924. *The Reaction of Some Alkyl Benzyl and Benzyl Cycloalkyl Ethers with t-Butoxy-radicals.*

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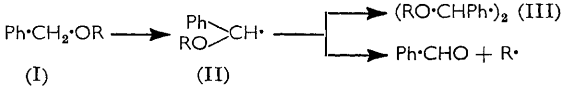
In hydrogen abstraction by t-butoxy-radicals from a benzyl ether $Ph{\cdot}CH_2{\cdot}OR$ (R = s-butyl, cyclopentyl, or cyclohexyl) attack is directed mainly at the benzylic α-hydrogen atom, but also appreciably at the tertiary hydrogen atom in R. The relative extents to which the latter attack occurs afford the following scale of reactivity: cyclopentyl > cyclohexyl ~ s-butyl.

Abstraction from benzyl phenethyl and di-(α-methylbenzyl) ether, as well as from cyclohexyl methyl and t-butyl ether, has also been studied. The radicals derived from these ethers decompose or dimerise according to whether the former process does or does not generate a relatively stable secondary radical.

Hydrogen-abstraction by free t-butoxy-radicals from the benzyl ether (I) has been shown [1] to occur at the benzylic α-carbon atom to generate the radical (II) which then either dimerises, or disproportionates to benzaldehyde and the radical R•, or undergoes both processes, as follows:



(I) (II)

From study of a series of benzyl ethers (I; R = Me, Et, Pr^i, Bu^t, Ph, $Ph{\cdot}CH_2$, and Ph_2CH), it has been established that the tendency of the radical (II) to decompose depends

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[1] Huang and Si-Hoe, *Proc. Chem. Soc.*, 1957, 354; Huang and Si-Hoe in "Vistas in Free-radical Chemistry," ed. W. A. Waters, Pergamon Press, London, 1959, p. 242.

on the relative stability of R· so produced. This tendency is predominant when R = $\mathrm{Ph{\cdot}CH_2}$, $\mathrm{Ph_2CH}$, or $\mathrm{Bu^t}$, for these radicals are stabilised by resonance; but it is very slight when R = Me or Ph for these are highly energised radicals. In the last cases, the radical (II) persists in solution until it dimerises. For radicals (II; R = Et or $\mathrm{Pr^i}$) which on fragmentation gives ethyl or isopropyl, of intermediate stability, both decomposition and dimerisation occur. This study has now been extended to five other benzyl ethers, namely, di-(α-methylbenzyl), benzyl phenethyl, benzyl s-butyl, benzyl cyclopentyl, and benzyl cyclohexyl ether. Two cyclohexyl ethers, namely, methyl and t-butyl, have also been studied. The earlier method of cleavage and of isolation of reaction products[1] has been considerably modified (see Experimental section).

Reaction of t-butyl peroxide at 125° with di-(α-methylbenzyl) ether gave only acetophenone and a mixture of *meso*- and racemic 2,3-diphenylbutane (see Table for results of cleavage experiments), indicating that the radical ·CMePh·O·CHMePh decomposes extensively, as expected. The fact that the substituted bibenzyl was formed in a yield nearly as high (nine-tenths) as that of acetophenone suggests that the α-methylbenzyl radical largely dimerises and hardly partakes in abstraction of hydrogen from the ether (to give ethylbenzene). Since, in the case of benzyl radicals, abstraction under comparable conditions has been shown to be slight,[2] the lack of activity of the α-substituted benzyl radical is to be expected.

Benzyl phenethyl ether gave a dimer as the main product, a little benzaldehyde and benzoic acid, and much polymer. Hydrolysis with hydrobromic acid to stilbene established the structure of the dimer as (III; R = $\mathrm{CH_2{\cdot}CH_2Ph}$) and thus also the identity of the intermediate radical as (II; R = $\mathrm{CH_2{\cdot}CH_2Ph}$). This radical is of the type expected to undergo dimerisation rather than decomposition, and has been found to do so. The alternative radical $\mathrm{Ph{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CHPh{\cdot}}$ could have been formed (although none of the dimer from it could be found), and, through the styryl derivative $\mathrm{Ph{\cdot}CH_2{\cdot}O{\cdot}CH{:}CHPh}$ which it forms by disproportionation with a like radical, could have given rise to polymers.

Benzyl s-butyl ether yielded a dimer, benzaldehyde and benzoic acid, and butanone. The dimer, obtained as a liquid, gave stilbene on degradation with hydrobromic acid, and must therefore have structure (III; R = $\mathrm{Bu^s}$), probably in a mixture of the *meso*- and racemic forms. Its high yield, relative to that of benzaldehyde, indicating extensive dimerisation of the radical (II; R = $\mathrm{Bu^s}$), is also in conformity with the established pattern. The isolation of butanone shows that with benzyl s-butyl ether abstraction of hydrogen occurred also in the s-butyl group, to generate the radical $\mathrm{Ph{\cdot}CH_2{\cdot}O{\cdot}CMeEt{\cdot}}$.

Ether	Ether, mmoles (g.)	Peroxide, mmoles (g.)	Cleavage products, mmoles (g.)				Intractable oils (g.)
			Ph·CHO	BzOH	Ketone	Dimer (III)	
$\mathrm{(Ph{\cdot}CHMe)_2O}$	120 (27)	30 (4·3)	—	—	COPhMe 18·0 (2·2) *	—	(2·3)
$\mathrm{Ph{\cdot}CH_2{\cdot}O{\cdot}CH_2{\cdot}CH_2Ph}$	170 (35)	43 (6·1)	1·0 (0·1)	0·01 (0·1)	—	5·0 (2·1)	(4·1)
$\mathrm{Ph{\cdot}CH_2{\cdot}OBu^s}$	230 (35)	53 (7·7)	10·5 (1·1)	1·0 (0·16)	COMeEt 6·5 (0·47)	27·1 (8·8)	(3·5)
$\mathrm{Ph{\cdot}CH_2{\cdot}O{\cdot}C_5H_9}$	100 (18)	25 (3·6)	5·9 (0·63)	—	Cyclopentanone 4·5 (0·38)	*meso* 4·2 (1·45) Rac. 5·0 (1·73)	(0·6)
$\mathrm{Ph{\cdot}CH_2{\cdot}O{\cdot}C_6H_{11}}$	130 (26)	33 (4·8)	4·7 (0·50)	—	Cyclohexanone 2·5 (0·24)	*meso* 7·0 (2·7) Rac. 3·2 (1·2)	(0·5)
$\mathrm{C_6H_{11}{\cdot}OBu^t}$	130(20)	30 (4·4)	—	—	,, 8·2 (0·80)	—	(3·5)
$\mathrm{C_6H_{11}{\cdot}OMe}$	450 (51)	113 (16·5)	—	—	,, 14·3 (1·4)	11 (2·4)	(6·6)

* Also isolated, 2,3-diphenylbutane in the *meso*- (1·0 g., 5 mmoles) and racemic form (0·62 g., 3 mmole).

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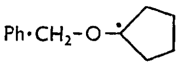
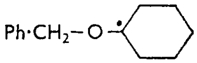
[2] Huang and Yeo, *J.*, 1959, 3190.

Since this radical is of the type which will readily decompose to free benzyl and butanone (and indeed no dimer from it could be isolated), the extent to which it was formed could be estimated approximately from the quantity of butanone produced. This quantity (6·5 mmoles), when compared with the yield (66 mmoles) of the alternative radical (II), in turn estimated from the yields of the dimer (III), benzaldehyde, and benzoic acid, gives an order of activity for the tertiary hydrogen atom in the s-butyl group of about one-tenth of that of the benzylic α-hydrogen atom.

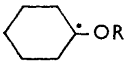
The products from benzyl cyclopentyl ether consisted of cyclopentanone, benzaldehyde, and two isomeric dimers. That these dimers were *meso*- and racemic forms of (II; R = C_5H_{11}) was indicated by their infrared absorption, and confirmed by their both being degraded to stilbene. By analogy with other diastereoisomeric substances the higher-melting, and less soluble, form was assumed to be the *meso*-isomer. The isolation of cyclopentanone indicates that, as in the previous case, abstraction occurred on both sides of the oxygen function, generating both the radicals (II) and (IV). By comparing the yield of cyclopentanone derived from (IV) on the one hand, and that of the dimers (III) and benzaldehyde derived from the radical (II), on the other, it is concluded that the rate at which the tertiary hydrogen atom in the cyclopentane ring suffers abstraction is ~0·18 that of the benzylic α-hydrogen atom. It is noted that formation of the dimer (III) again predominates over that of benzaldehyde, indicating that, for the radical (II), decomposition is not favoured.



(IV)



(V)



(VI: R = Me)
(VII: R = Bu^t)

From benzyl cyclohexyl ether were obtained cyclohexanone, benzaldehyde, and the dimer (III; R = C_6H_{11}) in both the *meso*- and the racemic form, the isomers being each degraded to stilbene in the usual way. The yields of the cleavage products show that the molar ratio in which the radicals (II) and (V) were formed was 1·0 : 0·10, and that the former radical dimerised preferentially.

Although our method is no better than semi-quantitative, the results obtained allow certain conclusions to be drawn. Hydrogen abstraction in all cases occur largely at the benzylic α-carbon atom, and this is probably due to resonance-stabilisation of the resulting radical by the benzene ring, as well as to polar effects to which the electronegative t-butoxy-radical is known to be subject.[2,3] The latter would understandably facilitate abstraction in the manner observed if the $-I$ effect of the benzene ring, coupled with the $+I$ effect of the alkyl group set up, through the polarisable C–O bonds, a relatively high electron density at the benzylic α-carbon atom.

From the activities, relative to that of the benzylic α-hydrogen atom, of the tertiary hydrogen atoms in the s-butyl, cyclopentyl, and cyclohexyl groups, namely, 0·10, 0·18, and 0·10, the following order of activity can be arranged: cyclopentyl > cyclohexyl ~ s-butyl. Although the accuracy of our method does not permit a distinction between the last two groups, the substantially higher activity of the cyclopentyl system is beyond doubt. Further, in the light of the behaviour of the radicals (II) under identical conditions, the tendency to decompose rather than dimerise is also in the order cyclopentyl > cyclohexyl ~ s-butyl (molar ratios of decomposition compared with dimerisation are ~0·3, 0·2, and 0·2, respectively). This tendency should give a rough measure of the relative stability of the radical R•, and the coincidence of the two scales in respect of the cyclic systems is to be expected if it is considered that in hydrogen-abstraction the factors other than radical stability which control the course of the reaction, namely, polar effect due to the t-butoxy-radical and steric factors (*F*-strain), should operate to approximately the same extent.

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[3] Huang, Lee, and Ong, *J.*, 1962, 3336.

These results agree with predictions based on Brown's *I*-strain theory,[4] and finds corroboration from findings on hydrogen-abstraction by free methyl radicals [5] and from work on cyclic azodinitriles.[6]

The radical (VI) afforded the dimer and some cyclohexanone, whereas (VII) gave only the ketone. This contrasting behaviour is to be expected: decomposition of (VI) would give the highly active free methyl and is not favoured, whereas that of (VII) liberates the relatively stable free t-butyl, probably with concomitant relief of steric strain, and hence occurs readily. The alkoxyalkyl radicals derived from benzyl and cyclohexyl ethers are thus analogous in behaviour to the α-aminobenzyl radicals derived from benzylamines, reported by one of us elsewhere,[7] and to the alkoxy-radicals recently studied by Kochi and by Greene and his co-workers.[8]

EXPERIMENTAL

Cleavage Experiments.—General procedure. A mixture of the ether and redistilled t-butyl peroxide was sealed under argon in a glass tube and heated at 125° for 24 hr. (In our earlier method [1] the reactants were heated in an open vessel at 115° for 96 hr.) Separation of aldehydes and/or ketones was by chromatographic adsorption of the 2,4-dinitrophenylhydrazones, as reported elsewhere,[3] and the yields were calculated from those of these derivatives. (The earlier method of estimating the yield of benzaldehydes from the weights of the bisulphite compounds obtained has been found to give somewhat exaggerated results, owing probably to coprecipitation of sodium bisulphite with the bisulphite compound.)

Di-(α-methylbenzyl) ether. The product from this ether (26·7 g.) and t-butyl peroxide (4·3 g.), on fractionation, gave (i) a mixture of acetone, butanol, and unchanged peroxide, (ii) acetophenone, b. p. 60—63°/4 mm., n_D^{26} 1·5340 (2·2 g.), identified as dinitrophenylhydrazone and semicarbazone, and (iii) a residue (22·1 g.). This residue on chromatography in benzene (alumina) gave (*a*) *meso*-2,3-diphenylbutane, m. p. 124° (1·0 g.), (*b*) racemic 2,3-diphenylbutane b. p. 84—86°/0·2 mm., n_D^{25} 1·5491 (0·62 g.) (Farmer and Moore [9a] and Hey *et al.*[9b] report, respectively, 124—125° and n_D^{23} 1·5495), (*c*) unchanged ether (19 g.), and (*d*) viscous oils (2·3 g.).

Benzyl phenethyl ether. The product from this ether (28·3 g.) and the peroxide (6·1 g.), after removal of benzaldehyde (0·10 g., identified as its dinitrophenylhydrazone and semicarbazone) by bisulphite extraction, and of unchanged ether (19·9 g.) by distillation, was chromatographed on alumina with light petroleum–benzene as eluant, to give (i) *αα'-di-(2-phenylethoxy)bibenzyl* (2·12 g.) which, recrystallised from ethanol, melted at 77° (Found: C, 84·8; H, 7·15. $C_{30}H_{30}O_2$ requires C, 85·3; H, 7·2%), and (ii) intractable oils (4·1 g.). The bibenzyl (0·21 g.) was boiled with a 1 : 2 mixture (*ca.* 20 c.c.) of 48% hydrobromic acid and glacial acetic acid for 3 hr. and the solution distilled until *ca.* 2 c.c. remained. The distillate, on being neutralised with sodium carbonate, precipitated stilbene, m. p. and mixed m. p. 124° (0·04 g.).

Benzyl s-butyl ether. This ether (35·2 g.) and the peroxide (7·7 g.) gave a product which was fractionated into (i) a liquid, b. p. 78°/760 mm. (3·12 g.), (ii) a liquid, b. p. 47°/126 mm. (3·42 g.), and (iii) a residue. The residue was shaken in light petroleum (30 c.c.) with saturated aqueous sodium hydrogen sulphite for 2 hr. and the bisulphite compound (2·21 g.) was filtered off and washed with ether. After extraction with 10% aqueous sodium hydrogen carbonate, the filtrate was dried ($MgSO_4$), concentrated, and distilled, giving fractions (iv) b. p. 54—55°/1·4 mm. (21·9 g.), (v) b. p. 130—136°/1·2 mm. (7·02 g.), (vi) b. p. 136°/1·0 mm. (2·06 g.), n_D^{25} 1·5102, and (vii) a residue (3·8 g.).

Fraction (i) was a mixture of t-butyl alcohol, acetone, and butanone. A portion (0·092 g.) was treated with an excess of a 2,4-dinitrophenylhydrazine phosphate solution and the mixture of hydrazones so obtained was chromatographed [3] on bentonite–kiesulguhr (eluant, chloroform), giving the dinitrophenylhydrazones of butanone (m. p. and mixed m. p. 117°; 0·024 g.) and

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[4] Brown, Fletcher, and Johannesen, *J. Amer. Chem. Soc.*, 1951, **73**, 212; cf. Brook, *Trans. Faraday Soc.*, 1957, **53**, 327.

[5] Trotman-Dickinson and Steacie, *J. Chem. Phys.*, 1951, **19**, 329.

[6] Overberger, Biletch, Finestone, Lilker, and Herbert, *J. Amer. Chem. Soc.*, 1953, **75**, 2078.

[7] Huang, *J.*, 1959, 1816.

[8] Kochi, *J. Amer. Chem. Soc.*, 1962, **84**, 1193; Greene, Savitz, Lau, Osterholtz, and Smith, *ibid.*, 1961, **83**, 2198; Greene, Savitz, Osterholtz, Lau, Smith, and Zanet, *J. Org. Chem.*, 1963, **28**, 55.

[9] (*a*) Farmer and Moore, *J.*, 1951, 131; (*b*) Hey, Pengilly, and Williams, *J.*, 1955, 6.

acetone (m. p. and mixed m. p. 126°; 0·053 g.). Fraction (ii) was unchanged peroxide containing butyl alcohol and butanone, a portion (1·01 g.) of which was treated with the same reagent, giving more butanone dinitrophenylhydrazone (0·32 g.), while another portion was converted into the semicarbazone, m. p. and mixed m. p. 145—146°. The total yield of butanone was 0·47 g. Fraction (iv) was mainly unchanged ether, b. p. 53—54°/1·0 mm., n_D^{25} 1·4852. Fraction (v), on distillation, gave three fractions of *αα′-di-s-butoxybibenzyl,* (*a*) b. p. 138°/1·5 mm., n_D^{26} 1·5102 (0·52 g.), (*b*) b. p. 140—144°/1·5 mm., n_D^{26} 1·5093 (2·60 g.), and (*c*) b. p. 144°/1·5 mm., n_D^{26} 1·5100 (3·57 g.) (Found: C, 80·6; H, 9·1. $C_{22}H_{30}O_2$ requires C, 80·9; H, 9·3%). The total yield of the bibenzyl derivative, including fraction (vi), was 8·8 g. A portion from each of the fractions (*a*), (*b*), and (*c*) was boiled with hydrobromic–acetic acid, as described earlier, each giving stilbene.

The aldehyde bisulphite compound was treated with 2N-sulphuric acid under nitrogen and the benzaldehyde liberated converted into the dinitrophenylhydrazone, m. p. and mixed m. p. 240° (3·00 g.), corresponding to a yield of aldehyde of 1·12 g. The sodium hydrogen carbonate extract, on acidification, gave benzoic acid (0·16 g.).

Benzyl cyclopentyl ether. The product from this ether (17·8 g.) and t-butyl peroxide (3·6 g.) was fractionated to give (i) volatile material, b. p. 60—83°/760 mm. (1·0 g.), (ii) a mixture of t-butyl peroxide, cyclopentanone, benzaldehyde, and unchanged ether (*ca.* 4 g.), b. p. up to 90°/0·8 mm. (N.B. distillate was collected in two receivers chilled to −80°; fraction was cut after unchanged ether had begun to distil, to ensure removal of all benzaldehyde), (iii) unchanged ether b. p. 90—92°/0·8 mm., n_D^{26} 1·5121 (4·95 g.), and (iv) a residue. Fraction (ii) was immediately treated with a solution of 2,4-dinitrophenylhydrazine and the mixture of hydrazones (3·36 g.) was analysed by chromatography in the usual way (the cyclopentanone derivative had m. p. and mixed m. p. 145°). The yields of cyclopentanone and benzaldehyde were 0·38 g. and 0·63 g., respectively.

The residue (iv), in contact with methanol, deposited meso-*αα′-dicyclopentyloxybibenzyl* (1·45 g.), which crystallised from methanol in plates, m. p. 117° [Found: C, 82·1; H, 8·8%; *M* (Rast), 351. $C_{24}H_{30}O_2$ requires C, 82·2; H, 8·6%; *M*, 350·5], very soluble in light petroleum, ether, and chloroform, $\nu_{max.}$ 3045, 2960, 2870, 1496, 1456, 1100, 1070, 1030, 944, and 675 cm.$^{-1}$. The methanolic filtrate slowly deposited racemic *αα′-dicyclopentyloxybibenzyl,* m. p. 59—65° (0·87 g.), which after recrystallisation from methanol and chromatography (alumina in light petroleum) and further recrystallisation gave the pure isomer as needles, m. p. 72° (Found: C, 82·4; H, 8·8%; *M*, 370), $\nu_{max.}$ 3045, 2960, 2870, 1496, 1456, 1090, 1070, 1030, 966, and 675. The mother-liquors from the recrystallisations were concentrated to an oil (5·07 g.), and a portion (3·59 g.) was evaporatively distilled, to give (i) unchanged ether (1·57 g.), (ii) the racemic bibenzyl (0·66 g.), and (iii) a brown viscous residue (0·36 g.).

The products were therefore cyclopentanone (0·38 g.), benzaldehyde (0·63 g.), the bibenzyl derivative in the *meso*- (1·45 g.) and the racemic (1·73 g.) form, and polymer (0·55 g.). Treatment of the racemic bibenzyl with hydrobromic acid in the usual manner gave stilbene (15%).

Benzyl cyclohexyl ether. The products from this ether (25·5 g.) and t-butyl peroxide (4·8 g.) were worked up as described for the previous experiment, to yield (*a*) cyclohexanone (0·24 g.), (*b*) benzaldehyde (0·50 g.), (*c*) meso-*αα′-dicyclohexyloxybibenzyl,* m. p. 118° (2·7 g.), prisms from methanol (Found: C, 82·4; H, 9·0. $C_{26}H_{34}O_2$ requires C, 82·5; H, 9·0%), $\nu_{max.}$ 3045, 2971, 2891, 1495, 1456, 1345, 1288, 1229, 1178, 1095, 1070, 1030, 975, and 625 cm.$^{-1}$), (*d*) the racemic *isomer,* needles (from methanol), m. p. 51—52° (1·2 g.) (Found: C, 82·8; H, 9·1%), $\nu_{max.}$ 3045, 2971, 2891, 1495, 1456, 1345, 1178, 1095, 1070, 1030, 1006, 990, and 625 cm.$^{-1}$), and (*e*) polymer (0·51 g.).

The *meso*- and racemic bibenzyl derivatives, on hydrolysis with hydrobromic acid, gave stilbene in 69% and 15% yield, respectively.

Cyclohexyl t-butyl ether. The product from this ether (19·8 g.) and the peroxide (4·4 g.), on distillation, gave (i) volatile material and unchanged peroxide, (ii) a liquid, b. p. 78—82°/35 mm., n_D^{26} 1·4361 (12·8 g.), (iii) unchanged ether, b. p. 57—64°/8 mm. (3·05 g.), n_D^{26} 1·4341, and (iv) a viscous residue (3·5 g.) which did not distil up to 170° (bath)/8 mm. Fraction (ii) contained unchanged ether admixed with cyclohexanone, and on extraction [10] with Girard's reagent P afforded the ketone (0·80 g.), identified through the dinitrophenylhydrazone and semicarbazone (m. p.s and mixed m. p.s). The residue (iv) was chromatographed but yielded no crystals.

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[10] Girard and Sandulesco, *Helv. Chim. Acta*, 1936, **19**, 1095.

Cyclohexyl methyl ether. The product from this ether (51·3 g.) and the peroxide (16·5 g.) was fractionated under argon, to give (i) volatile material, b. p. 84—122°/760 mm. (11·9 g.), (ii) material of b. p. up to 70°/1·7 mm. (49·2 g.), and (iii) a residue (9·3 g.). Fraction (ii) was extracted with Girard's reagent P, being thereby divided into a ketonic and a non-ketonic fraction, the former giving cyclohexanone which was isolated as dinitrophenylhydrazone (1·69 g.), and the latter being the unchanged ether, b. p. 131°/760 mm., n_D^{25} 1·4331 (47·0 g.). A portion (4·7 g.) of the residue (iii) was distilled, to give (iv) a little cyclohexanone and (v) 1,1'-*dimethoxybi*(*cyclohexyl*), b. p. 105°/0·7 mm., n_D^{25} 1·4745 (1·2 g.) [Found: C, 74·4; H, 11·2%; *M* (Rast), 254. $C_{14}H_{26}O_2$ requires C, 74·3; H, 11·6%; *M*, 226], and (vi) a residue. The products are thus cyclohexanone (1·4 g.), 1,1'-dimethoxybi(cyclohexyl) (2·4 g.), and polymer (6·5 g.).

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