1036. *The Oxidation of Ethers and Related Compounds. Part I. The Thermal and Photochemical Decomposition of t-Butyl Peroxide in Anisole.*

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Thermal decomposition of t-butyl peroxide in an excess of anisole at 140° has been shown to give mixtures of isomeric methoxytoluenes and phenoxymethylanisoles, but no 1,2-diphenoxyethane. These results, together with the high proportion of *ortho*-isomer in the phenoxymethylanisole mixture, are consistent with the initial production of phenoxymethyl radicals, which are sufficiently reactive at 140° to attack anisole at nuclear positions. As a further example of the reaction, 2,5-dimethoxybenzyl *p*-methoxyphenyl ether was obtained from the thermal decomposition of t-butyl peroxide in 1,4-dimethoxybenzene.

By contrast, the photochemical decomposition of t-butyl peroxide in anisole at 40° yielded no methoxytoluenes but gave 1,2-diphenoxyethane together with the isomeric phenoxymethylanisoles. The increasing order of reactivity of methyl groups towards t-butoxy-radicals at 140° is CMe, OMe, NMe; reasons for the differences are discussed.

CERTAIN atoms containing an unbonded electron pair are known to promote the attack of radical reagents at adjacent C–H bonds. Thus, tertiary alkylamines with t-butoxy-radicals give dialkylamino-substituted radicals that dimerise to derivatives of ethylenediamine [1] or, in the presence of oct-1-ene, add to this olefin.[2] In a study of benzyl ethers, Huang [3] has shown that t-butoxy-radicals cause a similar abstraction–dimerisation, but this cannot be strictly compared with the amine reactions because similar dimerisation *via* benzyl carbon occurs with toluenes in reaction with t-butyl peroxide,[4] *i.e.*, in the absence of the ether group.

Previous work with simpler ethers has been chiefly concerned with their reactions with acyl peroxides, especially benzoyl peroxide. Cass [5] showed that benzoyl peroxide reacts rather readily with dialkyl ethers, the products, formed in good yields, being benzoic acid and the α-benzoyloxy-ether. Kinetic studies [6,7] show that the peroxide decomposes both

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[1] Henbest and Patton, *J.*, 1960, 3557.
[2] Urry and Juveland, *J. Amer. Chem. Soc.*, 1958, **80**, 3322.
[3] Huang and Si-Hoe, " Vistas in Free Radical Chemistry," Pergamon Press, London, 1959, p. 242.
[4] Wilen and Eliel, *J. Amer. Chem. Soc.*, 1958, **80**, 3309, and references therein.
[5] Cass, *J. Amer. Chem. Soc.*, 1947, **69**, 500.
[6] Cass, *J. Amer. Chem. Soc.*, 1946, **68**, 1976.
[7] Nozaki and Bartlett, *J. Amer. Chem. Soc.*, 1946, **68**, 1686.

unimolecularly and by an induced chain mechanism, and tracer studies[8] have established that the first-formed ether radical attacks predominantly the peroxide oxygen of the peroxide in the induced decomposition.

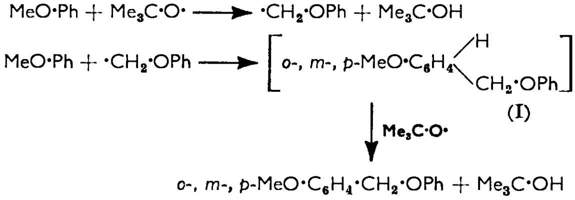
The reactions of alkoxy-radicals should in some ways be simpler than those of acyloxy-radicals, and the decomposition of t-butyl peroxide in anisole was chosen for investigation, this ether being the oxygen analogue of the previously studied dimethylaniline. Kinetic measurements have shown[7] that the decomposition of benzoyl peroxide in anisole is not a chain reaction, suggesting that nuclear substitution occurs in preference to abstraction of hydrogen from the methyl group, and this is supported by the isolation of methoxybiphenyls.[9] The methyl affinity[10] of anisole, however, is *less* than that of benzene. An interpretation of this result is that both hydrogen abstraction from the methyl group and nuclear substitution occur with methyl radicals.

The decomposition of t-butyl peroxide in anisole has been previously investigated by Cowley, Norman, and Waters,[11] who isolated (by vapour-phase chromatography, in unstated yield) an isomeric mixture of methoxytoluenes. The percentage composition of this mixture was shown to be: *o*- 74, *m*- 15, and *p*- 11. More recently, Johnston and Williams,[12] who made no reference to this previous work, obtained only " a dark involatile residue " on reaction of t-butyl peroxide with anisole.

We have investigated the decomposition of t-butyl peroxide in anisole induced thermally at 140° and photochemically at 40°, with ether and peroxide in the molar ratio of 10 : 1.

The thermal reaction, which was allowed to go to completion, gave isomeric mixtures of methoxytoluenes (*ca.* 29% based on acetone formed) and phenoxymethylanisoles (12% yield, see below). t-Butyl alcohol and acetone in the molar ratio 1·64 : 1 were also isolated, in 90% yield, together with small amounts of *o*-methoxybenzaldehyde and phenol. Careful examination failed to reveal any 1,2-diphenoxyethane and the remainder of the product consisted of resin from which no pure compound was isolated.

The identity of the phenoxymethylanisole fraction was demonstrated by hydrogenolysis and reduction by lithium–ammonia, which gave phenol and a mixture of isomeric methoxytoluenes in which the presence of the *ortho*- and *para*-isomers was shown by vapour-phase chromatography. The proportion (%) of each phenoxymethylanisole isomer (determined by vapour-phase chromatography which gave more satisfactory results in this instance than infrared analysis) was *o*- 70, *m*- 21, and *p*- 9. Phenoxymethylanisoles are considered to arise from nuclear substitution in anisole by phenoxymethyl radicals, which result from hydrogen abstraction from the methyl group of anisole by butoxy- or, to a smaller extent, by methyl radicals.



$$\mathrm{MeO{\cdot}Ph + Me_3C{\cdot}O{\cdot} \longrightarrow {\cdot}CH_2{\cdot}OPh + Me_3C{\cdot}OH}$$

$$\mathrm{MeO{\cdot}Ph + {\cdot}CH_2{\cdot}OPh \longrightarrow} \left[o\text{-}, m\text{-}, p\text{-}\mathrm{MeO{\cdot}C_6H_4}\!\left\langle\begin{matrix}\mathrm{H}\\ \mathrm{CH_2{\cdot}OPh}\end{matrix}\right.\right] \text{(I)}$$

$$\Big\downarrow \mathrm{Me_3C{\cdot}O{\cdot}}$$

$$o\text{-}, m\text{-}, p\text{-}\mathrm{MeO{\cdot}C_6H_4{\cdot}CH_2{\cdot}OPh + Me_3C{\cdot}OH}$$

The 12% yield of phenoxymethylanisoles is based on peroxide and these schemes; if the intermediate (I) is dehydrogenated by a process, *e.g.*, disproportionation, other than abstraction of hydrogen by a butoxy- or a methyl radical, the percentage yield given is too high. This scheme is supported by the isomer distribution which is typical of homolytic aromatic substitution[13] and may be compared with the values for methylation[11] and

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[8] Denney and Feig, *J. Amer. Chem. Soc.*, 1959, **81**, 5322; Drew and Martin, *Chem. and Ind.*, 1959, 925.

[9] Suehiro, *J. Chem. Soc. Japan*, 1951, **72**, 301.

[10] Heilman, Rembaum, and Szwarc, *J.*, 1957, 1127.

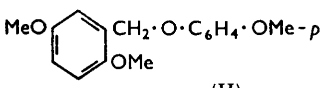
[11] Cowley, Norman, and Waters, *J.*, 1959, 1799.

[12] Johnston and Williams, *J.*, 1960, 1168.

[13] Augood and Williams, *Chem. Rev.*, 1957, **57**, 123.

phenylation[9] of anisole. Phenylation yields isomeric methoxybiphenyls in the ratio $o : m : p = 67 : 18 : 15$. Although the isomer ratios for phenoxymethylation, methylation, and phenylation of anisole are in good agreement, the values for phenoxymethylation do not necessarily indicate quantitatively the relative reactivities of the nuclear positions of anisole towards phenoxymethyl radicals, as the extent of further reactions of the phenoxymethylanisoles may vary with each isomer.

Material of higher molecular weight constituted the bulk of the product from the anisole–peroxide reaction at 140°. Much of this may arise from subsequent attack of radicals on the phenoxymethylanisoles, as reactions carried out with a 50 : 1 molar ratio of anisole to peroxide gave nearly twice the yield of the primary product. Subsequent attack can be envisaged to occur (i) by further nuclear substitution which would be slightly favoured with respect to anisole, and (ii) by abstraction of the benzyl hydrogen atom and dimerisation of the resulting radical. The latter reaction is known to occur with aryl benzyl ethers.[3] The radicals formed by hydrogen removal from the phenoxymethylanisoles may also decompose into other radicals, and the small amounts of phenol and *o*-methoxybenzaldehyde that were isolated probably arose in this way. Benzyl phenyl ether is known[14] to decompose, when heated, with formation of phenol and benzaldehyde, the reaction probably involving removal of benzyl hydrogen. The outcome of the anisole–peroxide reaction suggested that compound (II) should be the only primary product from the oxidation of 1,4-dimethoxybenzene. It was obtained in 19% yield (based on peroxide), its structure being confirmed by an alternative synthesis. Again, the major part of the product consisted of higher-boiling material.



(II)

The photochemically induced decomposition of t-butyl peroxide in anisole was carried out at 40° by irradiation with a mercury-arc lamp (principal wavelength 2570 Å). The products were markedly different from those obtained in the thermal reaction: 1,2-diphenoxyethane (11%) was obtained in addition to phenoxymethylanisoles (2%; essentially the *ortho*-isomer) (both yields based on peroxide consumed), and neither acetone nor methoxytoluene was detected. The yield of product of higher molecular weight was considerably lower than in the thermal reaction.

These results indicate that, at 140°, removal of phenoxymethyl radicals by nuclear substitution in anisole is too rapid to allow the occurrence of dimerisation, the rate of which depends on the square of the radical concentration. At 40°, however, nuclear substitution, with a higher energy of activation, becomes slower relative to dimerisation which consequently becomes observable. Moreover, it is concluded that alkyl radicals with an adjacent oxygen atom are considerably more reactive and hence shorter-lived than their nitrogen analogues which survive in a dialkylaniline solvent at 140° long enough to dimerise.[1]

This conclusion is supported by the observations that in *p*-methylanisole, butoxy-radicals abstract hydrogen from the *C*-methyl group[12] while in *NN*-dimethyl-*p*-toluidine, hydrogen is lost from an *N*-methyl group.[1] Further, when t-butyl peroxide was allowed to decompose in an equimolecular mixture of anisole and dimethylaniline, no *net* reaction with anisole was detected.

The reactivity of methyl groups towards t-butoxy-radicals increases in order CMe, OMe, NMe, as adduced by the yields of t-butyl alcohol (from reactions at 140°): 26% from t-butylbenzene,[15] *ca.* 55% from anisole, 100% from dimethylaniline,[1] and by the above competitive experiment. The greater reactivity of amines than of ethers is probably due to the greater capacity of amines to contribute a polar structure to the transition state (cf. the resonance polar effect discussed by Mayo and Walling[16] and Russell[17]). Electron

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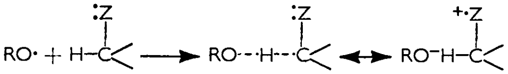
[14] Elkobaisi and Hickinbottom, *J.*, 1959, 1873.

[15] Raley, Rust, and Vaughan, *J. Amer. Chem. Soc.*, 1948, **70**, 1336.

[16] Mayo and Walling, *Chem. Rev.*, 1950, **46**, 191.

[17] Russell, *Tetrahedron*, 1959, **5**, 101; 1960, **8**, 101.

donation from the hetero-atom, with consequent lowering of the activation energy, occurs more readily when Z is nitrogen instead of oxygen:



$$\mathrm{RO\cdot} + \mathrm{H{-}}\overset{:\mathrm{Z}}{\overset{|}{\mathrm{C}}}\!< \;\longrightarrow\; \mathrm{RO\cdots H\cdots}\overset{:\mathrm{Z}}{\overset{|}{\mathrm{C}}}\!< \;\longleftrightarrow\; \mathrm{RO^{-}H{-}}\overset{+\cdot\mathrm{Z}}{\overset{|}{\mathrm{C}}}\!<$$

This is in accord with values for the ionisation potentials of amines and ethers, the energies required for excitation of a lone-pair electron being 7·84 ev for trimethylamine,[18] 9·53 ev for diethyl ether,[19] and 8·20 ev for anisole.[19] In general, alkyl halides have higher ionisation potentials than ethers and it is unlikely therefore that the reactivity of carbon–hydrogen bonds, adjacent to halogen, towards electron-accepting radicals will be appreciably enhanced by the electron-donating effect. α-Carbon chlorination and fluorination of n-butyl halides [20] is, in fact, slightly retarded by the halogen substituent.

Differences in the reactivities of $R_2N{\cdot}CR_2{\cdot}$ and $RO{\cdot}CR_2{\cdot}$ radicals when formed, notably the fact that amine radicals are longer lived, indicate that, as in the transition states for their formation, resonance stabilisation by electron donation is greater with adjacent nitrogen than with adjacent oxygen.

EXPERIMENTAL

Extracts were dried over $MgSO_4$. Light petroleum (b. p. 40—60°) was used. Anisole was washed with aqueous 10% sodium hydroxide and water, and then dried and fractionated, the middle fraction of b. p. 151° being collected; its vapour-phase chromatogram (polyethylene glycol–Celite; 75°; argon) showed a single peak. t-Butyl peroxide (Laporte) was gas-chromatographically homogeneous and was used without purification.

Decomposition of t-Butyl Peroxide in Anisole.—Anisole (32·3 g., 10 mol.) and the peroxide (4·33 g., 1 mol.) were kept under nitrogen in a sealed tube at 140° for 60 hr. t-Butyl alcohol (2·41 g.) and acetone (1·15 g.) in the mixture were determined by vapour-phase chromatography (trixylyl phosphate–Celite, 18°, nitrogen) with propan-1-ol as internal standard. In a separate experiment, acetone and t-butyl alcohol were distilled from the reaction mixture, and acetone was characterised as the 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 125°. The mixture was washed with aqueous 5% sodium hydroxide which extracted phenol (0·105 g.) estimated as the tribromo-derivative (0·369 g.), m. p. and mixed m. p. 88°. Slow distillation up to 70°/30 mm. gave a fraction consisting of anisole containing methoxytoluenes (see below). The residue was fractionally distilled: the fore-run, b. p. 60—106°/0·2 mm., showed a carbonyl band at 1680 cm.$^{-1}$ and gave a 2,4-dinitrophenylhydrazone (0·05 g.) which, after chromatography on bentonite–kieselguhr, had m. p. 248—250°, alone or mixed with *o*-methoxybenzaldehyde 2,4-dinitrophenylhydrazone (m. p. 250°). The main fraction (0·75 g.), b. p. 108—130°/0·2 mm. (Found: C, 78·1; H, 6·7. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%), showed an ether band at 1240 cm.$^{-1}$ and treatment with aqueous 48% hydrogen bromide gave phenol but no dibromomethane or 1,2-dibromoethane (vapour-phase chromatography).

A portion (0·8 g.) of the main fraction in ethanol (20 ml.) was hydrogenated over 5% palladised charcoal (0·22 g.). After absorption (50 ml.) had ceased, ether (100 ml.) was added and the suspension was filtered. Extraction of the filtrate with aqueous 5% sodium hydroxide gave phenol (0·06 g.) estimated as the tribromo-derivative (0·210 g.). Distillation of the ethereal solution gave a fraction (0·08 g.), b. p. 83°/25 mm., n_D^{18} 1·5236, which showed *ortho-*, *meta*, and *para*-substitution in the 690—850 cm.$^{-1}$ region and the vapour-phase chromatogram (trixylyl phosphate; 130°, nitrogen) showed two peaks with the retention times of *o*- (13·4 min.) and *p*-methoxytoluene (15·5 min.), respectively. A higher yield (55%) of the methoxytoluenes was obtained by reduction of the fraction with lithium (100% excess) in liquid ammonia (Found: C, 78·55; H, 8·6. Calc. for $C_8H_{10}O$: C, 78·7; H, 8·3%).

The distillation residue (2·24 g.) was chromatographed on alumina, yielding only amorphous solids of indefinite m. p. Reductive cleavage as above gave phenol as the only identifiable product.

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[18] Watanabe and Mottl, *J. Chem. Phys.*, 1957, **26**, 1773.

[19] Watanabe, *J. Chem. Phys.*, 1957, **26**, 542.

[20] Fredricks and Tedder, *J.*, 1960, 144.

In a separate experiment, the reaction mixture was distilled into three fractions of b. p. <200°: (i) 80—152°/760 mm.; (ii) 152°/760 mm.; (iii) 50°/10 mm. Each was examined by vapour-phase chromatography (trixylyl phosphate–Celite, 121°); apart from anisole, fractions (ii) and (iii) showed a peak with the retention time of *o*-methoxytoluene, possessing a shoulder (on the later side) due to the *meta*- and *para*-isomers. Owing to the relatively small sizes of these peaks, the total yield of methoxytoluenes could only approximately be estimated, at 29% ± 5% (based on acetone; dimethylaniline as internal standard).

Anisole–Peroxide Reactions at Higher Molar Ratios.—(i) Anisole (159 g., 50 mol.) and peroxide (4·3 g., 1 mol.) were heated at 140° for 60 hr. (reflux condenser) in a slow stream of nitrogen. After removal of the fraction containing phenol and anisole as before, distillation of the residue gave an isomeric mixture of phenoxymethylanisoles (1·48 g., 23·5%), b. p. 106—110°/0·11 mm. (ii) Repetition of Johnston and Williams's [12] experiment with anisole (108 g.) and peroxide (4 g.) at 110° for 72 hr. (reflux condenser) gave phenoxymethylanisoles (0·25 g., 4·3%), b. p. 140°/4 mm. The infrared spectrum was identical with that of the phenoxymethylanisole fractions obtained above.

o-*Phenoxymethylanisole.*—2-Methoxybenzyl chloride, b. p. 122—124°/28 mm., n_D^{22} 1·5481, was obtained by treatment of 2-methoxybenzyl alcohol [21] with thionyl chloride in benzene [22] (lit.,[21] b. p. 110—114°/14 mm.). The chloride (9·9 g.) was heated under reflux for 8 hr. with phenol (6·5 g.) and a suspension of anhydrous potassium carbonate (30 g.) in acetone (40 ml.). The mixture was filtered and the residue, from evaporation of the filtrate, was washed in ether (300 ml.) with aqueous 10% sodium hydroxide, dried, and evaporated. Distillation of the residue gave recovered chloride (1·1 g.), b. p. 58—62°/0·1 mm., and then the *ether* (8·8 g.), b. p. 116—120°/0·1 mm., $n_D^{19.5}$ 1·5800 (Found: C, 78·5; H, 6·3%).

m-*Phenoxymethylanisole.*—3-Methoxybenzyl chloride [23] was treated with phenol under the above conditions, yielding the *ether* (57%), b. p. 134—136°/0·2 mm., n_D^{18} 1·5790 (Found: C, 78·0; H, 6·7%).

p-*Phenoxymethylanisole.*—4-Methoxybenzyl chloride [24] was converted as before into the *ether* (58%), b. p. 124—126°/0·4 mm., m. p. 76—80°, raised to 92—92·5° (from benzene–light petroleum) (Found: C, 78·5; H, 6·6%).

Reaction of p-*Dimethoxybenzene with t-Butyl Peroxide.*—Reactions were carried out as for the anisole reactions with the ether (32 g.) and peroxide (3·38 g.). When reaction was complete the mixture, in chloroform (250 ml.), was extracted with aqueous 5% sodium hydroxide. Chloroform and the excess of the ether were removed and distillation of the residue gave 2,5-*dimethoxybenzyl* p-*methoxyphenyl ether* (1·2141 g.), b. p. 150—160°/0·2 mm., m. p. 50—54° raised to 62—63° (from benzene–light petroleum) (Found: C, 70·0; H, 6·8. $C_{16}H_{18}O_4$ requires C, 70·1; H, 6·6%) alone or mixed with an authentic specimen (below). Attempts to obtain recognisable products from the residue (2·2 g.), by chromatography on alumina or sodium–ammonia reduction, failed.

2,5-*Dimethoxybenzyl* p-*Methoxyphenyl Ether.*—Treatment of 2,5-dimethoxybenzoic acid [25] with methanol and sulphuric acid gave *methyl* 2,5-*dimethoxybenzoate*, b. p. 95—98°/1 mm., $n_D^{17.5}$ 1·5416 (Found: C, 60·9; H, 6·0. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·2%). Reduction of the ester (8 g.) with lithium aluminium hydride (4·5 g.) in ether (250 ml.) gave 2,5-dimethoxybenzyl alcohol (4·1 g.), b. p. 122—125°/1 mm., n_D^{17} 1·5490 (lit.,[26] b. p. 85—90°/0·025 mm.), which was converted with thionyl chloride in benzene into 2,5-dimethoxybenzyl chloride, m. p. 66° (lit.,[27] 70—72°). The chloride (0·6 g.) was refluxed for 40 hr. with *p*-methoxyphenol (0·5 g.) and a suspension of potassium carbonate (10 g.) in acetone (25 ml.). The mixture was filtered and ether (100 ml.) was added to the filtrate. The excess of *p*-methoxyphenol was removed with aqueous sodium hydroxide and evaporation of the ethereal solution gave the ether (0·3 g.), m. p. 62—62·5° (from benzene–light petroleum) (Found: C, 70·3; H, 6·7%).

Determination of the Ratios of Isomeric Phenoxymethylanisoles from the Anisole–Peroxide Reaction.—Duplicate experiments were carried out as previously described except that in

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[21] Cragoe and Pietrusykiewicz, *J. Org. Chem.*, 1957, **22**, 1338.
[22] Newman, *J. Amer. Chem. Soc.*, 1940, **62**, 2295.
[23] Tsukamoto, Yoshimura, and Toki, *Pharm. Bull.* (*Japan*), 1955, **3**, 239.
[24] Quelet, *Compt. rend.*, 1934, **198**, 102.
[25] Graebe and Martz, *Annalen*, 1905, **340**, 213.
[26] Shulgin and Gal, *J.*, 1953, 1316.
[27] Harley-Mason and Jackson, *J.*, 1954, 1165.

addition the reaction mixtures were extracted with saturated aqueous sodium hydrogen sulphite to remove aldehydes. The yields of phenoxymethylanisoles were 0·78 g. and 0·72 g., respectively [Found: (i) C, 78·2; H, 6·2; (ii) C, 78·1; H, 6·8%]. Vapour-phase chromatography (7% polyphenyl ether–Celite at 183°; argon) of the isomeric mixtures gave complete resolution of the isomers and peak areas were measured with a planimeter. The area–concentration dependence was checked with mixtures of the individual isomers of known compositions.

TABLE 1.

Isomer ratio determinations on mixtures of phenoxymethyl anisoles.

	Found (%)			Known (%)		
	o-	*m*-	*p*-	*o*-	*m*-	*p*-
Expt. (i)	69	22	9	—	—	—
Expt. (ii)	71	20	9	—	—	—
Synthetic mixture (i)	74	20	6	75·5	19·2	6·3
Synthetic mixture (ii)	68	24·7	7·3	69	23	8

Photochemical Decomposition of t-Butyl Peroxide in Anisole.—t-Butyl peroxide (4·32 g.) in anisole (32·1 g.), contained in a quartz flask, was irradiated with a Hanovia mercury arc lamp type 590/10 (principal wavelength of emission 2570 Å), the temperature of the solution being kept at 40—45°. After 96 hr., decomposed peroxide, t-butyl alcohol, and anisole were distilled off. The distillate was shown to contain 70% of the original peroxide and the absence of acetone was established by vapour-phase chromatography (trixylyl phosphate–Celite; 18°; nitrogen). The higher-boiling fraction, in benzene, was washed with aqueous 5% sodium hydroxide and, after removal of the solvent, distillation of the residue gave a fraction (0·24 g.), b. p. 125°/0·3 mm., m. p. 25—40°. 1,2-Diphenoxyethane (0·21 g.) and phenoxymethylanisoles (43 mg., essentially the *ortho*-isomer) in this fraction were determined by vapour-phase chromatography (polyphenyl ether–Celite; 183°; argon). The distillation residue (0·55 g.) was not further investigated. In another experiment, the "dimer" fraction was crystallised from ethanol, to give 1,2-diphenoxyethane, m. p. and mixed m. p. 97°, with an infrared spectrum identical with that of an authentic sample.

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