

NOVEL NITROSATION OF CYCLIC N-ALKYL ENAMINES<sup>1</sup>

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We have recently reported the synthesis of oximino-macrolides and N-acetyl oximino-lactams by the hydrolytic nitrosation of the corresponding cyclic enol-ethers and N-acetyl enamines.<sup>2,3</sup> In contradistinction, the same reaction when attempted with the cyclic N-ethyl enamines(I),<sup>4</sup> yielded the oximino enamines(IV) instead of the desired oximino-lactams(III).<sup>5</sup> Only once, in one case (I,n=2), has the oximino-lactam(III,n=2) been also isolated, although in very low yield.

The new compounds were characterized by elemental analysis and i.r. and <sup>1</sup>H n.m.r. spectra.<sup>6</sup> Some of their physical data are recorded in table 1. The n.m.r. spectra of oximino-enamine(IV,n=2) is reproduced in fig. 1 for quick inspection. The n.m.r. spectra of other oximino-enamine homologs(IV; n=3 and 4) show broad similarity to fig. 1; the saturated methylene region( $\delta$ 1.5-2.0) having 2 and 4 more hydrogens, respectively.

The drastic difference in the reaction behaviour of the N-alkyl enamines is due to their increased basicity over the N-acetyl analogs and the enol-ethers. The first reaction in the present series seems to be the formation of the N-nitrosoammonium ion (A), which then transfers the nitroso group to the C-atom bearing a 1:3 peri relationship to it (see scheme). To check this point of view, the peri position was substituted to prevent oxime formation. In accordance with expectation, the enamine mixture(V)<sup>4</sup> proved unreactive towards nitrosation<sup>5</sup> and was largely recovered on elaboration of the reaction mixture. In contrast, the N-acetyl enamine mixture(VI) reacted normally to furnish the expected oximino-lactam(VII).

Evidently, the behavior of N-alkyl enamines towards nitrosation is like that of the tertiary amines.<sup>7</sup> Smith and Loepky have demonstrated the formation of N-nitrosoammonium salts in the nitrosation of tertiary amines.<sup>7a</sup> In the present case, a circumstantial evidence for N-nitrosation was the immediate appearance of yellow colour instead of the blue, as noticed in our earlier studies involving C-nitrosation.<sup>2,3</sup> Moreover, tertiary amines in highly acidic solution (pH below 3) and quaternary ammonium salts are known to be unreactive towards nitrosation.<sup>7</sup> Accordingly, in the present case, the nitrosation failed in solutions with pH below 3 and the starting material could be recovered, though with a considerable work-up loss. In nitrosation experiments conducted with 1.1 equivalent of perchloric acid, the perchlorate of enamine (I; n=2: colorless needles, m.p. 240-241<sup>o</sup>; max.(KBr)1672 and 1087 cm<sup>-1</sup>) could be directly isolated after evaporation of the nitrosation mixture.

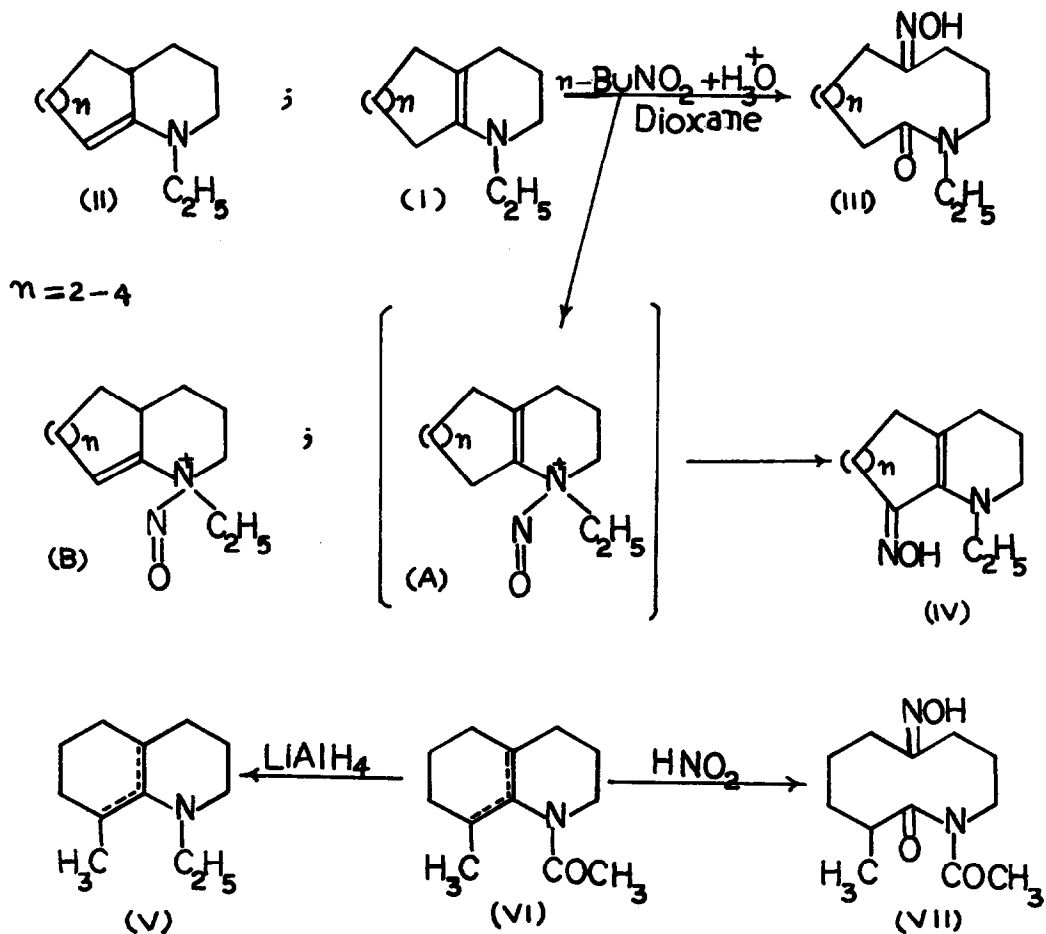
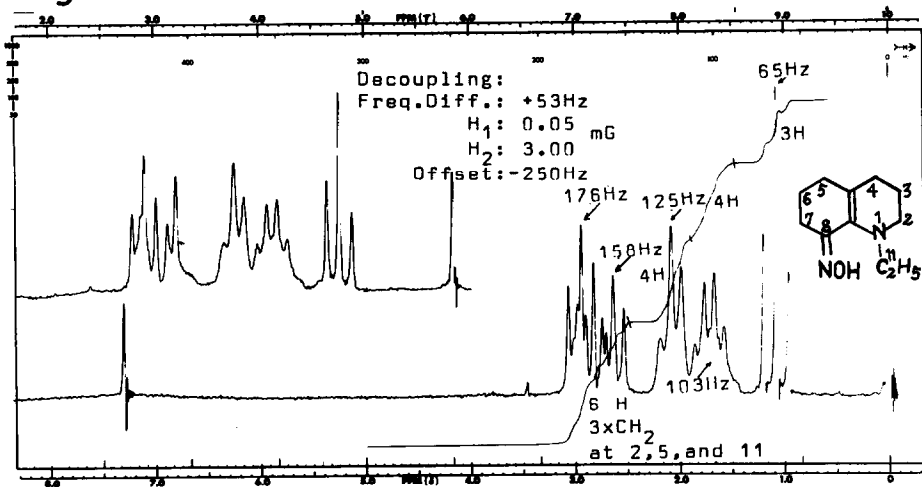
It is tempting to assume that the reaction proceeds through the isomeric form (II), but there was no detectable evidence (n.m.r.) for its presence in the starting material even after refluxing for a couple of hours in chloroform or ethanol, containing acid or base.

Nitrosation studies at different controlled pH as well as those directed to shed more light on the mechanism of the reaction are under way and will be reported in the detailed publication.

TABLE 1

Compound	M.P.	C ; H ; N %	$\nu_{\max.} (\text{cm}^{-1})$
(IV;n=2)	151-152 <sup>o</sup>	Found:67.95; 9.11; 14.27	3135,1631,1610
C <sub>11</sub> H <sub>18</sub> N <sub>2</sub> O		Calcd:68.01; 9.34; 14.42	
(IV;n=3)	125-127 <sup>o</sup>	Found:69.11; 9.49; 13.63	3226,1631,1618
C <sub>12</sub> H <sub>20</sub> N <sub>2</sub> O		Calcd:69.19; 9.68; 13.45	
(IV;n=4)	101-103 <sup>o</sup>	Found:70.30; 9.82; 12.44	3175,3067,1656,1634
C <sub>13</sub> H <sub>22</sub> N <sub>2</sub> O		Calcd:70.23; 9.97; 12.60	
(VII)	140-142 <sup>o</sup>	Found:59.72; 8.14; 11.48	3344,1724,1661,1550
C <sub>12</sub> H <sub>20</sub> N <sub>2</sub> O <sub>3</sub>		Calcd:59.98; 8.39; 11.66	

Fig.1



## REFERENCES AND NOTES

1. G.A.L. Ferreira, J.R. Mahajan, H.C. de Araújo e B.J. Nunes, *Resumos S.B.P.C., Ciência e Cultura*, 25, 118 (1973).
2. J.R. Mahajan, G.A.L. Ferreira, and H.C. Araújo, *Chem. Comm.*, 1078 (1972).
3. J.R. Mahajan, G.A.L. Ferreira, H.C. Araújo, and B.J. Nunes, *Synthesis*, 313 (1973).
4. The N-ethyl enamines were prepared from the corresponding N-acetyl enamines (ref. 3) by reduction with  $\text{LiAlH}_4$ . Enamine (V) was obtained as a 17:83 mixture (n.m.r.) of the  $\Delta^{8,9}$  :  $\Delta^{9,10}$  compound.
5. The nitrosation experiments were conducted between 10 to 25<sup>o</sup> using equimolar quantities of the enamine and n-butyl nitrite in aqueous dioxane solution, containing a drop or two of 10% hydrochloric acid (pH ca. 8-9).
6. The infrared spectra (KBr disc) were taken on a Perkin Elmer 137 instrument. The <sup>1</sup>H n.m.r. spectra ( $\text{CDCl}_3$ ) were taken on a Varian A60-D instrument. The elemental analysis were carried out by Alfred Bernhardt, West Germany.
7. (a) P.A.S. Smith and R.N. Loeppky, *J. Am. Chem. Soc.*, 89, 1147 (1967); (b) G.E. Hein, *J. Chem. Educ.*, 40, 181 (1963). These two papers describe an instructive account of the over a century-old controversy about the nitrosation of tertiary amines.