The oil was then dissolved in 20 ml. of ether and washed with two 20-ml. portions of saturated aqueous sodium bicarbonate solution which were combined and washed with a little ether. The combined ether phase was dried over anhydrous magnesium sulfate, and the ether then was removed under reduced pressure to give 540 mg. of a yellow, mobile oil possessing a camphor-like odor. The oil was distilled (bulb to bulb, air bath), b.p. 85° (0.035 mm.), to afford 353 mg. (46%) of colorless β-keto ester **16**, which gave a deep green color with ferric chloride: $\nu_{\max}^{\mathrm{CHCl_3}}$ 1748, 1721 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 72.05; H, 7.95.

Additional attempts at cyclization may be summarized as follows. Sodium methoxide in refluxing benzene[39] gave only tar along with recovered starting material. Potassium *t*-butoxide in dimethyl sulfoxide (100°) and sodium hydride in dimethyl sulfoxide[40,41] (100°) also produced tar and recovered diester and, in addition, a quantity of the diacid **13**.[31] Potassium *t*-butoxide either in refluxing *t*-butyl alcohol or in a mixture of *t*-butyl alcohol and dimethyl sulfoxide at 100° also failed to effect ring closure. In addition to tar and starting diester, a mixture of resinous half-esters was obtained from which **14** could be reconstituted by methylation.

Decarboxylation of β-Keto Ester 16. 12-Oxo-6,9-ethano-*cis*-$\Delta^{1,2}$-octalin (17).—A solution of 214 mg. of β-keto ester **16**, 2.5 ml. of *p*-dioxane, 1 ml. of water, and 0.5 ml. of concentrated hydrochloric acid was refluxed under an atmosphere of nitrogen for 10 hr. The solution was cooled to room temperature, diluted with 40 ml. of water, and extracted repeatedly (*ca.* eight times) with small quantities of ether totaling 40 ml. The combined ether extract was washed with four small portions of dilute aqueous sodium carbonate solution followed by small portions of water until neutral. The combined carbonate and water washings were then washed with three portions of ether, totaling 20 ml., which were combined with the ether extract and dried over anhydrous magnesium sulfate. The ether was removed on a steam bath under a stream of nitrogen to give 175 mg. of dark oil which was distilled (bulb to bulb, air bath), b.p. 50° (0.015 mm.), to afford 125 mg. (77%) of colorless ketone which possesses a camphor-like odor: $\nu_{\max}^{\mathrm{CHCl_3}}$ 1721 cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 82.16; H, 9.15.

Gas chromatography gave the following retention times: 13.2 min. (20% SF 96, 5 ft × 0.25 in., 173°); 11.1 min. (20% DEGS, 6 ft. × 0.25 in., 218°); 25 min. (20% NPGS, 6 ft × 0.25 in., 205°); 1.95 min. (0.35% silicone grease on glass beads, 6 ft. × 0.25 in., 183°).

A 2,4-dinitrophenylhydrazone was prepared as orange needles, m.p. 153.5–155.0°.

Anal. Calcd. for $C_{18}H_{20}N_4O_4$: C, 60.67; H, 5.66; N, 15.72. Found: C, 60.37; H, 5.73; N, 15.78.

A semicarbazone was prepared, recrystallized twice from chloroform–isohexane solution, and sublimed (140–160° at 0.02 mm.), m.p. 197.0–198.0° dec.

Anal. Calcd. for $C_{13}H_{19}N_3O$: C, 66.92; H, 8.21. Found: C, 66.93; H, 7.90.

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(39) N. N. Gerber, *J. Am. Chem. Soc.*, **82**, 5216 (1960).

(40) J. J. Bloomfield and P. V. Fennessey, *Tetrahedron Letters*, 2273 (1964).

(41) E. J. Corey, R. B. Mitra, and H. Uda, *J. Am. Chem. Soc.*, **86**, 485 (1964).

The α-Bromobenzyl Alkyl Ether as an Intermediate in the Reaction of Benzyl Alkyl Ethers with Free-Radical Reagents

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The yields of benzaldehyde (the major product) from the reaction of a series of benzyl alkyl ethers with N-bromosuccinimide, bromotrichloromethane, *t*-butyl hypobromite, and *t*-butyl peroxide in carbon tetrachloride have been determined. The yields are insensitive to changes in the alkyl group, R, and are not much affected by replacement of the free-radical halogenating agents by a nonhalogenated radical source (*t*-butyl peroxide). These results, while not definitive enough to allow extended comment on the reaction mechanism, are discussed briefly in terms of the nature of the intermediate steps involved in the formation of benzaldehyde from the benzyl ether radical ($C_6H_5\dot{C}HOR$). There is little change in the relative reactivities of the various benzyl alkyl ethers ($C_6H_5CH_2OR$) with changes in the hydrogen abstracting species ($Br\cdot$, $CCl_3\cdot$, t-$BuO\cdot$) or with changes in R. Apparently, the stabilizing influence of the ether oxygen on the benzyl ether radical is not strongly dependent on the structure of the R group.

The major product of the reaction of *p*-benzhydrylbenzyl methyl ether (I) with N-bromosuccinimide has been identified as *p*-benzhydrylbenzaldehyde (II)

$(C_6H_5)_2CHC_6H_4CH_2OCH_3$-*p*
I

$(C_6H_5)_2CHC_6H_4CHO$-*p*
II

(60–65% yield).[1] Included among the products are *p*-methoxymethyltriphenylmethyl bromide (III) (6–7% yield) and an unidentified halogen-containing material. It has been suggested, because of its behavior in solvolytic processes, that this substance may be the α-bromo ether IV. On the basis of these observations, two alternate paths have been proposed by which the radical V, presumed to be a precursor of the various products, may be consumed. This sequence of reactions is illustrated in eq. 1–3. The isolation of the material thought to be *p*-benzhydryl-α-bromobenzyl methyl ether (IV) has raised doubts about the suggestion made by previous investigators[2,3] that, in the reaction of benzyl alkyl ethers with free-radical halogenating agents, the α-bromo ether serves as an unstable intermediate in the formation of the benzaldehyde in the products.

$(C_6H_5)_2CBrC_6H_4CH_2OCH_3$-*p*
III

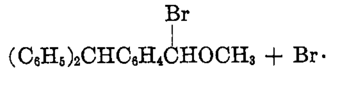
$(C_6H_5)_2CHC_6H_4CHBrOCH_3$-*p*
IV

$(C_6H_5)_2CHC_6H_4\dot{C}HOCH_3$
V

$$I + Br\cdot \longrightarrow (C_6H_5)_2CHC_6H_4\dot{C}HOCH_3 + HBr \qquad (1)$$

$$(C_6H_5)_2CHC_6H_4\dot{C}HOCH_3 \longrightarrow (C_6H_5)_2CHC_6H_4CHO + CH_3\cdot \qquad (2)$$

$$(C_6H_5)_2CHC_6H_4\dot{C}HOCH_3 + Br_2 \longrightarrow$$



$$(C_6H_5)_2CHC_6H_4\overset{\overset{\textstyle Br}{|}}{C}HOCH_3 + Br\cdot \qquad (3)$$

The present investigation was initiated to explore this matter in more detail through study of the relationship between alkyl group structure and the relative yields of benzaldehyde in the reaction of a series

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[1] R. E. Lovins, L. J. Andrews, and R. M. Keefer, *J. Org. Chem.*, **28**, 2847 (1963).

[2] R. L. Huang and K. H. Lee, *Tetrahedron Letters*, 711 (1963).

[3] R. Filler, *Chem. Rev.*, **63**, 21 (1963).

TABLE I

COMPETITIVE RATES OF REACTION OF BENZYL ALKYL ETHERS WITH N-BROMOSUCCINIMIDE, BROMOTRICHLOROMETHANE, AND *t*-BUTYL HYPOBROMITE[a]

Compound A[b]	Compound B[b]	A_0, mmoles	B_0, mmoles	A, mmoles	B, mmoles	Initial free-radical reagent, mmoles	k_A/k_B
		N-Bromosuccinimide					
$C_6H_5CH_2OCH_3$	$C_6H_5CH(CH_3)_2$	30.6	30.6	16.0	25.0	22.0	3.2
		48.4	57.7	24.0	47.7	39.0	3.6
$C_6H_5CH_2OC_2H_5$	$C_6H_5CH(CH_3)_2$	41.6	71.6	17.4	57.5	35.2	4.0[c]
		41.6	53.5	15.8	41.2	35.2	3.7[c]
$C_6H_5CH_2OCH(CH_3)_2$	$C_6H_5CH(CH_3)_2$	54.2	71.3	21.8	59.7	40.4	5.0[c]
		48.8	62.9	14.8	51.2	45.8	5.6
$C_6H_5CH_2OC(CH_3)_3$	$C_6H_5CH(CH_3)_2$	55.3	71.6	24.1	62.6	45.4	6.0
		46.3	62.9	20.5	53.9	39.6	5.3
$C_6H_5CH_2OCH_2C_6H_5$	$C_6H_5CH(CH_3)_2$	48.6	78.9	20.3	66.8	40.6	5.3
		50.9	67.7	21.5	57.8	41.3	4.4
		Bromotrichloromethane					
$C_6H_5CH_2OC_2H_5$	$C_6H_5CH_2OCH_3$	58.4	58.4	36.0	38.7	31.1	1.2[c]
		58.1	67.0	38.3	50.0	30.7	1.4[c]
$C_6H_5CH_2OCH(CH_3)_2$	$C_6H_5CH_2OCH_3$	60.3	65.4	46.8	54.6	33.9	1.4
		61.6	53.5	54.2	47.7	31.4	1.2
$C_6H_5CH_2OC(CH_3)_3$	$C_6H_5CH_2OCH_3$	40.5	58.1	25.9	44.9	42.1	1.7
		43.2	54.1	30.6	46.1	39.5	2.0
$C_6H_5CH_2OCH_2C_6H_5$	$C_6H_5CH_2OCH_3$	53.8	66.8	27.9	50.6	34.1	2.4[c]
		56.8	59.3	29.1	46.5	33.6	2.7[c]
		t-Butyl Hypobromite					
$C_6H_5CH_2OC_2H_5$	$C_6H_5CH_2OCH_3$	22.6	23.3	16.3	17.5		1.1
		22.0	23.6	15.3	16.5		1.0
$C_6H_5CH_2OCH(CH_3)_2$	$C_6H_5CH_2OCH_3$	20.0	21.9	13.7	15.7		1.1
		19.4	22.7	13.1	17.5		1.5
$C_6H_5CH_2OC(CH_3)_3$	$C_6H_5CH_2OCH_3$	24.6	23.2	16.3	17.2		1.4
		22.8	23.6	14.0	17.4		1.6
$C_6H_5CH_2OCH_2C_6H_5$	$C_6H_5CH_2OCH_3$	24.3	22.4	19.2	20.2		2.3
		23.4	23.0	14.9	17.8		1.8

[a] At 77° in CCl_4. The initial concentration of *t*-butyl hypobromite was 14 ± 1 mmoles in each case. An exact determination of the *t*-butyl hypobromite concentration by weighing was not feasible because of its volatility and extreme reactivity with the benzyl ethers. [b] Total volume of A, B, and carbon tetrachloride was 50 ml. at room temperature. [c] In these determinations, the total amount of hydrocarbon consumed, $(A_0 + B_0) - (A + B)$, was in excess of the amount of halogenating agent initially present.

of benzyl alkyl ethers with *t*-butyl peroxide, *t*-butyl hypobromite, bromotrichloromethane, and N-bromosuccinimide.

Experimental Section

Materials.—Commercial samples of benzyl methyl ether, benzyl ethyl ether, dibenzyl ether, cumene, bromotrichloromethane, toluene (Eastman Organic Chemicals), benzaldehyde (Aldrich Chemical Co. Inc.), *t*-butyl peroxide (K and K Laboratories, Inc.), and N-bromosuccinimide (Arapahoe Chemical, Inc.) were used without further purification. Benzyl isopropyl ether, b.p. 53–54° (2 mm.),[4] and benzyl *t*-butyl ether, b.p. 55–56° (2 mm.),[4] were prepared from α-chlorotoluene (Eastman Organic Chemicals) and sodium isopropoxide and potassium *t*-butoxide, respectively, by the procedure described by Huang and Si-Hoe.[4] *t*-Butyl hypobromite, b.p. 40–42° (75 mm.),[5] was prepared in 30% yield by the method outlined by Walling and Padwa.[5] α,α'-Dimethoxydibenzyl, m.p. 82–85°, was prepared from the reaction of benzyl methyl ether and *t*-butyl peroxide without the addition of solvent, in the manner described by Huang and Si-Hoe.[4] Eastman Organic Chemicals Spectro Grade carbon tetrachloride was used as the reaction medium.

Relative Rates of Reaction of the Benzyl Alkyl Ethers with N-Bromosuccinimide.—For each determination a carbon tetrachloride solution of known volume which contained weighed quantities of the benzyl alkyl ether and the reference hydrocarbon (cumene) was prepared. The solution was treated with a limited quantity of N-bromosuccinimide. The mixture was irradiated with a 500-w. projection lamp under a nitrogen atmosphere for 10–15 min. The heat from the lamp was sufficient to cause the carbon tetrachloride solution to remain at reflux temperatures during the reaction. Without separating the solid succinimide formed in the reaction, the liquid portion of the product mixture was analyzed for unreacted ether and reference hydrocarbon by vapor phase chromatography. The chromatographic column was packed with Chromosorb W (45–60 mesh) impregnated with SE-30 silicone gum rubber and was operated at temperatures ranging from 130 to 210°. Table I contains a list of typical k_A/k_B values [the ratio of rate constants for reaction of benzyl alkyl ether (A) and the reference material (B) with N-bromosuccinimide] for the various compounds investigated. The ratios were calculated from the initial ($[A_0]$ and $[B_0]$) and final ($[A]$ and $[B]$) concentrations of the benzyl alkyl ether (A) and the reference compound (B) using the following equation. Values of *r*

$$k_A/k_B = \frac{\log([A_0]/[A])}{\log([B_0]/[B])}$$

reported later in Table III are k_A/k_B values for the condition that B is benzyl methyl ether; that is, for benzyl methyl ether $r = 1$. The values of *r* were calculated from the k_A/k_B and $k_{\text{benzyl methyl ether}}/k_B$ values which are recorded in Table I. Each *r* value is an average based on the results of at least two or more separate experiments at different reactant concentrations. In all but three cases the total amount of hydrocarbon and ether consumed was in good agreement with the amount of N-bromosuccinimide initially present in the reaction mixture. In three determinations the amount of hydrocarbon and ether consumed was about 10% in excess of the amount of N-bromosuccinimide used. The source of this error has not been determined.

Relative Rates of Reaction of the Benzyl Alkyl Ethers with

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[4] R. L. Huang and S. S. Si-Hoe, "Vistas in Free Radical Chemistry," W. A. Waters, Ed., Pergamon Press Inc., New York, N. Y., 1959, p. 245.

[5] C. Walling and A. Padwa, *J. Org. Chem* ., **27**, 2976 (1962).

Bromotrichloromethane.—Procedures like those outlined for reaction with N-bromosuccinimide were used to measure the relative rates of reaction with bromotrichloromethane. Benzyl methyl ether was substituted for cumene as the reference hydrocarbon in these experiments, and the irradiation time was extended to 5 hr. The values of k_A/k_B for the compounds studied again are reported in Table I. The total amount of ether and reference hydrocarbon consumed was in four cases in excess of the amount of bromotrichloromethane initially present in the mixture. The source of these errors is as yet not known.

Relative Rates of Reaction of the Benzyl Alkyl Ethers with *t*-Butyl Hypobromite.—A procedure similar to that outlined for the reactions with bromotrichloromethane was used to determine the relative rates of reaction of the benzyl alkyl ethers with *t*-butyl hypobromite (see Table I). In these experiments the irradiation times were reduced to 2–3 min.

Quantitative Determination of Benzaldehyde Production in the Reaction of Benzyl Alkyl Ethers with N-Bromosuccinimide, Bromotrichloromethane, *t*-Butyl Hypobromite, and *t*-Butyl Peroxide. A. N-Bromosuccinimide.—A carbon tetrachloride solution (50-ml. initial volume) containing a weighed amount of the benzyl alkyl ether was treated with a weighed amount of N-bromosuccinimide (0.5–0.7 mole of NBS/mole of ether). After irradiation of the mixture in a nitrogen atmosphere for 10 min. with a 500-w. projection lamp, the cooled reaction mixture was analyzed for unreacted ether and also for benzaldehyde produced by vapor phase chromatography using the equipment already described. The results of these experiments, along with those of studies described in sections B–D below, are listed in Table II in the Results section and are expressed as moles of benzaldehyde formed per mole of benzyl alkyl ether consumed. In order to determine whether benzaldehyde was being consumed by reaction with N-bromosuccinimide, a solution initially containing 66 mmoles of benzyl methyl ether and 42 mmoles of benzaldehyde (50 ml. initial volume) was allowed to react with 36 mmoles of N-bromosuccinimide. The product mixture from the reaction contained 23 mmoles of benzyl methyl ether and 65 moles of benzaldehyde. The amount of benzaldehyde produced in excess of the amount initially present (23 mmoles) agrees (within experimental error) with the yield of aldehyde obtained in a control reaction in which the carbonyl compound was not initially present.

B. Bromotrichloromethane.—The method outlined above (section A) was used with slight modification in studying the reactions with bromotrichloromethane. Again an initial ratio of 0.5–0.7 moles of bromotrichloromethane/mole of ether was employed, but the irradiation time was extended to 5 hr. The product mixture from the reaction of a carbon tetrachloride solution initially containing 64 mmoles of benzyl methyl ether, 51 mmoles of benzaldehyde, and 40 mmoles of bromotrichloromethane (50 ml. initial volume) contained 48 mmoles of ether and 66 mmoles of benzaldehyde. The amount of benzaldehyde produced in excess of the quantity initially present in the reaction mixture (15 mmoles) again agrees (within experimental error) with the yield of aldehyde obtained from reactions in which no aldehyde is present initially.

C. *t*-Butyl Hypobromite.—Carbon tetrachloride solutions of of benzyl alkyl ether were treated with 13–15 mmoles of *t*-butyl hypobromite using procedures similar to those described above. Irradiation was limited to 2–3 min. Consumption of benzaldehyde by *t*-butyl hypobromite was observed in a reaction in which the initial mixture contained 21 mmoles of benzyl methyl ether, 15 mmoles of benzaldehyde, and approximately 10 mmoles of *t*-butyl hypobromite (50 ml. initial volume). The product mixture obtained contained 14 mmoles of unreacted ether and 14 mmoles of benzaldehyde. The observed loss of benzaldehyde is reflected in the low values obtained (see Table II) when no benzaldehyde was initially present.

D. *t*-Butyl Peroxide.—The yields of benzaldehyde from the reaction of benzyl alkyl ethers with *t*-butyl peroxide were determined by the general procedure outlined in section A above. The irradiation time was 5 hr. Even when the initial ratio of *t*-butyl peroxide to ether was relatively low (0.3 or less), it was found that the aldehyde produced in the reaction was partially consumed by the *t*-butyl peroxide. For example, the product mixture from reaction of a carbon tetrachloride solution initially containing 65 mmoles of benzyl methyl ether, 42 mmoles of benzaldehyde, and 22 mmoles of *t*-butyl peroxide was found to contain 40 mmoles of unreacted ether and 34 mmoles of benzaldehyde (8 mmoles less than initially present). When 39 mmoles of benzyl methyl ether underwent reaction with 33 mmoles of *t*-butyl peroxide in carbon tetrachloride, no aldehyde was obtained from the mixture. However, in the reaction of 72 mmoles of benzyl methyl ether and 22 mmoles of *t*-butyl peroxide in carbon tetrachloride, 10 mmoles of benzaldehyde was formed and 22 mmoles of ether was consumed. When 65 mmoles of benzyl methyl ether was treated with 12 mmoles of *t*-butyl peroxide in carbon tetrachloride, 13 mmoles of benzaldehyde was produced while 20 mmoles of ether was consumed. To minimize consumption of aldehyde by the peroxide it was decided to limit the ratio of *t*-butyl peroxide to ether to values no higher than 0.1 to 0.2 in experiments conducted to determine aldehyde yield.

The Formation of α,α'-Dimethoxydibenzyl in the Reaction of Benzyl Methyl Ether with *t*-Butyl Peroxide and N-Bromosuccinimide.—A carbon tetrachloride solution initially containing 39 mmoles of benzyl methyl ether and 33 mmoles of *t*-butyl peroxide (50 ml. initial volume) was irradiated for 5 hr. and then was distilled under reduced pressure to remove carbon tetrachloride and unreacted ether (12 mmoles). The residue from the reaction (approximately 0.5 g.) was analyzed for α,α'-dimethoxydibenzyl by vapor phase chromatography using a synthetic sample of the dimer for reference purposes. The analysis revealed that no detectable quantity of the α,α'-dimethoxydibenzyl was formed in the reaction. When the product mixture from the reaction of 74 mmoles of benzyl methyl ether with 45 mmoles of N-bromosuccinimide in carbon tetrachloride (50 ml. initially) was analyzed as described above, it was again observed that no detectable amount of α,α'-dimethoxydibenzyl had been formed in the reaction.

The Reaction of α,α'-Dimethoxydibenzyl with *t*-Butyl Peroxide.—A solution initially containing 3.5 mmoles of α,α'-dimethoxydibenzyl and 3.4 mmoles of *t*-butyl peroxide in carbon tetrachloride (50 ml. initially) was irradiated under a nitrogen atmosphere for 5 hr. and then analyzed by vapor phase chromatography. The product mixture contained 2.4 mmoles of unreacted α,α'-dimethoxydibenzyl. While the products of the reaction were not identified, it was observed from the chromatographic analysis that benzaldehyde was not present in the product mixture. This suggests that any dimer formed in the reactions of benzyl alkyl ethers with *t*-butyl peroxide does not react further to contribute to the over-all yield of benzaldehyde formed in the reaction.

The Reaction of Toluene with *t*-Butyl Peroxide in Carbon Tetrachloride.—A solution initially containing 56 mmoles of toluene and 23.4 mmoles of *t*-butyl peroxide in carbon tetrachloride (50 ml. initial volume) was irradiated for 5 hr. with a 500-w. projection lamp and then was analyzed by vapor phase chromatography by the methods described. The analysis showed that, while 2 mmoles of toluene had been consumed, no benzyl chloride was generated in the reaction. Walling and Padwa[5] have previously reported that the product of the irradiation of toluene with *t*-butyl hypochlorite in bromotrichloromethane for 3–4 hr. contained 97% benzyl chloride and 3% benzyl bromide. Zavitsas[6] has shown that the solvent is not directly involved in the reaction of toluene with *t*-butyl hypochlorite in carbon tetrachloride. These several observations are cited as evidence that the reaction of *t*-butoxy radicals with carbon tetrachloride to form *t*-butyl hypochlorite (which then attacks the ether) is not of primary importance in the reaction of *t*-butyl peroxide with a benzyl alkyl ether, since it has been shown that benzyl methyl ether is at least 30 times more reactive than toluene.[1]

Results

In the course of a study of the reaction of benzyl alkyl and benzyl aryl ethers with *t*-butoxy radicals, Huang and Si-Hoe[4] demonstrated that the substituted benzyl radicals VI, assumed to be produced in the first

$$C_6H_5\dot{C}HOR$$

VI

step (eq. 4), may cleave to produce aldehyde (eq. 5) and also may couple (eq. 6). The yield of aldehyde as opposed to dimer increases as the stability of the alkyl

$$C_6H_5CH_2OR + (CH_3)_3CO\cdot \longrightarrow C_6H_5CHOR + (CH_3)_3COH \quad (4)$$

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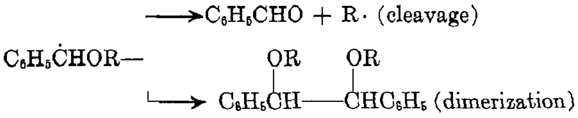
[6] A. A. Zavitsas, *J. Org. Chem.*, **29**, 3086 (1964).

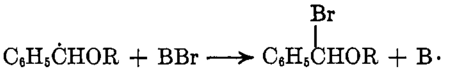


$$C_6H_5\dot{C}HOR\text{—}\begin{cases}\longrightarrow C_6H_5CHO + R\cdot \text{ (cleavage)} & (5)\\ \longrightarrow C_6H_5\overset{OR}{\overset{|}{C}}H\text{—}\overset{OR}{\overset{|}{C}}HC_6H_5 \text{ (dimerization)} & (6)\end{cases}$$

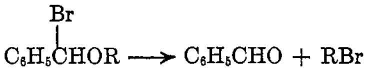
radical (R·) resulting from the cleavage reaction increases [$\cdot CH_3 < \cdot C_2H_5 < \cdot CH(CH_3)_2 < \cdot C(CH_3)_3 < \cdot CH_2C_6H_5$]. Benzyl methyl ether was found to react predominantly to form α,α′-dimethoxydibenzyl (eq. 6) and only traces of benzaldehyde (eq. 5). The radical derived from dibenzyl ether is reported to cleave (eq. 5) to give benzaldehyde in good yield. Substantial amounts both of cleavage and dimerization products are reported to form from the other ethers studied (where R = ethyl, isopropyl, and *t*-butyl). It should be emphasized that in every case Huang and Si-Hoe carried out these reactions of *t*-butyl peroxide with the benzyl alkyl ether without the use of a third substance as solvent.

As noted previously, it has been suggested[2] that, when a halogenating agent such as N-bromosuccinimide is used instead of *t*-butyl peroxide, the course of the reaction of the benzyl alkyl ethers is altered. Supposedly, the radical VI formed initially reacts with the halogenating agent (BBr) to form the α-bromo ether (eq. 7–9) instead of cleaving or dimerizing as in the

$$C_6H_5CH_2OR + B\cdot \longrightarrow C_6H_5\dot{C}HOR + BH \qquad (7)$$



$$C_6H_5\dot{C}HOR + BBr \longrightarrow C_6H_5\overset{Br}{\overset{|}{C}}HOR + B\cdot \qquad (8)$$



$$C_6H_5\overset{Br}{\overset{|}{C}}HOR \longrightarrow C_6H_5CHO + RBr \qquad (9)$$

reaction with *t*-butyl peroxide (eq. 7–9 depict the reactions under consideration).[7] This suggestion stems from the observation that the major product of reaction of benzyl methyl ether with N-bromosuccinimide and with bromotrichloromethane is benzaldehyde rather than α,α′-dimethoxydibenzyl, the main product of the *t*-butyl peroxide reaction.

This point has now been checked. The yields of benzaldehyde formed in the reactions of a series of benzyl alkyl ethers with various radical sources (N-bromosuccinimide, bromotrichloromethane, *t*-butyl hypobromite, and *t*-butyl peroxide) in carbon tetrachloride as determined in the present investigation are compared in Table II. The yields of the aldehyde from the reactions of benzyl methyl ether with N-bromosuccinimide and bromotrichloromethane agree with those reported earlier (NBS, 63%, and $BrCCl_3$, 75%).[2] The composition of the products formed in the reactions of the various benzyl alkyl ethers with *t*-butyl peroxide as determined in this investigation (Table II) are, however, considerably different from those reported by Huang and Si-Hoe.[4] In the present study, the dominant product from the reaction of all the benzyl alkyl ethers with *t*-butyl peroxide as well as with the various radical-type halogenating agents is benzaldehyde, and no significant amount of dimer, $(C_6H_5CHOR)_2$, has been observed to form (see Experimental Section). In addition, the yield of benzaldehyde is relatively insensitive to the nature of the alkyl group both in the reaction with *t*-butyl peroxide and with the free-radical halogenating agents. The differences in the products of reaction of the benzyl alkyl ethers with *t*-butyl peroxide as obtained in the present work and as reported by Huang and Si-Hoe[4] are considered to reflect the influence of an inert solvent. When, as in this investigation, a solvent is used, the concentration of substituted benzyl radicals VI in the reaction mixtures is always sufficiently low so that the number of effective collisions to form dimer become extremely small relative to the rate of decomposition by cleavage to generate benzaldehyde. In the absence of solvent it is possible that the rate of diffusion of pairs of radicals VI, produced in the reaction of the ethers with *t*-butyl peroxide, away from each other is low enough so that the rate of dimerization is at least competitive with that of the cleavage process.[8]

Table II

Yields of Benzaldehyde[a] from the Reaction of Benzyl Alkyl Ethers ($C_6H_5CH_2OR$) with N-Bromosuccinimide, Bromotrichloromethane, *t*-Butyl Hypobromite, and *t*-Butyl Peroxide[b]

	—Moles of benzaldehyde produced/mole of ether consumed—			
R	NBS[c]	$BrCCl_3$	*t*-BuOBr[d]	(*t*-BuO)$_2$[d]
CH_3	0.66 ± 0.03[e]	0.86 ± 0.03[e]	0.58 ± 0.05[e]	0.73 ± 0.07[e]
C_2H_5	0.60 ± 0.04	0.71 ± 0.02	0.57 ± 0.02	0.76 ± 0.02
$CH(CH_3)_2$	0.88 ± 0.04	0.72 ± 0.02	0.54 ± 0.05	0.75 ± 0.07
$C(CH_3)_3$	0.70 ± 0.04	0.66 ± 0.03	0.53 ± 0.01	0.72 ± 0.09
$CH_2C_6H_5$	0.97 ± 0.04	0.80 ± 0.06	1.3 ± 0.3[f]	0.74 ± 0.03

[a] It has been demonstrated (see Experimental Section) that benzaldehyde is not produced from the reaction of α,α′-dimethoxydibenzyl with *t*-butyl peroxide. In addition, the possibility that the solvent (carbon tetrachloride) may react with *t*-butyl peroxide to form *t*-butyl hypochlorite, which might then react with the benzyl ether to produce benzaldehyde, has been investigated (see Experimental Section) and discounted. [b] In CCl_4 at 77°. [c] N-Bromosuccinimide. [d] Because of consumption of benzaldehyde by reaction with *t*-BuOBr and (*t*-BuO)$_2$, these ratios are to be considered as minimum values (see Experimental Section). [e] The uncertainty expressed is the average deviation from the mean of two or more determinations. [f] No satisfactory explanation has been found for high yield of aldehyde in the reaction of dibenzyl ether with *t*-butyl hypobromite.

As is mentioned in the introduction, the previously observed difference in the major product of reaction of benzyl methyl ether with *t*-butyl peroxide (α,α′-dimethoxydibenzyl) and with N-bromosuccinimide or bromotrichloromethane (benzaldehyde) has been explained on the assumption that an α-bromo ether is produced as an unstable intermediate in the latter reaction. The results of the present investigation are not sufficiently definitive to warrant extended comment on the nature of the intermediates in the formation of benzaldehyde from the reaction of benzyl ethers with free-radical halogenating agents. They do, however, indicate that the formation of benzaldehyde by the cleavage of the substituted benzyl radical VI (eq. 5), as previously suggested,[1] cannot be eliminated as a possible alternative to the process in which the bromether is an intermediate.

The relative rates of reaction of the several benzyl alkyl ethers under investigation are insensitive to changes in structure of the radical brominating agent (see Table III). That is, these relative rates are not very dependent on the nature of the hydrogen-abstracting species. In addition, the reactivities of the

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(7) See G. A. Russell, C. DeBoer, and K. M. Desmond, *J. Am. Chem. Soc.*, **85**, 365 (1963), for a detailed mechanism for radical halogenation by N-bromosuccinimide.

(8) A referee has suggested that in the absence of solvent, regenerative chain transfer ($C_6H_5\dot{C}HOR + C_6H_5CH_2OR \rightarrow C_6H_5CH_2OR + C_6H_5\dot{C}HOR$) may occur, with the consequent preservation of C_6H_5CHOR until coupling takes place.

TABLE III

RELATIVE RATES OF REACTION OF BENZYL ALKYL ETHERS WITH N-BROMOSUCCINIMIDE, BROMOTRICHLOROMETHANE, AND *t*-BUTYL HYPOBROMITE[a]

Ether	r^b NBS	BrCCl$_3$	*t*-BuOBr
$C_6H_5CH_2OCH_3$	1.00	1.00	1.00
$C_6H_5CH_2OC_2H_5$	1.1 ± 0.1^c	1.3 ± 0.1^c	1.1 ± 0.1^c
$C_6H_5CH_2OCH(CH_3)_2$	1.5 ± 0.1	1.3 ± 0.1	1.3 ± 0.2
$C_6H_5CH_2OC(CH_3)_3$	1.7 ± 0.1	1.8 ± 0.2	1.5 ± 0.1
$C_6H_5CH_2OCH_2C_6H_5$	0.8 ± 0.1	1.3 ± 0.1	1.0 ± 0.1

[a] These reactions, initiated by irradiation with a 500-w. tungsten lamp, were carried out in refluxing (77°) carbon tetrachloride (see Experimental Section). [b] *r* is the relative reactivity per benzylic hydrogen atom. [c] The uncertainties expressed are average deviations from the mean of two or more determinations.

various ethers ($C_6H_5CH_2OR$) increase only slightly as R changes in the sequence CH_3, C_2H_5, $CH(CH_3)_2$, $C(CH_3)_3$, $CH_2C_6H_5$. In other words, the favorable influence of the ether function on the benzyl hydrogen abstraction process[1] is not much affected by alterations in the structure of the alkyl group. It is interesting to recall that the relative reactivities observed for the reactions of $C_6H_5CH_3$, $C_6H_5CH_2CH_3$, $C_6H_5CH(CH_3)_2$, $C_6H_5CH_2C_6H_5$, and $(C_6H_5)_3CH$ with N-bromosuccinimide are, in contrast to those of the benzyl alkyl ethers, substantially different from those observed in reactions with bromotrichloromethane. That is, the reactivity ratios of these hydrocarbons are appreciably altered when Br· is replaced by the more selective ·CCl_3 radical as the hydrogen-abstracting species.[7]

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Steroids. CCLXXXII.[1] Some Reactions of 5β,19-Cyclo 6-Oxygenated Steroids in Acid Media

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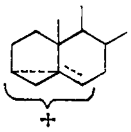
Treatment of 3β-hydroxy-5β,19-cycloandrostane-6,17-dione (Ic) and 3β,6α-dihydroxy-5β,19-cycloandrostan-17-one (Id) with hydrochloric acid afforded the corresponding 19-chloro derivatives IIa, b, and IV, respectively. With hydrofluoric and sulfuric acids, 3β,6α-dihydroxy-5β,19-cycloandrostan-17-one (Id) and the acetate Ia rearranged to afford a multiplicity of products, including B-homo-19-nor steroids. Product formation is rationalized on the basis of classical carbonium ion intermediates.

The solvolysis of the *p*-toluenesulfonates of 3β-hydroxy-Δ^5 steroids in buffered medium frequently yields 3α,5α-cyclo derivatives,[4] which in turn may be rearranged to the parent Δ^5-3β alcohols in the presence of dilute mineral acid.[5] These well-known transformations have been studied extensively, and their mechanistic aspects have been explained on the basis of the nonclassical homoallylic cation.[4]



In recent communications from our laboratory[6] and from several others[7,8] it was reported that the closely related 19-tosyloxy-Δ^5 steroids underwent solvolytic displacement of tosylate with participation of the olefinic double bond to yield 5β,19-cyclo-6α-hydroxy steroids. Tadanier and Cole[8] also made the interesting observation that the 5β,19-cyclo-6α-hydroxy system was not converted to the parent 19-hydroxy-Δ^5 steroid in the presence of aqueous sulfuric acid. Instead, rearrangement to a B-homo-$\Delta^{5(10)}$-estrane derivative took place.

We have also investigated in detail the behavior of several 5β,19-cyclo 6-oxygenated steroids in hydrochloric, hydrofluoric, and sulfuric acid mixtures. It was found that both 19-substituted and more complex rearrangement products were formed and that the outcome of the rearrangement was dependent upon the acid employed. An account of our work is reported in this paper.

At the same time as these investigations were in progress, other Syntex researchers examined the action of diethyl-(2-chloro-1,1,2-trifluoroethyl)amine on 19-hydroxy-Δ^5 steroids.[9] Several products resulted, including two reported here. The same carbonium ions are considered to be generated as in our work, with the observed variance in product mix being a consequence of the different mode of collapse of the intermediate charged species.

Three cyclopropyl steroids were utilized in the present investigation: 3β-hydroxy-5β,19-cycloandrostane-6,17-dione (Ic), 3β,6α-dihydroxy-5β,19-cycloandrostan-17-one (Id), and the corresponding acetate Ia which has been described previously.[6] Compounds Ic and Id were obtained from the acetate Ia by unexceptional methods, as outlined in the Experimental Section.

Treatment of 3β-hydroxy-5β,19-cycloandrostane-6,-17-dione (Ic) with hydrochloric acid in tetrahydrofuran

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(1) Steroids. CCLXXXI: A. D. Cross and L. J. Durham, *J. Org. Chem.*, **30**, 3200 (1965).

(2) This work was reported earlier in theses submitted by A. C. B. and M. G. T. M. to the Universidad de Vera Cruz (1964) and the Universidad Nacional Autonoma de Mexico (1965), respectively.

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(4) For a recent summary of the *i*-steroid rearrangement, see N. L. Wendler in "Molecular Rearrangements," part 2, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p. 1075.

(5) See L. F. Fieser and M. Fieser in "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, pp. 315, 316.

(6) O. Halpern, P. Crabbé, A. D. Cross, I. Delfin, L. Cervantes, and A. Bowers, *Steroids*, **4**, 1 (1964).

(7) M. Akhtar and D. H. R. Barton, *J. Am. Chem. Soc.*, **86**, 1528 (1964).

(8) J. Tadanier and W. Cole, *Tetrahedron Letters*, 1345 (1964).

(9) See L. H. Knox, *et al.*, *J. Org. Chem.*, **30**, 4160 (1965).