68. *Halogenated Ketones. Part III. The Preparation of Bromomethyl Ketones by the Diazomethane Reaction.*

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The preparation of eight bromomethyl ketones, by reaction of acyl bromides with diazomethane followed by decomposition of the diazo-ketones with hydrogen bromide, is described.

The direct bromination of unsymmetrical ketones usually gives rise to two isomeric monobromoketones (Parts I and II, preceding papers) which in certain cases can be separated by careful fractional distillation. Since a series of pure bromomethyl alkyl ketones was required for investigation of their physiological properties it seemed desirable to use a preparative method which would yield the pure ketones directly, uncontaminated with any isomers. The diazomethane reaction with acyl halides, originally discovered by Clibbens and Nierenstein (*J.*, 1915, **107**, 1491 and subsequent papers; see also Bradley, Robinson, and Schwarzenbach, *J.*, 1928, 1310, 1545, 2904), was especially suitable for this purpose. The appropriate pure acid bromides were allowed to react with two moles of diazomethane, and the ethereal solutions of the resulting diazo-ketones were then treated with anhydrous hydrogen bromide.

When first prepared these strongly lachrymatory bromomethyl ketones are colourless liquids; they all show a marked tendency to darken and resinify on storage, but this is almost completely inhibited by the presence of a little magnesium oxide.

The ethyl and propyl ketones proved to be identical with those obtained by the direct bromination method (Parts I and II).

Experimental.

The acid bromides were prepared by heating the acid (1 mol.) with phosphorus tribromide (0·5 mol.) for 1·5—2 hours at 150°. They were distilled from the mixture and then redistilled in order to free them from phosphorus compounds and hydrogen bromide.

Diazomethane was obtained in the usual manner by distillation from a mixture of ether, potassium hydroxide solution, and nitrosomethylurea, the latter being prepared in quantity by the very satisfactory method due to Arndt, Loewe, and Avan (*Ber.*, 1940, **73**, 606).

General Method for Bromomethyl Ketones.—The acid bromide (1 mol.) was added slowly to an ice-cold ethereal solution of diazomethane (2 mols.) (dried for at least 3 hours over potassium hydroxide); nitrogen was then evolved and the yellow colour of the diazomethane disappeared rapidly. After 30 minutes at 0°, dry hydrogen bromide was passed in until it was obvious that excess was present; the solution was kept at 0° for a further 30 minutes and then washed with water and sodium hydrogen carbonate solution. The dried ethereal solution was evaporated, and distillation of the residual oil under reduced pressure gave a small first fraction of methyl ester, followed by the bromomethyl ketone.

The properties of the compounds prepared by this method are listed below, all except the first two being new.

Bromomethyl ketone.	Yield, %.	B. p.	n_D.	Found, %.	Req., %.
Ethyl	55	154—155°	1·4670 (20°)	Br, 52·8	Br, 53·0
Propyl	27	92/50 mm.	1·4575 (20)	48·9	48·5
iso*Propyl*	46	86/50 mm.	1·4467 (14·5)	48·9	48·5
n-*Butyl*	50	108/50 mm.	1·4486 (15·5)	45·1	44·7
iso*Butyl*	70	101—102/50 mm.	1·4595 (17)	45·1	44·7
n-*Amyl*	70	96/14 mm.	1·4645 (18)	41·8	41·5
3-*Chloropropyl*	80	114/13 mm.	1·5009 (19·5)	Ag halide, 4·18 mg.	Ag halide, 4·16 mg.
Benzyl	62	106/0·2 mm.	1·5593 (15·5)	Br, 37·2	Br, 37·5

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