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HETEROLYSIS OF N-CHLORO-1,2,3,4-TETRAHYDRO-1,4-IMINONAPHTHALENES AND RELATED SYSTEMS; EFFECTS OF STRUCTURE AND OF SOLVENT ON REACTION PATHWAYS

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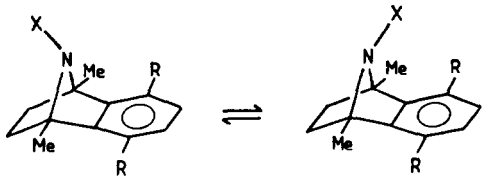
Summary Replacement of hydrogen by methyl at the 1,4-positions of 1,2,3,4-tetrahydro-1,4-iminonaphthalenes substantially modifies the Ag(I)-catalysed solvolytic behaviour of this system giving tetrahydrobenzazepine derivatives; small amounts of methanol in non-polar solvents have a profound effect favouring heterolytic, rather than homolytic, N-Cl cleavage. Methanoquinolines are produced via secondary rearrangement. Bridgehead methyl substituents also divert the reactions of N-chloro-1,4-dihydro-1,4-iminonaphthalenes, leading to quinoline derivatives.

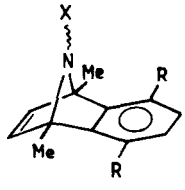
As part of our interest in the structure and the inversion process at nitrogen in derivatives of the 7-azabicyclo[2.2.1]heptane ring system[1] and in the chemistry of the derived N-chloroamines,[2] we have prepared the 1,4-dimethyl-substituted compounds (1)-(5).[3]



anti- (1) X = H
(2) X = Cl
(3) X = Br

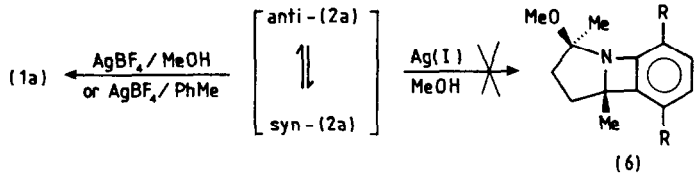
syn-

[a, R = OMe; b, R = H]



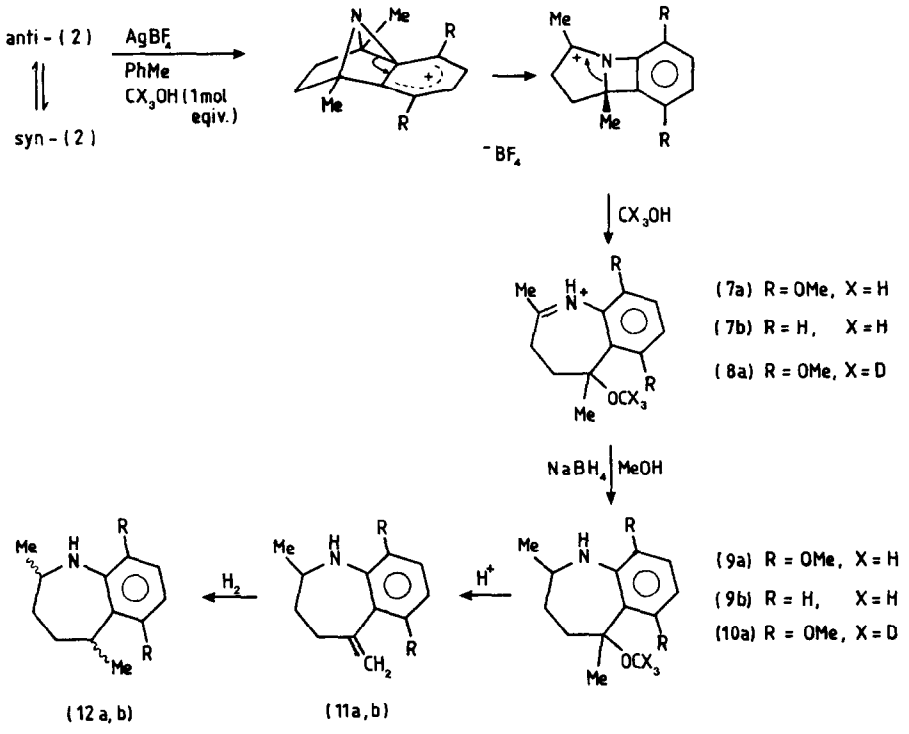
(4) X = H
(5) X = Cl

The N-chloroamine (2a)[3] was treated with Ag(I) in methanol in the expectation[2] that rearrangement would proceed entirely via the anti-Cl invertomer to yield the benzazetidine derivative (6) which was required for other work.



(6)

In fact, no (6) was observed. The only product was the 'parent' amine (1a) formed in 97% yield via homolysis of the NCl bond. An attempt to suppress homolysis using $AgBF_4$ in toluene[4] was unsuccessful, giving (1a) in 96% yield. However, when the same reaction was performed with $AgBF_4$ in toluene but with the addition of a small amount (ca. 1 mole equivalent) of methanol, the picture changed completely [Scheme 1].



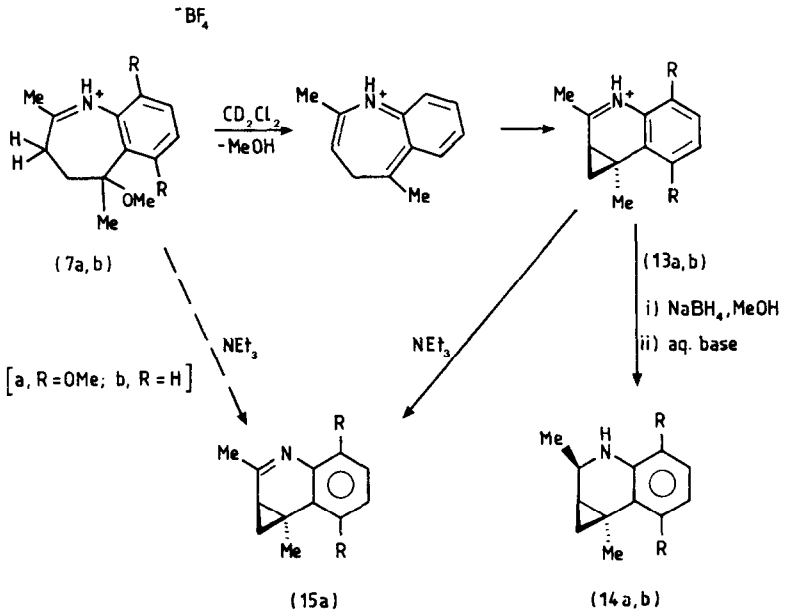
SCHEME 1

A precipitate was formed which on treatment with $NaBH_4$ in methanol gave the tetrahydrobenzazepine derivative (9a). The structure of (9a) was fully confirmed by ^{13}C and ^{1}H nmr including homonuclear spin-decoupling studies. That the methoxyl group originated from the methanol used in the first step (and not during the reduction in methanol) was confirmed by performing the heterolysis reaction in the presence of CD_3OH (1 mole equiv.) which gave (8a) and thence (10a). Thus, the first-formed precipitate was (7a) [68% isolated yield], a structure fully confirmed by its chemical and spectroscopic behaviour.

The presence of a small amount of methanol clearly encourages heterolysis at the expense of the, otherwise dominant, homolytic route.[5] The bridgehead methyl groups also alter the balance of reactivity, leading to the 7-ring iminium salt (7) rather than the isomeric salt of the more highly strained amine (6).

On standing in solution, (9a) lost methanol slowly to give (11a) [the reaction occurred immediately in the presence of trifluoroacetic acid to give the trifluoroacetate salt of (11a)]. Catalytic hydrogenation of (11a) yielded a 1:1 mixture of diastereoisomeric tetrahydrobenzazepine derivatives (12a) which could be partially separated by recrystallisation.

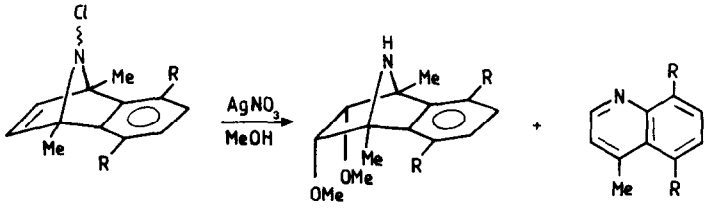
The iminium salt (7a) suffered rearrangement with loss of methanol on standing in CD_2Cl_2 solution; the liberation of methanol coincided with the appearance of upfield signals in the ^1H nmr spectrum at δ 0.74 typical of a cyclopropyl ring and occurred more rapidly in the presence of d-$_5$-pyridine. The product (13a) [94% yield] was converted quantitatively into the free 2,4-dimethyl-3,4-methano-5,8-dimethoxy-3,4-dihydroquinoline (15a) on treatment with triethylamine. The reduction of (13a) with $NaBH_4$ in methanol occurred with stereospecific attack from the less-hindered face to give (14a) [>95%; Scheme 2].



SCHEME 2

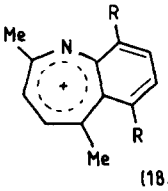
In like fashion, the N-chloroamine (2b) was treated with $AgBF_4$/toluene/methanol (1 mole equiv.) followed by immediate reduction with $NaBH_4$ in methanol to give (9b) in 31% overall yield together with 62% of (1b). The yield of (9b) could be raised to almost 50% by using the minimum of benzene solvent containing 2.5 molar equivalents of methanol.[6a] Further rearrangements/reductions of (2b) are summarised in Schemes 1 and 2. These reactions led, variously, to the separation of (9b), (14b) [2 diastereoisomers], (11b) [plus the 5-methyl-4-ene tautomer], and (12b); no attempt was made to optimise conditions or yields. A significant increase in the yield of rearranged products was obtained by using the N-bromoamine (3b).[6] The primary product (7b) was partially converted into (13b) on standing overnight; borohydride reduction then gave (9b), 56% and (14b), 17% (an isolated yield of heterolysis products totalling 73%). No attempt was made to maximise either the yield of (9b) by early work-up with borohydride, or the yield of (14b) by encouraging complete rearrangement of (7b) into (13b).

A syn/anti- mixture of the etheno-bridged N-chloroamine (5a) was prepared by chlorination at low temperature. This was stirred overnight at 0°C with $AgNO_3$ in MeOH to give a mixture of the amine (16a) [presumably via syn-(5a)][2] and, unexpectedly, 4-methyl-5,8-dimethoxyquinoline (17a) in good yield. The analogue (5b) reacted similarly to yield (16b) and (17b). The anti-invertomers of (5) and the benzazatropylium ions (18a) are probably implicated in the deep-seated rearrangements to (17); further mechanistic investigations are planned.



(5a,b) (16a,b) (17a,b)

[a, R=OMe; b, R=H]



(18a,b)

References

1. J.W. Davies, J.R. Malpass, J. Fawcett, L.J.S. Prouse, R. Lindsay, and D.R. Russell, J. Chem. Soc., Chem. Commun., in the press; J.W. Davies, J.R. Malpass, and R.E. Moss, Tetrahedron Letters, 1985, 26, 4533.

2. J.R. Malpass and M.L. Durrant, J. Chem. Soc., Chem. Commun., 1981, 1028.

3. Prepared by addition of the appropriate benzyne to N-trimethylsilyl-2,5-dimethylpyrrole followed by hydrolysis; hydrogenation gave the ethano-bridged compounds. Chlorination/bromination with NCS/NBS respectively provided the N-halo-compounds. We thank Mr Ian Dee for assistance with the preparation of (1b).

4. F.M. Schell and R.N. Ganguly, J. Org. Chem., 1980, 45, 4069.

5. The presence of a small amount of methanol has a similar, dramatic effect in other cases, also: A. Bathgate, J.W. Davies, and J.R. Malpass, unpublished results. E.g., the reaction of N-chloro-1,2,3,4-tetrahydro-1,4-iminonaphthalene with $AgNO_3$/MeOH or $AgBF_4$/toluene gives only homolysis products, whereas treatment of the same compound (6% syn-/94% anti-) with $AgBF_4$/toluene in the presence of MeOH (1 mole equiv.) at -20°C gives an 81% isolated yield of 2-methoxy-6,7-benzo-1-azabicyclo[3.2.0]heptane via heterolysis.

6. (a) In all cases, the heterolysis/homolysis ratio varied with concentrations of silver salt and methanol; homolysis products were never totally absent.

   (b) Small amounts of 1-azabicyclo[3.2.0]heptane derivatives [c.f. (6)] were observed on occasion in reactions of N-bromoamines.

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