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-diaminocyclobutendiylium-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.

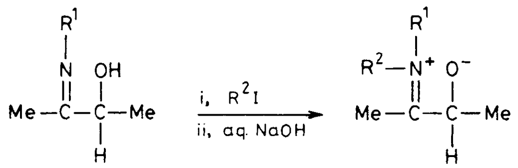
The imines (**1a**)—(**1c**) have not been reported and they were prepared by the following procedure. A mixture of 3-hydroxybutan-2-one (acetoin) (0.1 mol), propylamine (0.1 mol), and benzene (20 ml) was kept at room temperature for 15 h and then distilled under reduced pressure to give crude 3-(propylimino)butan-2-ol (**1a**) [39%, ^{1}H n.m.r. (*J* in Hz) δ 0.91 (t, 3H, *J* 6.5, $CH_2CH_2CH_3$), 1.24 (d, 3H, *J* 7.0, CH_3CHOH), 1.35—1.67 (m, 2H, $CH_3CH_2CH_2$), 1.95 (s, 1H, OH), 2.16 (s, 3H, $CH_3C{=}N$), 2.48 (t, 2H, *J* 7.0, $CH_3CH_2CH_2$), and 3.34 (q, 1H, *J* 7.0, CH_3CHOH); 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. ^{1}H 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**) [^{1}H n.m.r. (*J* in Hz) δ 0.93 (t, 3H, *J* 7.5, $CH_2CH_2CH_3$), 1.10 (d, 3H, *J* 7.0, CH_3CHO^-), 1.51 (sextet, 2H, *J* 7.5, $CH_3CH_2CH_2$), 2.21 and 2.24 (2 × s, 3H for each, $CH_3C{=}N^+CH_3$), 2.38 (t, 2H, *J* 7.5, $CH_3CH_2CH_2$), and 3.24 (q, 1H, *J* 7.0, CH_3CHO^-); ν_{max} 1705s cm^{-1}; *m/z* 141 (M − 2H), 100 ($M - CH_3CHO^- + H$), 58 ($M - Pr^n - CH_3CHO^- + 2H$), and 43 ($Pr^n$)].

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**) [^{1}H n.m.r. (*J* in Hz) δ 0.93 (t, 3H, *J* 7.5, $CH_2CH_2CH_3$), 1.10 (d, 3H, *J* 6.5, CH_3CHO^-), 1.50 (sextet, 2H, *J* 7.5, $CH_3CH_2CH_2$), 2.30 (s, 3H, $CH_3C{=}N^+$) 2.45 (t, 2H, *J* 7.5, $CH_3CH_2CH_2$), 3.05—3.25 (m, 2H, $CH_2CH{=}CH_2$), 3.51 (q, 1H, *J* 6.5, CH_3CHO^-), 5.20—5.48 (m, 2H, $CH_2CH{=}CH_2$), and 5.76—6.10 (m, 1H, $CH_2CH{=}CH_2$); ν_{max} 1710s cm^{-1}; *m/z* 167 (M − 2H), 126 ($M - CH_3CHO^- + H$), 84 ($M - Pr^n - CH_3CHO^- + 2H$), and 43 ($Pr^n$)].

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 × product/(imine used − imine unchanged). The six betaines showed weak u.v. absorption; (**2a**) λ_{max} (EtOH) 305 nm, (ε 130.5 mol^{-1} l 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 ^{1}H n.m.r. spectroscopy using benzene as solvent in order to ascertain the possible intervention of a hydroxy immonium



(**1**) (**2**)

a; $R^1 = Pr^n$
b; $R^1 = Pr^i$
c; $R^1 = Bu^t$

a; $R^1 = Pr^n$, $R^2 = Me$
b; $R^1 = Pr^n$, $R^2 = Et$
c; $R^1 = Pr^n$, $R^2 = CH_2{=}CHCH_2$
d; $R^1 = Pr^i$, $R^2 = Me$
e; $R^1 = Pr^i$, $R^2 = CH_2{=}CHCH_2$
f; $R^1 = Bu^t$, $R^2 = Me$

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† 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^2I	Product[b]	Reaction time	Unchanged imine, %[c]	% Yield[c] Actual	% Yield[c] Corrected
(**1a**)	MeI	(**2a**)	5 h	6	24	26
(**1a**)	EtI	(**2b**)	1 week	9	20	22
(**1a**)	$CH_2=CH-CH_2I$	(**2c**)	15 h	20	36	45
(**1b**)	MeI	(**2d**)	24 h	11	28	31
(**1b**)	$CH_2=CH-CH_2I$	(**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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