

### 170. Alkyl-Oxygen Fission in Carboxylic Esters. Part V.

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The resolution of *p*-phenoxybenzhydrol, and reactions of its hydrogen phthalate, similar to those recorded in previous papers, are described. The hydrogen phthalate in aqueous alkali has at room temperature less tendency, and at 80° more tendency, to alkyl-oxygen fission than has the hydrogen phthalate of *p*-methoxybenzhydrol. Homophthalates and diphenates of *p*-phenoxybenzhydrol are described.

The aralkylating action of some of the hydrogen phthalates which react by alkyl-oxygen fission is illustrated by their reactions with *p*-toluenesulphonic acid, thio-*p*-cresol, phenol,  $\beta$ -naphthol, and ammonia, giving the corresponding sulphones, thioethers, ethers, and amines. Some of the carbinols also are shown to give the sulphones and thioethers. The *O*-aralkylations of  $\alpha$ -oxime salts and of the sodium salt of *p*-bromophenylnitromethane by reaction with the sodium salt of *p*-methoxybenzhydrol hydrogen phthalate are described.

THE (+)hydrogen phthalate of *p*-phenoxybenzhydrol, obtained by fractional crystallisation of the quinidine salt of the *dl*-phthalate, yields, on hydrolysis in alcoholic sodium hydroxide, (+)-*p*-phenoxybenzhydrol. The (+)carbinol is also obtained when the hydrolysis is conducted in the cold with *N*-sodium hydroxide, indicating that the tendency to acyl-oxygen fission is greater in this carbinol than in *p*-methoxybenzhydrol, which is largely racemised on aqueous hydrolysis of its phthalate. Similarly, (+)-*p*-phenoxybenzhydrol hydrogen phthalate can be recovered unchanged from solution in a slight excess of aqueous alkali, whereas under these conditions *p*-methoxybenzhydrol hydrogen phthalate yields the neutral ester. When warmed with a greater excess (2 mols. or more) of aqueous alkali, *p*-phenoxybenzhydrol hydrogen phthalate reacts by alkyl-oxygen fission, yielding the neutral diphenate if the concentration of hydrogen phthalate is above 4%, and carbinol at low concentration (below 20 g./l.). At the lower concentrations, the probability of a liberated kation reacting with a molecule of hydrogen phthalate is decreased, and the probability of reaction with a water molecule or hydroxyl ion is, therefore, increased. In the case of *p*-methoxybenzhydrol hydrogen phthalate, on the other hand, increase in temperature or concentration of alkali results in some acyl-oxygen fission (retention of optical activity). These results indicate the dual capacity of the *p*-phenoxy-groups for electron attraction (which assists co-ordination of the hydroxyl group and so promotes acyl-oxygen hydrolysis in the cold), or for electron release (which in conjunction with thermal energy promotes some alkyl-oxygen fission on heating).

*p*-Phenoxybenzhydrol hydrogen phthalate yields, by methods previously described, the *p*-tolyl sulphone and the methyl and ethyl ethers: the methyl ether has also been obtained from the neutral phthalate on heating in methyl alcohol. The carbinol itself yields di-*p*-phenoxybenzhydrol ether on heating, and the chloride on warming with concentrated hydrochloric acid. These reactions in general occur less readily than with *p*-methoxybenzhydrol, and further evidence of a lesser tendency to alkyl-oxygen fission in the *p*-phenoxybenzhydrol is given by the formation of the acetate (instead of the chloride, cf. Part II) on reaction with acetyl chloride.

Neutral di-esters of diphenic and homophthalic acids have been obtained on warming the corresponding acid esters of *p*-phenoxybenzhydrol and anisyl-1-naphthylcarbinol in a slight excess of aqueous sodium hydroxide, and from the acid esters of *o*-methoxyphenyl-1-naphthylcarbinol in the cold. Also a *p*-tolyl sulphone was obtained from the acid diphenate of *p*-phenoxybenzhydrol.

In general, the reactions of esters of benzhydrol and related carbinols may be summarised by describing

them as effective aralkylating agents, the reactions proceeding to completion on account of the precipitation of one or other product from the reaction mixtures. This is further illustrated by the reactions of a number of the hydrogen phthalates in chloroform solution (see experimental section) with *p*-toluenesulphonic acid, thio-*p*-cresol, phenol, or  $\beta$ -naphthol to give the corresponding sulphones, thioethers, or ethers. The hydrogen phthalate of *p*-methoxybenzhydrol (at room temperature) and of anisyl-1-naphthylcarbinol and *p*-phenoxybenzhydrol (at 100°) react with concentrated aqueous ammonia to give the substituted benzhydramines: those of benzhydrol and anisyl alcohol, on account of their lesser tendency to alkyl-oxygen fission, only undergo hydrolysis to the carbinol, slowly at room temperature, and more rapidly on heating. In aqueous ammonia, the concentration of hydroxyl ions is low compared with that of ammonia (or solvated ammonia) molecules, with which the *p*-substituted benzhydryl cations, therefore, preferentially react to give the amines. In aqueous methylamine, with which *p*-methoxybenzhydryl hydrogen phthalate reacts to give the benzhydrol, the concentration of hydroxyl ions is higher, and the amine is to a large extent present in the form of  $\text{MeNH}_3^{\oplus}$ , carrying a charge which will diminish interaction with benzhydryl cations: these, therefore, react preferentially with the hydroxyl ions.

The aralkylating action of the *p*-methoxybenzhydryl phthalic ester is also shown by its reaction (*i.e.*, in the presence of a slight excess of sodium hydroxide) with the sodium salts of  $\alpha$ -oximes (*o*-methoxybenzaloxime and *p*-nitrobenzaloxime) to give *O*-oxime ethers (cf. Brady, Dunn, and Goldstein, *J.*, 1926, 2386) on *O*-alkylation of  $\alpha$ -oximes by methyl sulphate. An *O*-ether of *o*-methoxybenzaloxime has also been obtained from the hydrogen phthalate of *o*-methoxyphenyl-1-naphthylcarbinol. The sodium salt of *p*-methoxybenzhydryl hydrogen phthalate reacts with cupferron, giving a compound which is presumably one of the two possible *O*-ethers,\* and with the sodium salt of *p*-bromophenylnitromethane, giving the nitronic ester by *O*-alkylation (cf. Arndt and Rose, *J.*, 1935, 1, on *O*-alkylation of *aci*-nitro-compounds).

In the reactions in chloroform solution, the phthalate ionises (involving the first dissociation of phthalic acid,  $K$ ,  $1.3 \times 10^{-3}$ ) and the kation displaces a hydrogen ion from the reactant. In aqueous sodium hydroxide, the second dissociation of phthalic acid ( $K$ ,  $3.1 \times 10^{-6}$ ) is involved, and the kation reacts with another benzhydryl phthalate anion to give the neutral ester, or with a water molecule to give the hydrol, according to the relative concentrations. Though the separation of the products takes several hours, the reactions are probably very rapid (see Part I). If anions (*e.g.*, of hydroxyl, sulphinate, oxime salt, or of *aci*-nitro-compound) or molecules (ammonia) of high co-ordinating power are present, or if anions (*e.g.*, bivalent phthalate anion; Part I) are present in high concentration, the reaction is diverted to these. There are two anomalous cases: *p*-substituted benzhydryl benzoate is not formed when sodium benzoate is present in equimolar concentration (Part I) or in five-molar excess (subsequent experiments), and a mixed phthalic ester is not formed when octyl hydrogen phthalate is present in five-molar excess (Part I: the observation there given, that the neutral phthalate which is formed is racemic, is not anomalous; the neutral ester was not separated until 7 days after deposition, and it is shown in Part I that it racemises during this time). Though both the benzoate and the octyl phthalate anions might be described as not of high co-ordinating power, in the sense used above, they would be expected when present in excess to react in a similar way to the bivalent phthalate anion.

In aqueous sodium hydroxide, acid succinates of certain of these hydrols and carbinols (Part III and IV) react to give *p*-tolyl sulphones, as is to be expected from the similar strengths of the second dissociations of succinic ( $K$ ,  $2.8 \times 10^{-6}$ ) and phthalic acids. Some neutral succinates are also formed, but there is a tendency for the hydrols to be formed from the succinates, under conditions where the phthalates give neutral esters. This may be related to the lower strength of the first dissociation of succinic acid ( $K$ ,  $6.6 \times 10^{-5}$ ) compared with phthalic acid, resulting in a higher concentration of hydroxyl ions when acid succinates are dissolved in an equimolar amount of alkali, and, therefore, greater tendency of liberated kations to react with hydroxyl ions to give the hydrol or carbinol.

Some further reactions of the substituted benzhydrols and related carbinols (see experimental section), involving separation of the hydroxyl group, have been observed: the formation of sulphones on refluxing with *p*-toluenesulphonic acid in chloroform solution (see also Part III), and of thioethers with thio-*p*-cresol in the same solvent. Separation of water from the chloroform presumably drives these reactions to completion. In this connection mention should be made of the work of Fosse, who showed (*Compt. rend.*, 1907, 145, 1291) that *C*-aralkylation of keto-methylene systems occurs when benzhydrol and its *p*-substituted homologues react in acid solution with, *e.g.*, acetoacetic ester or benzoylacetone, and formulated the reactions as involving removal of the hydroxyl groups of the hydrols, *i.e.*, alkyl-oxygen fission. Xanthhydrol was found by Fosse (*Compt. rend.*, 1912, 155, 1019) to undergo this type of reaction with great ease—its structure must produce a very strong tendency to electron release—and he records the formation of its disulphide and peroxide on reaction with sodium sulphide and hydrogen peroxide respectively.

In Part III it is shown that anisyl alcohol and its hydrogen phthalate and acetate can react with alkyl-oxygen fission, though less readily than the benzhydrols, and this is further illustrated by reactions of the hydrogen phthalate with *p*-toluenesulphonic acid, thio-*p*-cresol, and ethyl alcohol. It also yields the neutral diphtalate when heated in chloroform solution (compare the formation of anisyl-1-naphthylcarbinyl diphtalate in chloroform solution, Part IV). Alkyl-oxygen fission, with resulting formation of neutral ester, occurs in chloroform solution when it involves ionisation of the first dissociation constant of phthalic acid, but not in

\* Further examination of this substance, which might throw light on the structure of cupferron (Taylor and Baker, "Sidgwick's Organic Chemistry of Nitrogen," 1942, p. 456), has not yet been attempted.

aqueous sodium hydroxide (Part III), in which ionisation of the second carboxyl group would be involved (see Part IV).

*p*-Methoxybenzhydryl ether (Part II, *loc. cit.*) is very smoothly prepared by heating the hydrol with a solution of *p*-toluenesulphonic acid in water.

## EXPERIMENTAL.

*dl*- and (+)-*p*-Phenoxybenzhydryl and their Hydrogen Phthalates.—*p*-Phenoxybenzophenone (m.p. 71°, from diphenyl ketone by Friedel-Crafts reaction; Kipper, *Ber.*, 1905, 38, 2492) was reduced (100 g.) with powdered sodium hydroxide (100 g.) and zinc dust (100 g.) in ethyl alcohol by refluxing (3 hours). The solution was filtered and poured into ice-water. The precipitate, recrystallised from boiling ligroin, gave *p*-phenoxybenzhydryl, long silky needles, m. p. 76.5°. Overall yield, 130 g. of recrystallised hydrol from 100 g. of diphenyl ether. The hydrol (13.8 g.), phthalic anhydride (7.4 g.), and pyridine (7 g.) were heated at 60° for 6 hours, diluted with acetone, and poured slowly into excess of dilute hydrochloric acid at 0°. The oil was redissolved in acetone and reprecipitated with hydrochloric acid to remove excess of pyridine. The resulting solid hydrogen phthalate (20 g.; m. p. 138—139°) crystallised from most organic solvents as short needles, m. p. 143° (Found, on rapid titration with 0.1*N*-NaOH: *M*, 426. Calc. for C<sub>27</sub>H<sub>20</sub>O<sub>5</sub>: *M*, 424). The hydrogen phthalate (85 g.) and quinidine (72 g.) were dissolved in warm acetone (250 c.c.); the salt which was deposited (102 g.) was recrystallised four times from acetone, yielding the quinidine salt of the (+)phthalate (42 g.), m.p. 137—138°. This was dissolved in warm acetone, and the (+)phthalate precipitated by iced hydrochloric acid: it was reprecipitated thrice in this way to remove all the quinidine; (+)-*p*-phenoxybenzhydryl hydrogen phthalate, clusters of short needles, m. p. 100—101° (*M*, as above, 426), had in benzene solution (*l*, 2; *c*, 2.553; *t*, 23°), [α]<sub>D</sub><sup>20</sup><sub>5893</sub> + 8.0°, [α]<sub>D</sub><sup>20</sup><sub>5893</sub> + 11.8°, [α]<sub>D</sub><sup>20</sup><sub>5780</sub> + 12.2°, [α]<sub>D</sub><sup>20</sup><sub>5761</sub> + 13.9°, [α]<sub>D</sub><sup>20</sup><sub>4358</sub> + 28.3°, and in carbon disulphide (*l*, 2; *c*, 1.182; *t*, 20°), [α]<sub>D</sub><sup>20</sup><sub>5893</sub> + 14.0°, [α]<sub>D</sub><sup>20</sup><sub>5780</sub> + 16.9°, [α]<sub>D</sub><sup>20</sup><sub>5461</sub> + 18.6°. The above solution in benzene after 70 days at room temperature had [α]<sub>D</sub><sup>20</sup><sub>5893</sub> + 6.0°, and had deposited needles of almost pure *dl*-phthalate, m. p. 103—104°, [α]<sub>D</sub><sup>20</sup><sub>5893</sub> + 0.6° in benzene (*l*, 2; *c*, 0.958).

The (+)hydrogen phthalate (2 g.) was warmed for a few minutes with sodium (2 g.) in 98% ethyl alcohol (60 c.c.). On dilution with water, (+)-*p*-phenoxybenzhydryl separated (1.25 g.); it recrystallised from carbon disulphide-ligroin in masses of long silky needles, m. p. 81—82°. In carbon disulphide (*l*, 2; *c*, 2.485; *t*, 19.5°) it had [α]<sub>D</sub><sup>20</sup><sub>5893</sub> + 11.9°, [α]<sub>D</sub><sup>20</sup><sub>5780</sub> + 13.7°, [α]<sub>D</sub><sup>20</sup><sub>5461</sub> + 15.9°, [α]<sub>D</sub><sup>20</sup><sub>4358</sub> + 31.4°. Hydrolysis of the (+)phthalate (1 g.) with 0.3*N*-sodium hydroxide (34 c.c.) at room temperature (2 days) gave the (+)hydrol with m. p. 81—82°, [α]<sub>D</sub><sup>20</sup><sub>5893</sub> (without previous recrystallisation), + 11.6° in carbon disulphide (*l*, 2; *c*, 1.91).

Reactions of *p*-Phenoxybenzhydryl Hydrogen Phthalate with Aqueous Sodium Hydroxide.—2—4 G. portions of hydrogen phthalate were used. The reaction conditions and products are summarised in the Table and further discussed in the notes below. *dl*-Phthalate was used except when otherwise stated.

	Molar ratio : NaOH/hydrogen phthalate.	Concn., g. hydrogen phthalate/l.	Temp.	Products.	
				Neutral phthalate as % of maxi- mum theoretical. (after 3 weeks)	Other products.
1	1	125	20°	0	Sodium salt.
2	1.4	110	20	20	Unchanged hydrogen phthalate.
3	1.8	65	80	60	Hydrol (30%).
4	3	40	80	50	"
5	6	25	80	60	"
6	15	125	80	85	None
7	4.5	15	20	0	Hydrol (quantitative).
8	4	4	80	0	" "

*Expt.* 1. Separation of the sodium salt as an oil or gum usually occurs when hydrogen phthalates (diphenates or homophthalates) of benzhydrols and related carbinols are dissolved in aqueous sodium hydroxide in high concentration (over 100 g./l.), and is encouraged by the presence of other sodium salts, *e.g.*, toluenesulphinate.

*Expts.* 3—6. Isolation of neutral ester and hydrol (compare Part II, *loc. cit.*). The gums which separated were washed with ethyl ether and water, dried, and extracted thrice with hot methyl alcohol (5-c.c. portions) followed by rapid cooling. The neutral ester separated and the hydrol was isolated from the methyl alcohol. A little ethyl ether was added to the neutral ester and the solvents removed under reduced pressure, leaving a glassy solid which softened at 47°. This was extracted with ligroin, dissolved in ether, and washed with alkali and with water, and the solvents were removed by distillation under reduced pressure at room temperature, leaving *p*-phenoxybenzhydryl phthalate as a glassy solid (Found: C, 81.2; H, 5.3. C<sub>26</sub>H<sub>24</sub>O<sub>6</sub> requires C, 80.9; H, 5.0%). Further evidence on the course of the reactions was obtained by drawing up balance sheets of (i) initial weight of hydrogen phthalate, (ii) alkali consumed in the reactions, (iii) yield of unchanged hydrogen phthalate (usually nil), (iv) neutral ester in crude gum, as determined by hydrolysis with 0.5*N*-sodium hydroxide, (v) alkali consumed in hydrolysis of phthalate to hydrol, from (i), (iii), and (iv). These calculations gave results agreeing with the determined weights of neutral ester and carbinol formed.

*Expt.* 4. From (+)hydrogen phthalate, the glassy, solid neutral ester had [α]<sub>D</sub><sup>20</sup><sub>5893</sub> + 17.7° in carbon disulphide (*l*, 2; *c*, 2.58). On hydrolysis with alcoholic potash it gave *dextro*-hydrol with [α]<sub>D</sub><sup>20</sup><sub>5893</sub> + 6.0° in carbon disulphide (*l*, 2; *c*, 2.69), *i.e.*, half the rotatory power of the (+)hydrol (cf. Part II, *loc. cit.*).

Reactions of *p*-Phenoxybenzhydryl Hydrogen Phthalate.—(i) 2.12 G. in 19 c.c. of 0.3*N*-sodium hydroxide, added to 1.8 g. of sodium *p*-toluenesulphinate in water (22 c.c.), did not react during 3 days at room temperature. After 15 minutes at 90°, *p*-tolyl *p*-phenoxybenzhydryl sulphone (2.1 g.) separated as prismatic needles, m. p. after recrystallisation from ethyl alcohol or acetic acid, 164—165° (Found: S, 7.7. C<sub>26</sub>H<sub>22</sub>O<sub>3</sub>S requires S, 7.7%). From (+)phthalate, *dl*-sulphone was obtained. (ii) (+)Phthalate (10 g.) in methyl alcohol (200 c.c.) was slowly distilled (4 hours). The residual oil was dissolved in ether and extracted with aqueous ammonia (which removed 3.8 g. of phthalic acid). The oil obtained from the ethereal solution had b. p. 207—210°/8 mm. (4.7 g.) and set to a crystalline mass of *dl*-*p*-phenoxybenzhydryl methyl ether, m. p. and mixed m. p. (see below), 27—28°. (iii) *dl*-Phthalate with ethyl alcohol as in (ii) above yielded 3.6 g. of phthalic acid and 7.0 g. of *p*-phenoxybenzhydryl ethyl ether, b. p. 227—228°/12 mm., which crystallised from ethyl alcohol in clusters of needles, m. p. 38—39° (Found: C, 82.6; H, 6.6. C<sub>21</sub>H<sub>20</sub>O<sub>4</sub> requires C, 82.9; H, 6.6%).

*Di*-*p*-phenoxybenzhydryl ether (3 g.) in methyl alcohol (70 c.c.), as in (ii) above, gave the methyl ether (2.1 g.) which, crystallised from methyl alcohol, had m. p. 27° (Found: C, 82.7; H, 6.3. C<sub>20</sub>H<sub>18</sub>O<sub>2</sub> requires C, 82.8; H, 6.2%).

Reactions of *p*-Phenoxybenzhydryl.—(iv) The hydrol (10 g.) was heated at 160° for 10 hours, then diluted with ethyl ether. The crystalline precipitate of *di*-*p*-phenoxybenzhydryl ether (4.1 g.; m. p. 175—190°) was soluble only in dioxan and cyclohexane, and after many recrystallisations from the latter plus ether had m. p. 202° (Found: C, 85.2; H, 5.6. C<sub>33</sub>H<sub>30</sub>O<sub>2</sub> requires C, 85.4; H, 5.6%). (v) Hydrol (3 g.) was triturated with concentrated hydrochloric acid at 60°.

The chloride (3 g.) solidified on cooling; washed and dried (lime), it had m. p. 48—50°. Recrystallised from ligroin, it formed clusters of pale yellow needles, m.p. 49—50° (Norris and Blake, *J. Amer. Chem. Soc.*, 1928, **50**, 1809, give m. p. 49—50°) (Found, by reaction with excess of 0.1N-sodium hydroxide: *M*, 292. Calc.: *M*, 294). The chloride (1.5 g.) in benzene solution on shaking with water yielded the di-ether, m. p. and mixed m. p. (iv above) 201—202°. (vi) The hydrol (1 g.) was dissolved in acetyl chloride. After 2 hours at room temperature, the excess of acetyl chloride was removed under reduced pressure. The residual *p*-phenoxybenzhydryl acetate crystallised from ligroin in needles, m. p. 51—52° (Found, by hydrolysis with 0.1N-sodium hydroxide: *M*, 312. Calc. for  $C_{21}H_{18}O_3$ : *M*, 318). (vii) 3 G. of *dextro*-hydrol ( $[\alpha]_{D}^{18} + 8.0^\circ$  in carbon disulphide) by Einhorn's method gave 2.9 g. of *dextro*-benzoate,  $[\alpha]_{D}^{18} + 28.9^\circ$  in carbon disulphide (*l*, 2; *c*, 3.97). *dl*-Hydrol in the same way gave *dl*-benzoate, rosettes of needles, m. p. 61—62° (Found: C, 81.8; H, 5.4.  $C_{26}H_{20}O_3$  requires C, 82.1; H, 5.3%).

*p*-Phenoxybenzhydryl hydrogen diphenate was prepared from the hydrol (13.8 g.), diphenic anhydride (11.2 g.), and pyridine (12 c.c.) warmed for 10 hours at 70°. The crude diphenate (22 g.) was purified by running a benzene solution into a column of magnesium oxide (activated by 4 hours' heating at 200°) then washing out with benzene containing 10% of ethyl alcohol. The first fraction of washings contained the hydrogen diphenate (2.5 g.), glassy solid, m. p. 150—151° (Found, by titration with 0.1N-sodium hydroxide: *M*, 498. Calc. for  $C_{33}H_{24}O_5$ : *M*, 500). By the usual methods, the hydrogen diphenate gave the *p*-tolyl sulphone (m. p. and mixed m. p. 163—164°) on heating the reactants at 90° for 30 minutes, and the neutral *p*-phenoxybenzhydryl diphenate (0.6 g. from 1.0 g. of hydrogen diphenate) on boiling the reactants for 10 minutes. The neutral ester was purified by the methods described under Expts. 3—6 above [Found: C, 82.5; H, 5.2; *M* (Rast), 730.  $C_{52}H_{38}O_8$  requires C, 82.3; H, 5.0%; *M*, 758]. The following acid and neutral esters were prepared by exactly comparable methods:

	Temp. of prepn.	M. p.	Analysis.
<i>p</i> -Phenoxybenzhydryl hydrogen homophthalate	60°	140°	<i>M</i> , 434. Calc. for $C_{28}H_{22}O_5$ : <i>M</i> , 438.
Di- <i>p</i> -phenoxybenzhydryl homophthalate	80	Oil	306 Mg. yielded 79 mg. of homophthalic acid (Calc.: 73 mg.).
<i>o</i> -Methoxyphenyl-1-naphthylcarbonyl hydrogen diphenate	60	135—136	<i>M</i> , 485. Calc. for $C_{32}H_{24}O_6$ : <i>M</i> , 488.
<i>o</i> -Methoxyphenyl-1-naphthylcarbonyl diphenate	20	Glassy solid	2.0 G. gave 1.4 g. of carbinol and 0.6 g. of diphenic acid (Calc., 1.4 and 0.6 g.).
Anisyl-1-naphthylcarbonyl hydrogen homophthalate	50	133	<i>M</i> , 419. Calc. for $C_{27}H_{22}O_5$ : <i>M</i> , 426.
Anisyl-1-naphthylcarbonyl homophthalate	20	Glassy solid	1 G. gave 0.75 g. of carbinol and 0.21 g. of acid (Calc., 0.62 and 0.21 g.).

*Further Reactions of Hydrogen Phthalates.*—Hydrogen phthalates of the following carbinols were used: (I) *p*-Methoxybenzhydrol (see Part II, but, contrary to the description therein, the preparation of the hydrogen phthalate is best conducted at room temperature over several days); (II) anisyl alcohol (see Part III); (III) *p*-phenoxybenzhydrol (see above); (IV) anisylmethylcarbinol (see Part IV); (V) (+)anisylnaphthylcarbinol (see Part IV). *p*-Tolyl sulphones were obtained by heating solutions of the hydrogen phthalates with *p*-toluenesulphonic acid (approx. equal weight) in chloroform, heating being continued for some time after separation of phthalic acid ceased (1—20 hours). *p*-Tolyl thioethers and phenyl ethers, and a 1-naphthyl ether, were obtained in exactly the same way with the appropriate reactants. Yields approximately quantitative in all cases.

<i>p</i> -Tolyl sulphone of (I)	M. p. and mixed m. p. 160°.
<i>p</i> -Tolyl sulphone of (II)	M. p. 120° from ethyl alcohol (Found: S, 11.7. Calc. for $C_{15}H_{16}O_3S$ : S, 11.6%).
<i>p</i> -Tolyl thioether of (I)	M. p. 87—88° from ethyl alcohol. Gives the sulphone (m. p. and mixed m. p. 160°) on oxidation with hydrogen peroxide—glacial acetic acid.
<i>p</i> -Tolyl thioether of (II)	M. p. 66—67° from methyl alcohol (Found: S, 12.9. $C_{15}H_{16}OS$ requires S, 13.1%).
<i>p</i> -Tolyl thioether of (IV)	M. p. 58° from methyl alcohol (Found: S, 12.6. $C_{16}H_{18}OS$ requires S, 12.4%).
Phenyl ether of (I)	M. p. 83—84° from methyl alcohol (Found: C, 82.4; H, 6.0; OMe, 9.9. $C_{20}H_{18}O_2$ requires C, 82.7; H, 6.2; OMe, 10.7%).
[ <i>dl</i> - from (+)phthalate]	M. p. 104° from ethyl alcohol (Found: C, 85.0; H 6.0; <i>M</i> (Rast), 334. $C_{24}H_{20}O_2$ requires C, 84.7; H, 5.9%; <i>M</i> , 340).
Phenyl ether of (V)	M. p. 122—123° from ethyl alcohol (Found: C, 85.2; H, 6.1; <i>M</i> (Rast), 360. $C_{24}H_{20}O_2$ requires C, 84.7; H, 5.9%; <i>M</i> , 340).

*Reactions with Aqueous Ammonia and Methylamine.*—From a solution of *dl*-*p*-methoxybenzhydryl hydrogen phthalate (9 g.) in concentrated aqueous ammonia (90 c.c.) at room temperature an oil separated, which was combined with ether washings from the supernatant liquid, washed with alkali and with water, dried, and concentrated. From the resulting impure *p*-methoxybenzhydrylamine (1 g.), warmed with acetic anhydride for a few minutes and poured into water, the acetyl derivative, silky needles, m. p. 159—160° from ethyl alcohol, was obtained (Hantzsch and Kraft, *Ber.*, 1891, **24**, 3513, give m. p. 159°). The impure amine (0.8 g.), with sodium hydroxide (4 c.c. of 2.5N) and benzoyl chloride (0.6 g.), gave the benzoyl derivative, m. p. 180—181° from ethyl alcohol (Busch and Lefhelm, *J. pr. Chem.*, 1908, **77**, 20, give m. p. 174°) (Found: C, 79.7; H, 6.2; N, 4.0. Calc. for  $C_{16}H_{17}O_2N$ : C, 79.5; H, 6.0; N, 4.4%).

From 3 g. of the same phthalate in 20 c.c. of aqueous methylamine solution (33% w/v), *p*-methoxybenzhydrol (1.6 g.) separated after 48 hours at room temperature, m. p. and mixed m. p. 64—65°.

From *dl*-*p*-phenoxybenzhydryl hydrogen phthalate (3 g.) in aqueous ammonia (20 c.c.) after 30 minutes at 100° (sealed tube), impure *p*-phenoxybenzhydrylamine (1.4 g.) separated, yielding with acetic anhydride the *acetyl* derivative, needles from methyl alcohol, m. p. 166° (Found: N, 4.7.  $C_{21}H_{19}O_2N$  requires N, 4.5%). Similarly, from the hydrogen phthalate of anisyl-1-naphthylcarbinol (3 g.) in concentrated aqueous ammonia (20 c.c.) at 100° and acetylation of the crude amine, the *acetyl* derivative of anisyl-1-naphthylmethylamine was obtained, m. p. 197° from ethyl alcohol (Found: C, 79.0; H, 6.0; N, 4.5.  $C_{21}H_{19}O_2N$  requires C, 78.7; H, 6.2; N, 4.6%).

From a solution of benzhydryl phthalate (2 g.) in aqueous ammonia (15 c.c.) after 7 days at room temperature, benzhydrol (0.2 g.; m. p. and mixed m. p. 68°) separated, but most of the phthalate was recovered unchanged. From a solution of anisyl hydrogen phthalate (9 g.) in aqueous ammonia (20 c.c.) after 2 hours at 100° (sealed tube), anisyl alcohol (m. p. and mixed m. p. 22°) was obtained quantitatively.

*Reactions of p-Methoxybenzhydryl Hydrogen Phthalate with Oxime and aci-Nitro Salts.*—(viii) (+)Phthalate (7.2 g.) was dissolved in a solution of *o*-methoxy-*a*-benzaloxime (4.5 g.; m. p. 92°) in 150 c.c. of 0.3N-sodium hydroxide. An oil separated from the filtered solution after 12 hours; it was solidified by trituration with light petroleum and recrystal-

lised from ethyl alcohol, yielding the *O*-*p*-methoxybenzhydryl ether of *o*-methoxybenzaloxime (4.2 g.), m. p. 81° (Found: C, 75.9; H, 6.4; N, 4.1.  $C_{22}H_{21}O_3N$  requires C, 76.1; H, 6.1; N, 4.0%). This ether (1 g.) was dissolved in glacial acetic acid (25 c.c.) and reduced with zinc dust (2 g., activated by shaking with acidified 3% copper sulphate solution). The zinc dissolved at room temperature, and the solution was filtered, made alkaline, and extracted with ether. The oil isolated from the ether was dissolved in ethyl acetate; on addition of hydrochloric acid, *o*-methoxybenzylamine hydrochloride separated, shining plates from ethyl alcohol-ether, m. p. 150° (Goldschmidt and Ernst, *Ber.*, 1890, **23**, 2742, give m. p. 150°) (Found: N, 8.2; Cl, 20.5. Calc. for  $C_8H_{11}ON \cdot HCl$ : N, 8.1; Cl, 20.4%). (ix) Phthalate (3.6 g.) was added to a solution of *p*-nitro-*a*-benzaloxime (3.3 g.), m. p. 129° (Gabriel and Herzbert, *Ber.*, 1883, **16**, 2000), in sufficient 0.3*N*-sodium hydroxide for complete solution. The oil, (2.9 g.) which separated (24 hours) hardened on trituration with ligroin. The *O*-*p*-methoxybenzhydryl ether of *p*-nitro-*a*-benzaloxime, small yellow prisms from ethyl alcohol or ligroin, had m. p. 115—116° (Found: N, 7.8.  $C_{21}H_{18}O_2N_4$  requires N, 7.7%).

(x) Phthalate (3.6 g.) and cupferron (3 g.) were dissolved in sodium hydroxide solution (38 c.c.; 0.3*N*). The oil which separated (18 hours) crystallised from hot ethyl alcohol. Repeated crystallisation (alcohol or benzene) and decolorisation (charcoal) gave the *p*-methoxybenzhydryl ether of *N*-nitrosophenylhydroxylamine, m. p. 114° (decomp.) (Found: N, 8.1.  $C_{20}H_{18}O_3N_2$  requires N, 8.4%).

(xi) *p*-Bromobenzyl bromide (Schramm, *Ber.*, 1884, **17**, 2922) was converted into the cyanide (Jackson and Lowery, *J. Amer. Chem. Soc.*, 1881, **3**, 242) and this into the sodium salt of *p*-bromophenylisnitromethane (Wislicenus and Elvert, *Ber.*, 1908, **41**, 4121). From a solution of this sodium salt (3.0 g.) and the phthalate (3.6 g.) in 0.3*N*-sodium hydroxide (40 c.c.) a sticky solid separated, which was dissolved in ether, washed with alkali, and dried. The needles which crystallised from the ether (1.4 g.; m. p. 170—190°) crystallised from most organic solvents, giving the *p*-methoxybenzhydryl ether (nitronic ester) of *p*-bromophenylnitromethane, m. p. 192° [Found: C, 61.4; H, 4.4; N, 3.2; Br, 18.9; *M* (Rast), 448.  $C_{21}H_{15}O_3NBr$  requires C, 61.2; H, 4.4; N, 3.4; Br, 18.9%; *M*, 412]. This substance was insoluble in hot alkali, gave no coloration with ferric chloride, and did not liberate iodine from hydriodic acid or absorb bromine from alcoholic solution. The solution decanted from the crude ether yielded *p*-methoxybenzhydrol (1 g.) and a little of its neutral phthalic ester. (xii) From the phthalate and the sodium salts of phenylnitromethyl cyanide, phenylnitromethane, and nitromethane, by methods as in (x) above, oils separated, which after being washed with alkali, contained nitrogen (*i.e.*, were probably crude nitronic esters) but could not be crystallised or distilled.

From the hydrogen phthalate (2.1 g.) of *o*-methoxyphenyl-1-naphthylcarbinol (Part III) the *O*-ether of *o*-methoxybenzaloxime (1.8 g.) was obtained as in (viii) after 1 week at room temperature; m. p. 144—145° from methylene chloride (Found: N, 3.6.  $C_{26}H_{23}O_3N$  requires N, 3.5%).

**Reactions of Carbinols.**—These were done with carbinols (I)–(V) listed above, and 3 : 4-dimethoxybenzhydrol (VI), anisylxenylicarbinol (VII), *p*-dimethylaminobenzhydrol (Part III) (VIII), and triphenylcarbinol (IX). (VI), m. p. 99°, was obtained by reduction (zinc dust in alcoholic sodium hydroxide) of the ketone (Friedel-Crafts reaction on veratrole; Sachs and Thonet, *Ber.*, 1904, **37**, 3332; Brüggeman, *J. pr. Chem.*, 1896, **53**, 253). *Anisylxenylicarbinol* (VII), m. p. 108—109° from benzene-ligroin (Found: C, 82.5; H, 6.3.  $C_{20}H_{19}O_2$  requires C, 82.8; H, 6.2%), was obtained by similar reduction of *anisyl xenyl ketone*, m. p. 157—158° from ligroin (Found: C, 83.1; H, 5.6.  $C_{20}H_{18}O_2$  requires C, 83.3; H, 5.6%), the ketone having been obtained by Friedel-Crafts reaction from anisoyl chloride and diphenyl. The reactions (products listed below) were conducted by heating the carbinols under reflux in chloroform with approximately equal weights of *p*-toluenesulphonic acid or thio-*p*-cresol, respectively for 4—18 hours. Yields approximately quantitative.

<i>p</i> -Tolyl sulphone of (I)	M. p. and mixed m. p. 87—88°.
<i>p</i> -Tolyl sulphone of (III)	M. p. and mixed m. p. 164°; <i>dl</i> -sulphone from (+)carbinol.
<i>p</i> -Tolyl sulphone of (VI)	M. p. 146—147° from ethyl alcohol (Found: S, 8.4. $C_{23}H_{22}O_4S$ requires S, 8.4%).
<i>p</i> -Tolyl sulphone of (VII)	M. p. 165° from ethyl alcohol (Found: S, 7.7. $C_{27}H_{26}O_3S$ requires S, 7.5%).
<i>p</i> -Tolyl thioether of (I)	M. p. and mixed m. p. 87—88°.
<i>p</i> -Tolyl thioether of (III)	M. p. 55—56° from methyl alcohol (Found: S, 8.2. $C_{26}H_{22}OS$ requires S, 8.3%).
<i>p</i> -Tolyl thioether of (IV)	M. p. 58° from methyl alcohol (Found: S, 12.6. $C_{16}H_{18}O_5$ requires S, 12.6%).
<i>p</i> -Tolyl thioether of (VI)	M. p. 74—75° from methyl alcohol (Found S, 8.7. $C_{22}H_{22}O_2$ requires S, 9.2%).
<i>p</i> -Tolyl thioether of (VIII)	M. p. 91° from methyl alcohol (Found: S, 9.8. $C_{22}H_{23}NS$ requires S, 9.6%).
<i>p</i> -Tolyl thioether of (IX)	M. p. 149° from methyl alcohol (Found: S, 8.7. $C_{26}H_{22}S$ requires S, 8.7%).

Anisyl hydrogen phthalate (10 g.), heated under reflux in 30 c.c. of ethyl alcohol, yielded the ethyl ether (2.7 g.), b. p. 115°/13 mm., 116—117°/14 mm.,  $n_D^{21}$  1.5060 (Späth, *Monatsh.*, 1914, **35**, 330, gives b. p. 111—113°/11 mm.). From a solution of the same phthalate (20 g.) after heating under reflux in chloroform (40 c.c.) for 45 hours phthalic acid separated; unchanged hydrogen phthalate was removed from the chloroform by washing with dilute aqueous sodium hydroxide, and evaporation of the chloroform then yielded anisyl phthalate (6.2 g.), an undistillable oil which on hydrolysis yielded anisyl alcohol (m. p. and mixed m. p. 22°) and phthalic acid.

*Di-p*-methoxybenzhydryl ether (Part II, *loc. cit.*). The hydrol (2.1 g.) with *p*-toluenesulphonic acid (5.2 g.) in water (20 c.c.) was warmed on the steam-bath for 20 minutes. The resulting oil crystallised (1.9 g.) from ligroin in glassy plates and after one recrystallisation from ethyl alcohol had m. p. and mixed m. p. 120—121°.

Thanks are due to the Government Grants Committee of the Royal Society and to Imperial Chemical Industries Ltd. for grants: and to the Czechoslovak Government (Department of Education) for a maintenance grant (R.W.).

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[Received, February 28th, 1946.]