359. *The Sommelet Reaction. Part V.** N-*Heteroaromatic Aldehydes.*

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In the pyridine and benzopyridine series α- and γ-aldehydes cannot be obtained by the Sommelet reaction but β-aldehydes are readily prepared. 4-Formyl-2-phenylthiazole, though an α-aldehyde, could be obtained in good yield.

THE Sommelet reaction, best suited for yielding aromatic aldehydes, has not been used for the preparation of heteroaromatic aldehydes, except in the thiophen series (*e.g.*, Hartough, " Thiophene and Its Derivatives," Interscience Publ., New York, 1952, p. 310; Wiberg, *Org. Synth.*, 1949, **29**, 87). Since *N*-heteroaromatic aldehydes are generally difficult to obtain by other methods, it seemed worth while to explore the scope of the Sommelet reaction in their preparation.

The halogenomethyl compounds are not particularly suitable starting materials because in the *N*-heteroaromatic series they are mostly inaccessible or unstable. The aminomethyl compounds, on the other hand, are stable and available through the hydrogenation of nitriles.

2-Bromomethylquinoline, which is conveniently prepared (Hammick, *J.*, 1926, 1302), was first used but gave no aldehyde. Experience with aliphatic aldehydes (preceding paper) suggested that 2-formylquinoline may be unstable under the conditions of the Sommelet reaction, and this proved to be the case: short heating with a solution of hexamine destroyed it. 2-Formylpyridine and 3-formyl*iso*quinoline behaved similarly; the latter, expected to be more stable because of the lower bond order of the $N-C_{(3)}$ bond, was, in fact, converted into a black tar almost immediately by hexamine in boiling dilute acetic acid. It is clear therefore that α-aldehydes of pyridine and benzopyridines cannot be prepared by the Sommelet reaction.

4-Formylpyridine proved to be more stable: most of it was recovered after 10 min.', but none after 2 hr.', heating. Nevertheless experiments designed to remove it quickly by steam-distillation from a reaction mixture of 4-aminomethylpyridine and hexamine failed to yield any of the aldehyde.

By contrast, the β-aldehydes are stable and can be prepared by the Sommelet reaction; *e.g.*, 3-formylpyridine, not readily available by other methods, is obtained easily from 3-aminomethylpyridine. 4-Formyl*iso*quinoline was obtained in 50% yield from the corresponding aminomethyl compound.

In the thiazole series, 4-formyl-2-phenylthiazole—though an α-aldehyde—was readily prepared but the isomeric 2-formyl-4-phenylthiazole could not be obtained by this method. Yet the latter compound, when prepared by other methods (Olin and Johnson, *J. Amer. Chem. Soc.*, 1931, **53**, 1470), was stable under the Sommelet conditions. 4-Chloromethyl-2-methylthiazole was too unstable to be of use in the Sommelet reaction, not even the hexaminium salt being obtainable.

Attempts to prepare furfuraldehyde from 2-aminomethylfuran failed.

EXPERIMENTAL

M. p.s are corrected. Microanalyses are by Mrs. E. Bielski.

3-*Formylpyridine*.—A mixture of 3-aminomethylpyridine (11·4 g.) (Huber, *J. Amer. Chem. Soc.*, 1944, **66**, 876), hexamine (18 g.), concentrated hydrochloric acid (26 ml.), acetic acid (4 ml.), and water (24 ml.) was boiled under reflux for 6 hr. After having been adjusted to pH 5, the mixture was saturated with sodium nitrate and extracted several times with chloroform (200 ml. in all). The solvent was removed through a short column (the aldehyde is

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* Part IV, preceding paper.

somewhat volatile with chloroform), and the residue distilled, to give 6·4 g. (57%) of the aldehyde, b. p. 95—97°/15 mm. The *dinitrophenylhydrazone*, crystallised from aqueous pyridine, had m. p. 259° (Found: N, 24·1. $C_{12}H_9O_4N_5$ requires N, 24·4%). The oxime melted at 150°; Craig and Hixon (*J. Amer. Chem. Soc.*, 1931, **53**, 4367) report m. p. 148°.

pH 5 was used for extraction as a compromise: at lower pH's very little aldehyde is extracted and at higher pH's much of it is present as Schiff's bases. These are not absent even at pH 5, as shown by the substantial residue left on distillation of the aldehyde; the actual yield of 3-formylpyridine is probably higher than stated.

4-*Aminomethyl*iso*quinoline*.—4-Cyano*iso*quinoline (19·8 g.) was hydrogenated at room temperature and pressure with Raney nickel in anhydrous ethanol saturated with ammonia. The reaction stopped when 4·2 l. of hydrogen had been taken up; after removal of the catalyst and solvent the mixture was distilled and fractions of the following b. p. were collected: (i) 80—100°/3 mm. (2·6 g.), (ii) 140—160°/2 mm. (6·7 g.), (iii) 210—215°/2 mm. (5·5 g.). The first consisted mainly of *iso*quinoline, b. p. 224—226° (picrate, m. p. 223°; methiodide, m. p. 158°; both identified by mixed m. p.). In view of the unusual nature of this reaction it was ascertained that *iso*quinoline was not an impurity of the starting material. Fraction (ii) was neutralised to pH 6·5 with hydrochloric acid, evaporated, and crystallised from ethanol–ethyl acetate, giving 4-*aminomethyl*iso*quinoline hydrochloride* (5·0 g., 20%), m. p. 208—209°. For analysis it was sublimed at 165°/0·003 mm. and then melted at 209—210° (Found: C, 61·5; H, 5·6; N, 14·5. $C_{10}H_{11}N_2Cl$ requires C, 61·7; H, 5·7; N, 14·4%). The free amine boils at 179—181°/6 mm. and readily forms a dihydrochloride, insoluble in ethanol. The *picrate* melts at 215° (Found: N, 17·65. $C_{16}H_{13}O_7N_5$ requires N, 18·1%).

The unsatisfactory yield could not be improved by increasing the pressure of the hydrogenation. When both pressure and temperature were increased, none of the expected amine was obtained.

4-*Formyl*iso*quinoline*.—A solution of 4-aminomethyl*iso*quinoline hydrochloride (1·57 g.) and hexamine (2 g.) in 50% acetic acid (10 ml.) was boiled under reflux for 2 hr. The mixture was then diluted with water and extracted with ether, the ether evaporated, and the residue crystallised from water, to give the *aldehyde* (0·63 g., 50%), m. p. 100°. Another crystallisation raised the m. p. to 103° (Found: N, 9·05. $C_{10}H_7ON$ requires N, 8·9%). The *semicarbazone*, m. p. 253°, crystallised from much ethanol (Found: N, 26·5. $C_{11}H_{10}ON_4$ requires N, 26·2%). The phenylhydrazone, m. p. 201°, crystallised from dilute acetic acid.

4-*Formyl-2-phenylthiazole*.—4-Chloromethyl-2-phenylthiazole (2·0 g.) (Hooper and Johnson, *J. Amer. Chem. Soc.*, 1934, **56**, 484) and hexamine (1·6 g.) in 50% acetic acid (10 ml.) were boiled for 45 min. On cooling and dilution with water an oil separated which was taken up by ether and converted into the bisulphite compound. This was decomposed by sodium carbonate solution, to give the *aldehyde* (1·0 g., 56%), m. p. 49°. Being very soluble in organic solvents it is not readily crystallised; for analysis it was twice sublimed *in vacuo* and then melted at 52° (Found: N, 7·3. $C_{10}H_7ONS$ requires N, 7·4%). The *semicarbazone* formed needles (from methanol or ethyl acetate), m. p. 198° (Found: C, 53·45; H, 4·2. $C_{11}H_{10}OSN_4$ requires C, 53·65; H, 4·1%). A sample of the aldehyde was oxidised by permanganate to 2-phenylthiazole-4-carboxylic acid, m. p. 175°; Huntress and Pfister (*J. Amer. Chem. Soc.*, 1943, **65**, 1669) report m. p. 175—176·5°.

2-Formyl-4-phenylthiazole was prepared according to Olin and Johnson's method (*loc. cit.*). Though it was described as an oil, it readily crystallised on steam-distillation, and had m. p. 62°. It gave a bisulphite compound.

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