Reaction of a Quinone Methide with Triethyl Phosphite[1]

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Quinone methide (1) reacts with triethyl phosphite in *n*-heptane or benzene solution at 25–30° to form bisphenol (2) (65–75%), a trimer tentatively identified as trisphenol (3) (12–17%), phosphonate (4) (2–5%), and minor by-products. The phosphite functions as a true catalyst for the unusual carbon–carbon condensations leading to 2 and 3, and rate measurements show that the disappearance of 1 follows strict second-order kinetics (first order in 1, first order in phosphite). In the presence of ethanol, phosphonate 4 becomes the principal product, while in the presence of benzaldehyde equivalent amounts of triethyl phosphate and stilbenol (20) are formed in a major competing process. The immediate precursor of bisphenol 2 is shown to be quinone methide (11), whose rearrangement to 2 can be accelerated by carrying out the reaction in the presence of triethylamine. On the basis of these data and other facts, it is shown that the reaction of 1 with triethyl phosphite can be rationalized by a mechanism involving ylides (8 and 12) as key intermediates. Addition of 8 or 12 to 1, followed by prototropic rearrangements and loss of triethyl phosphite, accounts for the formation of bisphenol 2 and trisphenol 3, respectively.

In recent years the reactions of carbonyl compounds with trivalent phosphorus nucleophiles have been studied extensively.[3] However, at the time the present work was begun there appeared to be no information available in the literature regarding reactions of these nucleophiles with quinone methides.[4] Our interest in this area was prompted by observations made earlier in connection with studies relating to the mechanism of action of synergistic antioxidant systems containing hindered phenols and compounds of trivalent phosphorus.[1a] Under certain conditions it appeared that appropriately substituted phenols could be converted to quinone methides in inhibitor systems of this type,[1a] and for this reason it was felt that insight into the over-all inhibition process might be forthcoming from separate studies of quinone methide–P(III) nucleophile reactions. An investigation of the products and mechanism of such a reaction, *viz.*, the reaction of quinone methide 1 with triethyl phosphite, is described in the present paper.

Results and Discussion

Quinone methide 1 cannot be isolated as such because of its tendency to undergo spontaneous self-condensation in concentrated solutions.[5] However, dilute solutions of 1 in inert solvents are reasonably stable and easy to prepare; under these conditions reactions of 1 with added reagents can be studied readily. In the present work the quinone methide was generated *in situ* by dehydrochlorination of 2,6-di-*t*-butyl-4-chloromethylphenol with triethylamine. This reaction proceeds very rapidly at room temperature in hydrocarbon solvents and has been shown to give the desired product in quantitative yield.[5c,6]

Dilute solutions of 1 in *n*-heptane or benzene were allowed to react at room temperature with various amounts of triethyl phosphite (0.20–2.0 mol/mol of 1). In some of these experiments the reaction mixtures also contained triethylamine (0.0–1.0 mol/mol of 1). Under all conditions studied the major product of the reaction was found to be bisphenol 2, a substance which is *not* formed during the quinone methide's spontaneous self-condensation.[5] Several of the product mixtures were analyzed quantitatively by means of programmed temperature vpc; Scheme I shows the identified products and their yields for a series of runs carried out in *n*-heptane solution [1, 0.04 *M*; $P(OEt)_3$, 0.04–0.08 *M*; Et_3N, 0.00–0.01 *M*]. Although the structure assigned to 3 should be regarded as tentative (see Experimental Section), the high resolution mass spectrum of the material clearly shows it to be a trimer of 1. Compounds 5 and 6 are the products expected to result from the self-reaction of 1,[5b,c] a minor path at most under these conditions. A notable feature of the reaction is the almost complete absence of products containing phosphorus. Analyses by vpc showed that the amounts of triethyl phosphite consumed were equivalent (within experimental error) to the low yields of phosphonate 4; thus the phosphite must have functioned as a true catalyst for the conversion of the quinone methide to bisphenol 2 and the trimer, 3. This unusual catalytic aspect of the reaction was of particular interest, and it provided a strong incentive for detailed study of the reaction mechanism.

A further reaction of 1 (0.02 *M*) with triethyl phosphite (0.016 *M*) was carried out in *n*-heptane containing triethylamine (0.002 *M*) and a large excess of styrene (0.87 *M*). Polystyrene was not formed, and no new products were detected by vpc, a result which can be taken as evidence against free radical intermediates. Additional evidence for the absence of radicals was provided by the nmr spectra of mixtures undergoing reaction (*vide infra*), in that no paramagnetic line

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[1] (a) Paper V of a series on oxidation inhibitors. Paper IV: W. H. Starnes, Jr., and N. P. Neureiter, *J. Org. Chem.*, **32**, 333 (1967). (b) Presented in part at the 24th Southwest Regional Meeting of the American Chemical Society, Austin, Texas, Dec 5, 1968.

[2] (a) Summer employee, 1965; (b) summer employee, 1968.

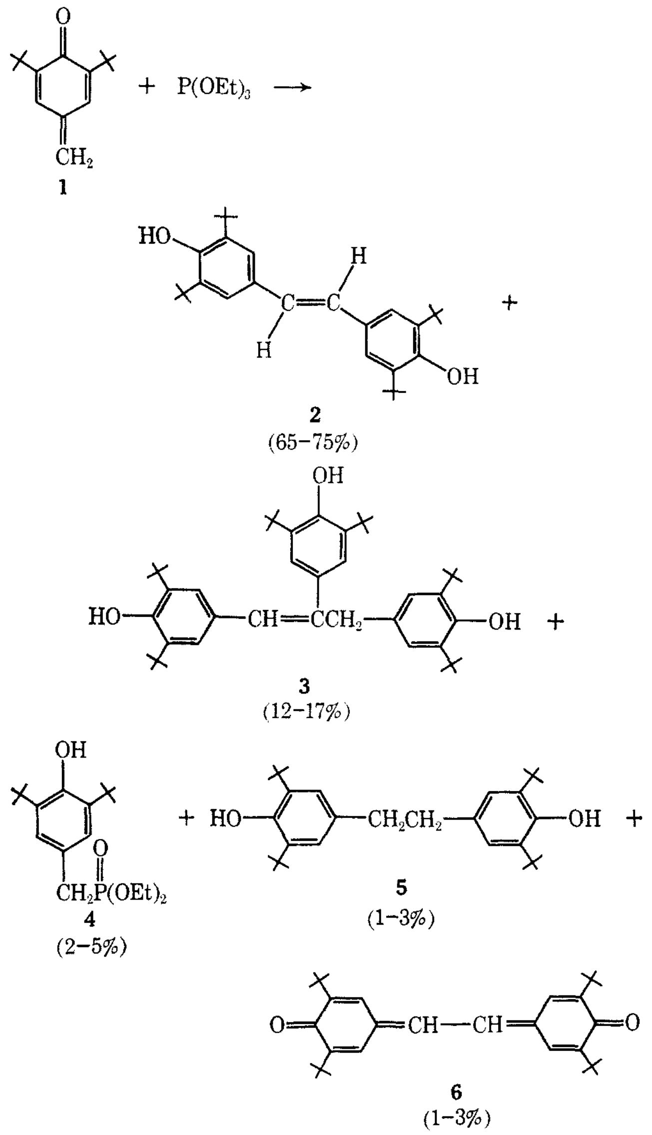
[3] For reviews, see (a) F. Ramirez, *Pure Appl. Chem.*, **9**, 337 (1964); (b) B. A. Arbusow, *ibid.*, **9**, 307 (1964); (c) F. Ramirez, *Bull. Soc. Chim. Fr.*, 2443 (1966); (d) F. Ramirez, *Accounts Chem. Res.*, **1**, 168 (1968); (e) R. G. Harvey and E. R. de Sombre in "Topics in Phosphorus Chemistry," Vol. 1, M. Grayson and E. J. Griffith, Ed., John Wiley & Sons, Inc., New York, N. Y., 1964, pp 57–111; and (f) A. J. Kirby and S. G. Warren, "The Organic Chemistry of Phosphorus," Elsevier Publishing Co., Amsterdam, The Netherlands, 1967, Chapter 3.

[4] (a) The reaction of triethyl phosphite with 10-methyleneanthrone has been described in two recent reports: A. N. Al-Khafaji, Ph.D. Thesis, University of Texas, Austin, Texas, 1966; and B. A. Arbuzov, V. M. Zoroastrova, and N. D. Ibragimova, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 687 (1967). Diethyl 9-(10-ethoxyanthryl)methylphosphonate was obtained in both studies, and no other products were identified. (b) B. E. Ivanov, L. A. Valitova, and T. G. Vavilova [*ibid.*, 741 (1968)] have recently described a similar reaction which is believed to involve attack of triethyl phosphite on an *o*-quinone methide generated *in situ*.

[5] (a) L. J. Filar and S. Winstein, *Tetrahedron Lett.*, No. 25, 9 (1960); (b) R. H. Bauer and G. M. Coppinger, *Tetrahedron*, **19**, 1201 (1963); (c) N. P. Neureiter, *J. Org. Chem.*, **28**, 3486 (1963).

[6] W. H. Starnes, Jr., *ibid.*, **31**, 3164 (1966).

SCHEME I



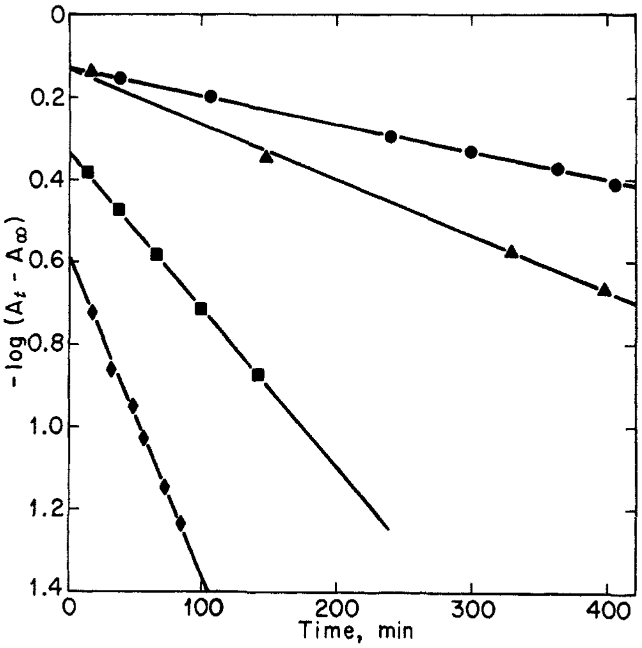


Figure 1.—Kinetic plots for reactions of quinone methide **1** with P(OEt)$_3$ in n-heptane at 30.0°. ●, run 1; ▲, run 4; ■, run 7; ◆, run 8. For experimental conditions, see Table I.

TABLE I

RATE CONSTANTS FOR REACTIONS OF QUINONE METHIDE 1 WITH TRIETHYL PHOSPHITE IN n-HEPTANE AT 30.0°

Run	**1**, $M \times 10^2$	Et$_3$N,[a] $M \times 10^2$	P(OEt)$_3$, $M \times 10^2$	$10^5\ k'$, sec^{-1}
1	4.00	0.40	0.80	2.79
2	4.00	0.00	1.60	5.39
3	4.00	0.40	1.60	5.28
4	4.00	0.80	1.60	5.22
5	4.00	2.00	1.60	5.67
6	2.00	0.20	1.60	5.58
7	4.00	0.40	4.00	14.4
8	4.00	0.40	8.00	27.9

[a] Amine in excess of that required for quantitative formation of **1** from 2,6-di-t-butyl-4-chloromethylphenol.

broadening was observed.[7] In order to obtain direct evidence against the rather unlikely possibility that **2** was formed by dimerization of a carbene, a reaction of **1** (0.04 M) with triethyl phosphite (0.008 M) was carried out in n-heptane containing triethylamine (0.004 M) and excess cyclohexene (4.6 M). No new products were formed, and the product distribution did not differ significantly from the distribution found for a parallel run performed in the absence of added olefin.

The kinetics of the reaction of **1** with triethyl phosphite were investigated in n-heptane at 30°, using the strong infrared band at 918 cm^{-1} to follow rates of disappearance of the quinone methide. Results are summarized in Table I. The reaction was found to be cleanly first order in quinone methide concentration, as is evident from the typical kinetic plots shown in Figure 1. Triethylamine had no effect on the rate. However, a plot of apparent first-order rate constants, k', $vs.$ phosphite concentration gave an excellent straight line extrapolating directly through the origin.[8] Hence, $k' = k[\mathrm{P(OEt)_3}]$, where k is the true second-order rate constant. The rate law is therefore $-\mathrm{d}[\mathbf{1}]/\mathrm{d}t = k[\mathrm{P(OEt)_3}][\mathbf{1}]$, with $k = 3.5 \times 10^{-3}$ l. mol^{-1} sec.$^{-1}$

Scheme II shows a mechanism for the reaction which is consistent with the data presented thus far. Attack of the methylene group of **1** by triethyl phosphite (eq 1) seems eminently reasonable, since many other nucleophiles have been found to attack p-quinone methides at this position exclusively.[9] Equation 1 is subject to much less steric hindrance than other possible reaction modes, has the advantage of generating a resonance-stabilized phenoxide moiety, and finds a direct analogy in the mechanism which apparently operates in the reaction of triethyl phosphite with 10-methyleneanthrone.[4a] The benzylic protons of betaine **7** should be relatively acidic; thus in solvents of low polarity **7** might be expected to undergo rapid rearrangement to

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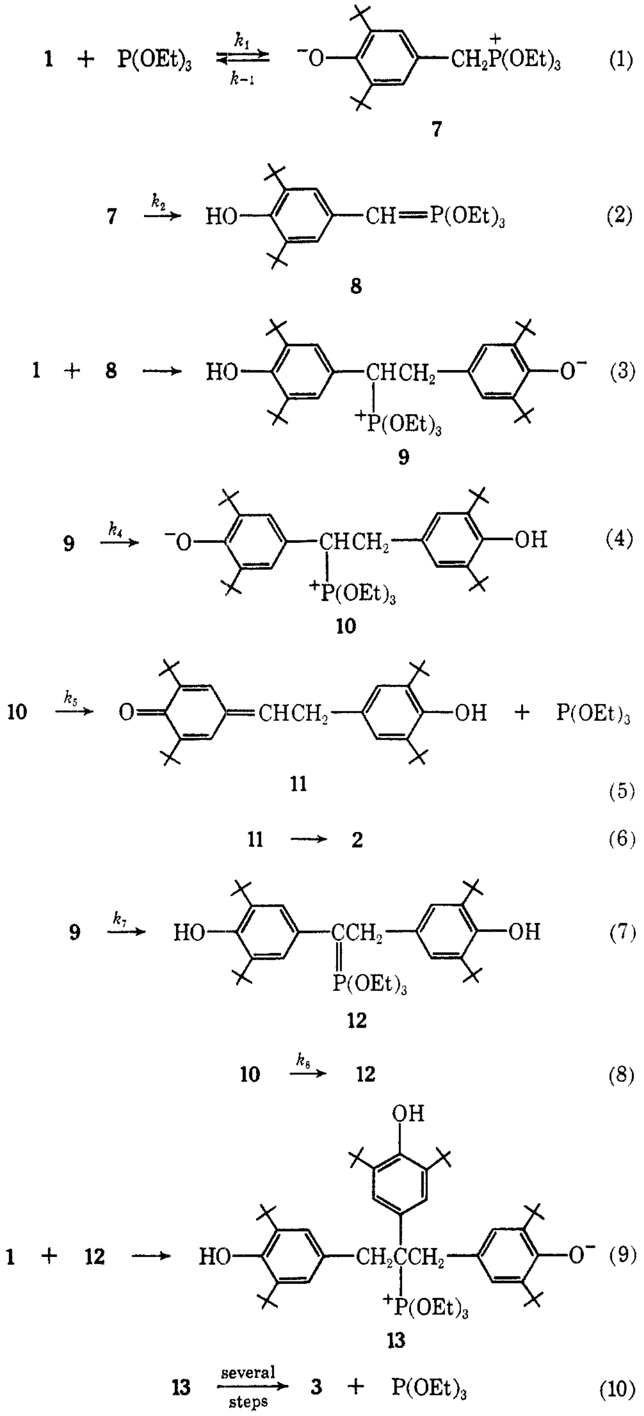
[7] Hindered phenoxy radicals are known to be involved in the spontaneous conversion of quinone methide **1** into bisphenol **5** and stilbenequinone **6** [see ref 5b, 5c, and B. R. Loy, *J. Org. Chem.*, **31**, 2386 (1966)]. However, these radicals would not be expected to be efficient initiators for styrene polymerization, and their concentration was undoubtedly quite low under the conditions of our experiments.

[8] These results show that the spontaneous self-condensation[5] of **1** was not fast enough to compete effectively with the phosphite-catalyzed condensation under the conditions used for the kinetic runs. However, product analyses indicated that the spontaneous reaction did occur to a minor extent in all of these experiments.

[9] A. B. Turner, *Quart. Rev.* (London), **18**, 347 (1964), and references therein.

SCHEME II



ylide **8** (eq 2),[10] a stable species with reduced dipolar character. Ylide **8** should be highly nucleophilic and should therefore react quickly with another quinone methide molecule to produce a new betaine, **9** (eq 3). In principle, **9** could undergo a β-elimination reaction leading directly to triethyl phosphite and bisphenol **2**. However, the nmr spectra of reacting mixtures (see Experimental Section) showed that **2** *was not an initial product*, and that it must have been formed by a mechanism involving quinone methide **11** as an intermediate. Direct conversion of betaine **9** to triethyl phosphite and bisphenol **2** is thus ruled out, leaving the path shown in eq 4–6 as the only reasonable alternative. By analogy with eq 2, betaine **9** and/or betaine **10** might also rearrange to ylide **12** (eq 7 and 8), whose reaction with **1** would give betaine **13** (eq 9). This betaine could then be converted to the trimer, **3**, *via* a sequence of reactions (eq 10) analogous to eq 4–6.

By making the usual steady-state assumption for reactive intermediates **7**–**10** and **12**, it can readily be shown that Scheme II predicts the clean second-order kinetics actually observed. For example, if all steps are assumed to be irreversible and **12** is considered to be formed from both **9** and **10**, the rate constant k may be set equal to $2k_1 + [k_1k_7/(k_4 + k_7)] + [k_1k_4k_8/(k_4 + k_7)(k_5 + k_8)]$. If eq 1 is reversible, $k = [2k_1k_2/(k_{-1} + k_2)] + [k_1k_2k_7/(k_{-1} + k_2)(k_4 + k_7)] + [k_1k_2k_4k_8/(k_{-1} + k_2)(k_4 + k_7)(k_5 + k_8)]$. Simpler expressions result if k_7 (or k_8) = 0, and second-order kinetics are also predicted by several other variations of the mechanism which take into account the possibility of reversibility in other steps and the occurrence of bimolecular prototropic shifts. Discussion of all the possible variations would serve no useful purpose at this time, for we have no real basis for deciding which one of these mechanisms is actually operative. The point we do wish to emphasize here is that the general mechanistic picture shown in Scheme II has been found to be entirely consistent with our kinetic results.

Other conceivable routes to the trimer, **3**, would involve addition of ylide **8** to quinone methide **11** and/or bisphenol **2**, followed by appropriate sequences involving prototropic shifts and loss of triethyl phosphite. However, steady-state analysis shows that such mechanisms will not give second-order kinetics unless the fraction of **8** reacting with **1** remains constant with time—a requirement which obviously cannot be met under the circumstances. Since the dimeric products, **2** and **11**, would certainly not be expected to undergo addition of ylide **8** at identical rates,[11] changing the relative amounts of **2** and **11** present during the reaction should change the relative amounts of **2** and **3** present in the final products if the trimer were actually formed from one (or both) of the dimers. This possibility was investigated by carrying out a reaction of **1** (0.04 *M*) with triethyl phosphite (0.08 *M*) in *n*-heptane containing a high concentration of triethylamine (0.43 *M*). Nmr measurements showed that the **11**:**2** ratio remained very low ($\ll$1) throughout the course of this experiment. However, the yields of the final products did not differ significantly from the yields obtained in a parallel run carried out under conditions such that the **11**:**2** ratio remained high (>1) during most of the reaction (see Experimental Section). These observations provide compelling evidence against trimer formation *via* quinone methide **11** and/or bisphenol **2**.[12]

Scheme III shows another mechanism that has been considered for the reaction of **1** with triethyl phosphite. The initial step of this mechanism (eq 11) seems less likely than eq 1 for reasons which were given above. On the other hand, eq 11 cannot be excluded auto-

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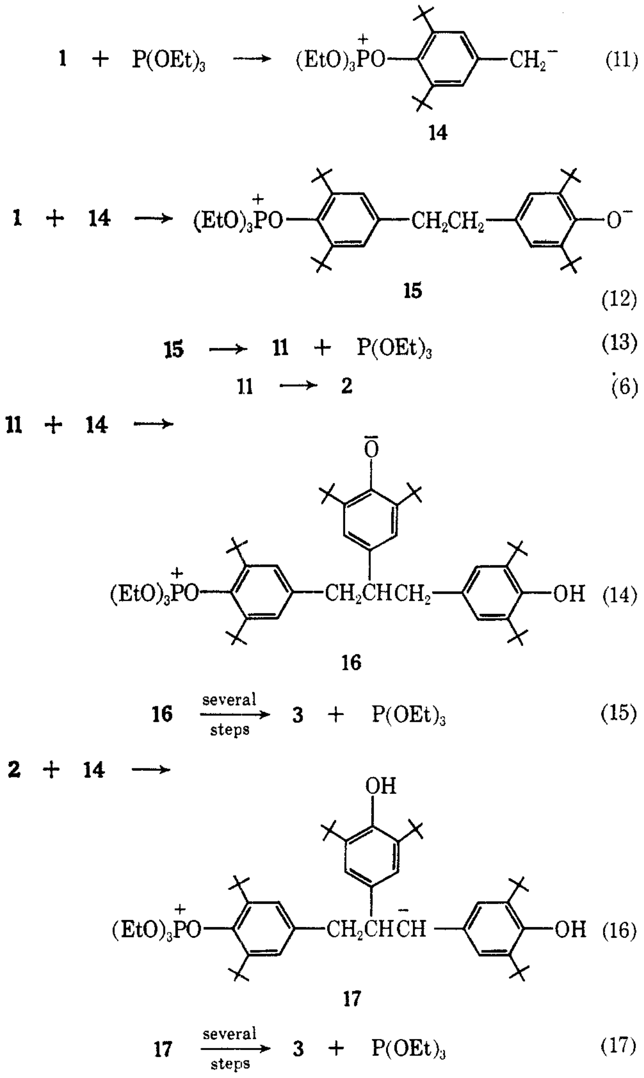
[10] (a) A few phosphitemethylenes (trialkoxyalkylidenephosphoranes) have previously been described in the literature, but their chemistry has not been investigated extensively. For other examples of phosphitemethylenes, see (b) F. Ramirez, O. P. Madan, and C. P. Smith, *J. Org. Chem.*, **30**, 2284 (1965); (c) E. J. Corey and G. Märkl, *Tetrahedron Lett.*, 3201 (1967); (d) G. H. Birum, U. S. Patent 3,058,876 (1962); and (e) W. J. Middleton, U. S. Patent 3,067,233 (1962).

[11] Quinone methide **11** should obviously be much more reactive.

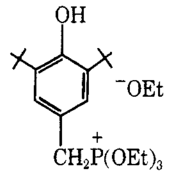
[12] It should be noted that all of our arguments relating to the mechanism of trimer formation will apply regardless of the trimer's structure.

SCHEME III



matically, for the phosphorus atom of trivalent phosphorus nucleophiles is known to attack carbonyl oxygen in many other reactions.[13] If occurrence of eq 11 is accepted, formation of bisphenol **2** can be accounted for by eq 12, 13, and 6, whereas the only reasonable routes to **3** would now appear to be either of two sequences: eq 14 and 15, or eq 16 and 17. However, a simple steady-state treatment shows that Scheme III also fails to predict clean second-order kinetics. Moreover, the insensitivity of the yields of the final products to changes in the **11**:**2** ratio (*vide supra*) clearly constitutes additional strong evidence against a mechanism of this type.

Further evidence in favor of Scheme II was obtained by carrying out the reaction of **1** (0.04 *M*) with triethyl phosphite (0.08 *M*) in *n*-heptane containing triethylamine (0.004 *M*) and a large amount of ethanol (1.7 *M*). The major product was phosphonate **4** (61%); bisphenol **2** (22%), trisphenol **3** (2%), and unidentified minor products were also formed. The immediate precursor of **4** is evidently ion pair **18**, which could have resulted from ethanol-catalyzed addition of triethyl phosphite to the quinone methide. This route to **18** seems unlikely, however, since a control run without phosphite showed that addition to **1** of ethanol itself



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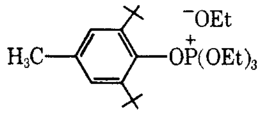

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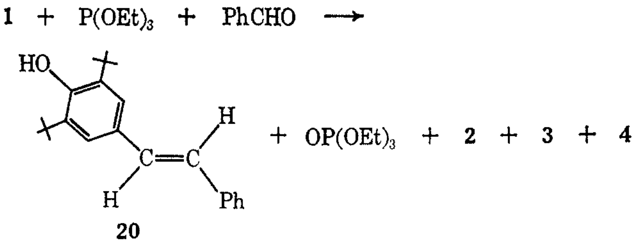
was extremely slow under these conditions. The most probable routes to **18** are therefore considered to be those involving reaction of ethanol with betaine **7** and/or ylide **8**.[14] In the presence of 1.7 *M* ethanol a very strong base such as **14** would have been expected to undergo very rapid and essentially irreversible protonation.[15] The ion pair (**19**) thus formed should then have reacted to give products such as diethyl(2,6-di-*t*-butyl-*p*-tolyl) phosphate, ethyl(2,6-di-*t*-butyl-*p*-tolyl) ether, or 2,6-di-*t*-butyl-*p*-cresol. However, vpc analysis provided no evidence for the formation of either of these substances in the experiment with added ethanol, and the nmr spectrum of the total product mixture showed that nuclear methyl groups were absent.

In a direct test for the intermediacy of ylide **8**, a reaction of **1** (0.04 *M*) with triethyl phosphite (0.08 *M*) was carried out in *n*-heptane containing triethylamine (0.004 *M*) and benzaldehyde (1.6 *M*). The identified products were stilbenol **20** (26%), triethyl phosphate (22%), phosphonate **4** (29%),[16] bisphenol **2** (19%), and trisphenol **3** (3%). Formation of stilbenol and phosphate in essentially equivalent amounts (within experimental error) is clearly best rationalized in terms of a Wittig-type reaction between ylide **8** and benzaldehyde.[17] An alternative route to the Wittig products



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[13] For examples of carbonyl oxygen attack that are of special interest within the context of the present work, *cf.* the reaction of trialkyl phosphites with *p*-benzoquinone and its homologs [F. Ramirez and S. Dershowitz, *J. Org. Chem.*, **23**, 778 (1958); F. Ramirez, E. H. Chen, and S. Dershowitz, *J. Amer. Chem. Soc.*, **81**, 4338 (1959); V. A. Kukhtin, N. S. Garif'yanov, and K. M. Orekhova, *J. Gen. Chem. USSR*, **31**, 1070 (1961)] and the reaction of triethyl phosphite with 4-tribromomethyl-4-methyl-2,5-cyclohexadien-1-one [B. Miller, *J. Amer. Chem. Soc.*, **88**, 1841 (1966)]. F. Ramirez, C. P. Smith, J. F. Pilot, and A. S. Gulati [*J. Org. Chem.*, **33**, 3787 (1968)] have recently discussed the factors influencing C *vs.* O attack in reactions of carbonyl groups with trivalent phosphorus nucleophiles.

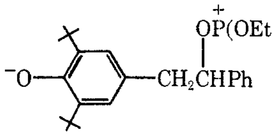
[14] It is somewhat surprising to find that the phenoxide moieties of Scheme II do not induce Arbuzov-type valence expansions analogous to that involved in the conversion of **18** into **4**. This failure is presumably due to increased steric hindrance and decreased nucleophilicity of the phenoxide species compared with ethoxide ion.

[15] The pK_a's of ethanol and toluene are *ca.* 18 and 35–37, respectively [D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, Chapter I, and references therein], and the pK_a of the conjugate acid of **14** should not differ greatly from that of toluene. Dilution with *n*-heptane probably reduces the acidity of ethanol to some extent [*cf.* E. C. Steiner and J. M. Gilbert, *J. Amer. Chem. Soc.*, **85**, 3054 (1963)]; however, under our conditions ethanol should still be an acid of sufficient strength to protonate **14** at a rate approaching the diffusion-controlled limit [see M. Eigen, *Angew. Chem. Intern. Ed. Engl.*, **3**, 1 (1964)].

[16] The rather high yield of **4** obtained in this reaction may have been caused by minor amounts of acidic impurities in our redistilled benzaldehyde (*cf.* the high yield of **4** obtained in the presence of ethanol).

[17] Other phosphitemethylenes have been found to undergo the Wittig reaction with benzaldehyde.[10c]

would involve β-elimination of a proton and triethyl phosphate from betaine **21**. This betaine might be considered to arise *via* addition of phosphite to the aldehyde carbonyl group, followed by reaction of the adduct with quinone methide **1**, or by reaction of the aldehyde with betaine **14** to form betaine **22**, followed by rearrangement of **22** into **21**. However, neither of these paths appears reasonable. The reaction of triethyl phosphite with benzaldehyde alone occurs only at temperatures above 100°;[18] this fact militates against the first path. The second path is rendered untenable by our previous evidence against **14** and by the results of a further reaction of **1** (0.04 *M*) with triethyl phosphite (0.08 *M*) and benzaldehyde (1.6 *M*) which was carried out in *n*-heptane containing triethylamine (0.004 *M*) and a large excess of ethanol (0.69 *M*). Under these conditions betaine **22** should have been trapped (at least in part) by protonation, thereby giving a new ion pair capable of undergoing conversion to one or more new products. However, as anticipated, no such products were formed, and those actually present were shown to be stilbenol **20** (46%), triethyl phosphate (47%), phosphonate **4** (51%), and bisphenol **2** (2%).



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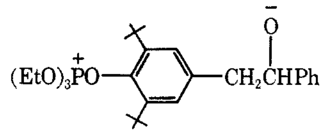

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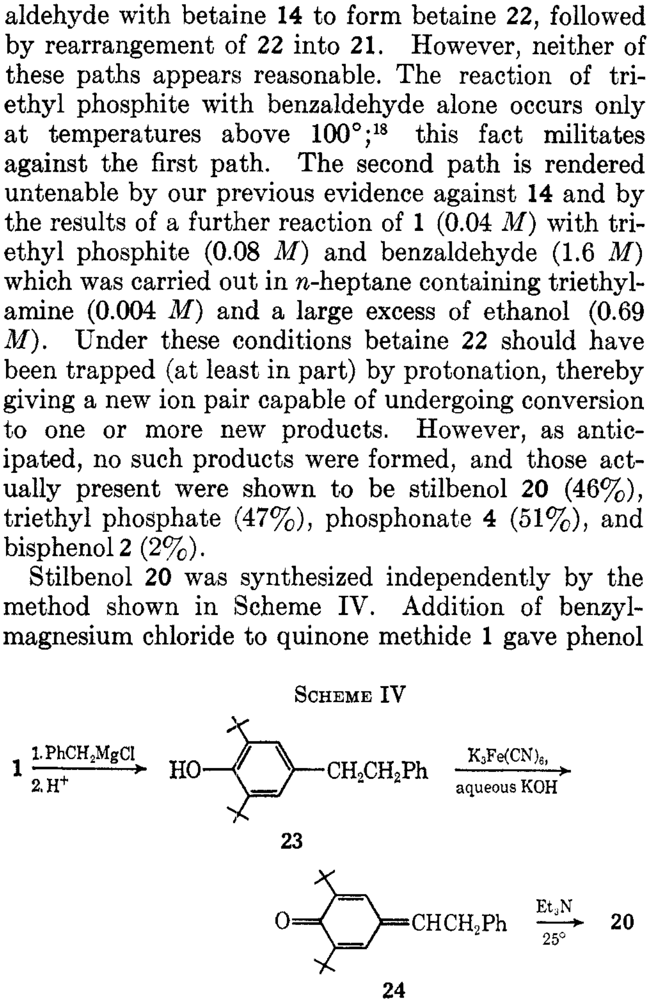
Stilbenol **20** was synthesized independently by the method shown in Scheme IV. Addition of benzylmagnesium chloride to quinone methide **1** gave phenol **23** in 77% yield. Oxidation of petroleum ether solutions of **23** with aqueous, basic ferricyanide gave high yields of the new quinone methide, **24**. This quinone methide showed little tendency to isomerize in the two-phase system used for its preparation, evidently because of its limited solubility in aqueous caustic. However, **24** underwent quantitative conversion to **20** when it was allowed to stand in hydrocarbon solvents containing triethylamine. This facile rearrangement provides an excellent analogy for our postulated isomerization of quinone methide **11** (eq 6).

Scheme IV



In view of the foregoing observations, the mechanism of Scheme II is now considered to constitute an adequate rationale (at least in a qualitative sense) for the interaction of quinone methide **1** with triethyl phosphite. We have not explored the scope of this unusual reaction, nor have we established its effect (if any) on the over-all mechanism of action of synergistic antioxidant systems containing phosphites and hindered phenols. The latter topic is clearly an intriguing subject for speculation; however, we feel that such speculation can hardly be justified here in the absence of needed information.

Experimental Section[19]

Materials.—Triethyl phosphite was distilled under vacuum in a nitrogen atmosphere and stored under nitrogen at −15°; it contained no impurities detectable by vpc or nmr analysis. Triethylamine, styrene, cyclohexene, and benzaldehyde were also purified by means of appropriate distillation techniques. Reagent grade heptane (Humble Oil & Refining Company) was usually percolated through silica gel and then stored under nitrogen; sodium-dried material gave equivalent results. Literature procedures were used to prepare 2,6-di-*t*-butyl-4-chloromethylphenol[6] and pure reference samples of *trans*-1,2-bis(3,5-di-*t*-butyl-4-hydroxyphenyl)ethylene[20] (**2**), diethyl 3,5-di-*t*-butyl-4-hydroxybenzylphosphonate[21] (**4**), 1,2-bis(3,5-di-*t*-butyl-4-hydroxyphenyl)ethane[20c] (**5**), and 3,5,3′,5′-tetra-*t*-butylstilbene-4,4′-quinone[22] (**6**). All other chemicals used were highly purified commercial products. Purities were checked by spectral measurements, vpc analyses, and the determination of appropriate physical constants.

Instrumental Analysis.—Infrared, 100-MHz nmr, and high resolution mass spectra were recorded with Perkin-Elmer Model 21, Varian Model HA-100, and AEI MS-9 spectrometers, respectively. The nmr measurements were made at ambient temperature on dilute solutions containing TMS as the internal standard. Nmr peak multiplicities are abbreviated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Exact mass measurements are referred to $C = 12$ amu. Programmed temperature vpc analyses were done with an F & M instrument (Model 500) using helium as the carrier gas; column temperature was increased at the rate of 8°/min in the 100–350° range. The following columns were employed: A, 6 ft × 0.25 in. (o.d.), stainless steel, packed with SE-30 (5%) on 40–60 mesh Chromosorb W, acid washed DMCS; B, 12 ft × 0.25 in. (o.d.), stainless steel, packed with SE-30 (2%) on 45–60 mesh Chromosorb W. The areas of vpc peaks were measured with a planimeter.

Reactions of Quinone Methide 1 with Triethyl Phosphite. A. Product Studies.—Stock solutions of triethyl phosphite (0.400 *M*), 2,6-di-*t*-butyl-4-chloromethylphenol (0.200 *M*), and triethylamine (0.200 *M*) were prepared in dry *n*-heptane and stored under nitrogen. In a typical run, the desired amounts of the solutions of phenol and amine were pipetted into a small flask, and the mixture was stirred magnetically for 5–10 min. (Excess amine was ordinarily used to insure complete reaction. Control runs showed that the phenol was quantitatively converted to **1** under all conditions studied.) The mixture was then quickly filtered under slight vacuum through a fritted-glass funnel ("medium" porosity) into a 50-ml volumetric flask containing the desired amounts of ethanol, benzaldehyde, styrene, or cyclohexene, together with the internal standard(s) to be used for vpc analysis. Several small portions of *n*-heptane were used to wash the recovered triethylamine hydrochloride and the vessel used for preparation of **1**. The washings were filtered directly into

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[18] F. Ramirez, S. B. Bhatia, and C. P. Smith, *Tetrahedron*, **23**, 2067 (1967), and references therein.

[19] Boiling points and melting points are uncorrected. The melting points were determined with a Fisher-Johns apparatus. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. All reactions were run under nitrogen. Drierite was used as the drying agent. Evaporations were carried out on rotary evaporators at room temperature under 5–10 mm pressure. Much of the instrumental analytical work was performed by the Analytical Section of this laboratory.

[20] (a) C. D. Cook, *J. Org. Chem.*, **18**, 261 (1953). (b) That this compound is indeed the pure *trans* isomer is clearly shown by its nmr spectrum, which exhibits only two sharp singlets in the olefinic–aromatic region (*vide infra*), and by the ir spectrum, which contains a typical *trans* olefin CH out-of-plane bending band at 957 cm^{-1} (CS$_2$). *Cf.* (c) C. R. Bohn and T. W. Campbell, *ibid.*, **22**, 458 (1957).

[21] L. E. Goddard and J. D. Odenweller, U. S. Patent 3,006,945 (1960).

[22] C. D. Cook, N. G. Nash, and H. R. Flanagan, *J. Amer. Chem. Soc.*, **77**, 1783 (1955).

the flask containing the original filtrate. After addition (pipet) of the desired quantity of phosphite solution, the solution was diluted to the mark with more *n*-heptane, degassed by bubbling with nitrogen for 10–15 min, stoppered tightly under nitrogen, and allowed to stand at room temperature until the reaction was complete (vpc trace invariant with time). Solutions were analyzed by programmed temperature vpc using appropriate standard mixtures for calibration. Products were identified by comparing their retention times and the spectra of trapped fractions with those of authentic specimens. All constituents except triethyl phosphite were analyzed on column A using *n*-eicosane as the internal standard; the sensitivity factor for the trimer, **3**, was assumed to be equal to that of **2**. Triethyl phosphite was analyzed on column B using *n*-tetradecane for internal standardization. Nonquantitative material balances are probably due to several factors: the presence in some runs of minor by-products (detected by vpc but not identified), mechanical losses incurred during the transfer of solutions of **1**, use of an incorrect vpc sensitivity factor for the trimer, and the usual uncertainties (estimated to be ±3%) in the other sensitivity factors. A trapped sample of the trimer exhibited the following spectral characteristics: ir (CS_2) 3663 cm^{-1} (strong, sharp, hindered phenol OH), no C=O absorption; nmr (CCl_4) δ 1.1–1.5 (m containing at least seven sharp singlets, 54, *t*-butyls), 3.51 and 3.82 (broad singlets having approximately equal areas, total area 2, two ArCH$_2$'s), 4.6–5.0 (envelope with apparent maxima at 4.74 and 4.89 ppm, ~3, OH's), and 6.2–7.3 ppm (m, 7, olefinic and aromatic H); mass spectrum (70 eV) *m/e* 654.5005 (strong parent peak; calcd for $C_{45}H_{66}O_3$, 654.5012). These data are in reasonable accord with the presence of approximately equal amounts of *cis*- and *trans*-trisphenol **3** in the trapped trimer fraction.

Several reactions were followed by nmr spectroscopy, using aliquot portions of mixtures prepared in the manner described above. In a typical experiment, the initial concentrations of **1**, triethyl phosphite, and triethylamine were 0.04, 0.08, and 0.02 *M*, respectively. At the outset the only peaks present in the 4–8 δ region of the spectrum were two sharp singlets produced by the quinone methide: δ 5.54 (2, =CH$_2$) and 6.85 ppm (2, two =CH—). As the reaction proceeded, these peaks decreased in intensity, and peaks assignable to quinone methide **11** appeared at δ 5.01 (s, 1, OH), 6.26 (t, 1, $J \cong 8$ Hz, CH$_2$CH), 6.76 (d, 1, $J \cong 2.5$ Hz, dienone =CH— *trans* to ArCH$_2$), 6.95 (s, 2, aromatic H), and 7.38 ppm (d, 1, $J \cong 2.5$ Hz, dienone =CH— *cis* to ArCH$_2$). Interference by heptane and triethyl phosphite prevented the observation of peaks arising from *t*-butyl groups and the CH$_2$ group of **11**. It should be noted that the chemical shifts and coupling constants assigned to the three olefinic protons of **11** are in good agreement with the values found for the structurally analogous compound, quinone methide **24**, in heptane solution (*vide infra*). After a major part of **1** had reacted, small peaks arising from bisphenol **2** were detected at δ 5.06 (s, 2, OH), 6.81 (s, 2, CH=CH), and 7.25 ppm (s, 4, aromatic H). When the reaction was complete (nmr spectrum constant with time), no trace of the peaks due to **1** and **11** remained, and the spectrum then consisted of strong peaks due to **2** and weak peaks arising from minor products. Similar experiments showed that higher amine concentrations caused higher rates of conversion of **11** into **2**.

In a small-scale preparative experiment, a dry benzene solution (200 ml) of triethyl phosphite (0.83 g, 5.0 mmol) and quinone methide **1** (20 mmol, generated in the usual way from 5.20 g of the corresponding chloromethylphenol and 2.05 g of triethylamine) was allowed to react at room temperature for 70 hr. Solvent was removed under vacuum, and the residue was triturated thoroughly with 25 ml of cold (−78°) petroleum ether (bp 30–60°) and filtered. After several washes on the filter with fresh portions of cold petroleum ether, the recovered solid weighed 2.42 g (55%) and melted at 242–243° (lit.[20a] mp 240–241°); it was shown to be essentially pure **2** by the usual variety of spectral comparisons with authentic material.[20a]

B. Kinetics.—Reaction mixtures were prepared in 50-ml volumetric flasks according to the procedure described in part A. The flasks were thermostated in an oil bath at 30.0 ± 0.1° and stoppered tightly with rubber serum caps after degassing. Fifteen minutes was allowed for thermal equilibration, and aliquots for infrared analysis were then removed at appropriate intervals by means of a hypodermic syringe. The absorbance, A_t, at 918 cm^{-1} was measured immediately; infinity points, A_∞, were taken after reactions had been allowed to run for at least 10 half-lives. Solvent was used in the reference cell for runs with low phosphite concentrations; in other runs *n*-heptane solutions of the phosphite (concentration identical with phosphite concentration in reaction mixture) were employed. Parallel experiments with no added phosphite showed that the spontaneous dimerization of **1** was too slow to effectively compete with the phosphite-catalyzed reaction under these conditions. Rate constants were calculated in the usual way from straight lines fitted by inspection; replicate runs gave rate constants agreeing to within ±6% or better. No curvature was detected in the first-order kinetic plots, even for runs followed up to 80–90% of completion. Most of the rate constants listed in Table I are average values obtained from duplicate experiments.

2,6-Di-*t*-butyl-4-phenethylphenol (23).—A freshly prepared solution of quinone methide **1**, obtained by reaction of 2,6-di-*t*-butyl-4-chloromethylphenol (20.38 g, 0.0800 mol) with triethylamine (8.10 g, 0.0800 mol) in dry ether (500 ml), was added during 5 min with stirring to a Grignard reagent prepared in the usual way from 4.080 g (0.168 g-atom) of magnesium, 20.24 g (0.160 mol) of benzyl chloride, and a crystal of iodine in dry ether (150 ml). Stirring was continued for 10 min at ambient temperature after the addition was complete; then the mixture was stirred under reflux for an additional 20 min, cooled, and poured into a large excess of dilute hydrochloric acid. The ether layer was separated, washed twice with sodium bicarbonate solution, dried, and evaporated. Fractionation of the semisolid residue through a short spinning-band column gave 2.07 g of unidentified forerun [bp 57–160° (1.0–1.2 mm)] and 19.05 g (77%) of pure **23** as a pale yellow oil [bp 160–162° (1.2 mm); lit.[23] bp 187–189° (1 mm) (?)] that solidified on cooling: mp 54.5–56.5° (lit.[23] mp 55–56°); ir (CS_2) 3585 cm^{-1} (strong, sharp, hindered phenol OH); nmr (CCl_4) δ 1.38 (s, 18, two *t*-Bu), 2.79 (distorted s, 4, CH$_2$CH$_2$), 4.82 (s, 1, OH), 6.76 (s, 2, H on tetrasubstituted ring), and 6.94–7.31 ppm (m, 5, H on monosubstituted ring); mass spectrum (70 eV) *m/e* 310.2291 (medium; calcd for $C_{22}H_{30}O$, 310.2297).

4-Benzylmethylene-2,6-di-*t*-butyl-2,5-cyclohexadien-1-one (24).—A solution of potassium ferricyanide (70 g) and potassium hydroxide (4 g) in water (275 ml) was degassed by bubbling with nitrogen and then added rapidly to a well-stirred, similarly degassed solution of phenol **23** (5.00 g, 16.1 mmol) in petroleum ether (bp 30–60°, 50 ml). Stirring was continued for 1.0 hr. The organic layer was then separated, washed several times with water (final wash had pH 7), dried, and concentrated by evaporation *in vacuo*. Chilling to −15° caused precipitation of pure **24** (2.27 g, 46%) as bright yellow crystals: mp 73.5–75.5°; ir (CS_2) 1623 (strong with shoulder at 1637 cm^{-1}, *p*-quinone methide system[5a]), 746 (strong, monosubstituted phenyl), and 695 cm^{-1} (strong, monosubstituted phenyl); nmr (CCl_4) δ 1.26 (s, 9, *t*-Bu), 1.32 (s, 9, *t*-Bu), 3.78 (d, 2, $J \cong 8$ Hz, CH$_2$), 6.30 (t, 1, $J \cong 8$ Hz, CH$_2$CH=), 6.76 (d, 1, $J \cong 2.5$ Hz, dienone =CH— *trans* to PhCH$_2$), and 7.02–7.38 ppm (m, 6, overlapping C_6H_5 envelope and d at 7.30 ppm with $J \cong 2.5$ Hz for dienone =CH— *cis* to PhCH$_2$); nmr (*n*-heptane) δ 3.70 (d, 2, $J \cong 8$ Hz, CH$_2$), 6.22 (t, 1, $J \cong 8$ Hz, CH$_2$CH=), 6.76 (d, 1, $J \cong 2.5$ Hz, dienone =CH— *trans* to PhCH$_2$), and 6.98–7.41 ppm (m, 6, overlapping C_6H_5 envelope and d at 7.35 ppm with $J \cong 2.5$ Hz for dienone =CH— *cis* to PhCH$_2$); mass spectrum (70 eV) *m/e* 308.2129 (strong; calcd for $C_{22}H_{28}O$, 308.2140).

Anal. Calcd for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.91; H, 9.42.

The mother liquor was shown by nmr analysis to contain **24** (2.08 g, 42%, total yield 88%), phenol **20** (0.34 g, 7%), and phenol **23** (0.30 g, 6% recovery). A similar experiment employing a reaction time of 1.5 hr gave 69% **24** having mp 72–73.5° and containing no impurities that could be detected by nmr measurements.

***trans*-3,5-Di-*t*-butyl-4-stilbenol (20).**—A solution of quinone methide **24** (5.00 g) and triethylamine (0.10 ml) in benzene (15 ml) was kept at room temperature for 9.3 hr and then evaporated under vacuum to recover **20** in quantitative yield as a pale brown solid, mp 89–91°. Three recrystallizations of the product from aqueous methanol gave white granules: mp 90–91°; ir (CS_2) 3572 (strong, sharp, hindered phenol OH), 956 (strong, *trans* olefin), 745 (strong, monosubstituted phenyl), and 689 cm^{-1} (strong, monosubstituted phenyl); nmr (CCl_4) δ 1.46 (s, 18, two

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[23] A. A. Volod'kin, V. V. Ershov, and N. V. Portnykh, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 384 (1967).

t-Bu), 5.07 (s, 1, OH), 6.88 (AB q,[24] 2, J = 16.1 Hz, CH=CHPh), and 7.01–7.52 ppm (m, 7, aromatic H); mass spectrum (70 eV) m/e 308.2148 (strong; calcd for $C_{22}H_{28}O$, 308.2140).

Anal. Calcd for $C_{22}H_{28}O$: C, 85.66; H, 9.15. Found: C, 85.71; H, 9.34.

Registry No.—**1**, 2607-52-5; **3**, 21363-59-7; **11**, 21363-60-0; **20**, 21449-69-4; **23**, 15017-98-8; **24**, 21363-62-2; triethyl phosphite, 122-52-1.

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(24) Analysis of this quartet (see J. A. Elvidge in "Nuclear Magnetic Resonance for Organic Chemists," D. W. Mathieson, Ed., Academic Press Inc., New York, N. Y., 1967, p 52) gives δ_A 6.94, δ_B 6.82. For comparison spectra, see H. Güsten and M. Salzwedel, *Tetrahedron*, **23**, 173 (1967).

Studies of Nitriles. I. Synthesis of Fumaro- and Maleonitrile by a Novel Pyrolytic Coupling Reaction[1]

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It was found that the pyrolysis of monohalogenoacetonitriles at 800–1000° under reduced pressure resulted in a novel pyrolytic coupling reaction to yield fumaro- and maleonitrile in 50–60% yields. Further refinements of the reaction led to a single-step synthesis of fumaro- and maleonitrile from acetonitrile and chlorine. Similarly, the pyrolysis of di- and trichloroacetonitrile and the mixed pyrolysis of chloroacetonitriles and acetonitrile were studied. Discussions are given on the mechanism of these reactions.

In recent years, three- and four-carbon unsaturated nitriles, prepared mainly by the gas-phase reactions,[2] have attracted much interest as basic building blocks for the production of a number of synthetic polymers. There are also several reports which describe the syntheses of more complicated nitriles, such as malononitrile,[3] cyanoacetylene,[4] dicyanoacetylene,[5] etc., by essentially gas-phase reactions. It should be noted that all these syntheses have been performed on the basis that the nitriles possess considerable stability at high temperatures. Our attention was therefore directed toward synthesizing the nitriles which are difficult to prepare in a liquid phase, by means of a vapor-phase reaction, and utilizing them for the synthesis of various heterocyclic compounds.[6]

To date, several syntheses of fumaronitrile have been reported which involve (a) dehydration of fumaroamide;[7] (b) the reaction of *trans*-diiodoethylene with cuprous cyanide;[8] (c) the reaction between β-chloroacrylonitrile and sodium cyanide;[9] and (d) the reaction of acetonitrile with hydrogen cyanide.[10] However, none of them so far recorded gave a satisfactory yield and all were far from being commercially feasible. Similarly, for the synthesis of maleonitrile, (a) the dehydration of maleoamide;[7] (b) the reaction of *cis*-diiodoethylene with cuprous cyanide;[8] and (c) the isomerization of fumaronitrile in the presence of hydrogen chloride[11] have been reported. A recent patent[12] claims that succinic acid can be converted into a mixture of fumaro- and maleonitrile in a single step over a complex metal oxide catalyst by the reaction with ammonia and oxygen. More recently, after completion of our experiments, another patent[13] appeared which claimed essentially the same reaction as our experiments. They disclosed that the reaction of chlorine with acetonitrile at high temperature afforded a mixture of fumaro- and maleonitrile in less than 20% yield.

We have found that the pyrolysis of monohalogenoacetonitriles at an elevated temperature (800–1000°) and under reduced pressure (5–20 mm) gave a mixture of fumaro- and maleonitrile in 50–60% yield. The pyrolytic coupling of other halogenoacetonitriles have also been investigated under various conditions.

Results

Pyrolysis of Monohalogenoacetonitriles.—The pyrolysis of monochloro- or monobromoacetonitrile was carried out in an unpacked quartz tube at 800–1000°

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(2) Some simple unsaturated nitriles such as acrylonitrile, methacrylonitrile, and benzonitrile are synthesized by the method known as ammoxidation from the corresponding hydrocarbons, *e.g.*, propene, isobutylene, and toluene. They are also made by the oxidation of the corresponding amines. Acrylonitrile has been produced by the addition of hydrogen cyanide to acetylene by a vapor-phase reaction.

(3) J. K. Dixon, U. S. Patent 2,553,406 (1951); *Chem. Abstr.*, **45**, 9081 (1951); U. S. Patent 2,606,917 (1952); *Chem. Abstr.*, **47**, 5964 (1953).

(4) L. J. Krebaum, U. S. Patent 3,079,424 (1963); *Chem. Abstr.*, **59**, 3777 (1963); *J. Org. Chem.*, **31**, 4103 (1966).

(5) E. I. Du Pont de Nemours and Co., Inc., U. S. Patent 3,070,622 (1962); *Chem. Abstr.*, **59**, 454 (1964); E. Ciganek and C. G. Krespan, *J. Org. Chem.*, **33**, 541 (1968).

(6) F. Johnson and R. Madronero, *Advan. Heterocycl. Chem.*, **6**, 95, (1966).

(7) (a) E. H. Keiser and J. J. Kessler, *Am. Chem. J.*, **46**, 523 (1911); (b) L. McMaster and F. B. Langreck, *J. Amer. Chem. Soc.*, **40**, 970 (1918); (c) J. de Wolf and L. van de Straete, *Bull. Classe Sci., Acad. Roy. Belges*, **21**, 216 (1935); *Chem. Abstr.*, **29**, 3985 (1935); (d) D. T. Mowry and J. M. Butler, *Org. Syn.*, **30**, 46 (1950); (e) J. de Wolf and L. van de Straete, *Bull. Soc. Chim. Belges*, **44**, 288 (1935); (f) A. T. Blomquist and E C. Winslow, *J. Org. Chem.*, **10**, 155 (1945); (g) H. A. Pace, U. S. Patent 2,438,019 (1948); *Chem. Abstr.*, **42**, 4606 (1948); (h) U. S. Patent 2,121,551 (1936); *Chem. Abstr.*, **32**, 6259 (1938).

(8) (a) J. Jennen, *Bull. Classe Sci., Acad. Roy. Belges*, **22**, 1169 (1936); *Chem. Abstr.*, **31**, 1010 (1937); (b) J. Jennen, *Bull. Soc. Chim. Belges*, **46**, 199 (1937); (c) C. A. Hochwalt, U. S. Patent 2,399,349 (1946); *Chem. Abstr.*, **40**, 4744 (1946).

(9) D. T. Mowry and W. H. Yanko, U. S. Patent 2,471,767 (1949); *Chem. Abstr.*, **43**, 7498 (1949).

(10) L. J. Krebaum, U. S. Patent 3,055,738 (1962); *Chem. Abstr.*, **58**, 2375 (1963).

(11) H. Mommaerts, *Bull. Soc. Chim. Belges*, **52**, 63 (1943). As for the thermal equilibrium between fumaro- and maleonitriles, see F. M. Lewis and F. R. Mayo, *J. Amer. Chem. Soc.*, **70**, 1533 (1948); and as for ultraviolet light induced isomerization, see J. Jennen, *Bull. Soc. Chim. Belges*, **46**, 258 (1937).

(12) Deutsche Gold- und Silber-Scheideanstalt vorm. Roessler, Netherlands Appl., **6**, 414,353 (1965); *Chem. Abstr.*, **63**, 17915 (1965).

(13) M. Taguchi, M. Aramaki, and T. Fujii, Japanese Patent 42-17965 (1967).