

1150. *The Reaction of Benzyl Methyl Ether and Benzaldehyde Dimethyl Acetal with Di-*t*-butyl Peroxide, N-Bromosuccinimide, and Bromotrichloromethane.*¹

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The reaction of benzyl methyl ether with *N*-bromosuccinimide or bromotrichloromethane gives, *via* the radical $\text{Ph}\cdot\dot{\text{C}}\text{H}\cdot\text{OMe}$, α -methoxybenzyl bromide which, on heating, breaks down into benzaldehyde and methyl bromide.

The action of *t*-butoxy-radicals on benzaldehyde dimethyl acetal involves a chain-reaction in which the radical $\text{Ph}\cdot\dot{\text{C}}(\text{OMe})_2$ is first generated, and then breaks down into methyl benzoate and free methyl, the latter being the chain-carrier. When liberated in the presence of *N*-bromosuccinimide or bromotrichloromethane, however, the radical $\text{Ph}\cdot\dot{\text{C}}(\text{OMe})_2$ abstracts a bromine atom to give the corresponding bromide. This then decomposes into methyl benzoate and methyl bromide.

THE abstraction of benzylic α -hydrogen atoms from benzyl methyl ether by the *t*-butoxy-radical has been shown² to generate the α -methoxybenzyl radical (I), which in solution persists until dimerisation. We now report the same reaction with benzaldehyde dimethyl acetal. The reaction of both the ether and the acetal with *N*-bromosuccinimide and with bromotrichloromethane has also been investigated.

Benzyl Methyl Ether.—The reaction of benzyl methyl ether with *N*-bromosuccinimide gives α -methoxybenzyl bromide(II), isolated in the form of its breakdown products, benzaldehyde and methyl bromide. The bromo-ether (II), as well as the chloro-derivative, have been prepared³ from benzaldehyde dimethyl acetal, and found to decompose readily on heating, into benzaldehyde and the corresponding methyl halides. The half-life at 120° of the chloro-ether was reported to be 34 minutes, and for analogues bearing the *para*-substituents NO₂, Cl, H, Me, and MeO, the ratio of half-lives was estimated as 10·8:2·8:1:0·41:0·03. The bromo-ether (II) is reportedly even more labile and its isolation was therefore not attempted in this work.

To establish the fact that the bromo-ether was the intermediate, an attempt was made to prepare the bromo-derivative from *m*-chlorobenzyl methyl ether since, judging from the relative stability of the chloro-ethers mentioned above, this would be expected to be considerably more stable than the unsubstituted ether. This expectation proved correct. Thus, treatment of the bromination product with sodium methoxide gave the dimethyl acetal of *m*-chlorobenzaldehyde, indicating the presence of the bromo-ether.³ Moreover, the same product showed an infrared spectrum, presumably that of the bromo-ether, completely different from that of the starting material and indicative of only a low concentration of *m*-chlorobenzaldehyde. After hydrolysis however, the presumed absorption due to the bromo-intermediate completely disappeared, with greatly increased absorption due to the aldehyde. By this method, it has also been shown that, after 10 minutes at 80°, decomposition of the bromo-ether did not exceed 16%. Previous work⁴ afforded no evidence for the formation of the bromo-ethers or of alkyl halides.

Results from the reaction of benzyl methyl ether with *N*-bromosuccinimide under a variety of conditions are summarised in Table 1. Estimation of the yield of α -methoxybenzyl bromide was made by gravimetric determination of the 2,4-dinitrophenylhydrazone of

¹ R. L. Huang and K. H. Lee, *Tetrahedron Letters*, 1963, 711.

² R. L. Huang and S. S. Si-Hoe, *Proc. Chem. Soc.*, 1957, 354; "Vistas in Free Radical Chemistry," ed. W. A. Waters, Pergamon Press, London, 1959, p. 242.

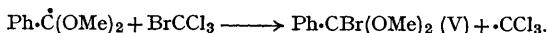
³ (a) F. Straus and H. Heinze, *Annalen*, 1932, 493, 191; (b) F. Straus and H. J. Weber, *ibid.*, 1933, 498, 101.

⁴ (a) D. G. Markees, *J. Org. Chem.*, 1958, 23, 1490; (b) L. L. Braun and J. H. Looker, *ibid.*, 1961, 26, 574; (c) R. E. Lovins, L. J. Andrews, and R. M. Keefer, *ibid.*, 1963, 28, 2874.

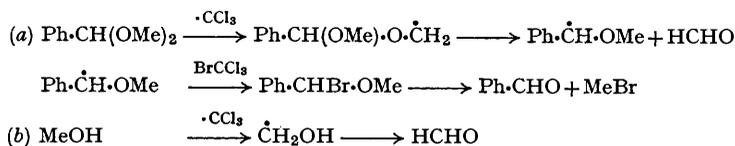
The absence of chain characteristics, one mole of ester being obtained from one of the bromoimide (in contrast to the reaction with di-*t*-butyl peroxide), supports the above mechanism.

Among related studies on acetals may be mentioned the transformation of benzaldehyde diethyl acetal¹² and *p*-nitrobenzaldehyde dimethyl acetal^{4a} into the corresponding esters, and of the cyclic acetal ethylene benzal,¹³ and benzaldehyde *cis*-1,2-cyclohexanol acetal¹⁴ into 2-bromoethyl benzoate and *trans*-2-bromocyclohexyl benzoate, respectively.

The reaction of benzaldehyde dimethyl acetal with bromotrichloromethane yielded methyl benzoate, methyl bromide, and chloroform (see Table 2), no doubt involving the same intermediate bromo-compound (V), formed as indicated:



Isolation of traces of dimethoxymethane indicated that formaldehyde had been formed during the reaction, probably *via* (a) and/or (b) :



Acetal exchange with the aromatic acetal present would then give dimethoxymethane. Such an exchange has indeed been shown to occur when paraformaldehyde and the acetal were mixed with a trace of hydrogen bromide and maintained at 70°. In addition to dimethoxymethane were isolated free benzaldehyde (6–7%) and methanol (traces). The former could have arisen from the acetal either through (a) above, or by acetal interchange with formaldehyde, or by inadvertent hydrolysis. The last reaction would also generate methanol which, when subjected to the same reaction conditions as the acetal, has indeed been found to yield some dimethoxymethane.

EXPERIMENTAL

All reactions, distillations, and filtrations were carried out under dry nitrogen.

Materials.—Carbon tetrachloride (Merck, C.P. grade) was shaken 3 times with concentrated sulphuric acid and then successively with water, 10% aqueous sodium hydroxide, and water, dried over potassium hydroxide pellets, and fractionated through a 50 cm. Vigreux column.

Bromotrichloromethane (Eastman) was washed 3 times with 2*N*-sodium hydroxide, 3 times with water, dried (CaCl₂), and fractionated through a 30 cm. Vigreux column, fractions having n_D^{25} 1.5032 being stored over anhydrous potassium carbonate (lit.,¹⁵ n_D^{25} 1.5030). Di-*t*-butyl peroxide (Light) was redistilled under reduced pressure. Methyl fluorene-9-carboxylate (Eastman white label) was used without further purification.

Benzyl Methyl Ether.—The ether was prepared in 65% yield from benzyl chloride and sodium methoxide in methanol (method A), b. p. 85–86°/35 mm., n_D^{25} 1.4995, and in 80% yield from the halide and potassium hydroxide in methanol (method B), b. p. 91–91.5°/45 mm., n_D^{25} 1.4994. It was freed of traces of benzaldehyde dimethyl acetal and the free aldehyde by shaking with 2*N*-hydrochloric acid saturated with 2,4-dinitrophenylhydrazine, washed with 2*N*-hydrochloric acid, water, dried, and redistilled through a 25 cm. Vigreux column, b. p. 91.0–91.5°/45 mm., n_D^{25} 1.4990 (lit.,² b. p. 113°/100 mm., n_D^{22} 1.5021), λ_{max} (cyclohexane) 237, 243, 248.5, 258.5, 264.5, 280, 289 m μ (ϵ 172, 182, 200, 203, 155, 12.6, 7.0), ν_{max} 3073w, 3040m, 2990m, 2929s, 2885s, 2857s, 2822s, 1497m, 1455s, 1383s, 1366m, 1313vw, 1203s, 1195s, 1185m, 1157vw, 1101vs, 1078m, 1029m, 966w, 928m, 901m, 841vw, 725m, 693vs cm.⁻¹. (Infrared spectra were recorded on a Hilger H800 double-beam spectrophotometer equipped with NaCl prism. Calibrated against polystyrene, the instrument accuracy and reproducibility were \pm 5 cm.⁻¹ in the range 4000–2000 cm.⁻¹ and \pm 1 cm.⁻¹ in range 2000–650 cm.⁻¹.)

¹² E. N. Marvell and M. J. Joncich, *J. Amer. Chem. Soc.*, 1951, **73**, 973.

¹³ A. Rieche, E. Schmitz, and E. Beyer, *Chem. Ber.*, 1958, **91**, 1935.

¹⁴ A. Rieche, E. Schmitz, W. Schade, and E. Beyer, *Chem. Ber.* 1961, **94**, 2926.

¹⁵ P. S. Skell and R. C. Woodworth, *J. Amer. Chem. Soc.*, 1955, **77**, 4638.

Benzaldehyde Dimethyl Acetal.—To a solution of benzaldehyde (106 g., 1 mole) and trimethyl orthoformate (106 g., 1 mole) in anhydrous methanol (50 ml.) was added methanol which had been saturated with hydrogen chloride (*ca.* 1 ml.). A vigorous reaction occurred after which the mixture was heated under reflux for 0.5 hr. After rapid cooling in ice and neutralisation with methanolic potassium hydroxide, the solution was concentrated under reduced pressure, dried (MgSO_4), and fractionated through a 20 cm. helix-packed column, b. p. 96–97°/35 cm. (137 g., 90%), n_D^{25} 1.4922. Its infrared spectrum showed presence of traces of benzaldehyde. Refractionation gave the carbonyl-free acetal, n_D^{25} 1.4900, which was stored under nitrogen in the dark (lit.,¹⁶ b. p. 194–196°/760 mm., n_D^{20} 1.4970), λ_{max} (cyclohexane) 251, 257, 261, 263, 267 μ (ϵ 129, 174, 96.0, 135, 43.5), ν_{max} 3073vw, 3040vw, 2997w, 2948m, 2897w, 2832w, 1494vw, 1446m, 1357m, 1313vw, 1206s, 1195m, 1176w, 1158vw, 1105vs, 1076s, 1056vs, 1031w, 984s, 930w, 913m, 697s cm^{-1} .

Quantitative Analysis by Infrared Spectrophotometry.—A set of variable path-length cells with sodium chloride end-plates supplied by Research and Industrial Instruments Co., London, was used. All calibrations and determinations were done in carbon tetrachloride solution. Plots of path-lengths (50–250 μ) against absorbance are linear in all cases, usually through the origin and up to 0.45 absorbance units. Apparent extinction coefficients for analytical peaks calculated from the linear plots are recorded elsewhere.¹⁷

Reaction of Benzyl Methyl Ether with N-Bromosuccinimide.—A mixture of benzyl methyl ether (3.66 g; 30 mmoles) and *N*-bromosuccinimide (2.685 g.; 15 mmoles) in carbon tetrachloride (50 ml.) was illuminated with a 150-watt lamp with magnetic stirring. A vigorous reaction commenced after *ca.* 3 min. and was over in 10 min., refluxing and stirring being continued for 50 min. The precipitated succinimide (1.04 g., 70%; identified by m. p. and mixed m. p.) was filtered and washed with carbon tetrachloride and the combined filtrate and washings were diluted to 100 ml. A 10 ml. aliquot was shaken for 1 hr. with 100 ml. of 2*N*-hydrochloric acid saturated with 2,4-dinitrophenylhydrazine in a stoppered flask. The carbon tetrachloride was removed under reduced pressure and the benzaldehyde 2,4-dinitrophenylhydrazone estimated gravimetrically, m. p. and mixed m. p. 238–239° (0.31 g.). The remaining 90 ml. of the solution was washed with aqueous sodium hydrogen carbonate, water, and dried (CaCl_2). Removal of the solvent and of benzyl methyl ether and benzaldehyde under reduced pressure left a thick oil (*ca.* 0.27 g.) which was chromatographed on alumina and eluted with benzene followed by benzene-methanol (9:1). The oil so obtained (160 mg.) did not crystallise from the usual solvents and was distilled, giving *N*- α -methoxybenzylsuccinimide, b. p. 125° (bath)/1 mm. (Found: C, 65.65; H, 5.95%; *M*, 204. $\text{C}_{12}\text{H}_{13}\text{NO}_3$ requires C, 65.75; H, 6.0%; *M*, 219), ν_{max} (CCl_4) 3068, 3032, 2995, 2937, 2827, 1787m, 1722vs, 1496, 1477, 1455, 1435, 1387, 1344s, 1314, 1292, 1247, 1216, 1196, 1173s, 1109s, 1100s, 1077, 1029, 971, 917, 861, 715, 693 cm^{-1} . (The spectrum of the chromatographed sample before distillation was identical.)

Methyl bromide was retained in an acetone-dry-ice trap and treated with a solution of methyl fluorene-9-carboxylate (1.12 g.; 5 mmoles) in dry methanol (10 ml.) containing sodium (0.23 g.), giving methyl 9-methylfluorene-9-carboxylate (0.65 g.), m. p. 108–109° (from cyclohexane) (lit.,¹⁸ 108–109°). Hydrolysis of the ester with methanolic potassium hydroxide yielded the acid, m. p. 171.5–172.5 (from cyclohexane) (lit.,¹⁸ 170–171°), ν_{max} 1376, 2891 ($\text{C}-\text{H}_3$), 1737 cm^{-1} ($\text{C}=\text{O}$) (lit.,¹⁹ ν_{max} 1735.5 cm^{-1}). The ester carbonyl of the reagent has a doublet at 1750 and 1740 cm^{-1} (lit.,¹⁹ 1750 and 1739 cm^{-1}).

Reaction of m-Chlorobenzyl Methyl Ether with N-Bromosuccinimide.—The ether²⁰ (0.86 g., 5.5 mmoles) in carbon tetrachloride (25 ml.) was treated with *N*-bromosuccinimide (0.89 g., 5.0 mmoles) as for the unsubstituted ether. The reaction was complete in 5 min. and refluxing was continued for 5 min. before the mixture was cooled rapidly to room temperature. The infrared spectrum of a sample of the solution showed a concentration of 0.64 mmole/25 ml. of free *m*-chlorobenzaldehyde (1711 cm^{-1}), and two strong peaks at 1230 and 1105 cm^{-1} . The compensated difference-spectrum assigned to *m*-chloro- α -methoxybenzyl bromide is given below and is compared with that of the ether :

m-Cl-C₆H₄-CHBr-OMe: 3072, 3015, 2940, 2839, 1601, 1579, 1478, 1462, 1448, 1368, 1361, 1282, 1230s, 1197, 1170, 1105vs, 1093s, 1080, 980s, 909, 883, 714, 686s cm^{-1} ; *m*-Cl-C₆H₄-CH₂-OMe: 3065,

¹⁶ S. Mamedov and M. A. Avanesyan, *Zhur. obshchei Khim.*, 1962, **32**, 2834.

¹⁷ K. H. Lee, Ph.D. Thesis, University of Malaya, 1964.

¹⁸ P. M. G. Bavin, *Analyt. Chem.*, 1960, **32**, 554.

¹⁹ K. Bowden, N. B. Chapman, and J. Shorter, *Canad. J. Chem.*, 1963, **41**, 2154.

²⁰ R. L. Huang and K. H. Lee, following Paper.

3029, 2987, 2922m, 2882m, 2852m, 2820m, 1497, 1456m, 1378m, 1367, 1205m, 1195m, 1186, 1155, 1103vs, 1029, 966, 926, 901, 725, 694vs cm^{-1} .

After shaking the mixture with a saturated aqueous solution of sodium hydrogen carbonate for 5 min. and drying (CaCl_2), the spectrum indicated an increased concentration of *m*-chlorobenzaldehyde (4.0 mmoles/25 ml.) with disappearance of the peaks at 1230 and 1105 cm^{-1} . The rest of the mixture was filtered into a stirred solution from sodium (0.23 g., 10 mmoles) in anhydrous methanol (25 ml.). A white precipitate formed instantaneously, and stirring was continued for 10 min. before water was added. The organic matter was extracted with methylene chloride, washed with water and aqueous sodium carbonate, and dried. After removal of the solvent, the infrared spectrum showed four strong peaks at 1111, 1089, 1078, 1058 cm^{-1} , indicative of an acetal. Distillation gave a liquid (0.46 g.), b. p. 51—52°/0.1 mm., n_D^{25} 1.5098, which had an identical infrared spectrum to that of *m*-chlorobenzaldehyde dimethyl acetal²⁰ (n_D^{25} 1.5084). It gave the 2,4-dinitrophenylhydrazone of *m*-chlorobenzaldehyde, m. p. and mixed m. p. 257—258.5°.

Reaction of Benzyl Methyl Ether with Bromotrichloromethane.—Benzyl methyl ether (3.66 g., 30 mmoles) and bromotrichloromethane (3.96 g., 20 mmoles) in carbon tetrachloride (10 ml.) was illuminated under reflux for 42 hr. Infrared absorption at 1709 cm^{-1} showed the presence of benzaldehyde (14.6 mmoles), unreacted ether (1101 cm^{-1}) (11.7 mmoles), and some benzoyl bromide (1779 cm^{-1}). Treatment of the solution with an excess of aniline gave benzanilide (0.28 g., 1.4 mmoles), m. p. 164—165.5° (from aqueous ethanol), undepressed by an authentic sample. Thus 27.7 mmoles (92.3%) of the ether was accounted for. Methyl bromide was characterised as described earlier.

*Reaction of Benzaldehyde Dimethyl Acetal with Di-*t*-butyl Peroxide.*—The acetal (6.08 g., 40 mmoles) and the peroxide (1.46 g., 10 mmoles) were weighed into a reaction tube which was then connected through a reflux condenser to a dry-ice trap, and heated at 110° for 40 hr. The solution was distilled under reduced pressure up to 70° (bath) to remove volatile material. Infrared analysis of this material and the residue showed the presence of methyl benzoate (1.96 g., 14.4 mmoles) (1275 and 1730 cm^{-1}), benzaldehyde dimethyl acetal (3.72 g., 24.5 mmoles) (1056 cm^{-1}), *t*-butyl alcohol (0.37 g., 5.0 mmoles), di-*t*-butyl peroxide (0.92 g., 6.3 mmoles), and acetone (0.11 g., 0.2 mmole). Thus, 96% of the acetal and 89% of the peroxide was accounted for.

Reaction of Benzaldehyde Dimethyl Acetal with N-Bromosuccinimide.—This was carried out as for benzylether. Because of the presence, in the reaction products, of traces of benzaldehyde which caused an inflexion in the infrared absorption at 1709 cm^{-1} , the peak at 1275 cm^{-1} was used for estimation of methyl benzoate.

Reaction of Benzaldehyde Dimethyl Acetal with Bromotrichloromethane.—The products were analysed by infrared spectroscopy in the usual way. Infrared difference-spectra showed the presence of chloroform (1218 cm^{-1}), and dimethoxymethane (strong maxima at 1142, 1112, 1046, and 929 cm^{-1} and identical with the spectrum of an authentic sample), the latter yielding the 2,4-dinitrophenylhydrazone of formaldehyde, m. p. and mixed m. p. 164—165°. In one experiment, in which the gaseous products were passed through a solution of 2,4-dinitrophenylhydrazine in 2*N*-hydrochloric acid, formaldehyde 2,4-dinitrophenylhydrazone (m. p. and mixed m. p.) was precipitated. The forerun from distillation of the reaction mixture gave more of the same hydrazone (total yield of 80 mg. from 30 mmoles of the acetal).

Acetal Exchange Reaction of Benzaldehyde Dimethyl Acetal.—A mixture of the acetal (7.6 g.), paraformaldehyde (1.5 g.), and 2 drops of 63% hydrobromic acid was kept at 70° for 3 hr. by which time 1.5 g. of dimethoxymethane had distilled over at 40—42°, n_D^{20} 1.3518 (lit.,²¹ b. p. 41°, n_D^{20} 1.3535), ν_{max} 2990, 2935, 2820, 2780, 1465, 1448, 1398, 1223, 1190, 1142, 1112, 1046, 929 cm^{-1} .

Reaction of Methanol with Bromotrichloromethane in the Presence of Benzaldehyde.—Methanol (3.20 g., 10 mmoles), benzaldehyde (5.62 g., 53 mmoles), and bromotrichloromethane (4.97 g., 25 mmoles), in carbon tetrachloride (10 ml.) were illuminated under reflux for 22 hr. Fractionation gave a forerun shown by infrared difference-spectra to contain chloroform and dimethoxymethane, the latter forming the 2,4-dinitrophenylhydrazone of formaldehyde (m. p. and mixed m. p.). Infrared analysis of the remaining fractions showed methyl benzoate (4.6 mmoles), benzaldehyde dimethyl acetal (3.1 mmoles), and benzaldehyde (44.6 mmoles).