. Soc. **1935,** 1396.
(23) ANDERSON: J. Chem. Soc. **1936,** 1024.
(24) ANDREYEVSKII: J. Russ. Phys. Chem. Soc. **40,** 770 (1908); Chem. Zentr. **1908, II,** 1434.
(25) ANSCHUTZ: Ann. **235,** 150 (1886).
(26) ANSCHUTZ: Ann. **235,** 299 (1886).
(27) ARBUZOV AND AKHMED-ZADE: J. Gen. Chem. (U.S.S.R.) **12,** 212 (1942); Chem. Abstracts **37,** 2733 (1943).
(28) ARDIS, BALTZLY, AND SCHOEN: J. Am. Chem. Soc. **68,** 591 (1946).
(29) ARNDT, EISTERT, AND PARTALE: Ber. **61,** 1107 (1928).
(30) ARNDT AND PARTALE: Ber. **60,** 446 (1927).
(31) ASHWORTH AND BURKHARDT: J. Chem. Soc. **1928,** 1791.
(32) v. AUWERS: Ber. **44,** 788 (1911).
(33) v. AUWERS: Ber. **44,** 3514 (1911).
(34) v. AUWERS: Ber. **45,** 2781 (1912).
(35) v. AUWERS: BER. **68,** 1346 (1935).
(36) v. AUWERS AND EISENLOHR: J. prakt. Chem. [2] **82,** 65 (1910); Chem. Zentr. **1910, II,** 721.
(37) v. AUWERS AND HESSENLAND: Ann. **352,** 273 (1907).
(38) v. AUWERS AND JULICHER: Ber. **55,** 2167 (1922).
(39) v. AUWERS AND KEIL: Ber. **36,** 1861 (1903).
(40) v. AUWERS AND KEIL: Ber. **36,** 3902 (1903).
(41) v. AUWERS AND KOCKRITZ: Ann. **352,** 288 (1907).
(42) v. AUWERS AND ZIEGLER: Ann. **425,** 280 (1921).
(43) BACHMAN AND LEWIS: J. Am. Chem. Soc. **69,** 2022 (1947).
(44) BAGCHEE, GAIND, AND RAY: J. Chem. Soc. **1938,** 657.
(45) BAKER: J. Chem. Soc. **1931,** 2416.
(46) BAKER AND WILSON: J. Chem. Soc. **1927,** 845.
(47) BALLA: Compt. rend. **198,** 947 (1934); Chem. Abstracts **28,** 3402 (1934).
(48) BALTZLY AND BUCK: J. Am. Chem. Soc. **62,** 164 (1940).
(49) BALTZLY AND BUCK: J. Am. Chem. Soc. **65,** 1984 (1943).
(50) BANUS AND VILA: Anales soc. españ. fís. y quím. **20,** 689 (1922); Chem. Zentr. **1923, III,** 1074.
(51) BARGER: J. Chem. Soc. **93,** 2081 (1908).
(52) BARGER, EISENBRAND, EISENBRAND, AND SCHLITTLER: Ber. **66,** 450 (1933).
(53) BARGER AND EWINS: J. Chem. Soc. **93,** 2086 (1908).
(54) BARGER AND JOWETT: J. Chem. Soc. **87,** 967 (1905).
(55) BARISH: J. prakt. Chem. [2] **20,** 173 (1879); Ber. **12,** 2020 (1879).
(56) BASLER: Ber. **16,** 3001 (1883).
(57) BAUMANN AND FROMM: Ber. **28,** 890 (1895).
(58) BAYER AND Co.: German patent 245,523; Frdl. **10,** 1192.
(59) BAYER AND Co.: German patent 254,861; Frdl. **11,** 1006.
(59a) BEER, CLARKE, KHORANA, AND ROBERTSON: J. Chem. Soc. **1948,** 1605.

(60) Behal: Bull. soc. chim. [2] **50,** 632 (1888); Ber. **22R,** 143 (1889).

(61) Behal: Ann. chim. [7] **20,** 425 (1900): Chem. Zentr. **1900, II,** 313.

(62) Benoit: Bull. soc. chim. [5] **6,** 708 (1939).

(63) Benoit and Herzog: Bull. sci. pharmacol. **42,** 34, 102 (1935); Chem. Zentr. **1936, II,** 4208.

(64) Bergel and Morrison: J. Chem. Soc. **1943,** 48.

(65) Bergmann and Blum-Bergmann: J. Chem. Soc. **1938,** 727.

(66) Bergmann and Bondi: Ber. **63,** 1158 (1930).

(67) Bergmann and Bondi: Ber. **66,** 278 (1933).

(68) Bergmann and Bondi: Ber. **66,** 286 (1933).

(69) Bergmann, Eschinazi, and Neeman: J. Org. Chem. **8,** 179 (1943).

(70) Bergmann and Schutz: Z. physik. Chem. **B19,** 395 (1932).

(71) Bernthsen and Bender: Ber. **15,** 1982 (1882).

(72) Berthelot: Bull. soc. chim. [2] **6,** 289 (1866).

(73) Berthelot: Ann. chim. [4] **9,** 466 (1866).

(74) Berthelot: Compt. rend. **64,** 786 (1867).

(75) Berthelot: Bull. soc. chim. [2] **7,** 274 (1867).

(76) Berthelot: Bull. soc. chim. [2] **7,** 303 (1867).

(77) Berthelot: Bull. soc. chim. [2] **7,** 310 (1867).

(78) Berthelot: Ann. **141,** 180 (1867).

(79) Berthelot: Ann. **142,** 251, 259 (1867).

(80) Berthelot: Compt. rend. **67,** 327 (1868).

(81) Berthelot: Compt. rend. **67,** 846 (1868).

(82) Berthelot: Bull. soc. chim. [2] **9,** 265 (1868).

(83) Bhatnagar, Chopra, Narang, and Ray: J. Indian Chem. Soc. **14,** 344 (1937).

(84) Biltz: Ann. **296,** 219 (1897).

(85) Biltz: Ann. **296,** 263 (1897).

(86) Biltz: Ber. **35,** 1528 (1902).

(87) Blyth and Hofmann: Ann. **53,** 289 (1845).

(88) Bock, Lock, and Schmidt: Monatsh. **64,** 399 (1934); Chem. Abstracts. **29,** 1405 (1935).

(89) Bockemuller and Pfeüffer: Ann. **537,** 178 (1939).

(90) Bodroux: Compt. rend. **208,** 1022 (1939);

(91) Böeseken and Bastet: Rec. trav. chim. **32,** 184 (1913); Chem. Zentr. **1914, I,** 647.

(92) Böeseken and Blumberger: Rec. trav. chim. **44,** 96 (1925).

(93) Böeseken and Derx: Rec. trav. chim. **40,** 519 (1921); Chem. Zentr. **1922, III,** 549.

(94) Böeseken and de Graaff: Rec. trav. chim. **41,** 199 (1922); Chem. Zentr. **1922, III,** 46.

(95) Böeseken and Kremer: Rec. trav. chim. **50,** 827 (1931); Chem. Abstracts **25,** 4867 (1931).

(96) Böeseken and Soesman: Rec. trav. chim. **52,** 874 (1933); Chem. Abstracts **28,** 4047 (1934).

(97) Böeseken and Stuurmann: Rec. trav. chim. **56,** 1034 (1939).

(97a) Bordwell and Rondestvedt: J. Am. Chem. Soc. **70,** 2429 (1948).

(98) Bordwell, Suter, Holbert, and Rondestvedt: J. Am. Chem. Soc. **68,** 139 (1946).

(99) Borsche and Heimburger: Ber. **48,** 452 (1915).

(100) Bottcher: Ber. **42,** 253 (1909).

(101) Bougault: Compt. rend. **131,** 528 (1900).

(102) Bourguel: Compt. rend. **176,** 751 (1923).

(103) Bourguel: Compt. rend. **178,** 1557 (1924).

(104) Bourguel: Bull. soc. chim. [4] **35,** 1629 (1924).

(105) Bourguel: Ann. chim. [10] **3,** 191 (1925).

(106) Bouveault and Wahl: Compt. rend. **134,** 1145 (1902).

(107) Bouveault and Wahl: Compt. rend. **135,** 41 (1902).

(108) Bouveault and Wahl: Bull. soc. chim. [3] **29,** 519 (1903).

(109) v. Braun: Ber. **49,** 2629 (1916).

(110) v. BRAUN: Ber. **50,** 45 (1917).
(111) v. BRAUN AND BLESSING: Ber. **56,** 2153 (1923).
(112) v. BRAUN AND ENGEL: Ber. **58,** 281 (1925).
(113) v. BRAUN, KARPF, AND GARN: Ber. **53,** 98 (1920).
(114) v. BRAUN AND KIRSCHBAUM: Ber. **54,** 597 (1921).
(115) v. BRAUN AND MOLDÄNKE: Ber. **54,** 618 (1921).
(116) v. BRAUN AND NEUMANN: Ber. **53,** 109 (1920).
(117) BRENECK AND MULLER: Ber. **75,** 554 (1942).
(118) BRETSCHNEIDER: Monatsh. **76,** 355 (1947).
(119) BRETSCHNEIDER: Monatsh. **76,** 368 (1947).
(120) BREUER AND ZINCKE: Ber. **11,** 1399 (1878).
(121) BREUER AND ZINCKE: Ber. **11,** 1403 (1878).
(122) BRINER AND GELBERT: Helv. Chim. Acta **22,** 1483 (1939).
(123) BRINER, GELBERT, AND PERROTTET: Helv. Chim. Acta **22,** 1491 (1939).
(124) BROWN, KHARASCH, AND SPROWLS: J. Org. Chem. **4,** 442 (1939).
(125) BROWN AND MARVEL: J. Am. Chem. Soc. **59,** 1176 (1937).
(126) BROWN AND ODELL: U. S. patent 1,907,317; Chem. Zentr. **1933, II,** 3192.
(127) BRUS AND PEYRESBLANQUES: Compt. rend. **190,** 685 (1930).
(128) BUCHNER: Ann. **273,** 214 (1893).
(129) BUCHNER AND GERONIMUS: Ber. **36,** 3782 (1903).
(130) BUCK: J. Am. Chem. Soc. **55,** 2593 (1933).
(130a) BUCK: J. Am. Chem. Soc. **55,** 3388 (1933).
(131) VAN DE BUNT: Rec. trav. chim. **48,** 121 (1929).
(131a) BURTON AND DUFFIELD: J. Chem. Soc. **1949,** 78.
(132) BUSCH AND WEBER: J. prakt. Chem. **146,** 1 (1936); Chem. Zentr. **1936, II,** 2883.
(133) CALVET AND MEJUTO: J. Chem. Soc. **1936,** 554.
(134) CARMACK AND DETAR: J. Am. Chem. Soc. **68,** 2029 (1946).
(135) CARTER AND VAN LOON: J. Am. Chem. Soc. **60,** 1077 (1938).
(135a) CHAIKIN AND BROWN: J. Am. Chem. Soc. **71,** 122 (1949).
(136) CHATTAWAY AND CALVET: J. Chem. Soc. **1928,** 2913.
(137) CHATTAWAY AND FARINBOLT: J. Chem. Soc. **1931,** 1828.
(138) CHATTAWAY AND PRATS: J. Chem. Soc. **1927,** 685.
(139) CLAISEN: Ber. **29,** 1005 (1896).
(140) CLAISEN: Ber. **29,** 2931 (1896).
(141) CLAISEN: Ber. **31,** 1020 (1898).
(141a) COFFMAN, BARRICK, CRAMER, AND RAASCH: J. Am. Chem. Soc. **71,** 490 (1949).
(142) COLEMAN AND CAMPBELL: J. Am. Chem. Soc. **50,** 2754 (1928).
(143) COLEMAN, CAMPBELL, AND MULLINS: Proc. Iowa Acad. Sci. **32,** 326 (1925); Chem. Abstracts **21,** 903 (1927).
(144) COMANDUCCI: Rend. accad. sci. fis. mat. Napoli (Soc. reale Napoli) **1908,** 5/12 (November, 1908); Chem. Zentr. **1909, I,** 1486.
(145) CONANT AND COYNE: J. Am. Chem. Soc. **44,** 2530 (1923).
(146) CORRIGAN, LANGERMAN, AND MOORE: J. Am. Chem. Soc. **67,** 1894 (1945).
(147) COURTOT AND PIERRON: Compt. rend. **190,** 1057 (1930).
(148) CREMER AND POLANYI: Z. physik. Chem. **B19,** 443 (1932); Chem. Zentr. **1933, I,** 1892.
(148a) CULVENOR, DAVIES, AND HEATH: J. Chem. Soc. **1949,** 278.
(149) CULVENOR, DAVIES, AND PAUSACKER: J. Chem. Soc. **1946,** 1050.
(149a) DANFORTH: U.S. patent 2,449,644; Chem. Abstracts **43,** 681 (1949).
(150) DANN, HOWARD, AND DAVIES: J. Chem. Soc. **1928,** 605.
(151) DAS-GUPTA: J. Indian Chem. Soc. **12,** 627 (1935).
(152) DAS-GUPTA: J. Indian Chem. Soc. **14,** 397 (1937).
(153) DAS-GUPTA: J. Indian Chem. Soc. **14,** 400 (1937).
(154) DATTA AND CHATTERJEE: J. Am. Chem. Soc. **45,** 480 (1923).

(155) Datta and Prosad: J. Am. Chem. Soc. **39,** 441 (1917).
(156) Dauben, Evans, and Meltzer: J. Am. Chem. Soc. **63,** 1883 (1941).
(157) De: J. Indian Chem. Soc. **5,** 29 (1928); Chem. Zentr. **1928, I,** 2393.
(157a) Degering: U.S. patent 2,466,655.
(158) Deluchat: Compt. rend. **192,** 1387 (1931).
(159) Detoeuf: Bull. soc. chim. [4] **31,** 176 (1922).
(160) Dharwarkar and Alimchandani: J. Univ. Bombay **9,** Pt. 3, 163 (1940).
(161) D'Ianni and Adkins: J. Am. Chem. Soc. **61,** 1675 (1939).
(162) Diels and Alder: Ann. **450,** 237 (1926).
(163) Dinesmann: Compt. rend. **141,** 201 (1905); Chem. Zentr. **1905, II,** 753.
(164) Dolliver, Gresham, Kistiakowsky, and Vaughan: J. Am. Chem. Soc. **59,** **831** (1937).
(165) Drake and Goldman: J. Org. Chem. **11,** 100 (1946).
(166) Drewsen: Ann. **212,** 150 (1882).
(167) Dufraisse: Compt. rend. **158,** 1691 (1914).
(168) Dufraisse: Compt. rend. **171,** 960 (1920).
(169) Dufraisse: Compt. rend. **172,** 67 (1921).
(170) Dufraisse: Compt. rend. **172,** 162 (1921).
(171) Dufraisse: Ann. chim. [9] **17,** 133 (1922).
(172) Dufraisse and Chaux: Bull. soc. chim. [4] **39,** 443 (1926).
(173) Dufraisse and Dequesnes: Bull. soc. chim. [4] **49,** 1880 (1931).
(174) Dufraisse and Viel: Bull. soc. chim. [4] **37,** 874 (1925).
(175) van Duin: Rec. trav. chim. **45,** 345 (1926).
(176) Dupont: Bull. soc. chim. [5] **3,** 1021 (1936).
(177) Duquenois: Bull. soc. chim. [5] **4,** 193 (1937).
(178) Durrans: J. Chem. Soc. **123,** 1424 (1923).
(179) Dyckerhoff: Ber. **10,** 119 (1877).
(180) Dyckerhoff: Ber. **10,** 531 (1877).
(181) Dykstra: J. Am. Chem. Soc. **56,** 1625 (1934).
(182) Eigel: Ber. **20,** 2527 (1887).
(183) Einhorn: Ber. **16,** 2208 (1883).
(184) Einhorn and Grabfield: Ann. **243,** 362 (1888).
(185) Einhorn and Hess: Ber. **17,** 2015 (1884).
(186) Eisenlohr and Schulz: Ber. **57,** 1808 (1924).
(187) Elovich and Zhabrova: J. Phys. Chem. (U.S.S.R.) **19,** 239 (1945); Chem. Abstracts **39,** 5160 (1945).
(188) Emde: Ann. **391,** 88 (1912).
(189) Emerson: J. Am. Chem. Soc. **67,** 516 (1945).
(190) Emerson: J. Org. Chem. **10,** 464 (1945).
(191) Emerson: U.S. patent 2,360,301; Chem. Abstracts **39,** 1178 (1945).
(192) Emerson: U.S. patent 2,372,562; Chem. Abstracts **39,** 3555 (1945).
(193) Emerson: U.S. patent 2,382,867; Chem. Abstracts **40,** 606 (1946).
(194) Emerson: U.S. patent 2,394,674; Chem. Abstracts **40,** 3135 (1946).
(195) Emerson: U.S. patent 2,397,412; Chem. Abstracts **40,** 4081 (1946).
(196) Emerson: U.S. patent 2,399,479; Chem. Abstracts **40,** 4395 (1946).
(196a) Emerson: U.S. patent 2,444,400; Chem. Abstracts **43,** 3461 (1949).
(197) Emerson and Agnew: J. Am. Chem. Soc. **67,** 518 (1945).
(197a) Emerson, Heyd, Lucas, Lyness, Owens, and Shortridge: J. Am. Chem. Soc. **69,** 1905 (1947).
(198) Engel: U.S. patent 2,417,548; Chem. Abstracts **41,** 3493 (1947).
(199) Erdmann: Ber. **17,** 412 (1884).
(200) Erdmann: Ber. **24,** 2771 (1891).
(201) Erlenmeyer: Z. Chem. **1864,** 545.
(202) Erlenmeyer: Ann. **135,** 122 (1865).

(203) Erlenmeyer: Ann. **137,** 327 (1866).
(204) Erlenmeyer: Ber. **12,** 1607 (1879).
(205) Erlenmeyer: Ber. **13,** 305 (1880).
(206) Erlenmeyer: Ber. **14,** 320 (1881).
(207) Erlenmeyer: Ber. **14,** 1867 (1881).
(208) Erlenmeyer: Ber. **16,** 152 (1883).
(209) Erlenmeyer and Leo: Helv. Chim. Acta **16,** 897 (1933); Chem. Zentr. **1933, II,** 3229.
(210) Erlenmeyer and Lipp: Ann. **219,** 179 (1883).
(211) Essex and Ward: U.S. patent 1,594,608; Chem. Zentr. **1926, II,** 1693.
(212) Essex and Ward: U.S. patent 1,626,398; Chem. Zentr. **1928, I,** 410.
(213) Evans, Mabbott, and Turner: J. Chem. Soc. **1927,** 1159.
(214) Evans and Morgan: J. Am. Chem. Soc. **35,** 54 (1913).
(215) Evans, Pearson, and Braithwaite: J. Am. Chem. Soc. **63,** 2574 (1941).
(216) Fabrykant: Chem. Zentr. **1930, I,** 2548.
(217) Ferratini: Gazz. chim. ital. [2] **23,** 409 (1893); Ber. **27R,** 123 (1894).
(218) Feuerstein and Heimann: Ber. **34,** 1468 (1901).
(219) Fischer: Ber. **29,** 205 (1896).
(220) Fittig and Binder: Ann. **195,** 131 (1879).
(221) Fittig and Claus: Ann. **269,** 1 (1892).
(222) Fittig and Erdmann: Ann. **216,** 179 (1883).
(223) Flood and Nieuwland: J. Am. Chem. Soc. **50,** 2566 (1928).
(224) Flürscheim: J. prakt. Chem. [2] **66,** 16 (1902).
(225) Flürscheim and Holmes: J. Chem. Soc. **1932,** 1458.
(225a) Fodor and Kovacs: J. Am. Chem. Soc. **71,** 1045 (1949).
(226) Fornet: Seifensieder-Ztg. **62,** 285 (1935); Chem. Abstracts **29,** 3780 (1935).
(227) Forrer: Ber. **17,** 982 (1884).
(228) Forster and Saville: J. Chem. Soc. **121,** 2595 (1922).
(229) Fosdick, Faucher, and Urbach: J. Am. Chem. Soc. **68,** 840 (1946).
(230) Fourneau, Benoit, and Firminich: Bull. soc. chim. [4] **47,** 858 (1930).
(231) Fourneau, Benoit, and Firminich: Bull. soc. chim. [4] **47,** 894 (1930).
(232) Fourneau and Chantalou: Bull. soc. chim. [5] **12,** 845 (1945).
(233) Fourneau and Tiffeneau: Compt. rend. **140,** 1595 (1905).
(234) Frank, Adams, Allen, Gander, and Smith: J. Am. Chem. Soc. **68,** 1365 (1946).
(235) Franzen and Schneider: J. prakt. Chem. [2] **90,** 547 (1914); Chem. Zentr. **1915, I,** 198.
(236) Freundlich and Salomon: Helv. Chim. Acta **17,** 88 (1934); Chem. Abstracts **28,** 2591 (1934).
(237) Friedel: Compt. rend. **67,** 1192 (1868).
(238) Friedel: Jahresber. **1868,** 410.
(239) Friedel: Z. Chem. **1869,** 123.
(240) Friedel: Ann. chim. [4] **16,** 360 (1869).
(241) Friedel and Balsohn: Bull. soc. chim. [2] **32,** 614 (1879); Ber. **12,** 2150 (1879).
(242) Friedel and Balsohn: Bull. soc. chim. [2] **35,** 54 (1881); Ber. **14,** 36 (1881).
(243) Friedländer and Lazarus: Ann. **229,** 233 (1885).
(244) Friedländer and Mähly: Ann. **229,** 210 (1885).
(245) Friedman: Beitr. chem. Physiol. Path. **8,** 95 (1906); Chem. Zentr. **1906, I,** 1618.
(246) Fries and Bestian: Ber. **69,** 715 (1936).
(247) Fries and Fickewirth: Ber. **41,** 367 (1908).
(248) Fries and Moskopp: Ann. **372,** 187 (1910).
(249) Fromm: Ann. **456,** 168 (1927).
(250) v. Fürth: Monatsh. **24,** 261 (1903); Chem. Zentr. **1903, II,** 301.
(251) Gabriel and Colman: Ber. **47,** 1866 (1914).
(252) Gabriel and Herzberg: Ber. **16,** 2036 (1883).

(253) GAL'PERN AND VINOGRADOVA: Petroleum Ind. (U.S.S.R.) No. 1, 59 (1936); Chem. Zentr. **1936, I,** 5015.
(254) GAL'PERN AND VINOGRADOVA: Chem. festen Brennstoffe **8,** 384 (1937); Chem. Zentr. **1938, I,** 133.
(255) GANGLOFF AND HENDERSON: J. Am. Chem. Soc. **39,** 1420 (1917).
(256) GAUTHIER AND GAUTHIER: Bull. soc. chim. [4] **53,** 323 (1933).
(256a) GEBHART: U.S. patent 2,459,423; Chem. Abstracts **43,** 3024 (1949).
(257) GELMAN: Compt. rend. acad. sci. U.R.S.S. **16,** 351 (1937); Chem. Zentr. **1939, I,** 363.
(258) GELMAN: Compt. rend. acad. sci. U.R.S.S. **20,** 307 (1938); Chem. Zentr. **1939, I,** 4023.
(259) GEVEKOHT: Ann. **221,** 323 (1883).
(260) GILMAN AND FOTHERGILL: J. Am. Chem. Soc. **51,** 3501 (1929).
(260a) GILMAN AND FULLHART: J. Am. Chem. Soc. **71,** 1478 (1949).
(261) GILMAN, HAUBEIN, O'DONNELL, AND WOODS: J. Am. Chem. Soc. **67,** 922 (1945).
(262) GILMAN AND KIRBY: Rec. trav. chim. **54,** 577 (1935).
(263) GILMAN, LANGHAM, AND MOORE: J. Am. Chem. Soc. **62,** 2327 (1940).
(264) GILMAN AND McGLUMPHY: Rec. trav. chim. **47,** 418 (1928); Chem. Zentr. **1928, I,** 1950.
(265) GILMAN, TOWNE, AND JONES: J. Am. Chem. Soc. **55,** 4689 (1933).
(266) GILMAN, ZOELLNER, AND SELBY: J. Am. Chem. Soc. **55,** 1252 (1933).
(267) GILMAN, ZOELLNER, SELBY, AND BOATNER: Rec. trav. chim. **54,** 584 (1935).
(268) GLASER: Compt. rend. **67,** 906 (1868).
(269) GLASER: Ann. **154,** 137 (1870).
(270) GLAVIS, RYDEN, AND MARVEL: J. Am. Chem. Soc. **59,** 707 (1937).
(271) GLYNN AND LINNELL: Quart. J. Pharm. Pharmacol. **5,** 480 (1932); Chem. Zentr. **1933, I,** 604.
(272) GOLDING AND McNEELY: J. Am. Chem. Soc. **68,** 1847 (1946).
(273) GOLUMBIC AND COTTLE: J. Am. Chem. Soc. **61,** 996 (1939).
(274) GRAVE AND CHRISTIANSEN: J. Am. Pharm. Assoc. **23,** 35 (1934).
(275) GREEN AND RICHTER: Biochem. J. **31,** 596 (1937); Chem. Abstracts **31,** 5397 (1937).
(276) GRIGNARD AND PERRICHON: Ann. chim. [10] **5,** 5 (1936).
(277) GRUNDMANN: Ann. **524,** 31 (1936).
(278) GWYNN AND DEGERING: J. Am. Chem. Soc. **64,** 2216 (1942).
(279) HAHN AND RUMPF: Ber. **71,** 2141 (1938).
(280) HAHN AND STIEHL: Ber. **71,** 2154 (1938).
(281) HALASZ: Ann. chim. **14,** 318 (1940); Chem. Abstracts **36,** 452 (1942).
(282) HANBY AND RYDON: J. Chem. Soc. **1946,** 114.
(283) HANHART AND INGOLD: J. Chem. Soc. **1927,** 997.
(284) HANZLIK AND BIANCHI: Ber. **32,** 2282 (1899).
(285) HARNIST: Ber. **63,** 2307 (1930).
(286) HARTUNG, CROSSLEY, AND MUNCH: J. pharm. chim. [8] **13,** 474 (1931); Chem. Zentr. **1931, II,** 2361.
(287) HARTWELL AND KORNBERG: J. Am. Chem. Soc. **68,** 868 (1946).
(288) HEDEN AND HOLMBERG: Svensk Kem. Tid. **48,** 207 (1936); Chem. Zentr. **1937, I,** 1156.
(289) HELLER AND TISCHNER: Ber. **42,** 4566 (1909).
(290) HENDERSON AND GRAY: J. Chem. Soc. **85,** 1041 (1904).
(291) HERMANS: Z. anorg. allgem. Chem. **142,** 83 (1925); Chem. Zentr. **1925, I,** 1574.
(292) HEROLD: Deut. Parfüm. Ztg. **17,** 246 (1931).
(293) HERRMANN AND VORLÄNDER: Abhandl. Naturforsch. Ges. Halle **21,** 251 (1899); Chem. Zentr. **70, I,** 730 (1899).
(294) HESS AND UIBRIG: Ber. **48,** 1974 (1915).
(295) HESSLER: J. Am. Chem. Soc. **44,** 425 (1922).

(296) Hessler: *Organic Syntheses*, Collective Vol. I, p. 438. John Wiley and Sons, Inc., New York (1941).

(297) Hibbert and Burt: J. Am. Chem. Soc. **47**, 2240 (1925).

(298) Hibbert and Burt: Org. Syntheses **8**, 102 (1928).

(299) Hickinbottom: J. Chem. Soc. **1934**, 319.

(300) Hoch: Compt. rend. **200**, 938 (1935); Chem. Abstracts **29**, 4337 (1935).

(301) Hoering: Ber. **41**, 173 (1908).

(302) Hoering: Ber. **41**, 1889 (1908).

(303) Hoessle: J. prakt. Chem. [2] **49**, 403 (1894); Ber **27R**, 396 (1894).

(304) Hohn and Bloch: J. prakt. Chem. [2] **82**, 511 (1910).

(305) Holleman: Ber. **20**, 3080 (1887).

(306) Holleman: Rec. trav. chim. **23**, 283 (1904).

(307) Holmberg: J. prakt. Chem. **141**, 93 (1934); Chem. Zentr. **1935, I**, 557.

(308) Holmberg: Arkiv Kemi, Mineral. Geol. **12A**, No. 28 (1938); Chem. Zentr. **1938, II**, 295

(309) Holmberg: Arkiv Kemi, Mineral. Geol. **12B**, No. 47 (1938); Chem. Zentr. **1938, I**, 4312.

(310) Holmberg: Arkiv Kemi, Mineral. Geol. **12B**, No. 48 (1938); Chem. Zentr. **1938, I**, 4618.

(311) Holmberg: Arkiv Kemi, Mineral. Geol. **13B**, No. 14 (1939); Chem. Abstracts **34**, 2341 (1940).

(312) Houben: Ber. **41**, 1027 (1908).

(313) Houben: Ber. **41**, 3708 (1908).

(314) Houben and Führer: Ber. **40**, 4990 (1907).

(315) Houben and Führer: Ber. **47**, 75 (1914).

(316) Hugel and Krassilchik: Chimie & industrie **23**, No. 3, 267 (1930).

(317) Hughes and Ingold: J. Chem. Soc. **1933**, 523.

(318) Hultzsch: J. prakt. Chem. **158**, 275 (1941); Chem. Abstracts **36**, 849 (1942).

(319) Hunt and Turner: J. Chem. Soc. **127**, 996 (1925).

(320) Hurd, McNamee, and Green: J. Am. Chem. Soc. **61**, 2979 (1939).

(321) Hurry and Meldrum: J. Indian Chem. Soc. **11**, 535 (1935).

(322) I. G. Farbenindustrie A.-G.: British patent 320,424; Chem. Zentr. **1930, I**, 737.

(323) I. G. Farbenindustrie A.-G.: British patent 327,382; Chem. Zentr. **1930, II**, 1320.

(324) I. G. Farbenindustrie A.-G.: British patent 381,459; Chem. Zentr. **1933, I**, 506.

(325) I. G. Farbenindustrie A.-G.: British patent 464,054; Chem. Zentr. **1937, II**, 1662.

(326) I. G. Farbenindustrie A.-G.: British patent 516,936; Chem. Abstracts **35**, 6822 (1941).

(327) I. G. Farbenindustrie A.-G.: French patent 620,799; Chem. Zentr. **1929, I**, 2697.

(328) I. G. Farbenindustrie A.-G.: French patent 724,105; Chem. Zentr. **1933, I**, 505.

(329) I. G. Farbenindustrie A.-G.: French patent 729,730; Chem. Zentr. **1932, II**, 3015.

(330) I. G. Farbenindustrie A.-G.: French patent 735,108; Chem. Zentr. **1933, II**, 1093.

(331) I. G. Farbenindustrie A.-G.: French patent 745,533; Chem. Zentr. **1933, II**, 2327.

(332) I. G. Farbenindustrie A.-G.: French patent 780,027; Chem. Zentr. **1937, I**, 430.

(333) I. G. Farbenindustrie A.-G.: German patent 484,360; Chem. Zentr. **1929, II**, 3251.

(334) I. G. Farbenindustrie A.-G.: German patent 525,836; Chem. Zentr. **1931**, II, 1191.

(335) I. G. Farbenindustrie A.-G.: German patent 526,087; Chem. Zentr. **1931, II**, 1056.

(336) I. G. Farbenindustrie A.-G.: German patent 559,521; Chem. Zentr. **1933, I**, 1843.

(337) I. G. Farbenindustrie A.-G.: German patent 573,535; Chem. Zentr. **1933, I**, 3628.

(338) I. G. Farbenindustrie A.-G.: German patent 615, 795; Chem. Zentr. **1935, II**, 3301.

(339) I. G. Farbenindustrie A.-G.: German patent 646,479; Chem. Zentr. **1937, II**, 1662.

(340) I. G. Farbenindustrie A.-G.: German patent 669,961; Chem. Abstracts **33**, 5415 (1939).

(341) Imperial Chemical Industries Ltd.: British patent 539,667; Chem. Abstracts **36**, 4133 (1942).

(342) Ingle: Ber. **27**, 2526 (1894).

(343) Ingle: J. Soc. Chem. Ind. **21**, 587 (1902).

(344) Ingle: J. Soc. Chem. Ind. **23,** 422 (1904).
(345) Ingold and Ingold: J. Chem. Soc. **1931,** 2354.
(346) Ingold and Smith: J. Chem. Soc. **1931,** 2742.
(347) Ingold and Weaver: J. Chem. Soc. **125,** 1456 (1924).
(348) Ingold and Weaver: J. Chem. Soc. **127,** 378 (1925).
(349) Inskeep and Deanin: J. Am. Chem. Soc. **69,** 2237 (1947).
(350) Ipatiev, Razuvayev, and Sysov: Ber. **63,** 174 (1930).
(351) Jacobs and Heidelberger: J. Biol. Chem. **21,** 403 (1915); Chem. Zentr. **1915, II,** 659.
(352) Jansen: Chem. Weekblad, **26,** 421 (1929).
(353) Jansen: Rec. trav. chim. **50,** 291 (1931); Chem. Zentr. **1931, I,** 2614.
(354) Johnson and McEwen: J. Am. Chem. Soc. **48,** 469 (1926).
(355) Jones and Burns: J. Am. Chem. Soc. **47,** 2966 (1925).
(356) Jordan: J. Am. Chem. Soc. **63,** 2687 (1941).
(357) Jowett: J. Chem. Soc. **85,** 192 (1904).
(358) Kadesch: J. Am. Chem. Soc. **68,** 41 (1946).
(358a) Kaelin: Helv. Chim. Acta **30,** 2132 (1947).
(359) Kafuku, Ishikawa, and Kato: Bull. Ind. Research Government of Formosa **24,** 1 (1928); Chem. Abstracts **23,** 1889 (1929).
(360) Kanao: J. Pharm. Soc. Japan, **49,** 238 (1929); Chem. Abstracts **23,** 5162 (1929).
(361) Kanao: J. Pharm. Soc. Japan **50,** 43 (1930); Chem. Zentr. **1930, II,** 1695.
(362) Kariyone: J. Pharm. Soc. Japan, **515,** 1 (1925); Chem. Zentr. **1925, I,** 2376.
(363) Kaufmann: German patent 404,175; Chem. Zentr. **1925, I,** 295.
(364) Kaufmann and Liepe: Ber. Pharm. **33,** 139 (1923).
(365) Kaufmann and Oehring: Ber. **59,** 187 (1926).
(366) Kawamura: J. Chem. Soc. Japan **62,** 259 (1941); Chem. Abstracts **37,** 4372 (1943).
(367) Kern, Shriner, and Adams: J. Am. Chem. Soc. **47,** 1147 (1925).
(368) Kharasch and Ashford: J. Am. Chem. Soc. **58,** 1733 (1936).
(369) Kharasch and Clapp: J. Org. Chem. **3,** 355 (1938).
(369a) Kharasch and Friedlander: J. Org. Chem. **14,** 239 (1949).
(370) Kharasch, Jensen, and Urry: J. Am. Chem. Soc. **68,** 154 (1946).
(371) Kharasch, Kane, and Brown: J. Am. Chem. Soc. **64,** 333 (1942).
(372) Kharasch, May, and Mayo: J. Am. Chem. Soc. **59,** 1580 (1937).
(373) Kharasch, May, and Mayo: J. Org. Chem. **3,** 175 (1938).
(374) Kharasch, May, and Mayo: Chemistry & Industry **57,** 774 (1938).
(375) Kharasch and Priestley: J. Am. Chem. Soc. **61,** 3425 (1939).
(376) Kharasch, Read, and Mayo: Chemistry & Industry **57,** 752 (1938).
(377) Kharasch, Schenk, and Mayo: J. Am. Chem. Soc. **61,** 3092 (1939).
(378) Kharasch, Seyler, and Mayo: J. Am. Chem. Soc. **60,** 882 (1938).
(378a) Kharasch, Urry, and Kuderna: J. Org. Chem. **14,** 248 (1949).
(379) Kindler and Brandt: Arch. Pharm. **273,** 478 (1935); Chem. Zentr. **1936, I,** 2539.
(380) Kindler, Brandt, and Gehlhaar: Ann. **511,** 209 (1934).
(381) Kindler and Peschke: Arch. Pharm. **269,** 581 (1931); Chem. Zentr. **1932, I,** 669.
(382) Kindler and Peschke: Ann. **519,** 291 (1935).
(383) Kindler, Peschke, and Brandt: Ber. **68,** 2241 (1935).
(384) King and McMillan: J. Am. Chem. Soc. **68,** 525 (1946).
(385) King and McMillan: J. Am. Chem. Soc. **68,** 2335 (1946).
(386) King and Wilkinson: J. Am. Chem. Soc. **54,** 3070 (1932).
(387) Kinney and Larsen: J. Am. Chem. Soc. **57,** 1054 (1935).
(388) Kinney and Ward: J. Am. Chem. Soc. **55,** 3796 (1933).
(389) Klages: Ber. **35,** 2245 (1902).
(390) Klages and Eppelsheim: Ber. **36,** 3584 (1903).
(391) Klages and Allendorff: Ber. **31,** 998 (1898).
(392) Klages and Keil: Ber. **36,** 1632 (1903).
(393) Klages and Stamm: Ber. **37,** 924 (1904).

(394) Kling: Ann. chim. [8] **5**, 471 (1905); Chem. Zentr. **1905, II**, 754.

(395) Kobayashi: Sci. Papers Inst. Phys. Chem. Research (Tokyo) **6**, 149 (1927); Chem. Abstracts **22**, 1345 (1928).

(396) Koenigs: Ber. **23**, 3144 (1890).

(397) Koenigs and Carl: Ber. **24**, 3889 (1891).

(398) Kohler and Drake: J. Am. Chem. Soc. **45**, 1281 (1923).

(399) Kohler and Engelbrecht: J. Am. Chem. Soc. **41**, 764 (1919).

(400) Kohler and Steele: J. Am. Chem. Soc. **41**, 1093 (1919).

(401) Kolker and Lapworth: J. Chem. Soc. **1925**, 307.

(402) Kolshorn: Ber. **37**, 2474 (1904).

(403) Komatsu and Mitsui: Rec. trav. chim. **57**, 586 (1938).

(404) Komppa: Dissertation, Helsingfors, 1893.

(405) Komppa: Ber. **26**, 2968 (1893).

(406) Kondo: J. Pharm. Soc. Japan **48**, 56 (1927); Chem. Zentr. **1928, II**, **55**.

(407) Kondo and Ishiwata: Ber. **64**, 1533 (1931).

(408) Kondo and Kondo: J. Pharm. Soc. Japan **48**, 324 (1928); Chem. Abstracts **22**, 3414 (1928).

(409) Kondo and Shinozaki: J. Pharm. Soc. Japan **49**, 267 (1927); Chem. Abstracts **24**, 5294 (1930).

(410) Kondo, Shinozaki, and Ishii: J. Pharm. Soc. Japan **48**, 169 (1928); Chem. Zentr. **1929, I**, 1112.

(411) Kopp: Compt. rend. **21**, 1376 (1844).

(412) Kosolapoff and Huber: J. Am. Chem. Soc. **68**, 2540 (1946).

(413) Koss and Pellegrini: Roczniki Farmacji **1928**, 1; Chem. Zentr. **1930, II**, **556**.

(414) Kotz and Schneider: J. prakt. Chem. [2] **90**, 136 (1914).

(415) Krabbe, Polzin, and Culemeyer: Ber. **73**, 652 (1940).

(416) Kraemer and Spilker: Ber. **23**, 3169 (1890).

(417) Kraemer and Spilker: Ber. **24**, 2785 (1891).

(418) Kraemer, Spilker, and Eberhardt: Ber. **23**, 3269 (1890).

(419) Krasuskii and Kiprianov: J. Russ. Phys. Chem. Soc. **56**, 1 (1925); Chem. Zentr. **1926, I**, 895.

(419a) Kropa and Nyquist: U. S. patent 2,468,713; Chem. Abstracts **43**, 5422 (1949).

(420) Kruber and Schade: Brennstoff-Chem. **14**, 124 (1933); Chem. Zentr. **1933, I**, 3840.

(421) Kunckell and Eras: Ber. **33**, 3264 (1900).

(422) Kunckell and Eras: Ber. **36**, 915 (1903).

(423) Kunckell, Eras, Müller, and Hildebrandt: Ber. Pharm. **23**, 188 (1913).

(424) Kunckell and Gotsch: Ber. **33**, 265 (1900).

(425) Kunckell and Koritzky: Ber. **33**, 3261 (1900).

(426) Kunckell and Vossen: Ber. **35**, 2291 (1902).

(427) Kunckell and Vossen: Ber. **35**, 2294 (1902).

(428) Kunz-Krause: Ber. **30**, 1617 (1897).

(429) Labbé: Bull. soc. chim. [3] **22**, 1077 (1899); Chem. Zentr. **1900, I**, 258.

(430) Ladenburg: Ann. **217**, 74 (1883).

(431) Ladenburg and Rügheimer: Ber. **13**, 2041 (1880).

(432) Langlois: Compt. rend. **168**, 1052 (1919).

(433) Lauer and Spielman: J. Am. Chem. Soc. **53**, 1533 (1931).

(434) Lauer and Spielman: J. Am. Chem. Soc. **55**, 4923 (1933).

(435) Laurent: Compt. rend. **22**, 789 (1844).

(436) Lebeau and Picon: Compt. rend. **157**, 223 (1913); Chem. Zentr. **1913, II**, 1128.

(437) Lebedev: J. Russ. Phys. Chem. Soc. **32**, 197 (1900); Chem. Zentr. **1900, II**, 326.

(438) Lebedev, Koblyanskii, and Yakubchik: J. Chem. Soc. **127**, 417 (1925).

(439) Lebedev, Koblyanskii, and Yakubchik: J. Russ. Phys. Chem. Soc. **56**, 265 (1925); Chem. Zentr. **1926, I**, 1131.

(440) van der Lee: Rec. trav. chim. **44**, 1089 (1925).

(441) van der Lee: Rec. trav. chim. **47,** 920 (1928).
(442) Leffler and Adams: J. Am. Chem. Soc. **59,** 2252 (1937.)
(443) Legerlotz: U. S. patent 1,932,347; Chem. Zentr. **1930, I,** 586; Austrian patent 17,037.
(444) Lespagnol, Herlemont, and Stern: J. pharm. chim. [8] **29,** 447 (1939); Chem. Zentr. **1939, II,** 1935.
(445) Lespieau and Deluchat: Compt. rend. **190,** 683 (1930).
(446) Levine and Cass: U. S. patent 2,193,823; Chem. Abstracts **34,** 4746 (1940).
(447) Lewis, Nierenstein, and Rich: J. Am. Chem. Soc. **47,** 1728 (1925).
(448) Ley: Ber. **51,** 1810 (1918).
(449) Ley and Rinke: Ber. **56,** 771 (1923).
(450) Liebermann: Ber. **27,** 2037 (1894).
(451) Liebermann and Sachse: Ber. **24,** 4112 (1891).
(452) Linstead and Williams: J. Chem. Soc. **1926,** 2735.
(453) Lipp: Ber. **17,** 1067 (1884).
(454) Lipp: Ber. **17,** 2507 (1884).
(455) Loehr: U. S. patent 1,787,205; Chem. Zentr. **1931, I,** 2394.
(456) Loevenich and Gerber: Ber. **63,** 1707 (1930).
(457) Lohmann: J. prakt. Chem. [2] **153,** 57 (1939).
(458) Lozovoi and Dyakova: J. Gen. Chem. (U.S.S.R.) **10,** 1 (1940); Chem. Abstracts **34,** 4728 (1940).
(459) Luginin: Compt. rend. **150,** 915 (1910); Chem. Zentr. **1910, I,** 1959.
(460) Luginin and Dupont: Compt. rend. **150,** 1346 (1910); Chem. Zentr. **1910, II,** 216.
(461) Lund: Kemisk **17,** 169 (1936); Chem. Zentr. **1937, I,** 3480.
(462) Lund: Ber. **70,** 1520 (1937).
(463) Lutz, Allison, Ashburn, Bailey, Clark, Codington, Deinet, Freek, Jordan, Leake, Martin, Nicodemus, Rowlett, Shearer, Smith, and Wilson: J. Org. Chem. **12,** 617 (1947).
(464) MacDougall, Lauer, and Spielman: J. Am. Chem. Soc. **55,** 4089 (1933).
(465) Madinaveitia: Bull. soc. chim. [4] **25,** 601 (1919).
(466) Mameli: Gazz. chim. ital. [1] **34,** 358 (1904); Chem. Zentr. **1904, II,** 214.
(467) Manchot: Ann. **417,** 93 (1918).
(468) Manchot: Ann. **421,** 316 (1920).
(469) Manchot, Withers, and Oltrogge: Ann. **387,** 278 (1912).
(470) Mannich and Davidsen: Ber. **69,** 2106 (1936).
(471) Mannich and Falber: Arch. Pharm. **267,** 601 (1929); Chem. Zentr. **1930, I, 77.**
(472) Mannich and Hahn: Ber. **44,** 1542 (1911).
(473) Mannich and Jacobsohn: Ber. **43,** 189 (1910).
(474) Mannich, Neumann, and Jacobsohn: Arch. Pharm. **248,** 127 (1910).
(475) Mannich and Thiele: Arch. Pharm. **253,** 181 (1915).
(476) Mannich and Walther: Arch. Pharm. **265,** 1 (1927); Chem. Zentr. **1927, I,** 1479.
(477) Mannich and Walther: Arch. Pharm. **265,** 11 (1927); Chem. Zentr. **1927, I,** 1481.
(477a) Markees and Burger: J. Am. Chem. Soc. **70,** 3329 (1948).
(478) Marvel, Hager, and Coffman: J. Am. Chem. Soc. **49,** 2323 (1927).
(479) Marvel and Moon: J. Am. Chem. Soc. **62,** 45 (1940).
(480) Marvel, Mueller, and Peppel: J. Am. Chem. Soc. **60,** 410 (1938).
(481) Marvel and Nichols: J. Org. Chem. **6,** 296 (1941).
(482) Marvel, Overberger, Allen, Johnston, Saunders, and Young: J. Am. Chem. Soc. **68,** 861 (1946).
(483) Marvel, Saunders, and Overberger: J. Am. Chem. Soc. **68,** 1085 (1946).
(484) Marvel and du Vigneaud: J. Am. Chem. Soc. **46,** 2093 (1924).
(485) Mason: J. Chem. Soc. **119,** 1078 (1921).
(486) Matsui: J. Soc. Chem. Ind. Japan **44,** 38 (1941).
(487) Maurer and Schiedt: J. prakt. Chem. **144,** 41 (1935).
(488) Medinger: Monatsh., **27,** 237 (1906).

(489) Medvedev and Tseitlin: J. Phys. Chem. (U.S.S.R.), **18**, 13 (1944); Chem. Abstracts **39**, 3196 (1945).

(490) Meinel: Ann. **510**, 129 (1934).

(491) Meisenheimer and Heim: Ber. **38**, 466 (1905).

(492) Meisenheimer and Heim: Ann. **355**, 260 (1907).

(493) Meister, Lucius and Brüning: German patent 157,300; Frdl. **7**, 689.

(494) Meister, Lucius and Brüning: German patent 193,634; Frdl., **8**, 1183.

(495) Meister, Lucius and Brüning: German patent 209,609; Frdl. **9**, 1024.

(496) Meister, Lucius and Brüning: German patent 209,610; Frdl. **9**, 1025.

(497) Meister, Lucius and Brüning: German patent 212,206; Frdl. **9**, 1026.

(498) Meldrum and Alimchandani: J. Indian Chem. Soc. **2**, 1 (1925); Chem. Zentr. **1926**, **I**, 67.

(499) Meldrum and Alimchandani: J. Indian Chem. Soc. **6**, 253 (1929).

(500) Meldrum and Kapadia: J. Indian Chem. Soc. **9**, 483 (1932).

(501) Meldrum and Lonkar: J. Univ. Bombay **16**, **II**, 116 (1937).

(502) Meldrum and Parikh: Proc. Indian Acad. Sci. **1A**, 431 (1935).

(503) Meldrum and Vaidyanathan: Proc. Indian Acad. Sci. **1A**, 510 (1935).

(504) Melnikov and Rokitskaya: J. Gen. Chem. (U.S.S.R.) **8**, 1768 (1938); Chem. Abstracts **33**, 4969 (1939).

(505) Merck Chemische Fabrik: German patent 469,782; British patent 280,574; Chem. Zentr. **1929**, **I**, 3144.

(506) Merck Chemische Fabrik: German patent 519,988; Chem. Zentr. **1931**, **I**, 2783.

(507) Meyer and Hohenemser: Helv. Chim. Acta **18**, 1061 (1935).

(508) Meyer and Lenhardt: Ann. **398**, 66 (1913).

(509) Meyer and Schuster: Ber. **55**, 815 (1922).

(510) Michael: Ber. **28**, 1633 (1895).

(511) Milas and Sussman: J. Am. Chem. Soc. **59**, 2345 (1937).

(512) v. Miller: Ann. **189**, 338 (1877).

(513) v. Miller: Ber. **11**, 1450 (1878).

(514) Mills and Bains: J. Chem. Soc. **127**, 2502 (1925).

(515) Moore and Greensfelder: J. Am. Chem. Soc. **69**, 2008 (1947).

(516) Morgan: J. Chem. Soc. **29**, 162 (1876).

(517) Mortenson and Spielman: J. Am. Chem. Soc. **62**, 1609 (1940).

(518) Moureu: Compt. rend. **137**, 259 (1903).

(519) Moureu: Compt. rend. **138**, 286 (1904).

(520) Moureu: Bull. soc. chim. [3] **31**, 493 (1904); Chem. Zentr. **1904**, **I**, 1602.

(521) Moureu: Bull. soc. chim. [3] **31**, 526 (1904).

(522) Moureu and Delange: Bull. soc. chim. [3] **25**, 302 (1901).

(523) Moureu and Dufraisse: Compt. rend. **178**, 824 (1924).

(524) Moureu, Dufraisse, and Badoche: Compt. rend. **187**, 1092 (1928).

(525) Müller: Ber. **20**, 1212 (1887).

(526) Musante: Gazz. chim. ital. **67**, 579 (1937); Chem. Zentr. **1938**, **I**, 2537.

(527) Nagai: British patent 118,298; J. Chem. Soc. **118**, 143 (1920).

(528) Nagai: U. S. patent 1,973,647; Chem. Zentr. **1935**, **I**, 751.

(529) Nagel: Ann. **216**, 323 (1883).

(530) Neber, Burgard, and Thier: Ann. **526**, 277 (1936).

(531) Nef: Ann. **308**, 264 (1899).

(532) Nenitzescu: Ber. **58**, 1063 (1925).

(533) Nenitzescu, Isăcescu, and Ionescu: Ann. **491**, 210 (1931).

(534) Nesmeyanov and Freidlina: J. Gen. Chem. (U.S.S.R.) **7**, 2748 (1937); Chem. Abstracts **32**, 2912 (1938).

(534a) Nystrom and Brown: J. Am. Chem. Soc. **70**, 3738 (1948).

(535) Oda and Tamura: Sci. Papers Inst. Phys. Chem. Research (Tokyo) **33**, 129 (1937); Chem. Zentr. **1938**, **I**, 2153.

(536) Oddo: Gazz. chim. ital. **41, I,** 320 (1911); Chem. Zentr. **1911, I,** 1856.
(537) Oliveri-Mandala: Gazz. chim. ital. **40, I,** 119 (1910); Chem. Zentr. **1910, I,** 1531.
(538) Orlov and Mustafin: Compt. rend. acad. sci. U.R.S.S. **16,** 107 (1937); Chem. Zentr. **1938, I,** 896.
(539) Orlov and Shalygin: Compt. rend. acad. sci. U.R.S.S. **14,** 341 (1937); Chem. Zentr. **1937, II,** 1576.
(540) Ovakimian, Kuna, and Levene: J. Biol. Chem. **135,** 91 (1940).
(541) Pace: Gazz. chim. ital. **59,** 578 (1929); Chem. Zentr. **1930, I,** 213.
(542) Palfray and Pannelier: Bull. soc. chim. [5] **4,** 1913 (1937).
(543) Palfray, Sabetay, and Sontag: Compt. rend. **193,** 941 (1931).
(544) Palfray, Sabetay, and Sontag: Compt. rend. **196,** 622 (1933).
(545) Passerini and Casini: Gazz. chim. ital. **67,** 785 (1937); Chem. Zentr. **1938, I,** 3623.
(546) Pauly: Ber. **36,** 2944 (1903).
(547) Pauly: Ber. **37,** 1388 (1904).
(548) Pauly and Neukam: Ber. **40,** 3488 (1907).
(549) Pauly and Neukam: Ber. **41,** 4151 (1908).
(550) Peratoner: Gazz. chim. ital. **22, II,** 65 (1892); Ber. **26R,** 18 (1893).
(551) Perkin: J. Chem. Soc. **32,** 663 (1877).
(552) Perkin: J. Chem. Soc. **39,** 409 (1881).
(553) Perkin: J. Chem. Soc. **59,** 150 (1891).
(554) Perkins and Bryner: U. S. patent 2,247,402; Chem. Abstracts **35,** 6267 (1941).
(555) Perrot: Compt. rend. **202,** 494 (1936).
(556) Perrot: Compt. rend. **203,** 329 (1936).
(557) Pestemer, Langer, and Manchen: Monatsh. **68,** 326 (1936).
(558) Petrenko-Krishchenko and Opotskii: Ber. **59,** 2131 (1926).
(559) Petrenko-Krishchenko, Opotskii, Dyakova, and Lozovai: Ber. **62,** 581 (1929).
(560) Pfeiffer: Ber. **47,** 1755 (1914).
(561) Phillips and Goss: Ind. Eng. Chem. **24,** 1436 (1932).
(562) Pictet and Gams: Ber. **42,** 2943 (1909).
(563) Pictet and Gams: Ber. **43,** 2384 (1910).
(564) Pope and Smith: J. Chem. Soc. **121,** 1166 (1922).
(565) Posner: Ber. **38,** 646 (1905).
(566) Posner: Ann. **389,** 1 (1912).
(567) Prausnitz: Ber. **17,** 595 (1884).
(568) Prelog, Hahn, Brauchli, and Beyerman: Helv. Chim. Acta **27,** 1209 (1944).
(569) Pressman and Young: J. Am. Chem. Soc. **66,** 705 (1944).
(570) Prévost: Compt. rend. **197,** 1661 (1933).
(571) Priebs: Ann. **225,** 319 (1884).
(572) Priewe: German patent 459,145; Chem. Zentr. **1928, II,** 1615.
(573) Prins: Chem. Weekblad **14,** 932 (1917); Chem. Zentr. **1918, I,** 168.
(574) Prins: Proc. Koninkl. Nederland. Akad. Wetenschappen **27,** 1496 (1919); Chem. Zentr. **1919, III,** 1001.
(575) Prins: Chem. Weekblad **16,** 1510 (1919); Chem. Zentr. **1920, I,** 423.
(576) Prins: Proc. Acad. Sci. Amsterdam **22,** 51 (1919); Chem. Abstracts **14,** 1662 (1920).
(577) Pyman: J. Chem. Soc. **93,** 1793 (1908).
(577a) Quattlebaum and Noffsinger: U. S. patent 2,466,737.
(577b) Quattlebaum and Noffsinger: U. S. patent 2,467,095.
(578) Quelet: Compt. rend. **186,** 764 (1928).
(579) Quelet: Bull. soc. chim. [4] **45,** 75 (1929).
(580) Quelet: Bull. soc. chim. [4] **45,** 255 (1929).
(581) Quelet: Compt. rend. **202,** 956 (1936).
(582) Quelet: Bull. soc. chim. [5] **7,** 205 (1940).
(583) Quelet and Allard: Bull. soc. chim. [5] **7,** 215 (1940).
(584) Quelet and Calcagni: Compt. rend. **222,** 88 (1946).

(585) Quelet and Ducasse: Compt. rend. **208,** 1317 (1939).
(586) Quelet and Galse: Compt. rend. **223,** 159 (1946).
(587) Quilico and Fleischner: Atti reale accad. naz. Lincei. [6] **7,** 1050 (1928); Chem. Zentr. **1929, I,** 385.
(588) Radzevanovskii and Schramm: Akad. Wiss. Krakau Feb., 61 (1898); Chem. Zentr. **1898, I,** 1019.
(589) Radziszewski: Ber. **6,** 492 (1873).
(590) Raffaeli: Industria chimica **8,** 575 (1933); Chem. Zentr. **1933, II,** 1025.
(591) Ralston and Vander Wal: U. S. patent 2,197,709; Chem. Abstracts **34,** 5466 (1940).
(592) Ralston and Vander Wal: British patent 528,312; Chem. Abstracts **35,** 7418 (1941).
(593) Rangier: Compt. rend. **220,** 246 (1945).
(594) Raymond: J. chim. phys. **28,** 480 (1931).
(595) Raymond-Hamet: Bull. sci. pharmacol. [36], **41** 224 (1934).
(596) Read and Andrews: J. Chem. Soc. **119,** 1774 (1921).
(597) Read and Campbell: J. Chem. Soc. **1930,** 2682.
(598) Read and Reid: J. Chem. Soc. **1928,** 1487.
(599) Read and Williams: J. Proc. Roy. Soc. N. S. Wales **51,** 558 (1917).
(600) Reich: Arch. sci. phys. et nat. [4] **45,** 191 (1918).
(601) Reich: Arch. sci. phys. et nat. [4] **45,** 259 (1918).
(602) Reich: Bull. soc. chim. [4] **21,** 217 (1917); Chem. Zentr. **1918, I,** 521.
(603) Reich and Chang: Helv. Chim. Acta **3,** 235 (1920).
(604) Reich and Koehler: Ber. **46,** 3727 (1913).
(605) Reich, van Wijck, and Waelle: Helv. Chim. Acta **4,** 242 (1921); Chem. Zentr. **1921, III,** 469.
(606) Reichert: Arch. Pharm. **274,** 505 (1936).
(607) Reichert: German patent 629,313; Chem. Abstracts **30,** 4875 (1936).
(608) Reichert and Koch: Ber. **68,** 445 (1935).
(609) Reichert and Koch: Arch. Pharm. **273,** 265 (1935).
(610) Reichstein: Helv. Chim. Acta **15,** 1450 (1932).
(611) Reihlen, Knopfle, and Sapper: Ann. **534,** 247 (1938).
(612) Reimer and Kamerling: J. Am. Chem. Soc. **55,** 4643 (1933).
(613) Reimer and Tobin: J. Am. Chem. Soc. **52,** 341 (1930).
(614) Reimer and Tobin: J. Am. Chem. Soc. **62,** 2515 (1940).
(615) Reimer and Tobin: J. Am. Chem. Soc. **63,** 2490 (1941).
(616) Reynhart: Rec. trav. chim. **46,** 72 (1927); Chem. Zentr. **1927, I,** 2301.
(617) Richter and Blaschko: J. Chem. Soc. **1937,** 601.
(618) Riegel and Wittcoff: J. Am. Chem. Soc. **68,** 1805 (1946).
(619) Riegel and Wittcoff: J. Am. Chem. Soc. **68,** 1913 (1946).
(620) Riley and Friend: J. Chem. Soc. **1932,** 2342.
(621) Robinson: J. Chem. Soc. **95,** 2167 (1909).
(622) Robinson and Sugasawa: J. Chem. Soc. **1931,** 3163.
(623) Rosenmund: Ber. **42,** 4778 (1909).
(624) Rosenmund: Ber. **43,** 3412 (1910).
(625) Rosenmund: Ber. **46,** 1034 (1913).
(626) Rosenmund: German patent 244,321; Frdl. **10,** 1234.
(627) Rosenmund and Kuhnhenn: Ber. **56,** 1262 (1923).
(628) Rosenmund, Nothnagel, and Riesenfeldt: Ber. **60,** 392 (1927).
(628a) Ross: U. S. patent 2,448,739; Chem. Abstracts **43,** 2628 (1949).
(629) Ross, Percy, Brandt, Gebhart, Mitchell, and Yolles: Ind. Eng. Chem. **34,** 924 (1942).
(630) Rubin and Day: J. Org. Chem. **5,** 54 (1940).
(631) Ruggli and Knecht: Helv. Chim. Acta **27,** 1108 (1944).
(632) Rügheimer: Ber. **14,** 428 (1881).
(633) Ruhemann: J. Chem. Soc. **79,** 918 (1901).

(634) Ruhemann: Ber. **46,** 3384 (1913).
(635) Ruhemann and Beddow: J. Chem. Soc. **77,** 984 (1900).
(636) Ruhemann and Beddow: J. Chem. Soc. **77,** 1119 (1900).
(637) Ruhemann and Stapleton: J. Chem. Soc. **77,** 1179 (1900).
(638) Ruhemann and Wragg: J. Chem. Soc. **79,** 1185 (1901).
(639) Rupe and Engel: Helv. Chim. Acta. **18,** 1190 (1935); Chem. Zentr. **1936, I,** 778.
(640) Rupe and Proske: Ber. **43,** 1231 (1910).
(641) Rupe and Rinderknecht: Ann. **442,** 61 (1925).
(642) Russell and VanderWerf: J. Am. Chem. Soc. **69,** 11 (1947).
(643) Ryden, Glavis, and Marvel: J. Am. Chem. Soc. **59,** 1014 (1937).
(644) Sabatier and Senderens: Compt. rend. **132,** 1254 (1901); Chem. Zentr. **1901, II,** 201.
(645) Sabetay: Bull. soc. chim. [4] **45,** 69 (1929).
(646) Sabetay: Compt. rend. **197,** 557 (1933); Chem. Zentr. **1933, II,** 2862.
(647) Sabetay and Bleger: Ann. chim. anal. [2] **12,** 261 (1930); Chem. Zentr. **1930, II,** 2808.
(648) Sawai: J. Pharm. Soc. Japan **49,** 260 (1929); Chem. Abstracts **23,** 3230 (1929).
(649) Schales: Ber. **68,** 1579 (1935).
(650) Schales: J. prakt. Chem. **144,** 214 (1936).
(651) Schering: French patent 831,131; Chem. Zentr. **1939, I,** 3590.
(652) Schering-Kahlbaum A.-G.: German patent 533,464; Chem. Zentr. **1931, II,** 3264.
(653) Schirm: U. S. patent 2,246,762; Chem. Abstracts **35,** 6264 (1941).
(654) Schlenk, Appenrodt, Michael, and Thal: Ber. **47,** 473 (1914).
(655) Schmidt: Z. physik. Chem. **A176,** 237 (1936); Chem. Zentr. **1937, I,** 826.
(656) Schmitt: Ann. **127,** 319 (1863).
(657) Schnider: U. S. patent 2,393,820; Chem. Abstracts **40,** 3475 (1946).
(658) Schönberg: Trans. Faraday Soc. **30,** 18 (1934).
(659) Schönberg and Mustafa: Nature **153,** 195 (1944).
(660) Schönberg and Mustafa: J. Chem. Soc. **1944,** 387.
(661) Schramm: Ber. **18,** 35 (1885).
(662) Schramm: Ber. **24,** 1332 (1891).
(663) Schramm: Ber. **26,** 1709 (1893).
(664) Schroeter: German patent 220,852; Frdl. **10,** 1309.
(665) Semmler: Ber. **42,** 584 (1909).
(666) Shah and Alimchandani: J. Indian Chem. Soc. **8,** 261 (1931).
(667) Shamshurin: J. Gen. Chem. (U.S.S.R.) **1,** 99 (1946).
(668) Shoesmith and Connor: J. Chem. Soc. **1927,** 2230.
(669) Shorygin, Tsagulyants, and Guseva: J. Gen. Chem. (U.S.S.R.) **63,** 506 (1931); Chem. Zentr. **1932, I,** 2948.
(670) Shorygin and Shorygina: J. Gen. Chem. (U.S.S.R.) **9,** 845 (1939); Chem. Abstracts **34,** 389 (1940).
(671) Shriner and Anderson: J. Am. Chem. Soc. **61,** 2705 (1939).
(672) Sigmund and Uchann: Monatsh. **51,** 234 (1929).
(673) Simon: Ann. **31,** 265 (1839).
(674) Simonoff and Hartung: J. Am. Pharm. Assoc. **35,** 306 (1946); Chem. Abstracts **41,** 2705 (1947).
(675) Sivadjian: J. pharm. chim. [8] **12,** 266 (1930); Chem. Zentr. **1931, I,** 1487.
(676) Skita: German patent 406,149; Chem. Zentr. **1925,** I, 1530.
(677) Skita and Keil: Ber. **65,** 424 (1932).
(678) Skita and Meyer: Ber. **45,** 3579 (1912).
(679) Slotta and Haberland: Angew. Chem. **46,** 766 (1933).
(680) Slotta and Heller: Ber. **63,** 1024 (1930).
(681) Slotta and Heller: Ber. **63,** 3029 (1930).
(682) Slotta and Kethur: Ber. **71,** 59 (1938).
(683) Slotta and Szyszka: J. prakt. Chem. [2] **137,** 339 (1933).
(684) Slotta and Szyszka: Ber. **68,** 184 (1935).

(685) Smith and Moll: U. S. patent 2,281,252; Chem. Abstracts **36**, 5586 (1942).
(686) Smith and Niederl: J. Am. Chem. Soc. **53**, 806 (1931).
(687) Smith and Opie: J. Org. Chem. **6**, 427 (1941).
(688) Société des usines chimiques Rhône-Poulenc: British patent 438,820; Chem. Abstracts **30**, 2993 (1936).
(689) Soday: U. S. patent 2,315,557; Chem. Abstracts **37**, 5606 (1943).
(690) Söderbäck: Ann. **443**, 142 (1925).
(691) Sommer: Ber. **28**, 1328 (1895).
(692) Sommer: Ber. **29**, 356 (1896).
(693) Sonn and Schellenberg: Ber. **50**, 1513 (1917).
(694) Sontag: Ann. Chim. [11] **1**, 359 (1934); Chem. Abstracts **28**, 4716 (1934).
(695) Späth: Monatsh. **35**, 319 (1914); Chem. Zentr. **1914**, **I**, 2089.
(696) Späth: Monatsh. **35**, 463 (1914).
(697) Späth: Monatsh. **36**, 1 (1914).
(698) Späth: Monatsh. **40**, 129 (1919).
(699) Späth, and Dobrowsky: Ber. **58**, 1274 (1925).
(700) Späth, Orechoff, and Kuffner: Ber. **67**, 1214 (1934).
(701) Spielman and Mortenson: J. Am. Chem. Soc. **61**, 666 (1939).
(702) Spilker and Schade: Ber. **65**, 1686 (1932).
(703) Spring and Marsenille: Bull. soc. chim. [3] **8**, 13 (1892).
(704) Stanley, Minkoff, and Youell: U. S. patent 2,248,518; Chem. Abstracts **35**, 6598 (1941).
(705) Staudinger and Rheiner: Helv. Chim. Acta **7**, 8 (1924); Chem. Zentr. **1924**, **I**, **1778**.
(706) Staudinger and Suter: Ber. **53**, 1092 (1920).
(707) Steinkopf and Kühnel: Ber. **75**, 1323 (1942).
(708) Stenhouse: Ann. **55**, 1 (1845).
(709) Stenhouse: Ann. **57**, 79 (1846).
(710) Stoermer and Biesenbach: Ber. **38**, 1958 (1905).
(711) Stoermer and Kippe: Ber. **36**, 3992 (1903).
(712) Straus: Ann. **342**, 190 (1905).
(713) Straus: Ber. **42**, 2866 (1909).
(714) Straus and Ehrenstein: Ann. **442**, 93 (1925).
(715) Straus and Thiel: Ann. **525**, 151 (1936).
(716) Stuurmann: Proc. Koninkl. Nederland. Akad. Wetenschappen **38**, 450 (1935); Chem. Zentr. **1935**, **II**, 991.
(717) Sudborough and Thompson: J. Chem. Soc. **83**, 666 (1903).
(718) Sugasawa and Shigehara: Ber. **74**, 459 (1941).
(719) Suknevich and Chilingaryan: Ber. **68**, 1210 (1935).
(720) Suter and Bordwell: J. Am. Chem. Soc. **65**, 507 (1943).
(721) Suter and Milne: J. Am. Chem. Soc. **65**, 582 (1943).
(722) Swarts: Ann. **137**, 229 (1866).
(723) Swarts: Bull. soc. chim. [4] **25**, 145 (1919).
(723a) Swern, Billen, and Knight: J. Am. Chem. Soc. **71**, 1152 (1949).
(724) Takebayashi: J. Chem. Soc. Japan **62**, 1107 (1947); Chem. Abstracts **41**, 3065 (1947).
(725) Takebayashi: J. Chem. Soc. Japan **63**, 280 (1942); Chem. Abstracts **41**, 3064 (1947).
(726) Takeda: J. Pharm. Soc. Japan **1917**, No. 426, 691; Chem. Abstracts **11**, 3241 (1919).
(727) Takeda and Kuroda: J. Pharm. Soc. Japan **449**, 561 (1919); Chem. Abstracts **14**, **179** (1920).
(728) Tanaka: Mem. Coll. Sci., Kyoto Imp. Univ. **A22**, 97 (1939); Chem. Abstracts **34**, 403 (1940).
(729) Tanaka and Midzuno: J. Pharm. Soc. Japan **49**, 47 (1929); Chem. Zentr. **1929**, **I**, 2978.
(730) Tanaka and Midzuno: J. Pharm. Soc. Japan **49**, 255 (1929); Chem. Abstracts **23**, 3214 (1929).
(731) Tausz: Petroleum **13**, 649 (1918); Chem. Zentr. **1919**, **II**, 125.

(732) Taylor: J. Chem. Soc. **1937,** 304.
(733) Taylor: J. Chem. Soc. **1937,** 343.
(734) Terent'ev and Gomberg: J. Gen. Chem. (U.S.S.R.) **8,** 662 (1938); Chem. Zentr. **1939, II,** 3066.
(735) Terent'ev, Vinogradova, and Gal'pern: Wiss. Ber. Moskauer Staatsuniv. **6,** 235 (1936); Chem. Zentr. **1937, II,** 1628.
(736) Thiele: Chem.-Ztg. **70,** 657 (1912).
(737) Thiele and Haeckel: Ann. **325,** 1 (1902).
(738) Thomas and Hochwalt: U. S. patent 2,372,615; Chem. Abstracts **39,** 3549 (1945).
(739) Thorpe: Z. Chem. **1871,** 130.
(740) Tiffeneau: Compt. rend. **135,** 1346 (1902).
(741) Tiffeneau: Compt. rend. **145,** 811 (1907).
(742) Tiffeneau: Ann. chim. [8] **10,** 322 (1907).
(743) Tiffeneau and Fourneau: Compt. rend. **146,** 697 (1908).
(744) Tiffeneau and Fourneau: Bull. soc. chim. [4] **13,** 971 (1913).
(745) Tiffeneau and Fourneau: Bull. soc. chim. [4] **15,** 275 (1914).
(746) Tiffeneau and Führer: Bull. soc. chim. [4] **15,** 162 (1914); Chem. Zentr. **1914, I,** 1338.
(747) Tiffeneau and Tchoubar: Compt. rend. **207,** 918 (1938).
(748) Tilden and Sudborough: J. Chem. Soc. **63,** 479 (1893).
(749) Ting and Robertson: J. Chem. Soc. **1947,** 628.
(750) Titley: J. Chem. Soc. **1926,** 508.
(751) Tomayo and Viguera: Anales fís. quím. (Madrid) **38,** 192 (1942); Chem. Abstracts **37,** 5034 (1943).
(752) Tomita and Watanabe: J. Pharm. Soc. Japan **58,** 783 (1938); Chem. Abstracts **33,** 2524 (1939).
(753) Tommila: Ann. Acad. Sci. Fennicae **39,** No. 11 (1934); Chem. Zentr. **1934, II,** 1758.
(754) Tönnies: Ber. **11,** 1511 (1878).
(755) Toennies: Ber. **13,** 1845 (1880).
(756) Toennies: Ber. **20,** 2982 (1887).
(756a) Trevoy and Brown: J. Am. Chem. Soc. **71,** 1675 (1949).
(757) Trillat: Bull. soc. chim. [3] **29,** 35 (1903).
(757a) Truce and Suter: J. Am. Chem. Soc. **70,** 3851 (1948).
(758) Tutin, Caton, and Hann: J. Chem. Soc. **95,** 2113 (1909).
(759) Urion and Namias: Bull. soc. chim. [5] **3,** 2333 (1936).
(760) Ushakov, Chistov, and Shlosberg: J. Gen. Chem. (U.S.S.R.) **5,** 1391 (1935); Chem. Zentr. **1937, I,** 3619.
(761) Vaughn: J. Am. Chem. Soc. **56,** 2064 (1934).
(762) Vaughn and Nieuwland: J. Am. Chem. Soc. **56,** 1207 (1934).
(763) Vaughn, Vogt, and Nieuwland: J. Am. Chem. Soc. **56,** 2120 (1934).
(764) Vavon and Jakes: Compt. rend. **183,** 299 (1926); Chem. Zentr. **1926, II,** 1638.
(765) Vavon and Jakes: Bull. soc. chim. [4] **41,** 90 (1927).
(766) Venkataraman: J. Indian Chem. Soc. **7,** 157 (1930).
(767) Vorländer and Herrmann: Ann. **320,** 66 (1901).
(768) Walling, Kharasch, and Mayo: J. Am. Chem. Soc. **61,** 2693 (1939).
(769) Ward: U. S. patent 2,321,440; Chem. Abstracts **37,** 6768 (1943).
(770) Warnat: Festschrift E. C. Barell, p. 255 (1936); Chem. Zentr. **1936, II,** 3911.
(771) Waterman and Kok: Rec. trav. chim. **53,** 1133 (1934).
(772) Weinmayr: U. S. patent 2,378,453; Chem. Abstracts **39,** 3939 (1945).
(773) Weinmayr: U. S. patent 2,398,483; Chem. Abstracts **40,** 4394 (1946).
(774) Weitzenbock: Monatsh. **39,** 307 (1918); Chem. Zentr. **1918, II,** 621.
(775) Wieland: Ber. **36,** 2558 (1903).
(776) Wieland and Dorrer: Ber. **63,** 404 (1931).
(777) Wieland and Fischer: Ann. **446,** 49 (1926).

(778) WIELAND AND SEMPER: Ann. **358,** 36 (1908).
(778a) WILEY AND HOBSON: J. Am. Chem. Soc. **71,** 2429 (1949).
(778b) WILEY AND SMITH: J. Am. Chem. Soc. **70,** 1560 (1948).
(778c) WILEY AND SMITH: J. Am. Chem. Soc. **70,** 2295 (1948).
(779) WILLSTÄTTER AND KING: Ber. **46,** 527 (1913).
(780) WISLICENUS AND BILHUBER: Ber. **51,** 1366 (1918).
(781) WITTIG AND HARBORTH: Ber. **77,** 315 (1944).
(782) WITTIG AND WITT: Ber. **74,** 1474 (1941).
(783) WOHL AND YASOLIMOSKII: Ber. **54,** 476 (1921).
(784) WOLFF: Ann. **394,** 68 (1912).
(785) WOLHEIM: Ber. **47,** 1440 (1914).
(786) WOLLRING: Ber. **47,** 108 (1914).
(786a) WOODCOCK: J. Chem. Soc. **1949,** 203.
(787) WOOSTER AND RYAN: J. Am. Chem. Soc. **56,** 1133 (1934).
(788) WORRALL: J. Am. Chem. Soc. **43,** 919 (1921).
(789) WORRALL: J. Am. Chem. Soc. **49,** 1598 (1927).
(790) WORRALL: J. Am. Chem. Soc. **60,** 2841 (1938).
(791) WORRALL: J. Am. Chem. Soc. **60,** 2845 (1938).
(792) WORRALL AND BENINGTON: J. Am. Chem. Soc. **60,** 2844 (1938).
(793) WORRALL AND BENINGTON: J. Am. Chem. Soc. **62,** 493 (1940).
(794) WORRALL AND FINKEL: J. Am. Chem. Soc. **61,** 2969 (1939).
(795) WORRALL AND WOLOSINSKI: J. Am. Chem. Soc. **62,** 2449 (1940).
(796) WRIGHT: J. Am. Chem. Soc. **57,** 1993 (1935).
(797) WRIGHT: J. Org. Chem. **1,** 457 (1936).
(798) YAVORSKII: J. Russ. Phys. Chem. Soc. **40,** 782 (1908); Chem. Zentr. **1908, II,** 1412.
(799) YOZICH AND FAVORSKII: J. Russ. Phys. Chem. Soc. **30,** 920 (1898); Chem. Zentr. **1899, I,** 606.
(800) YOZICH AND FAVORSKII: J. Russ. Phys. Chem. Soc. **30,** 998 (1898); Chem. Zentr. **1899, I,** 777.
(801) ZAL'KIND: J. Russ. Phys. Chem. Soc. **52,** 191 (1920); Chem. Zentr. **1923, III,** 1392.
(802) ZAL'KIND AND FUNDYLER: Ber. **69,** 128 (1936).
(803) ZAL'KIND AND FUNDYLER: J. Gen. Chem. (U.S.S.R.) **9,** 1725 (1939); Chem. Abstracts **34,** 3719 (1940).
(804) ZARTMAN AND ADKINS: J. Am. Chem. Soc. **54,** 1668 (1932).
(805) ZIEGLER AND BAHR: Ber. **61,** 253 (1925).
(806) ZIEGLER AND EWALD: Ann. **504,** 162 (1933).
(806a) ZIEGLER, JACOB, WOLLTHAN, AND WENZ: Ann. **511,** 66 (1934).
(807) ZIEGLER AND OCHS: Ber. **54,** 3003 (1921).
(808) ZIEGLER AND OCHS: Ber. **55,** 2257 (1922).
(809) ZIEGLER AND TIEMANN: Ber. **55,** 3406 (1922).
(810) ZINCKE: Ber. **10,** 996 (1877).
(811) ZINCKE: Ann. **216,** 286 (1883).
(812) ZINCKE: Ann. **240,** 137 (1887).
(813) ZINCKE AND BREUER: Ann. **226,** 23 (1884).
(814) ZINCKE AND LEISSE: Ann. **322,** 220 (1902).
(815) ZINCKE AND SCHWABE: Ber. **41,** 897 (1908).
(816) ZINCKE, SIEBERT, AND REINBACH: Ann. **322,** 174 (1902).