

XXXIV.—*The Quaternary Salts of Benzoxazoles.*

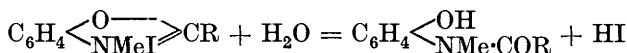
By LESLIE MARSHALL CLARK.

SINCE the pseudo-bases of the quaternary salts of substituted benzthiazoles have been shown to be *o*-acylmethylaminothiophenols (Mills, Clark, and Aeschlimann, *J.*, 1923, **123**, 2354; Clark, *J.*, 1925, **127**, 973), the corresponding benzoxazole compounds have now been investigated so that a comparison may be made between the properties of these analogous ring systems.

Benzoxazole methiodide was first prepared by Fischer (*J. pr. Chem.*, 1906, **73**, 435), who showed that when the salt was heated with hydrochloric acid, *o*-methylaminophenol was formed, whilst treatment with hot alkalis caused profound decomposition.

It has now been found that benzoxazole methiodide, on being dissolved in water, gives a solution, acid to litmus, from which, after addition of one equivalent of caustic alkali, *o*-formylmethylaminophenol can be obtained. In the same way, 1-methylbenzoxazole methiodide* and 1-phenylbenzoxazole methiodide readily hydrolyse in aqueous solution to *o*-acetylmethylaminophenol and *o*-benzoylmethylaminophenol, respectively, with the liberation of one equivalent of acid.

The reaction is therefore to be represented by the equation



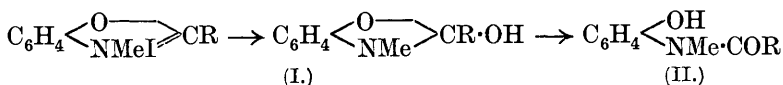
No such effect is apparent in these quaternary salts as was observed by Skraup (*Annalen*, 1919, **419**, 80), who found that in the 1-substituted benzoxazole bases resistance of the oxazole ring to fission increases with increasing volume of the substituent radical.

Attempts to reverse the hydrolysis were made by passing dry hydrogen iodide through a solution of *o*-benzoylmethylaminophenol in dry ether and by dissolving *o*-acetylmethylaminophenol in excess of concentrated perchloric acid. The hydriodide of the acylmethylaminophenol separated in the first case, but no 1-phenylbenzoxazole methiodide was obtained, and in the second the only substance isolated was the unchanged phenol.

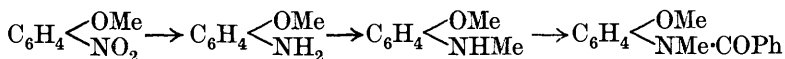
There appeared to be some possibility that the complete scheme

* Since this paper was prepared for publication, König and Meier (*J. pr. Chem.*, 1925, **109**, 324) have shown that 1-methylbenzoxazole methiodide on hydrolysis with water gives *o*-acetylmethylaminophenol.

for the action of alkalis on substituted benzoxazole quaternary salts might be represented thus :



Were this the case, methylation might be expected to yield a derivative of each of the compounds I and II. On treating an aqueous solution of 1-phenylbenzoxazole methiodide with a slight excess of sodium hydroxide and methyl sulphate, only *o*-benzoylmethylaminoanisole could be isolated, whose identity was established by synthesis in the following stages :



Under these conditions, therefore, no evidence for the presence of the carbinol base (I) is obtained. Although there is thus a measure of similarity between benzoxazonium and benzthiazolonium salts in their reactions with alkalis, two important differences must be noticed :

(a) Benzoxazonium salts are hydrolysed by water alone, whereas benzthiazolonium salts are stable in aqueous solution.

(b) In consequence of this behaviour, benzoxazole quaternary salts cannot be obtained by treatment of the *o*-acylmethylaminophenols with acids, whereas benzthiazole methiodide is readily recovered from the sodium salt of formylmethylaminothiophenol (Mills, Clark, and Aeschlimann, *loc. cit.*).

EXPERIMENTAL.

Benzoxazole Methiodide.—Benzoxazole was prepared by Ladenburg's method (*Ber.*, 1876, **9**, 1924) by heating together *o*-aminophenol and formic acid. Fischer (*loc. cit.*) obtained the methiodide by heating the base with excess of methyl iodide at 100° for 3 hours, and describes it as yellow, shining needles, m. p. 182° (decomp.). In this investigation, the two substances were combined at temperatures varying from 50° to 100°; the product was similar in colour to Fischer's but melted at 202° (decomp.). The purest material was obtained by heating the base with 10% excess of methyl iodide at 60° for 8 hours and extracting the crushed product with dry ether (Found: C, 37.1, 37.25; H, 3.0, 3.1; N, 5.2; I, 48.8. Calc., C, 36.8; H, 3.1; N, 5.4; I, 48.6%).

Action of Potassium Hydroxide on Benzoxazole Methiodide.—From mixed aqueous solutions of the methiodide (10 g.) and potassium hydroxide (rather more than 1 equiv.), *o*-formylmethylaminophenol crystallised on cooling, and a further crop was

obtained by passing carbon dioxide through the mother-liquor. It crystallised from benzene in colourless needles (yield, 5 g.), m. p. 103—104° (Found: C, 63·6; H, 5·8; N, 9·0. Calc., C, 63·6; H, 6·0; N, 9·3%).

The *formyl* compound (1 g.) was heated for 1 hour with concentrated hydrochloric acid (7·5 c.c.) and water (4 c.c.), the solution made slightly alkaline with sodium hydroxide, and the alkali neutralised with carbon dioxide; 0·7 g. of almost colourless, shining flakes of *o*-methylaminophenol was obtained, m. p. 95—96° (Lees and Shedden, *J.*, 1903, **83**, 756, give m. p. 96—97° and Fischer, *loc. cit.*, gives m. p. 86—87°).

For further characterisation of the product, a nitroso-derivative was prepared by Dieppolder's method (*Ber.*, 1899, **32**, 3519) from this compound, and from an authentic specimen of *o*-methylaminophenol. Both nitroso-derivatives and their mixture crystallised from alcohol in colourless, glistening plates, m. p. 125—126° (decomp.) (Found: N, 18·0. Calc., N, 18·4%).

1-Methylbenzoxazole Methiodide.—*1-Methylbenzoxazole*, prepared by Ladenburg's method (*Ber.*, 1876, **9**, 1524), was heated (13·5 g.) with methyl iodide (17 g.) for 8 hours at 100°. The yellow mass was extracted with dry ether and crystallised from acetone in colourless needles, which became light brown unless rapidly dried; m. p. 196° (decomp.) (Found: C, 39·5; H, 3·6; I, 46·1. Calc., for $C_9H_{10}ONI$, C, 39·3; H, 3·6; I, 46·2%).

1-Methylbenzoxazole Methoperchlorate.—The methiodide was dissolved in a little cold water and treated with excess of a saturated solution of sodium perchlorate. A mass of colourless plates was immediately precipitated, m. p. 165—170°. Recrystallisation from water lowered the melting point to 150—160°, evidently causing decomposition. A portion of the crude perchlorate was extracted with ether, whereby the hydrolysis product, *o*-acetylmethylaminophenol, m. p. 150°, was removed. The purified *perchlorate* had m. p. 173°, unchanged by crystallisation from acetone-ether (Found: N, 6·0. $C_9H_{10}O_5NCl$ requires N, 5·7%).

The salt (0·8 g.) was heated in aqueous solution for 1½ hours; colourless needles of *o*-acetylmethylaminophenol, m. p. 151°, crystallised on cooling (Found: N, 8·8. Calc., N, 8·5%).

1-Methylbenzoxazole methiodide in aqueous solution at laboratory temperature was hydrolysed incompletely after 8 hours and completely after 66 hours.

Action of Potassium Hydroxide on 1-Methylbenzoxazole Methiodide.—The reaction was carried out in the same way as for benzoxazole methiodide. The yield of *o*-acetylaminophenol, m. p. 151°, from 7 g. of salt was 2·1 g.

Action of Silver Oxide on 1-Methylbenzoxazole Methiodide.—The salt (1 g.) was dissolved in acetone (300 c.c.) and silver oxide freshly prepared from silver nitrate (3 g.) was added. Silver iodide was formed and after being shaken for 1 hour the acetone solution was evaporated: the residue was crystallised from benzene-light petroleum, colourless needles of *o*-acetylmethylaminophenol, m. p. 151°, being obtained.

1-Phenylbenzoxazole Methiodide.—1-Phenylbenzoxazole, prepared by Skraup's method (*loc. cit.*), was heated (3.8 g.) with methyl iodide (9 g.) at 100° for 36 hours. The product was extracted with dry ether and cautiously crystallised from absolute alcohol. The *methiodide* (yield 4.8 g.) separated in almost colourless needles, m. p. 196° (decomp.), which became brown on exposure to light (Found: C, 49.9; H, 3.6; I, 37.3. $C_{14}H_{12}ONI$ requires C, 49.9; H, 3.6; I, 37.6%).

Action of Water on 1-Phenylbenzoxazole Methiodide.—When the salt (3.37 g.) was dissolved in warm water (100 c.c.), a colourless, crystalline substance immediately began to separate. The acid solution on titration with sodium hydroxide and phenolphthalein required 10.4 c.c. of *N*-NaOH (Calc. for 1 equiv. of NaOH, 10.0 c.c.).

The solid crystallised from aqueous alcohol in plates, m. p. 163—164°, and was recognised as *o*-benzoylmethylaminophenol by analysis as well as by the method of preparation. Ransom (*Amer. Chem. J.*, 1900, **23**, 34) gives m. p. 162—163° (Found: C, 74.1; H, 5.6; N, 6.4. Calc., C, 74.0; H, 5.7; N, 6.2%).

The *urethane* was prepared by heating *o*-benzoylmethylaminophenol (1 g.) for 3 hours with phenylcarbimide (0.6 g.). The product was extracted with ether and crystallised from alcohol in colourless plates, m. p. 144° (Found: C, 73.3; H, 5.1; N, 8.2. $C_{21}H_{18}O_3N_2$ requires C, 72.8; H, 5.2; N, 8.1%).

o-Benzoylmethylaminoanisole.—*o*-Methylaminoanisole, prepared by the usual reactions from *o*-nitroanisole, was benzoylated with benzoyl chloride and sodium hydroxide. The product crystallised from aqueous alcohol in small, colourless prisms, m. p. 115° (Found: C, 74.4; H, 6.1; N, 5.7. $C_{16}H_{15}O_2N$ requires C, 74.7; H, 6.2; N, 5.8%).

When 1-phenylbenzoxazole methiodide (1.5 g.) was shaken with sodium hydroxide and methyl sulphate in slight excess, a paste formed which was crystallised from aqueous alcohol. It melted at 115°, and did not depress the melting point of *o*-benzoylmethylaminoanisole prepared as described above (Found: N, 5.8%).