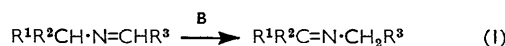


Synthesis of Carbonyl Compounds *via* Transamination of Schiff Bases

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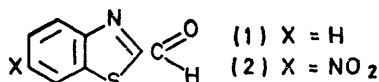
Benzothiazole-2-carbaldehyde or 6-nitrobenzothiazole-2-carbaldehyde can be used for the synthesis of aldehydes or ketones starting from the corresponding amines *via* transaminations. The method has wide applications and the yields are generally greater than 80%.

THE formation of a carbonyl group in a more complex substrate, *e.g.*, in compounds of biological interest, can be accomplished by mild oxidation of the corresponding amino-derivative. A large variety of oxidising agents have been used for this purpose.^{1,2} The conversion of primary amine into carbonyl compounds by means of base-catalysed prototropic rearrangement of Schiff bases [equation (1)] has been achieved by Corey and



Achiwa.³ The crucial factor in such 'transaminations,' is the ability of the residue linked to the carbonyl group to delocalise efficiently the negative charge produced by deprotonation of the Schiff base. During the course of our investigation on the reactivity of 2-halogenobenzothiazoles toward nucleophiles,⁴ we observed that the benzothiazole system has a strong ability to delocalise the negative charge.

For this reason we used benzothiazole-2-carbaldehyde (1) or 6-nitrobenzothiazole-2-carbaldehyde (2) as car-



bonyl compounds in the transamination. The aldehydes were found to react quantitatively with primary amines yielding the corresponding Schiff bases which in turn undergo a spontaneous isomerisation when dissolved in

¹ (a) H. Ruschig, W. Fritsch, J. Schmidt-Thome, and W. Haede, *Chem. Ber.*, 1955, **88**, 883; (b) W. E. Bachmann, M. P. Cava, and A. S. Dreiding, *J. Amer. Chem. Soc.*, 1954, **76**, 5554; (c) L. Labler and F. Šorm, *Coll. Czech. Chem. Comm.*, 1959, **42**, 4962.

² (a) R. G. R. Bacon and D. Stewart, *J. Chem. Soc. (C)*, 1966, 1384; (b) R. G. R. Bacon, W. J. W. Hanna, and D. Stewart, *ibid.*, p. 1388; (c) R. G. R. Bacon and W. J. W. Hanna, *J. Chem. Soc.*, 1965, 1962.

Hexametapol. The isomerisation is strongly accelerated by small amounts of bases, such as triethylenediamine (DABCO) or sodium methoxide. The isomeric Schiff bases are easily hydrolysed in acid. Some relevant results are reported in the Table.

Oxidation of amines by benzothiazole-2-carbaldehyde (1) and 6-nitrobenzothiazole-2-carbaldehyde (2)

Amine	M.p. (°C) ^a of Schiff base derived from (1) and (2)	Conditions for isomerisations, equiv. of base (t/h)	Yield of carbonyl compound (%)
Benzylamine	(1) 91—92	0.1 DABCO (1.5) (2.5)	69
	(2) <i>b</i>		74
α -Phenylethylamine	(1) 49—50	0.1 DABCO (3.5) (6.0)	97
	(2) 134—135		96
Diphenylmethylamine	(1) 148—149	0.1 DABCO (1.5) (3.5)	94
	(2) 121—122		93
Cyclopentylamine	(1) 50—51	0.1 NaOMe (1.0) (0.7)	86
	(2) 120—121		76
Cyclohexylamine	(1) 77—78	0.1 NaOMe (1.5) (1.0)	69 ^c
	(2) 184—185		65 ^c

^a Elemental analyses for C, H, and N were in agreement with calculated values (errors; C \pm 0.4, H \pm 0.8, and N \pm 0.2%).

^b This Schiff base was unstable on heating. ^c Yield determined by g.l.c. analysis; all other yields refer to isolated product.

The ready formation and isomerisation of Schiff bases, the high yields, the mild conditions used, and the wide applications of the reaction make the benzothiazole-carbaldehydes convenient reagents for transaminations.

EXPERIMENTAL

Reagents.—Benzothiazole-2-carbaldehyde, m.p. 73—74° (lit.,⁵ 75°), and 6-nitrobenzothiazole-2-carbaldehyde, m.p.

³ E. J. Corey and K. Achiwa, *J. Amer. Chem. Soc.*, 1969, **91**, 1429 and references therein.

⁴ P. E. Todesco, *Boll. sci. Fac. Chim. ind. Bologna*, 1965, **23**, 107.

⁵ V. M. Zubarovskii, *Doklady Akad. Nauk S.S.S.R.*, 1952, **87**, 759 (*Chem. Abs.*, 1954, **48**, 164e).

178—179° (lit.,⁶ 174°), were prepared by oxidation of the corresponding alcohols^{5,6} with selenium dioxide (0.5 mol) in dioxan at reflux. Hexametapol was distilled, dried on molecular sieves, and redistilled.

The following procedure illustrates general preparative technique. A solution (0.5 mol) of amine and aldehyde was refluxed in dry benzene generally for 0.5—1 h. After removal of the solvent, the resulting Schiff base was dissolved in Hexametapol (to give a 1M solution) containing base. The rate of isomerisation was determined approximately by n.m.r. measurements. After complete isomerisation, the mixture was diluted with a five-fold volume of methanol-water (9:1 v/v) and acidified to pH 2—3 by adding oxalic acid. After 2 h, the solution was poured in

water and the carbonyl compound was extracted with ether. The crude product was separated by t.l.c. [preparative scale; silica gel PF 254; eluant hexane-ether (5:2 v/v)]. The carbonyl compounds were identified by comparison (i.r. and g.l.c.) with authentic samples. Yields are in the Table. Slightly higher (by 5%) yields were determined on the ether extract by means of g.l.c. analysis using aldehydes or ketones with similar structures as internal standards.

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⁶ V. M. Zubarovskii, *Zhur. obshchei Khim.*, 1954, **24**, 1664 (*Chem. Abs.*, 1955, **49**, 13,223*d*).
