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SYNTHESIS AND REACTIONS OF 2-AMINO-1-AZIRINES

Maurice Rens and Léon Ghosez
Laboratoire de Chimie Organique de Synthèse
Université Catholique de Louvain, 96, Naamsestraat, Louvain, Belgium

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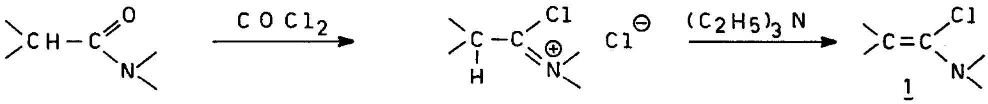
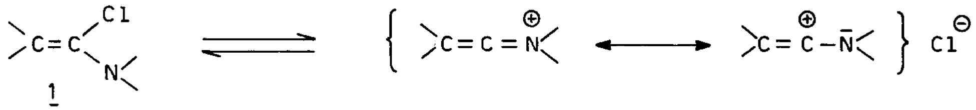
α-Chloroenamines (1) 1 have been shown to be readily available from the reaction of phosgene with tertiary amides followed by elimination of HCl with weak bases.

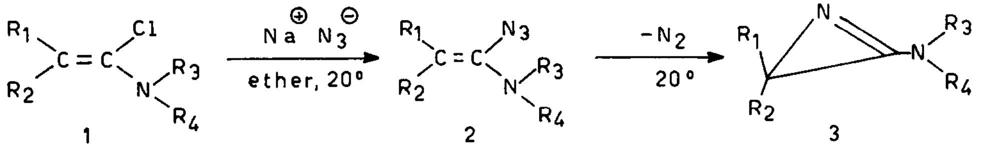


According to their formulation as keteniminium or aminovinylium chlorides (2,3), alkylsubstituted α-chloroenamines react readily in substitution reactions involving reagents of variable nucleophilicity (1).



We wish to report the reaction of alkylsubstituted α-chloroenamines with azide ion which gives the previously unknown 2-amino-1-azirines. Together with the recently described aziridine imines (4), these 2-amino-1-azirines are the first representatives of three-membered ring amidines.

Stirring a suspension of sodium azide (3 equivalents) in ether containing 1 equivalent of the α-chloroenamines 1 a-c for a few hours at room temperature yields the corresponding 2-amino-1-azirines 3 a-c and the theoretical amount of nitrogen as measured with a gas burette. The reaction probably involves the intermediate formation of α-azidoenamines 2 a-c ; in the case of the reaction of 2 c with azide ion, this hypothesis was confirmed by the appearance of an absorption band at 2140 cm^{-1} which gradually disappeared while nitrogen was evolved.



1 2 3

a : $R_1 = R_2 = -CH_3$; $R_3 = R_4 = CH_3-CH_2-$ 94 %

b : $R_1 = R_2 = -CH_3$; $R_3, R_4 = -(CH_2)_5-$ 95 %

c : $R_1, R_2 = -(CH_2)_5-$; $R_3 = R_4 = CH_3-CH_2-$ 92 %

These aminoazirines are colourless, thermally unstable liquids which show the following properties :

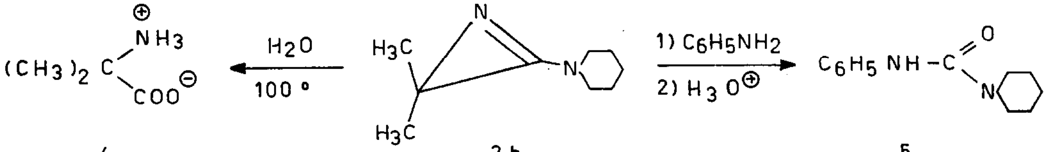
3 a : b.p. 42°/1 mm. Mass spectrum : m/e $(M^+)=140$ (13.5 %). IR (film, cm^{-1}): 1768 (C=N stretching). NMR ($CDCl_3$, δ) : 1.16 (t, 6 H, CH_3 groups, J=7.1 cps), 1.3 (s, 6 H, ring CH_3), and 3.24 (q., 4 H, CH_2 groups).

3 b : b.p. 48-49°/0.3 mm. Mass spectrum : m/e $(M^+)=152$ (68.3 %). IR (film, cm^{-1}) : 1768 (C=N stretching). NMR ($CDCl_3$, δ) : 1.3 (s, 6 H, ring CH_3), 1.6 (m, 6 H), 3.35 (broad m, 4 H, CH_2 groups α to the piperidine nitrogen)

3 c : b.p. 62-63°/0.2 mm. Mass spectrum : m/e $(M^+)=180$ (71 %) IR (film, cm^{-1}): 1768 (C=N stretching). NMR ($CDCl_3$, δ) : 1.35 (t, 6 H, CH_3 groups, J=7.6 cps), 1.63 (m, 10 H, ring CH_2), 3.41 (q, 4 H, CH_2 groups).

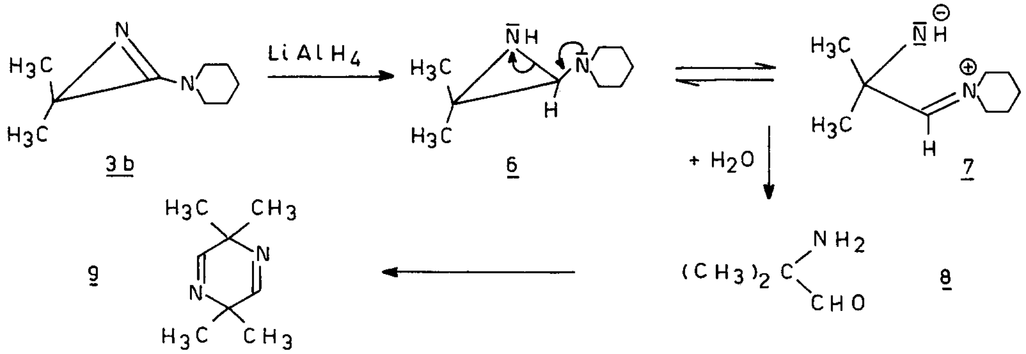
These data are consistent with the proposed structures which were further confirmed by chemical evidence.

Hydrolysis of 3 b in boiling water gave the crystalline aminoacid 4 (42 %) identified by comparison with an authentic sample. By heating 3 b for a short period in an excess of aniline at 170° and hydrolysing the reaction mixture with 2N HCl, ureide 5 was formed in 17 % yield and was identified by comparison with an authentic sample prepared from piperidine and phenylisocyanate.

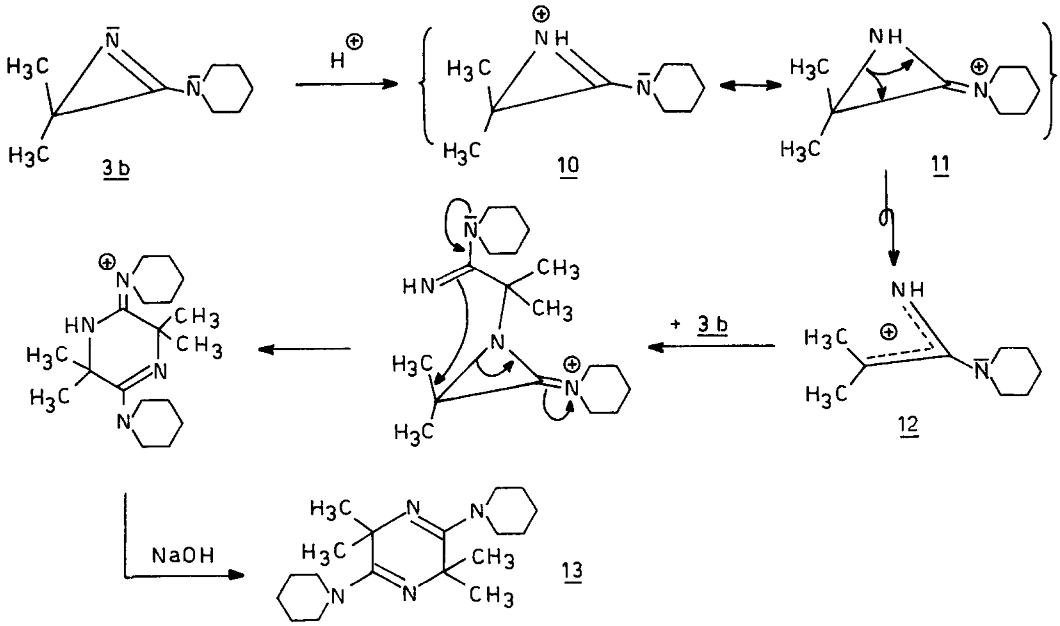


4 3 b 5

These observations are analogous to the behaviour of simpler azirines studied by Hassner (5) and Smolinsky (6). The addition of 1 equivalent of lithium aluminium hydride to an ether solution of 3 b resulted in a very exothermic reaction. Hydrolysis of the mixture gave 3,3,6,6 tetramethyldihydropyrazine, 9 m.p. 84°3 in 55 % yield. A likely pathway for this reduction involves the primary formation of a 2-amino-aziridine 6 (7). The instability of these probably results from their tendency to undergo ring opening to form the stabilised 1,3 dipole 7 . Addition of water and elimination of piperidine gives the aminoaldehyde which dimerises to 9 .



The protonation of 2-amino-1-azirines is an obvious source of 2-amino-1-azirinium ions 10 which we can also formulate as iminium forms 11 of α-lactams. As expected these cations are very unstable and undergo a very rapid rearrangement analogous to the cyclopropyl-allyl transformation. In the absence of other nucleophiles, the opened cations 12 react readily with a second molecule of 2-amino-1-azirine to give quantitatively a dihydropyrazine derivative. When an ether solution of HCl was gradually added to 3 b in ether, an immediate precipitation occurred. The free base 13 was isolated by treatment of the salt with 2N NaOH. The ready availibility of 2-amino-1-azirines as well as their possible transformations to various interesting intermediates such as the aminoaziridine or aminoazirinium cations make them promising reagents for the synthetic chemist. Other aspects of the chemistry of these reactive molecules are currently investigated in these laboratories.



3b 10 11 12 13

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