Isolation and *X*-Ray Structure Determination of Single Invertomers of *N*-Chloroamines

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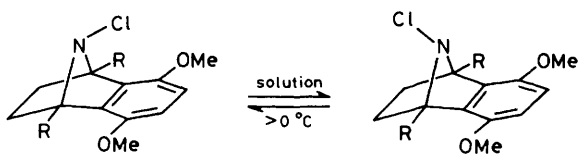
syn- and *anti*-*N*-Chloro-derivatives of substituted 1,2,3,4-tetrahydro-1,4-iminonaphthalenes have been isolated as crystalline, configurationally stable compounds at ambient temperature; *X*-ray crystal structures and single crystal dissolution experiments at low temperature allow secure structural and n.m.r. correlations whilst at higher temperatures rapid inversion occurs in solution leading to a mixture of invertomers in each case.

Rapid inversion at nitrogen precludes meaningful discussion of stereochemistry in most amines and their reactions. An exception is provided by aziridines where barriers to inversion have long been studied and where derivatives having a fixed configuration at nitrogen have been isolated. The presence of a heteroatom such as chlorine on nitrogen has played a key part in raising the inversion barrier but the major factor in aziridines is bond-angle strain; theory and observation are in good agreement.[1] Other monocyclic *N*-chloroamines display much lower barriers.[2]

Amongst bicyclic amines, the 7-azabicyclo[2.2.1]heptanyl skeleton is unique in having inversion barriers close to those in aziridines;[3a] other tightly constrained bicyclic systems have considerably lower barriers.[3b] We have earlier taken advantage of the slow inversion in 7-azabicyclo[2.2.1]heptanyl derivatives to study inversion barriers, invertomer preferences, and the stereochemical consequences of reactions at nitrogen[4] and have commented on unusual deshielding of bridging nitrogen in ^{15}N n.m.r. studies.[5] Detailed structural data are a pre-requisite for a better understanding of this ring system and we now report the isolation of two *N*-chloroamines in this series, (**1**) and (**2**),† as stable, crystalline, single diastereoisomers, each of which retains its stereochemistry indefinitely in the solid state at ambient temperature. The



syn-(**1**) R = H
syn-(**2**) R = Me
anti-(**1**) R = H
anti-(**2**) R = Me

† Compounds (**1**) and (**2**) were prepared by addition of 3,6-dimethoxybenzyne to the appropriate *N*-trimethylsilylpyrrole (or its 2,5-dimethyl derivative) followed by desilylation, hydrogenation, and chlorination with *N*-chlorosuccinimide in CH_2Cl_2. Samples were recrystallised from methanol.

Table 1. Selected n.m.r. data and invertomer ratios for *N*-chloroamines (**1**) and (**2**).

Amine	Nucleus	*syn* δ[b]	*anti* δ[b]	Invertomer ratio (*syn* : *anti*)[a] Single crystal dissolution at −50 °C	After thermodynamic equilibration	Ratio from 'kinetic'[d] chlorination
(**1**)	^{1}H: *exo*-H^2,H^3	2.17	2.44	<7 : >93	54 : 46[c]	5 : 95
	aryl H	6.72	6.65			
(**1**)	^{13}C: 2,3-C	23.4	23.3			
	5,10-C	132.7	131.2			
(**2**)	^{1}H: *exo*-H^2,H^3	1.91	2.13	100 : 0	71 : 29	21 : 79
	aryl H	6.70	6.68			
(**2**)	^{13}C: 2,3-C	31.5	32.8			
	5,10-C	134.0	132.0			

[a] Chlorine *syn* or *anti* to dimethoxyaryl ring. [b] In $CDCl_3$–$SiMe_4$; δ values varied with temperature; ^{1}H values are quoted at 298 K (400 Mhz), ^{13}C measurements at 250 K (75 MHz). Numbering is as shown in Figures 1 and 2. We thank Dr. O. Howarth of the S.E.R.C. 400 MHz N.M.R. service at Warwick for exploratory low-temperature dissolution studies. [c] Slow inversion at ambient temperature. [d] Ref. 4b.

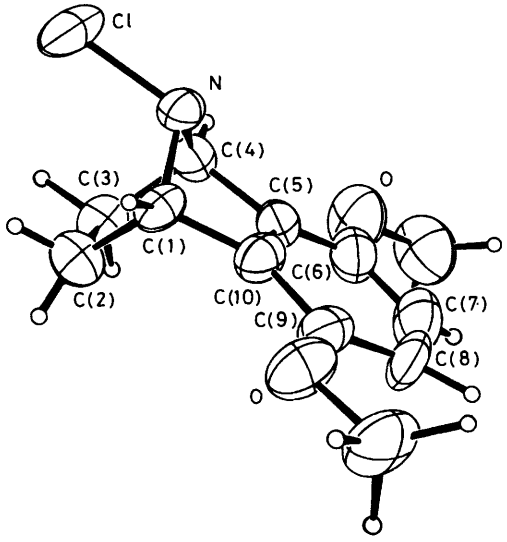


Figure 1. Crystal structure of *anti*-(**1**).

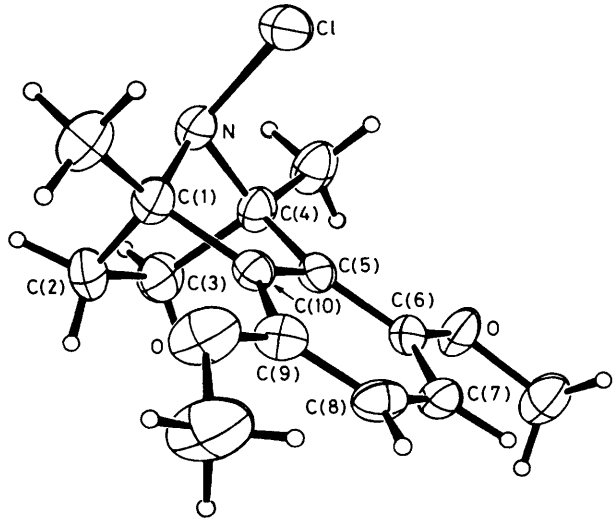


Figure 2. Crystal structure of *syn*-(**2**).

crystal structures for (**1**) and (**2**) are shown in Figures 1 and 2 respectively;‡ they establish the configuration of the chlorine in the solid state as *anti*- to the aryl ring for (**1**) and *syn*- to the aryl ring for (**2**). The C–C, C–N, and N–Cl bond lengths lie within normal ranges; the CNC bond angles are 95.7 and 97.3° respectively for (**1**) and (**2**), close to the value for norbornane.[6] These CNC bond angles are greater than those in azetidines (dihydroazetes) where the inversion barrier is lower[2] and we are not convinced that bond angle strain alone is a sufficient explanation for the high barriers in 7-azabicyclo[2.2.1]heptanyl systems.

The bond angles at the bridgehead carbons in (**1**) and (**2**) are unusual. The CNC bridge is tilted significantly towards the aryl ring in *anti*-(**1**) and away from the aryl ring in *syn*-(**2**) (Figure 3). The N–Cl bond in *syn*-(**2**) is almost antiperiplanar to the plane contained by C(1)C(2)C(3)C(4) (torsion angle 173.2°); the corresponding relationship for *anti*-(**1**) is even closer to antiperiplanarity (176.9°). These observations point to stabilising interactions between the N–Cl bond and the antiperiplanar C–C bonds which are sufficient to distort the molecules substantially. Such ground-state stabilisation together with the angle strain at nitrogen in the transition state for inversion may go some way to explaining the unusually high inversion barriers in this series. The lower inversion

‡ *Crystal Data:* (**1**), $C_{12}H_{14}ClNO_2$, M = 239.70, trigonal, space group $P\bar{3}$, a = 16.094(1), c = 7.80(1) Å, U = 1745.06 Å^3, Z = 6, λ(Mo-K_α) 0.7107 Å. The intensities of 1447 unique reflections with $7 < 2\theta < 45°$ were measured with a Stoe STADI-2 Weissenberg diffractometer; of these 1172 reflections had $|F_o| > 2.5\sigma(|F_o|)$. The structure was solved by direct methods and refined to R = 0.0845, R_w = 0.0770. The hydrogen atoms of the methoxy group were included in calculated positions (d_{C-H} = 1.08 Å); the remaining hydrogens were located and refined.

(**2**), $C_{14}H_{18}ClNO_2$, M = 267.76, monoclinic, space group $P2_1/a$, a = 17.010(2), b = 6.859(2), c = 12.490(1) Å, β = 107.8(1)°, U = 1387.47 Å^3, Z = 4. The intensities of 1713 unique reflections with $7 < 2\theta < 45°$ were measured using a Stoe STADI-2 Weissenberg diffractometer; of these 1241 reflections had $|F_o| > 3\sigma(|F_o|)$. The structure was solved by direct methods and refined to R = 0.037, R_w = 0.0385. All hydrogen atoms were located and refined as normal atoms.

Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1, 1986.

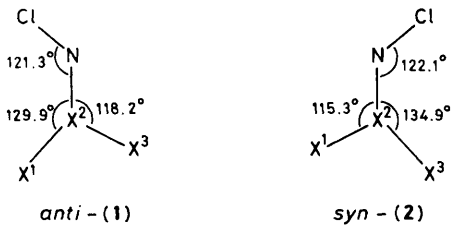


Figure 3. Side views of *anti*-(**1**) and *syn*-(**2**); X^1, X^2, and X^3 are the mid-points of C(2)C(3), C(1)C(4), and C(5)C(10), respectively (numbering as shown on the crystallographic structures, Figures 1 and 2).

barrier for (**2**) (20.5 kcal mol^{-1}; 1 cal = 4.184 J) compared to (**1**) (>22.6 kcal mol^{-1}) is consistent with the slightly wider CNC bond angle for (**2**). Calculations by Wiberg[7] have shown that bridgehead methyl groups should increase the non-bonded C(1)–C(3) distance in bicyclo[1.1.1]pentanes as a result of increased electron density in the bridgehead orbitals and increased mutual repulsion. A similar effect could be operating in (**2**); further variation of bridgehead substituents should offer a unique opportunity for systematic investigation of the relationship between CNC bond angles and nitrogen inversion barriers.

In earlier work, assignment of stereochemistry at nitrogen has been based on n.m.r. studies (chemical shift analogies, contact shift studies, and ^{13}C compression shifts) and on relative reactivities; there has been disagreement over invertomer preferences in some cases.[8] In order to provide a firm point of reference for invertomer assignments using n.m.r. spectroscopy in these *N*-chloroamines, we have taken single crystals of *anti*-(**1**) and *syn*-(**2**) and dissolved them in pre-cooled (−50 °C) $CDCl_3$–$SiMe_4$ in n.m.r. tubes in order to measure the ^1H and ^{13}C n.m.r. spectra of each single invertomer under conditions of little or no inversion. Selected n.m.r. data are shown in Table 1 together with ratios resulting from thermal equilibration to give the 'thermodynamic' invertomer ratios and, for reference, the ratios from 'kinetic' chlorination.[4b] These results confirm our earlier assignments of chlorine configuration in this family of compounds using relative reactivity studies and ^1H n.m.r. spectroscopy (in particular the deshielding effect of the *anti*-chlorine on the *exo*-2,3 protons). The aryl carbons γ to Cl also appear to be deshielded by the *syn*-Cl (Table 1) but the relative ^{13}C shifts of C(2) and C(3) do not correlate with orientation of the Cl.[8b]

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1 See, for example, W. B. Jennings and S. D. Worley, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1512, and references cited therein. The barrier for *N*-chloro-2-methylaziridine is 26.7 kcal mol^{-1}.
2 *E.g. N*-chloroazetidine: 13.4 kcal mol^{-1}, *N*-chloropyrrolidine: 10.3 kcal mol^{-1}; J. B. Lambert, *Top. Stereochem.*, 1971, **6**, 19. A recent, surprising, claim that the inversion barrier for azetidine itself is about 17.9 kcal mol^{-1} (B. R. Friedman, J. P. Chauvel, and N. S. True, *J. Am. Chem. Soc.*, 1984, **106**, 7638) has been shown to be in error (F. A. L. Anet, *J. Am. Chem. Soc.*, 1985, **107**, 4335).
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4 (a) M. L. Durrant and J. R. Malpass, *J. Chem. Soc., Chem. Commun.*, 1981, 1028; (b) J. R. Malpass and M. P. Walker, *ibid.*, 1979, 585.
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7 K. B. Wiberg, *Tetrahedron Lett.*, 1985, **26**, 599.
8 (a) G. R. Underwood and H. S. Friedman, *J. Am. Chem. Soc.*, 1977, **99**, 27; J. B. Grutzner, *ibid.*, 1976, **98**, 6385, and references therein. (b) We have observed deshielding of aryl carbons γ to the *syn*-Cl in other derivatives of this ring system. This contrasts with the well-known shielding effect on γ-carbons brought about by steric compression in *N-alkyl* amines. Our use of this 'γ-effect' shows that the preferred invertomer has the *N*-substituent consistently *syn*- to the aryl ring (contrary to some earlier suggestions) in a wide range of *N*-methyl-1,4-dihydro- and -1,2,3,4-tetrahydro-1,4-imino-naphthalenes and anthracenes (which have much lower barriers than the *N*-chloro-compounds). We thank Professor G. W. Gribble for details of a recent *X*-ray study of one of these compounds which has the methyl *syn*- in the solid state also (M. P. Byrn, C. E. Strouse, G. W. Gribble, and C. S. LeHoullier, *Acta Crystallogr., Sect. C*, 1985, **41**, 238).