Formal Dyotropic Rearrangements of *N*-Chloroamines catalysed by Alumina

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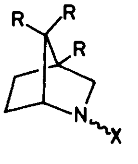
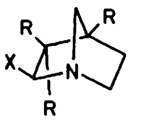
Rearrangement of *N*-chloro-2-azabicyclo[2.2.1]heptanes, [2.2.1]hept-5-enes, and [2.1.1]hexanes involving 1,2-migration of an sp^3 or an sp^2 carbon to nitrogen accompanied by 2,1-migration of chlorine occurs cleanly and efficiently on chromatographic alumina.

1,2-Migration of a neighbouring carbon during solvolytic loss of a nucleofuge from carbon has seen intense study, typically in the norbornyl system. The corresponding reaction involving loss of a nucleofuge from nitrogen and 1,2-migration to nitrogen has also been observed in the Ag^I-assisted methanolysis of *N*-chloroamines in which the skeletally rearranged carbenium ion is generally intercepted by an appropriate nucleophile such as MeOH solvent.[1a] An unusual example is provided by (**1a**) which rearranges in MeOH–AgNO$_3$ to give only small amounts of the methyl ether (**2c**) [and some amine (**1c**)]; the major product (**2a**) results from rearrangement with *retention* of chlorine.[1b] We now report the use of chromatographic alumina as a mild catalyst which achieves clean rearrangement involving retention of chlorine in a reaction which appears to be general for a wider range of strained *N*-chloroazabicycles.

After introduction of (**1a**)[2a] onto a column of neutral alumina[3] in the minimum of CH$_2$Cl$_2$, the column was eluted with petrol and the flow was halted after 5 min. After 3 h, the column was then simply stripped with dry MeOH and the solvent evaporated to leave only (**2a**) as a white solid, m.p. 120—122 °C, in 94% yield with no other product. In a similar manner, the trinor system (**1b**) was converted into (**2b**) as the sole isolated product in 70% yield.[1c]





(**1a**) R = Me, X = Cl ⟶ (**2a**) R = Me, X = Cl

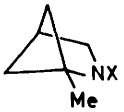
(**1b**) R = H, X = Cl ⟶ (**2b**) R = H, X = Cl

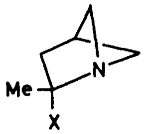
(**1c**) R = Me, X = H

(**2c**) R = Me, X = OMe

(**2d**) R = H, X = OMe

(**2e**) R = H, X = ONO$_2$



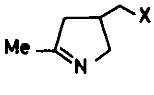


(**3a**) X = Cl ⟶ (**4a**) X = Cl

(**3b**) X = H

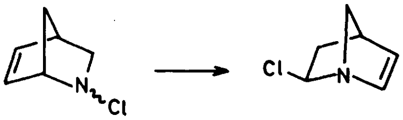
(**4b**) X = + ve charge

(**4c**) X = OMe



(**5a**) X = OMe

(**5b**) X = OH



(**6**) (**7**)

Rearrangement of 1-methyl-2-chloro-2-azabicyclo[2.1.1]-hexane (**3a**) occurred [alumina; 30 min] to give (**4a**),† a derivative of the previously unrecorded 1-azabicyclo-[2.1.1]hexane ring system, in 70% yield.[2b] The retention of chlorine in (**4a**) is a most surprising result. On the basis of earlier work[1a] it might reasonably be expected that the presence of a methyl group on an α-N carbon would encourage the formation of a discrete tertiary carbenium ion (**4b**) and that this ion would be intercepted by solvent [*e.g.* MeOH to give (**4c**)]. In the absence of any detectable chlorine-free products, it must be assumed that rearrangement is complete before elution with MeOH and that any water present on the alumina is an ineffective trap. The reaction may be viewed formally as a dyotropic shift[4] or, alternatively, as producing an intimate ion pair in which the build-up of positive charge is, predictably, at carbon rather than nitrogen. In any event, there appears to be effective σ-bond participation in the reaction together with a most effective retention of chlorine in the product. In contrast, treatment of (**3a**) with AgBF$_4$ in MeOH gave a precipitate of AgCl and no detectable chlorine-containing organic material; the major isolated compound was the pyrroline (**5a**)† which may reasonably arise *via* removal of chloride ion and attack by methanol at C-5 or C-6 of the tertiary carbenium ion (**4b**) with relief of ring strain. The relative mildness of the alumina catalysis is thus emphasised. The *C*-chloroamine (**4a**) is relatively stable in AgBF$_4$–MeOH and is therefore not a precursor of (**5a**) in the reaction above. Treatment of (**4a**) with anhydrous HCl gave a crystalline salt but attempted regeneration of (**4a**) with dilute aqueous base led, again, to C–N bond cleavage giving (**5b**).†

The participation of π-electrons in displacement of halide from nitrogen has hardly been studied[5,6] despite the wide occurrence of π-participation in displacements from carbon. The reaction of 2-chloro-2-azabicyclo[2.2.1]hept-5-ene (**6**)[2a] with AgNO$_3$–MeOH is complex.[6] In contrast, treatment of (**6**) with alumina followed by elution with MeOH gave only the rearrangement product (**7**)† as a pale yellow oil in 70% yield. The observation of migration of an sp^2 carbon to an incipient electron-deficient nitrogen is of interest in view of the recent report of an unusual 1,2-migration of an acyl group in the rearrangement of an *N*-chlorodiaziridine.[7]

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† The structures of all new compounds have been confirmed by spectroscopic means; details will be reported in the full paper.

Further study may throw light on the controversial question of homolytic *vs.* heterolytic mechanisms in the rearrangements of *N*-chloroamines and, in particular, on the proposed intermediacy of nitrenium ions in these reactions.[8] This formal dyotropic rearrangement of *N*-chloro- to *C*-chloro-amines induced by alumina appears to be a general, efficient reaction in strained systems‡ and offers a practical approach to functionalised derivatives of saturated and unsaturated, strained bicyclic systems having bridgehead nitrogen.

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References

1 (a) P. G. Gassman, *Acc. Chem. Res.*, 1970, **3**, 26, and references cited therein; (b) P. G. Gassman and R. L. Cryberg, *J. Am. Chem. Soc.*, 1969, **91**, 2047; (c) conversion of (**1b**) into (**2b**) has also been reported to occur (footnote 17 in ref. 1a). We found that treatment of (**1b**) with $AgNO_3$–MeOH gave a pale yellow oil containing small amounts of (**2d**) and (**2e**); preparative g.l.c. was necessary to separate pure (**2b**).

2 (a) For preparation of (**1a**), (**2a**), and (**6**) see J. R. Malpass and N. J. Tweddle, *J. Chem. Soc., Perkin Trans.* 2, 1978, 120. In all cases there is rapid inversion at nitrogen. The preferred invertomers are *endo*-(**1a**) >95%; *exo*-(**1b**) 75%; *endo*-(**6**) 88%. Thus the reactions occur *via* the *exo*-invertomer even in (**1a**) and (**6**) where the *endo*-invertomer is preferred overwhelmingly; (b) compound (**3b**) was prepared from 1-ethoxycarbonyl-2-azabicyclo[2.1.1]hexane (*cf.* M. C. Pirrung, *Tetrahedron Lett.*, 1980, 4577; P. Hughes, M. Martin, and J. Clardy, *ibid.*, 4579) by sequential treatment with $LiAlH_4$; toluene-*p*-sulphonyl chloride–pyridine; $LiAlH_4$; H_2–Pd,C. It was converted into the *N*-chloroamine (**3a**) with aqueous sodium hypochlorite; (**3a**) was handled in $CFCl_3$ solution.

3 See G. Posner, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 487 for a review of organic reactions at alumina surfaces.

4 See M. T. Reetz, *Tetrahedron*, 1973, **29**, 2189 for a discussion of dyotropic rearrangements.

5 See M. L. Durrant and J. R. Malpass, *J. Chem. Soc., Chem. Commun.*, 1981, 1028.

6 M. L. Durrant, J. R. Malpass, and M. P. Walker, following communication.

7 S. N. Denisenko, G. V. Shustov, and R. G. Kostyanovsky, *J. Chem. Soc., Chem. Commun.*, 1983, 1275.

8 See A. Heesing and W. Herdering, *Chem. Ber.*, 1983, **116**, 1081 for references to recent mechanistic work, especially on the complex solvolysis reactions of *N*-tosyl azabicycles.

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‡ A degree of strain in the system seems to be essential. In preliminary attempts to achieve the corresponding rearrangement of 2-chloro-2-azabicyclo[2.2.2]octane on alumina, no material whatsoever was eluted from the column in methanol.