

Heterocycles in Organic Synthesis. Part 26.¹ Conversion of Primary Amines into Aldehydes

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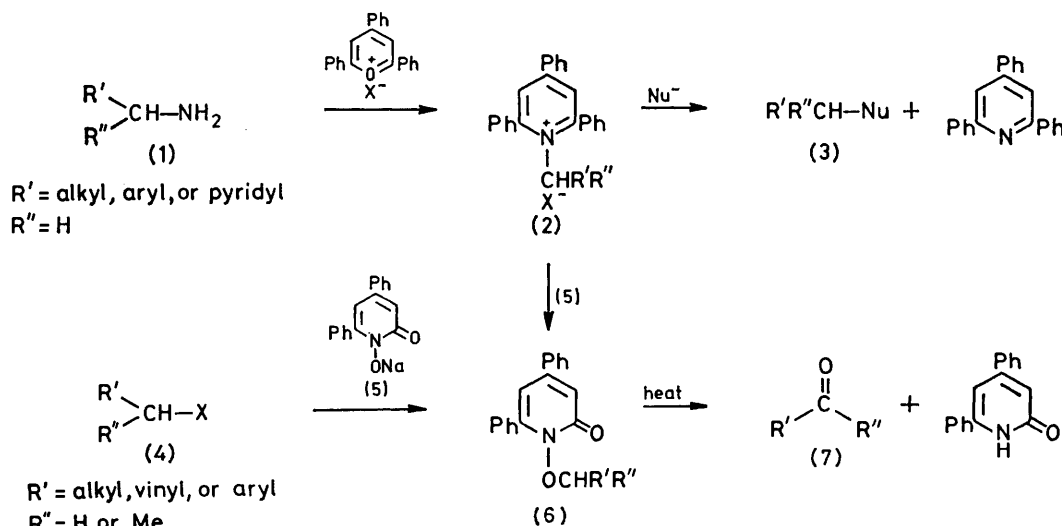
Triphenylpyridinium tetrafluoroborate derivatives, derived from alkyl, allyl, benzyl, and picolyl primary amines and triphenylpyrylium salts, react with sodium 1-oxido-4,6-diphenyl-2-pyridone to yield aldehydes, formed by thermolysis of intermediate 1-alkoxy-pyridones

VARIOUS synthetically useful procedures are available for the conversion of primary amines into aldehydes and ketones. The commonly used Ruschig route² involves generation of the *N*-halogeno-amine followed by elimination to give the imine (*cf.* also ref. 3), and imines have also been identified, or are likely intermediates, in direct oxidation⁴ and photochemical methods.⁵ A conceptually elegant and very different approach mimics the biologically important transamination pathway: here, Schiff-base formation is followed by prototropic isomerisation and hydrolysis.⁶ Oxidation of amines to oximes,⁷ and application of the Sommelet reaction⁸ provide feasible pathways, and attractively simple routes include oxidation of imine derivatives followed by hydrolysis of the oxaziridine product,⁹ elimination of sulphinate from a sulphonamide,¹⁰ and, for benzylamines, diazotisation in dimethyl sulphoxide.¹¹ Reaction sequences have also been reported using a triazolium salt and diethyl azodicarboxylate,¹² cuprous chloride and oxygen,¹³ and *t*-butyl nitrite and cupric halides.¹⁴

In the present paper we report a novel conversion under neutral and non-oxidative conditions which utilises features of two synthetic methods recently developed in these laboratories. The first, (1)→(2)→(3), provides a method of nucleophilic displacement of an amino-group,^{15,16} and the second, (4) + (5)→(6)→(7), gives access to aldehydes and ketones from halides by thermolysis of the intermediate 1-alkoxy-pyridone (6).¹⁷

The key to the present method lies in the one-step combined generation and cleavage of (6) on heating (2) with (5).

Preparation of Compounds.—With one exception the pyridinium tetrafluoroborates (2; X = BF₄) (Table) were readily prepared by the procedure described earlier.^{16,18} For (2; R' = R'' = Me, X = BF₄) the preparation was modified by using absolute ether as solvent and a reaction time of 30 h. Admixture of these salts with sodium 1-oxido-4,6-diphenyl-2-pyridone (5)¹⁷ afforded aldehydes when the reaction mixtures were heated, either under vacuum or in a nitrogen atmosphere, depending upon the volatility of the product (Table). The reaction proceeds most favourably for benzyl and picolyl derivatives and appears to provide a method of particular value for compounds sensitive to acids, bases, or oxidising reagents. The yields of benzaldehyde and substituted benzaldehydes (expts. IV—VII) fall in the range 47—74% and for the pyridinecarbaldehydes (VIII—X) satisfactory yields (41—57%) were also obtained. The reported yield of benzaldehyde, obtained from benzylamine by the Ruschig method is 80%,^{2d} by various direct oxidations, *ca.* 27—96%,^{4a-g} and by transamination methods, 55—78%.⁶ The Sommelet method has been used to convert 3-aminomethylpyridine into pyridine-3-carbaldehyde in 57% yield,^{8c} but the Sommelet reaction failed for the 2- and 4-isomers. The present method is less satisfactory for the



SCHEME

Conversion of amines R'R''CH-NH₂ into carbonyl compounds R'R''C=O [(1)→(2)→(7)]

Expt. no.	Amine (1)		Triphenylpyridinium tetrafluoroborates (2)				Pyrolyses to carbonyl compounds (7) ^a					Ref.
	R'	R''	Yield	M.p. (°C)	Lit. m.p. (°C)	Temp. (°C)	Press.	Time (h)	Yield (%)	M.p. (°C)	Lit. m.p. (°C)	
I	n-C ₃ H ₇	H	90	201—202	201—202 ^b	240	(N ₂ atm.)	3.5	22	119—121	122	c
II	n-C ₇ H ₁₅	H	65	155	d	210—230	0.1 mmHg	3	5 ^e	104—106	106	c
III	CH ₂ =CH	H	46	169—170	f	215	(N ₂ atm.)	3	20	163—164	165	c
IV	C ₆ H ₅	H	65	195	196—197 ^b	200	15 mmHg	2.5	73	235	237	c
V	4-MeC ₆ H ₄	H	80	130—132	g	200—220	0.1 mmHg	3.5	74	247—248.5	239	c
VI	2-ClC ₆ H ₄	H	77	200—202	200 ^h	225	15 mmHg	3	55	205—206	207	c
VII	2,4-Cl ₂ C ₆ H ₃	H	77	239—241	239 ^h	185	15 mmHg	4	47	221—223	224—225	i
VIII	2-C ₅ H ₄ N	H	58	219	218—219 ^b	245	(N ₂ atm.)	2.5	47	210	213	j
IX	3-C ₅ H ₄ N	H	74	167	166—168 ^b	230	(N ₂ atm.)	3.5	57	258	260	k
X	4-C ₅ H ₄ N	H	77	198—200	l	225	15 mmHg	3	41	280	283	k
XI	PhCH ₂	H	77	272	271 ^m	200—230	6.0 mmHg	4	0 ⁿ			
XII	Me	Me	52	171—173	o	200—220	(N ₂ atm.)	2.5	0 ^p			

^a Yields and m.p. data refer to the 2,4-dinitrophenylhydrazone derivative. ^b Ref. 16. ^c Ref. 19. ^d Not reported hitherto; Found: C, 73.2; H, 6.8; N, 2.8. C₃₁H₃₄BF₄N requires C, 73.4; H, 6.8; N, 2.8%. ^e 38% of n-octyl alcohol was obtained. ^f Not reported hitherto; Found: C, 72.1; H, 5.2; N, 3.0. C₂₆H₂₂BF₄N requires C, 71.8; H, 5.1; N, 3.2%. ^g Not reported hitherto; Found: C, 74.6; H, 5.5; N, 2.8. C₃₁H₂₆BF₄N requires C, 74.6; H, 5.3; N, 2.8%. ^h A. R. Katritzky, U. Gruntz, A. A. Ikizler, D. H. Kenny, and B. P. Leddy, *J.C.S. Perkin I*, 1979, 436. ⁱ W. Davies, N. H. Olver, and B. W. Wilson, *Austral. J. Sci. Research*, 1952, **A5**, 198 (*Chem. Abs.*, 1952, **46**, 10154^j). ^j P. Dyson and D. L. Hammick, *J. Chem. Soc.*, 1939, 781. ^k P. Grammaticakis, *Bull. Soc. chim. France*, 1956, 109. ^l Not reported hitherto; Found: C, 71.6; H, 4.7; N, 5.6. C₂₉H₂₃BF₄N₂ requires C, 71.6; H, 4.8; N, 5.8%. ^m B. P. Leddy, M.Sc. Thesis, University of East Anglia, 1975. ⁿ Styrene was isolated in 75% yield. ^o Not reported hitherto; Found: C, 71.1; H, 5.6; N, 2.9. C₂₆H₂₄BF₄N requires C, 71.4; H, 5.5; N, 3.2%. ^p Propene, isolated as 1,2-dibromopropane, was obtained in 51% yield.

preparation of aliphatic aldehydes, yields being ca. 20% for butyraldehyde and acrylaldehyde (expts. I and III) and only 5% for octanal, from which the main product isolated was octan-1-ol (*cf.* ref. 1). The method does not appear to work for ketones, as pyrolysis of the isopropyl derivative gave ca. 50% of propene [an identical yield was obtained without any pyridone salt (5)]. Moreover the attempted preparation of phenylacetaldehyde afforded styrene as the only product isolated.

EXPERIMENTAL

M.p.s were determined with a Reichert hot-stage microscope.

Preparation of Aldehydes and Ketones.—In a typical experiment 1-benzyl-2,4,6-triphenylpyridinium tetrafluoroborate (1.32 g, 2.7 × 10⁻³ mol) and sodium 1-oxido-4,6-diphenyl-2-pyridone¹⁷ (5) (0.80 g, 2.8 × 10⁻³ mol) were powdered together to give an intimate mixture and placed in a distillation unit equipped with a receiver cooled to -78 °C. The mixture was dried for 2 h at 110 °C and 0.2 mmHg and then heated at 200 °C and 15 mmHg, under which conditions the mixture was molten. After 3 h the benzaldehyde in the cooled receiver was characterised and quantitatively estimated as the 2,4-dinitrophenylhydrazone derivative (0.57 g, 73%), m.p. 235 °C (lit.,¹⁹ 237 °C).

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REFERENCES

- Part 25, A. R. Katritzky, M. J. Cook, S. B. Brown, R. Cruz, G. Millet, and A. Anani, *J.C.S. Perkin I*, 1979, preceding paper.
- (a) *e.g.* G. Ehrhart, H. Ruschig, and W. Aumüller, *Angew. Chem.*, 1939, **52**, 363; (b) H. Ruschig, W. Fritsch, J. Schmidt-Thomé, and W. Haede, *Chem. Ber.*, 1955, **88**, 883; (c) L. Lábler and F. Šorm, *Coll. Czech. Chem. Comm.*, 1959, **24**, 2975; (d) W. E. Bachmann, M. P. Cava, and A. S. Dreiding, *J. Amer. Chem. Soc.*, 1954, **76**, 5554; (e) E. J. Corey, N. H. Andersen, R. M. Carlson, J. Paust, E. Vedejs, I. Vlattas, and R. E. K. Winter, *J. Amer. Chem. Soc.*, 1968, **90**, 3245; (f) T. Masamune and K. Orito, *Tetrahedron*, 1969, **25**, 4551; (g) S. H. Dandegaonker and P. D. Pagar, *Current Sci.*, 1973, **42**, 539 (*Chem. Abs.*, 1973, **79**, 91724j).
- M. R. Czarny, *Synth. Comm.*, 1976, **6**, 285; R. V. Hoffman and R. Cadena, *J. Amer. Chem. Soc.*, 1977, **99**, 8226.
- (a) R. J. Highet and W. C. Wildman, *J. Amer. Chem. Soc.*, 1955, **77**, 4399; (b) R. J. Audette, J. W. Quail, and P. J. Smith, *Tetrahedron Letters*, 1971, 279; (c) R. G. R. Bacon and W. J. W. Hanna, *J. Chem. Soc.*, 1965, 4962; (d) R. G. R. Bacon and D. Stewart, *J. Chem. Soc. (C)*, 1966, 1384; (e) J. B. Lee and T. G. Clarke, *Tetrahedron Letters*, 1967, 415; (f) R. V. Hoffman, *J. Amer. Chem. Soc.*, 1976, **98**, 6702; (g) M. E. Kuehne and T. C. Hall, *J. Org. Chem.*, 1976, **41**, 2742.
- S. J. Cohen and R. J. Baumgarten, *J. Amer. Chem. Soc.*, 1965, **87**, 2996; J. A. Hyatt, *J. Org. Chem.*, 1972, **37**, 1254.
- E. J. Corey and K. Achiwa, *J. Amer. Chem. Soc.*, 1969, **91**, 1429; V. Caló, L. Lopez, and P. E. Todesco, *J.C.S. Perkin I*, 1972, 1652; see also F. G. Baddar and Z. Iskander, *J. Chem. Soc.*, 1954, 209.
- K. Kahr and C. Berther, *Chem. Ber.*, 1960, **93**, 132 and refs. therein; R. F. Merritt and J. K. Ruff, *J. Amer. Chem. Soc.*, 1964, **86**, 1392.
- (a) J. Graymore and D. R. Davies, *J. Chem. Soc.*, 1945, 293; (b) S. J. Angyal, D. R. Penman and G. P. Warwick, *J. Chem. Soc.*, 1953, 1737; (c) S. J. Angyal, G. B. Barlin, and P. C. Wailes, *J. Chem. Soc.*, 1953, 1740.
- D. St. C. Black and N. A. Blackman, *Austral. J. Chem.*, 1975, **28**, 2547; S. E. Dinizo and D. S. Watt, *J. Amer. Chem. Soc.*, 1975, **97**, 6900.
- J. B. Hendrickson, R. Bergeron, A. Giga, and D. Sternbach, *J. Amer. Chem. Soc.*, 1973, **95**, 3412.
- K. H. Scheit and W. Kampe, *Angew. Chem. Internat. Edn.*, 1965, **4**, 787.
- G. Doleschall, *Tetrahedron Letters*, 1978, 2131.
- T. Kametani, K. Takahashi, T. Ohsawa, and M. Ihara, *Synthesis*, 1977, 245.
- M. P. Doyle and B. Siegfried, *J.C.S. Chem. Comm.*, 1976, 433.
- J. B. Bapat, R. J. Blade, A. J. Boulton, J. Epszajn, A. R. Katritzky, J. Lewis, P. Molina-Buendia, Pai-Lin Nie, and C. A. Ramsden, *Tetrahedron Letters*, 1976, 2691; U. Gruntz, A. R. Katritzky, D. H. Kenny, M. C. Rezende, and H. Sheikh, *J.C.S. Chem. Comm.*, 1977, 701.
- A. R. Katritzky, U. Gruntz, D. H. Kenny, M. C. Rezende, and H. Sheikh, *J.C.S. Perkin I*, 1979, 430.
- M. J. Cook, A. R. Katritzky, and G. H. Millet, *Heterocycles*, 1977, **7**, 227.
- A. R. Katritzky, J. B. Bapat, R. M. Claramunt-Elguero, F. S. Yates, A. Dinculescu, A. T. Balaban, and F. Chiraleu, *J. Chem. Research*, 1978, (S) 395; (M) 4783.
- R. L. Shriner, R. C. Fuson, and D. Y. Curtin, 'The Systematic Identification of Organic Compounds,' 5th edn., Wiley, New York, 1964, p. 320.