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BASE CATALYSED DECOMPOSITION OF OXAZIRIDINES TO YIELD N-UNSUBSTITUTED ALDIMINES

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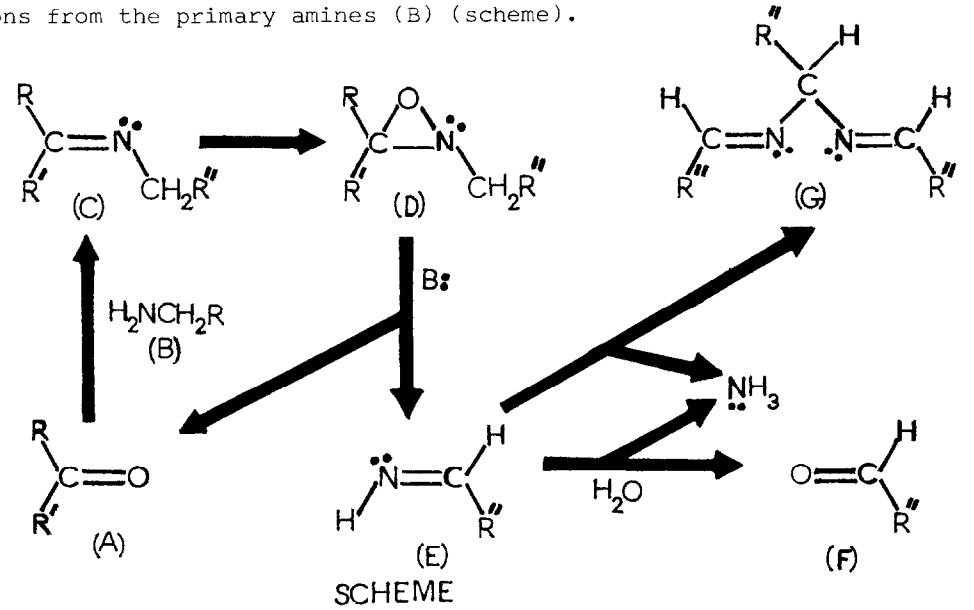
Summary: A range of oxaziridines bearing an α-hydrogen atom on the N-alkyl substituent react with tertiary amines at ambient temperature to yield N-unsubstituted aldimines.

The dehydrogenation of primary amines to yield highly unstable imine intermediates under oxidative conditions has been postulated to account for the formation of aldehydes (and ketones) using either chemical[1] or enzymatic[2,3,4] oxidants. Among the latter, hepatic microsomal fractions[2] and monoamine oxidases[3,4] are both reported to catalyse the dehydrogenation of primary amines (RCH_2NH_2) in the presence of dioxygen to yield N-unsubstituted aldimines (RCH=NH). D- and L- amino acid oxidases[4] similarly catalyse the oxidative deamination of α-amino acids to pyruvic acids via N-unsubstituted ketimine intermediates. The instability of these aldimines[5] and ketimines (which hydrolyse spontaneously in aqueous solution) has to date precluded their isolation after either the chemical or enzyme catalysed oxidation of the parent primary amines.

In the present communication is reported the synthesis and isolation of several N-unsubstituted aldimines (E) obtained indirectly under oxidative conditions from the primary amines (B) (scheme).



SCHEME

The N-alkyl aldimines and ketimines (C) (prepared by the condensation of A and B as previously reported[6,7]) upon peroxyacid oxidation yielded a range of oxaziridines[6,7] which were purified by column chromatography (silica-gel) prior to treatment with 1,4-diazabicyclo[2.2.2]octane (DABCO) or 1,5-diazabicyclo[4.3.0] non-5-ene (DBN).

Previous literature reports on the base[8,9] (and acid[10]) catalysed decomposition of oxaziridines bearing an α-hydrogen atom on the N-alkyl group indicated that aldehydes (or ketones) and ammonia are the major products. While the intermediacy of unstable N-unsubstituted imines has been proposed[9], the reaction conditions employed did not permit the isolation or detection of the aldimine intermediate.

Addition of DABCO or DBN (2 drops of a 20% solution in CCl_4 or toluene-d_8) to oxaziridines (D) (0.1 g in 0.5 ml CCl_4 or toluene-d_8) at ambient temperature rapidly produced a range of imine products (Table) depending on the nature of the group R".

(i) When R" was $-CH=CH_2$, or $-CMe=CH_2$, the products were the aldimines (E), which were purified by trap to trap distillation (0.001 mm). Since these compounds were previously reported[12] to decompose at $-70^{\circ}C$ in the neat state they were identified by their 90 MHz nmr spectra in CCl_4 at $20^{\circ}C$ and in toluene-d_8 at $-70^{\circ}C$ (on which extensive decoupling experiments were performed), and by their hydrolysis to the corresponding aldehydes by aqueous acid.

(ii) When R" = Ph or 4-Cl-C_6H_4, the initial products were the benzaldimines (E), identified by nmr and hydrolysis. On standing in solution, these were transformed over a period of minutes to hours into the hydrobenzamides[14,15] (G), identified by nmr comparison with authentic samples prepared from the aldehydes and methanolic NH_3.

(iii) When R" = ^{i}Pr or ^{t}Bu, the reaction was less facile, DBN but not DABCO giving the products rapidly at ambient temperature. The aldimines (E) could not be directly observed, the first products visible in the nmr being the known[12] bis-aldimines (G), and in the case of R" = ^{i}Pr also the compound $Me_2C=CH.N=CH.CHMe_2$.

Initial attempts to effect the base catalysed decomposition of analogous oxaziridines (D) derived from ketone (A : fluorenone or benzophenone) and amine (B : benzhydrylamine or α-phenylethylamine) using either DABCO or DBN at room temperature were unsuccessful. Since oxaziridines bearing the N-CHMePh substituent have been reported to give aldehydes, ketones and ammonia using stronger basic conditions[8,9] it is probable that unstable N-unsubstituted imines (E) were involved.

The results in the Table confirm the proposal[9,11] that oxaziridines bearing an α-hydrogen atom on the N-alkyl group can be converted into aldimines under basic conditions, by using a tertiary amine and an oxaziridine capable of transformation into a conjugated aldimine. The low stability observed for the N-unsubstituted aldimines (E) in the present work, even under these mild experimental conditions, is in agreement with the suggestion of Nielsen et al[5,13]

that unsubstituted aldimines are generally too reactive to permit their isolation in the neat state and that earlier reports of their synthesis, isolation and purification were erroneous. The oxaziridine ⟶ N-H aldimine reaction is shown to be general for oxaziridines derived from both N-alkyl aldimines and ketimines and adds to the relatively small number of known reactions of oxaziridines.

In conclusion, the enzyme catalysed transformation of primary amines into N-H substituted aldimines under oxidative conditions may now be emulated chemically at ambient temperature via N-alkyl imine and oxaziridine intermediates. Further work is in progress to fully examine the scope of this synthetic route and the reaction mechanism.

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TABLE: Aldimine and other products from base catalysed decomposition of oxaziridines.

	Oxaziridine (D) R	R'	R"	Aldimine (E)	Other identified products
1.	-Fl[a]-		CH_2=CH-	NH_E=CH_D-CH_C=$CH_A H_B$[b]	
2.	Ph	Ph	CH_2=CH-	" "	
3.	-Fl[a]-		CH_2=CMe-	NH_E=CH_D-CMe=$CH_A H_B$[c]	(F)
4.	"	"	Pr^i-	[NH=CH-Pr^i][d]	(G)
5.	"	"	Bu^t-	[NH=CH-Bu^t][d]	(G)
6.	"	"	Ph-	NH_E=CH_D-Ph[e]	(G)
7.	"	"	4-ClC_6H_4-	NH=CH—C_6H_4Cl-4	(G)
8.	4-NP[f]	H	Ph	NH=CH—Ph	(G)

a. Fl = fluorenyl;

b. nmr (at -70°C, $C_6D_5.CD_3$,) H_A(5.15,d), H_B(5.25,d), H_C(6.54,m), H_D(7.50, d of d), H_E(9.74,d), J_{AC} 17Hz, J_{BC} 10 Hz, J_{DC} 9 Hz, J_{DE} 16 Hz;

c. nmr (at -70°C, $C_6D_5.CD_3$,), Me(1.72,s), H_A(4.95,d), H_B(5.15,s), H_D(7.45,d), H_E(9.35,d), J_{DE} 16 Hz;

d. not detected by nmr.

e. nmr (at -70°C, $C_6D_5.CD_3$), H_D(7.76,d), H_E(9.70,d), J_{DE} 16Hz

f. 4-NP = 4-Nitrophenyl.

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