Electronic Control of Stereoselectivity in the Chlorination of 7-Azabenzonorbornenes† and 7-Azabenzonorbornadienes† with *N*-Chlorosuccinimide

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Summary The ratios of *syn* and *anti* *N*-chloroamines obtained from treatment of 7-azabenzonorbornenes and 7-azabenzonorbornadienes with *N*-chlorosuccinimide at −50 °C vary with the electronic character of the substituents on the benzenoid ring and differ substantially from the ratios observed under conditions of rapid inversion at nitrogen.

The stereochemical consequences of reactions at nitrogen (other than quaternisations of tertiary amines) can rarely be investigated due to rapid pyramidal inversion in the products. However, configurational stability at nitrogen at moderately low temperatures is an intriguing characteristic of derivatives of the 7-azanorbornane skeleton which bear an electronegative substituent on nitrogen.[1,2] We have therefore studied the reaction of the title compounds (**1**) and (**3**) with *N*-chlorosuccinimide under conditions of kinetic control (−50 °C in $CDCl_3$) to give the *N*-chloroamines (**2**) and (**4**) respectively. We find that the ratio of the *syn*-Cl and *anti*-Cl invertomers formed under these conditions varies with the pattern of substitution in the benzenoid ring. Attack of *N*-chlorosuccinimide on (**1a,b**) and (**3a,b**) occurs predominantly from the *anti* direction but an increasing tendency to approach nitrogen from over the benzenoid ring is observed as the substituents in that ring become more electron-withdrawing (**1c**; **3c,d**) culminating in a clear preference for *syn* attack on (**1d**) (Table).

TABLE. Invertomer ratios in the chlorination of 7-azabenzonorbornenes and 7-azabenzonorbornadienes with *N*-chlorosuccinimide.

Substrate	*syn*-Cl : *anti*-Cl product ratios: Under conditions of kinetic control[a]	Under conditions of thermodynamic control[b]
(**1a**)	(**2a**) 34 : 66	(**2a**) 67 : 33
(**1b**)	(**2b**) 28 : 72	(**2b**) 60 : 40
(**1c**)	(**2c**) 41 : 59	(**2c**) 82 : 18
(**1d**)	(**2d**) 68 : 32	(**2d**) 84 : 16
(**3a**)	(**4a**) 5 : 95	(**4a**) 54 : 46
(**3b**)	(**4b**) 6 : 94	(**4b**) 53 : 47
(**3c**)	(**4c**) 18 : 82	(**4c**) 71 : 29
(**3d**)	(**4d**) 20 : 80	(**4d**) 80 : 20
(**5**)	(**6**) 100 : 0[c]	(**6**) 100 : 0

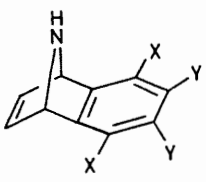
[a] Quantitative yields were obtained within 2—4 h at −50 °C in $CDCl_3$ and invertomer ratios remained constant under these conditions. Reactions were monitored by ^1H and ^{13}C n.m.r. spectroscopy and ratios were determined by integration of ^1H n.m.r. spectra. [b] Thermal equilibration was complete within 2 h at 25 °C. Inversion barriers vary with substituents in the benzenoid ring. Some decomposition of (**2a,b**) occurred; the remaining chloroamines were stable under these conditions. [c] Chlorination of the hindered amine (**5**) was complete within 20 h at −40 °C.

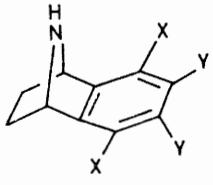
Significantly, the observed 'kinetic' ratios are contra-thermodynamic in almost every case; upon warming to 25 °C the *N*-chloroamines become free to invert and thereby demonstrate a general thermodynamic preference for the

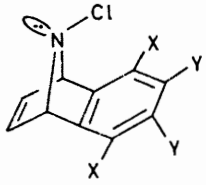
† It would be preferable to name these compounds as the 1,4-iminonaphthalene derivatives since the benzonorbornene-type names do not indicate unambiguously the state of hydrogenation, *e.g.* 1,4-dihydro- and 1,2,3,4-tetrahydro-1,4-iminonaphthalene.

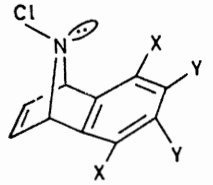
syn-Cl configuration. The *syn*/*anti* assignments for (**2b**) were based upon selective Ag^+-catalysed heterolyses of the N–Cl bonds.[2] In similar studies on (**2a**,**d**), the n.m.r. signals due to the thermodynamically preferred invertomers disappeared more rapidly (under conditions of negligible inversion) in agreement with the anticipated higher reactivity of the *syn*-Cl invertomers.[3] The assignments in the Table are consistent with close comparative analysis of ^1H and ^{13}C n.m.r. data on the range of amines. A further point of reference is provided by the rigid chloroamine *syn*-(**6**) which was the only product observed in the chlorination of (**5**) as a result of steric hindrance to *anti* attack.

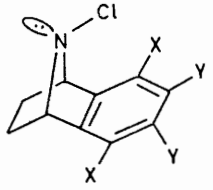
In view of the minimal steric differences within each of the series (**1a**—**d**) and (**3a**—**d**), the variation in the 'kinetic' stereoselectivity must be a result of electronic control. These results thus provide a parallel with recent reports of stereoselective additions to 7-isopropylidenenorbornene derivatives[4] in which the choice between the two bonding approaches to the *p*-orbital at C-7 varies with the balance of electronic factors in the substrates. In the 7-aza analogues, the choice is now between the (nominally) sp^3 hybridised lone pair of electrons in each of two rapidly equilibrating invertomers of (**1**) or of (**3**).‡ The relative favouring of the *syn* approach to nitrogen as the aromatic ring becomes less electron-rich may be rationalised by considering a transition state (**7**) modelled on the proposals in ref. 4a. An interaction between the developing negative charge on the trailing imide nitrogen and the aromatic ring would be expected to exert a greater stabilising influence as the electron density above the ring is reduced by electron withdrawal by Cl and F.

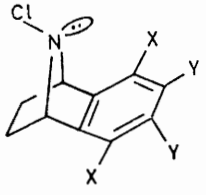

(1)


(3)

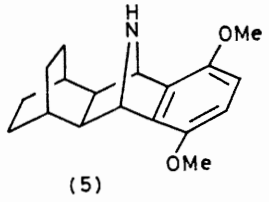

(2)—*syn*


(2)—*anti*


(4)—*syn*


(4)—*anti*

	X	Y
a;	OMe	H
b;	H	H
c;	Cl	Cl
d;	F	F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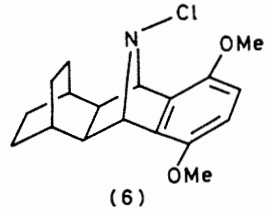
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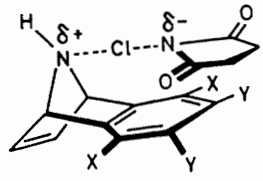
(7)

The decreased tendency for *anti*-attack in the series (**1**) as compared to the corresponding ethano-bridged series (**3**) is unexpected on steric grounds and may be due to a repulsive secondary orbital interaction[4b] between the π-bond in (**1**) and the incoming chlorine. Steric factors have, to date, played an overwhelming part in the rationalisation of stereoselectivity in the quaternisation of amines[5] and it seems probable that examples of electronic effects on stereoselectivity will also be found in this area.

As the benzenoid ring becomes more electron-deficient, the thermal relaxation of the *N*-chloroamines yields an increased proportion of *syn*-Cl invertomer at equilibrium. This preference is consistent with that expected of the negative end of an N–Cl dipole; certainly the nitrogen lone pair of electrons in an *N*-chloroamine is likely to play a subordinate role.

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‡ The *syn*:*anti* ratios observed at −50 °C are not simply a reflection of the lone pair preferences in the secondary amines (**1**) and (**3**) since a *syn*-lone pair is favoured in (**1b**) and (**3b**) (J. B. Grutzner, *J. Amer. Chem. Soc.*, 1976, **98**, 6385; G. R. Underwood and H. S. Friedman, *ibid.*, 1977, **99**, 27).

[1] J. M. Lehn, *Fortschr. Chem. Forsch.*, 1971, **15**, 311; J. B. Lambert, *Topics Stereochem.*, 1971, **6**, 19.

[2] V. Rautenstrauch, *Chem. Comm.*, 1969, 1122. The preparation and reactivity of (**2b**) were described in this key paper. A value for $\Delta G^{\ddagger}$ inversion of 23·5 kcal mol^{-1} was measured for (**2b**) by following the inversion kinetics of a partly equilibrated sample (1 cal = 4·184 J).

[3] Inversion and reactivity studies on the *N*-chloroamines described in the present work are in progress: M. L. Durrant, J. R. Malpass, and M. P. Walker, unpublished results.

[4] (a) L. A. Paquette, L. W. Hertel, R. Gleiter, and M. Böhm, *J. Amer. Chem. Soc.*, 1978, **100**, 6511 (we thank Professor Paquette for discussion of his results prior to publication); (b) K. Okada and T. Mukai, *ibid.*, p. 6509.

[5] A. T. Bottini, 'Selective Organic Transformations,' vol. 1, ed. B. S. Thyagarajan, Wiley-Interscience, New York, 1970, p. 89. *Added in proof*: Stereoselectivity has recently been observed in the quaternisation of the *N*-methyl derivatives of (**1d**) and (**3d**) with CD_3I; M. L. Durrant and J. R. Malpass, unpublished results.