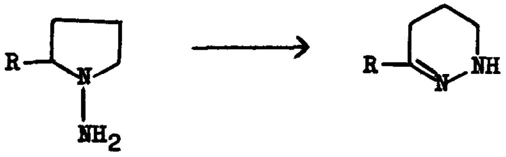
Tetrahedron Letters No. 52, pp 5025 - 5026.
0040-4039/79/1222-5025$02.00/0

NOVEL RING ENLARGEMENT OF 1-AMINOPYRROLIDINES[1]

N. Viswanathan* and A.R. Sidhaye
CIBA-GEIGY Research Centre, Goregaon, Bombay 400 063
India

Abstract : 1-Aminopyrrolidines undergo oxidative ring enlargement to 1,4,5,6-tetrahydropyridazines on treatment with silica gel in chloroform-methanol.

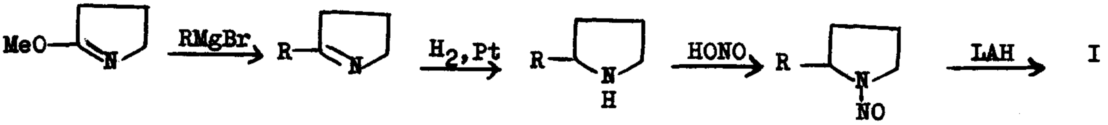
During a study of the reactions of 1-aminopyrrolidines (I), we have observed the facile oxidative ring enlargement of these to 1,4,5,6-tetrahydropyridazines (II). Experimentally, the aminopyrrolidine is either chromatographed on a column of silica gel in chloroform-methanol (98:2) or it is stirred overnight with silica gel in chloroform-methanol (98:2). The yields of isolated products, without optimisation, are in the range of 40-70%.



I II

a : H
b : phenyl
c : p-tolyl
d : p-anisyl
e : p-fluorophenyl

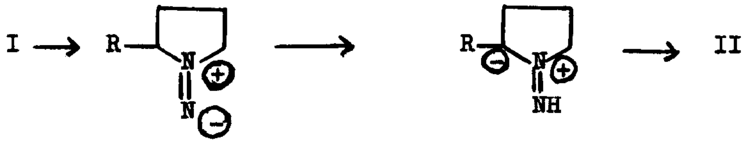
Whereas 1-aminopyrrolidine itself was available commercially, compounds Ib-Ie were prepared by the sequence outlined below[2]:



The products IIb-IIe were characterized as their tosylates, compound IIa alone being characterised as the adduct with phenylisothiocyanate. The structures of compounds IIb-IIe were confirmed by direct comparison with the authentic compounds prepared by reacting the corresponding γ-chlorobutyrophenones with hydrazine.

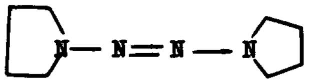
$$R.CO.(CH_2)_3.Cl \quad + \quad NH_2.NH_2 \longrightarrow II$$

The reaction proceeds as well in an atmosphere of nitrogen as in an atmosphere of oxygen. It does not proceed well when methanol alone is used as the solvent. The ring enlargement involves oxidation of the aminopyrrolidines by chloroform on the silica gel surface to the diazenes[3,4] (aminonitrenes) (III) and their subsequent re-arrangement.



III

The reaction represents a novel and facile method of generating the diazene. The fate of the diazenes is known to depend on the reaction conditions. It is noteworthy that the oxidation of 1-aminopyrrolidine Ia with mercuric oxide[5] which generates the diazene III (R=H) gives only the tetrazene IV and not the tetrahydropyridazine IIa.



IV

A second mode is the fragmentation of the diazene leading to the elimination of nitrogen and the formation of cyclobutanes[6]. The present is a special case of the third course, the diazene-hydrazone rearrangement[3,7].

The only two known cases[8] of the transformation of a pyrrolidine to a tetrahydropyridazine are the reaction of pyrrolidine with Angeli's salt (Na_2ONNO_2) and the fragmentation of the sodium salt of 1-benzenesulphonylaminopyrrolidine in protic solvents.

References and Notes :

1. Contribution No.564 from CIBA-GEIGY Research Centre.
2. Satisfactory analytical and spectral data were obtained for new compounds.
3. D.M. Lemal, F. Menger and E. Coats, J. Am. Cnem. Soc., 1964, 86, 2395.
4. R.A. Abramovitch and B.A. Davis, Chem. Rev. 1964, 64, 174.
5. D.M. Lemal, T.W. Rave and S.D. McGregor, J. Am. Chem. Soc., 1961, 85, 1944.
6. C.G. Overberger, M. Valentine and J.P. Anselme, J. Am.Chem. Soc., 1969, 91, 687.
7. W.H. Urry, and C.Ikoku, Abstracts of papers presented at the 146th National Meeting of the American Chemical Society, Denver, Colo., Jan.1964, p.25c.
8. D.M. Lemal and T.W. Rave, J. Am. Chem. Soc., 1965, 87, 393.

(Received in UK 2 October 1979)