

Reaction of Imines having an α -Hydroxy Group with Alkyl Iodides to give Betaines

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Reaction of 3-(alkylimino)butan-2-ol with alkyl iodides, followed by treatment with aqueous sodium hydroxide solution, gives the betaines, 2-(*N,N*-dialkyliminio)butan-3-olates.

It is known that the reaction of *N*-heterocyclic compounds including hydroxy groups or aromatic amines with alkyl halides or other electrophiles gives betaines such as 3-oxidopyridinium;¹ pyridazinium,² triazinium,³ and pyridinium phenoxides;⁴ and 3-oxidoanilinium.⁵ Betaines derived from squaric acid, which were considered to form a mesomeric 1,3-diaminocyclobutendiylum-2,4-diolate system, have been reported.⁶ However, acyclic analogues of such betaines have not been reported to our knowledge. We now show that the reaction of 3-(alkylimino)butan-2-ol with alkyl iodides gives betaines.

The imines (**1a**)—(**1c**) have not been reported and they were prepared by the following procedure. A mixture of 3-hydroxybutan-2-one (acetoin) (0.1 mol), propylamine (0.1 mol), and benzene (20 ml) was kept at room temperature for 15 h and then distilled under reduced pressure to give crude 3-(propylimino)butan-2-ol (**1a**) [39%, ¹H n.m.r. (*J* in Hz) δ 0.91 (t, 3H, *J* 6.5, CH₂CH₂CH₃), 1.24 (d, 3H, *J* 7.0, CH₃CHOH), 1.35—1.67 (m, 2H, CH₃CH₂CH₂), 1.95 (s, 1H, OH), 2.16 (s, 3H, CH₃C=N), 2.48 (t, 2H, *J* 7.0, CH₃CH₂CH₂), and 3.34 (q, 1H, *J* 7.0, CH₃CHOH); ν_{\max} 1705s and 3300br cm⁻¹]. Heating under reflux of a mixture of acetoin (0.1 mol), isopropylamine [or *t*-butylamine] (0.1 mol), and benzene (50 ml) for 1 h [10 h] gave crude 3-(isopropylimino)butan-2-ol (**1b**) [or crude 3-(*t*-butylimino)butan-2-ol (**1c**)] in 60 and 45% yield, respectively, after distillation under reduced pressure. ¹H N.m.r. and i.r. spectra of the main

fraction of (**1b**) or (**1c**) showed signals consistent with the structures proposed.[†]

After addition of MeI (0.01 mol) to a mixture of (**1a**) (0.01 mol), hexamethylphosphoric triamide (HMPA) (0.01 mol), and diethyl ether (15 ml), the mixture was kept for 5 h at room temperature, then treated with dilute aqueous NaOH. Distillation (kugelrohr) of the ether extract and g.l.c. separation (1.0 m Se-30, 15% on a Chromosorb W column) gave pure 2-(*N*-methyl-*N*-propyliminio)butan-3-olate (**2a**) [¹H n.m.r. (*J* in Hz) δ 0.93 (t, 3H, *J* 7.5, CH₂CH₂CH₃), 1.10 (d, 3H, *J* 7.0, CH₃CHO⁻), 1.51 (sextet, 2H, *J* 7.5, CH₃CH₂CH₂), 2.21 and 2.24 (2 \times s, 3H for each, CH₃C=N⁺CH₃), 2.38 (t, 2H, *J* 7.5, CH₃CH₂CH₂), and 3.24 (q, 1H, *J* 7.0, CH₃CHO⁻); ν_{\max} 1705s cm⁻¹; *m/z* 141 (*M* - 2H), 100 (*M* - CH₃CHO⁻ + H), 58 (*M* - Prⁿ - CH₃CHO⁻ + 2H), and 43 (Prⁿ)].

Similar reaction of (**1a**) with allyl iodide proceeded at a slightly slower rate than the reaction of MeI. Isolation of the product as before gave the pure 2-(*N*-allyl-*N*-propyliminio)butan-3-olate (**2c**) [¹H n.m.r. (*J* in Hz) δ 0.93 (t, 3H, *J* 7.5, CH₂CH₂CH₃), 1.10 (d, 3H, *J* 6.5, CH₃CHO⁻), 1.50 (sextet, 2H, *J* 7.5, CH₃CH₂CH₂), 2.30 (s, 3H, CH₃C=N⁺), 2.45 (t, 2H, *J* 7.5, CH₃CH₂CH₂), 3.05—3.25 (m, 2H, CH₂CH=CH₂), 3.51 (q, 1H, *J* 6.5, CH₃CHO⁻), 5.20—5.48 (m, 2H, CH₂CH=CH₂), and 5.76—6.10 (m, 1H, CH₂CH=CH₂); ν_{\max} 1710s cm⁻¹; *m/z* 167 (*M* - 2H), 126 (*M* - CH₃CHO⁻ + H), 84 (*M* - Prⁿ - CH₃CHO⁻ + 2H), and 43 (Prⁿ)].

The yields and conditions for the reactions of methyl, ethyl, or allyl iodide with the imines (**1a**), (**1b**), or (**1c**) are summarized in Table 1. Since some imine remained unchanged because of the slow reaction rate, corrected yields were calculated using the equation: 100 \times product/(imine used - imine unchanged). The six betaines showed weak u.v. absorption; (**2a**) λ_{\max} (EtOH) 305 nm, (ϵ 130.5 mol⁻¹ cm⁻¹), (**2b**) 304 (116.1), (**2c**) 303 (87.8), (**2d**) 304 (91.3), (**2e**) 307 (167.1), (**2f**) 306 (160.6).

The progress of the reaction of (**1a**) with MeI was followed by ¹H n.m.r. spectroscopy using benzene as solvent in order to ascertain the possible intervention of a hydroxy immonium

[†] For these imines coincidence of elemental analyses with the calculated values was not satisfactory because of decomposition during distillation.

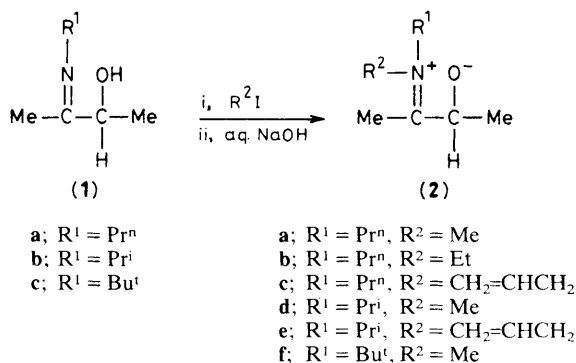


Table 1. Yields of betaines.^a

Imine	R ² I	Product ^b	Reaction time	Unchanged imine, % ^c	% Yield ^c	
					Actual	Corrected
(1a)	MeI	(2a)	5 h	6	24	26
(1a)	EtI	(2b)	1 week	9	20	22
(1a)	CH ₂ =CH-CH ₂ I	(2c)	15 h	20	36	45
(1b)	MeI	(2d)	24 h	11	28	31
(1b)	CH ₂ =CH-CH ₂ I	(2e)	3 days	34	28	42
(1c)	MeI	(2f)	2 weeks	30	35	50

^a 0.002 mol of the imine and 0.002 mol of the alkyl iodide in the presence of 0.002 mol of HMPA and a ten fold volume of ether. Reactions without HMPA were slow. ^b Elemental analyses of all products were satisfactory. ^c Amounts of imines or products were measured using *cis*- or *trans*-decalin as internal standard for g.l.c. analyses.

salt, and spectra due to compounds other than (1a) or (2a) were observed. Evaporation of the solvent *in vacuo* in order to isolate the intermediate gave a mixture whose spectrum showed obvious contamination from considerable amounts of (2a). This fact indicates the notable tendency of the intermediate to transform to the betaine, which makes isolation of the intermediate impossible.

Although some 3-oxidopyridinium betaines have been reported to rearrange to give 3-alkoxypyridine,^{1b} such a rearrangement was not observed with the betaines (2). Although protonation of (2) to afford water-soluble compounds was not observed under basic or neutral conditions, treatment of (2) with 0.1 M HCl (aq.) converted the betaines into water-soluble compounds. The short distance between N⁺ and O⁻ most likely contributes to the stability of betaines (2).

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