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Electronic Control of Stereoselectivity in the Chlorination of 1,4-Dihydro-1,4-iminonaphthalenes (7-Azabenzonorbornadienes) with N-Chlorosuccinimide

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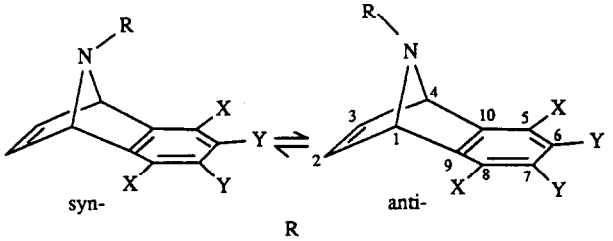
Key Words: 7-azabenzonorbornyl derivatives; N-chloroamines; stereoelectronic control; slow nitrogen inversion; inversion barriers; invertomer preferences.

Abstract *Chlorination of a range of secondary amines based on the 1,4-dihydro-1,4-iminonaphthalene (7-azabenzonorbornadiene) ring system is described. At low temperatures, the ratio of syn- and anti- N-chloroamines formed under conditions of kinetic control can be determined; this ratio is shown to be influenced substantially by variation in the electronic character of the aryl ring. At higher temperatures, inversion at nitrogen leads to different (thermodynamic) invertomer ratios which also vary as a function of substitution. Substituents in the aryl ring and in the bicyclic skeleton also influence the nitrogen inversion barrier.*

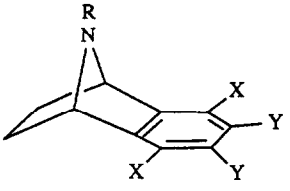
Introduction

The normal occurrence of rapid pyramidal inversion at neutral nitrogen means that stereochemistry at nitrogen and the stereochemical consequences of reactions at nitrogen can rarely be investigated. Aziridines provide a striking exception[1] but the 7-azabicyclo[2.2.1]heptane (7-azanorbornane) skeleton also offers a measure of configurational stability at nitrogen. N-Alkyl derivatives of this ring system undergo nitrogen inversion at a rate which is slow on the NMR time scale[2] but remains rapid in real terms. However, the presence of an electronegative substituent on nitrogen can raise the barrier to the level found in aziridines.[1,3] We have established earlier that nitrogen inversion barriers in N-halo derivatives of this system are sufficient to permit investigation of stereochemistry at bridging nitrogen and to allow a measure of control over stereochemistry.[4] We report here the results of a fuller study of the chlorination of a range of 1,4-dihydro-1,4-iminonaphthalene (7-azabenzonorbornadiene) derivatives and the establishment of invertomer preferences as a function of temperature. It was intended to probe the factors which affect invertomer preferences and to look for evidence bearing on the elusive 'bicyclic effect'.[1,2,6] It was also necessary to establish an unambiguous stereochemical foundation for reactivity studies.[5]

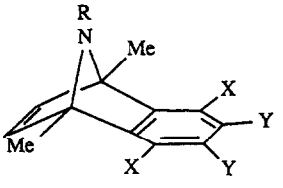
We chose to study a series of derivatives (**1a-e**) in which the substituents in the aryl ring were altered systematically in order to modify the electronic character of the aryl ring without introducing major changes to the shape of the molecule and to compare and contrast the analogues having a saturated 2,3-bridge (**2a-e**). The analogues (**3**) and (**4**) bearing methyl substituents at the bridgehead positions were included in the extended investigations together with the 1,4-dihydro-1,4-iminoanthracene system (**5**), and the 9,10-dihydro-9,10-iminoanthracenes (**6**) and (**7**). These latter systems appeared to offer the most appropriate way of achieving a contrast between the electronic factors which might influence the two nitrogen 'faces' but, at the same time, minimising the steric differences between the two faces.[7] Finally, the multicyclic systems (**8**) and (**9**) were included in order to provide points of reference for the spectroscopic assignments.



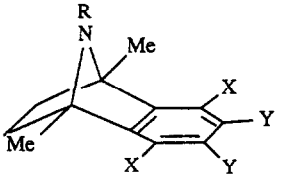
	R=H	R=Cl
(1a)	X=Y=Me	(11a)
(1b)	X=Y=H	(11c)
(1c)	X=OMe; Y=H	(11c)
(1d)	X=Y=Cl	(11d)
(1e)	X=Y=F	(11d)



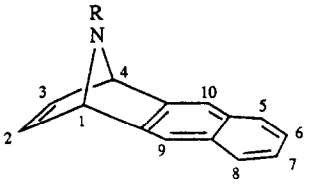
(2b)	(12b)
(2c)	(12c)
(2d)	(12d)
(2e)	(12e)



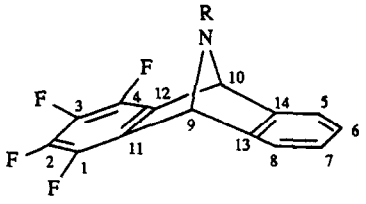
(3b)	(13b)
(3c)	(13c)



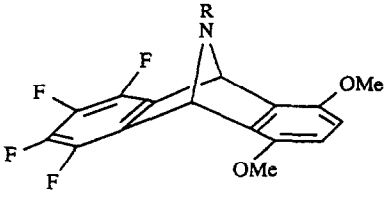
(4b)	(14b)
(4c)	(14c)



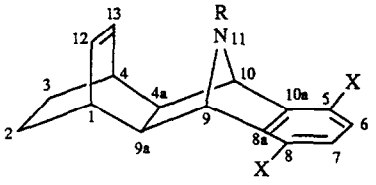
(5)	(15)



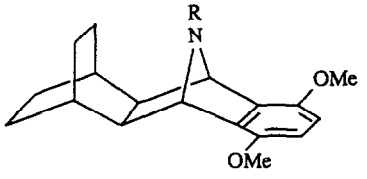
R=H (6) R=Cl (16)



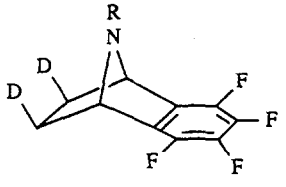
(7) (17)



(8b) X=H (18b)
(8c) X=OMe



(9c) (19c)



(10) (20)

Preparative Methods

Routes to the secondary amines (**1a-e**), (**2a-e**), (**5**), (**6**) and (**7**) have already been described.[2] The 1,4-dimethyl-1,4-iminonaphthalenes (**3**) and (**4**) were obtained by cycloaddition of the appropriate benzyne to N-trimethylsilyl-2,5-dimethylpyrrole; the trimethylsilyl group was readily cleaved during the work-up to give (**3b,c**) and hydrogenation gave (**4b,c**). The multicyclic amines (**8b**) and (**8c**) were synthesised by cycloaddition of cyclohexa-1,3-diene to (**1b**) and (**1c**) respectively in sealed tubes; hydrogenation of (**8c**) over palladium on carbon gave (**9c**). The amine (**10**), a deuterated analogue of (**2e**), was produced from (**1e**) by treatment with $LiAlD_4$.[8]

Chlorination of the secondary amines is discussed below.

Results and Discussion

Early work on the chlorination of the amine (**1b**) indicated that the ratio of invertomers produced at -5°C differed from the ratio obtained at higher temperatures at which equilibration occurred.[3] This was a significant result which, together with the promise of interesting solvolytic behaviour of the N-chloroamines, deserved further investigation.[5]

Chlorination of the secondary amines (**1**) and (**2**) with N-chlorosuccinimide (NCS) in $CDCl_3$ was performed at -50°C in order to prevent inversion at nitrogen in the products and thus preserve the ratio of N-chloroamine invertomers formed under conditions of kinetic control, reflecting the preferred direction of attack of the nitrogen lone pair on NCS. The reactions were followed by NMR spectroscopy and an example is shown in figure 1. The invertomer ratio shown in figure 1a remained unchanged at -50°C but on warming to ambient temperature, the intensity of the signals changed as the N-chloroamines began to undergo inversion. After complete equilibration, the invertomer preference was substantially reversed in the example shown. The ratio now reflected the balance of steric and electronic influences acting on the two invertomers under conditions of thermodynamic control.

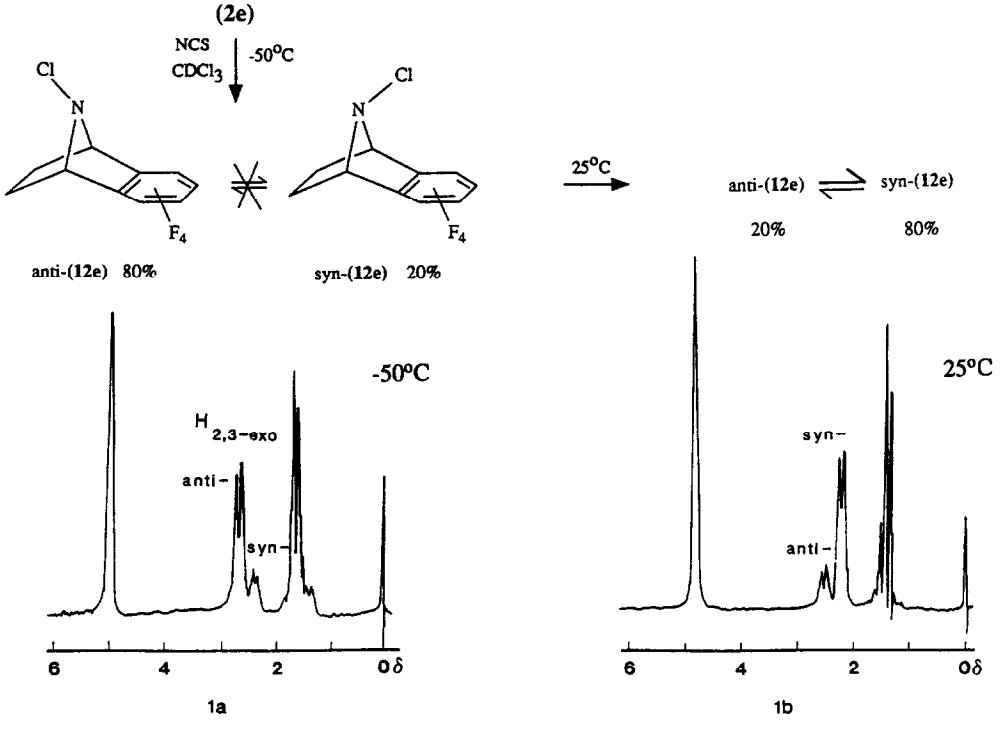


Figure 1. Chlorination of (**2e**) under conditions of kinetic (a) and thermodynamic (b) control

Qualitatively similar behaviour was seen along the series of compounds (**1a-e**) and (**2a-e**); the results are summarised in table 3 together with invertomer ratios for the remaining N-chloroamines obtained under conditions of kinetic and thermodynamic control. However, before discussing the results, it is necessary to justify the assignment of invertomer stereochemistry.

Assignment of Invertomer Stereochemistry

Assignment of stereochemistry was based initially on NMR spectra; ^{1}H NMR data are summarised in table 1 and ^{13}C data in table 2. Table 1 shows clearly the trends along the series **(11a)** - **(11e)**. For example the olefinic protons $H_{2,3}$ are consistently upfield (by 0.05 - 0.13 ppm) in the invertomer having the Cl *anti*- to the aryl ring (i.e. the Cl over the etheno-bridge) when compared to the *syn*- invertomer; **(13b)**, **(13c)** and **(15)** showed similar behaviour. The bridgehead protons $H_{1,4}$ in the *syn*- invertomer were consistently upfield (by 0.15 - 0.2 ppm) compared to the *anti*- for **(11)** and **(15)**. In table 2, it can be seen that the ^{13}C NMR signals due to $C_{2,3}$ in **(11)** are upfield (by 1.3 - 1.6 ppm) when the Cl is over this bridge (*anti*-Cl). The bridghead carbons $C_{1,4}$ are upfield in the *syn*- relative to the *anti*- invertomers of **(11)** and the $C_{9,10}$ signals are consistently deshielded (by 1.4 - 1.9 ppm) when the Cl is *syn*- . Confirmation of these invertomer assignments came from studies of the reactivity of the N-chloroamines under conditions of negligible inversion. Monitoring the relative intensity of the bridgehead signals of **(11e)** [$H_{1,4}$ at δ 5.43 (*anti*-Cl) and 5.27 (*syn*-Cl)] when treated with Ag^+/MeOH in an NMR tube at -30°C led to a change in the ratio from 31:69 (t=0) to 31:47 (t=15 min) to 31:35 (t=35 min) corresponding to more rapid loss of the *syn*-Cl invertomer due to participation of the π-electrons of the etheno- bridge (in preference to the negligible participation of the tetrafluoroaryl ring in loss of Cl^- from the *anti*- invertomer).

The saturated analogues **(12b-e)** showed the $H_{2,3}$ protons to be relatively downfield (by 0.27 - 0.33 ppm) in the *anti*-Cl invertomer and this pattern was continued in the bridgehead methyl compounds **(14b)** and **(14c)**. This agrees with the work of Cristol and Nachtigall[9] in analogous *syn*- and *anti*- 7-chloro-benzonorbornenes where a corresponding downfield shift of $H_{2,3\text{-exo}}$ was seen in the *anti*- isomer. The ^{13}C NMR spectra showed $C_{9,10}$ signals which were downfield in the *syn*- invertomers of **(12)** and **(14)** (by 1.4 - 2.6ppm) in agreement with the earlier observations for **(11)**. A point of reference here came from the sterically hindered multicyclic amine **(19c)** in which only the *syn*- invertomer is seen; there is an almost exact coincidence of the aryl signals for **(19c)** in the ^{1}H NMR spectrum with the corresponding signals for *syn*-**(12c)** but not with those for *anti*-**(12c)**.

Two final, irrefutable, points of reference came from the later isolation of single invertomers of **(12c)** and **(14c)** as pure crystalline compounds; the sample of **(12c)** was shown by X-ray crystallographic analysis to be the *anti*- invertomer and the sample of **(14c)** to be *syn*-.[4] In each case, dissolution of these crystalline samples at low temperature furnished solutions containing the appropriate single invertomer allowing unambiguous spectroscopic measurements and confirmation of the proposed assignments.[4,10]

In the case of the dibenzo-system **(16)**, the (*syn* → *anti*) increments for the bridgehead carbons $C_{9,10}$ mirrored those for the corresponding carbons $C_{1,4}$ in **(11b)**. A similar correspondence was seen in the behaviour of the signals due to $C_{5,8}$ in **(16)** and **(11b)** and also for $C_{6,7}$ in the same two compounds [note that the invertomers are defined with respect to the tetrafluoroaryl ring in **(16)**]. The ^{1}H NMR data showed correspondence between the (*syn* → *anti*) increments for the aryl protons and also for the O-methyl proton signals of **(17)** and **(11c)** but the assignments for **(17)** must be considered less rigorous. Nevertheless, a close correspondence of invertomer preferences between the N-chloro- **(11b)** and N-methyl- derivatives of the parent system has been noted[2] and the assignments for the N-chloroamines **(16)** and **(17)** maintain a consistent thermodynamic preference for the substituent at nitrogen to lie over the tetrafluoroaryl ring as already observed[2] for the N-benzyl and N-methyl analogues (where ^{13}C compression shifts allow unambiguous assignments to be made).

The obvious way to resolve the issue for **(16)** and **(17)** by comparing the reactivity of the two invertomers with Ag^+/MeOH under conditions of slow inversion (where the participatory abilities of the two rings differ markedly) was not applicable in this case. The two 9,10-iminoanthracene systems were much less reactive than the 1,4-iminoanthracenes and reaction only occurred at higher temperatures under conditions which allowed inversion at nitrogen to intrude. The Ag^+-catalysed solvolysis reactions of the family of compounds will be described elsewhere.[5]

Table 1. ^{1}H NMR Data for N-Chloroamines[a]

	Syn-Cl				*Anti-Cl*			
	Aryl	**$H_{2,3}$**	**$H_{1,4}$**	**OMe/ *CMe***	**Aryl**	**$H_{2,3}$**	**$H_{1,4}$**	**OMe/ *CMe***
(11a)		6.97	5.06			6.84	5.24	
(11b)	7.40-7.13 m	7.17 m $w_{\frac{1}{2}}$ 4.5Hz	4.86 m $w_{\frac{1}{2}}$ 4.5Hz		7.13-6.87 m	6.82 m $w_{\frac{1}{2}}$ 4Hz	5.06 m $w_{\frac{1}{2}}$ 4Hz	
(11c)	6.60 s	6.94 m $w_{\frac{1}{2}}$ 5Hz	5.09 m $w_{\frac{1}{2}}$ 5Hz	3.74 s	6.55 s	6.85 m $w_{\frac{1}{2}}$ 3.5Hz	5.26 m $w_{\frac{1}{2}}$ 3.5Hz	3.71 s
(11d)		6.99 m	5.10 m $w_{\frac{1}{2}}$ 5Hz			6.94 m	5.27 m $w_{\frac{1}{2}}$ 4Hz	
(11e)		7.10 m $w_{\frac{1}{2}}$ 5Hz	5.27 m			7.03 m $w_{\frac{1}{2}}$ 4Hz	5.43	
(12b)	7.18 m	~2.17 m[d] ~1.29 m	4.53 m		7.26	~2.46 m[d] ~1.41 m	4.53	
(12c)	6.72 s	~2.17 m[d] ~1.32 m	4.76 m	3.79 s	6.65	~2.44 m[d] ~1.47 m	4.76 m	3.75 s
(12d)		~2.22 m[d] ~1.31 m	4.74 m			~2.50 m[d] ~1.42 m	4.74 m	
(12e)		~2.24 m[d] ~1.37 m	4.81			~2.57 m[d] ~1.43 m	4.81	
(20)		1.40 s	4.83 s			1.47 s	4.83 s	
(13b)	~7.1 complex	6.75 s		*1.74 s*	~7.1 complex	6.40 s		*1.78 s*
(13c)	6.56 s	6.75 s		3.70 s *1.83 s*	6.57 s	6.45 s		3.70 s *1.90 s*
(14b)	7.29 s br	2.02 dd,[d] J=11.3, 4.9Hz *(exo)* 1.50 brm *(endo)*[b]		*1.78 s*	7.29 s br	2.24 dd,[d] J=12, 4Hz *(exo)* 1.44 dd, J=12, 4Hz *(endo)*		*1.78 s*
(14c)	6.70 s	1.91 dd,[d] J=12, 4.2Hz *(exo)* 1.52 dd, J=12, 4.2Hz *(endo)*		3.76 s *1.81 s*	6.68	2.13 dd,[d] J=12, 4.2Hz *(exo)* 1.48 dd, J=12, 4.2Hz *(endo)*		3.75 s *1.82 s*
(15)	7.78-7.22 m	6.86 m $w_{\frac{1}{2}}$ 4Hz	5.02 m $w_{\frac{1}{2}}$ 5Hz		7.78-7.22	6.76 m $w_{\frac{1}{2}}$ 5Hz	5.22 m $w_{\frac{1}{2}}$ 5Hz	
(18b)[c]	7.24 m		4.44 s					
(19c)[c]	6.73 s		4.63 s	3.85 s				
	Aryl		**$H_{9,10}$**	**OMe**	**Aryl**		**$H_{9,10}$**	**OMe**
(16)	7.50-7.04 m		5.67 s		7.50-7.04 m		5.60 s	
(17)	6.61 s		5.80 brs	3.77 s	6.64 s		5.80 brs	3.79 s

~ Indicates approximate values for centre of multiplets (peak overlap).
$w_{\frac{1}{2}}$ Indicates width at half height for unresolved multiplets.
a. Spectra measured under the conditions shown in table 3.
b. Obscured by *anti*-signal.
c. Partial data only; bridgehead signals (δ 4.44; 4.63) are numbered $H_{1,4}$ purely for comparison purposes. See experimental section for fuller ^{1}H NMR data.
d. The signals for $H_{2,3\text{-exo}}$ were downfield of those for $H_{2,3\text{-endo}}$ in compounds **(12)** and **(14)**; the data for **(20)** confirm the *exo-/endo-* assignments.

Table 2. ^{13}C NMR Data for N-Chloroamines[a]

		$C_{2,3}$	$C_{5,8}$	$C_{6,7}$	$C_{9,10}$	$C_{1,4}$	OMe	CMe
(11b)	*syn-*	141.6	125.6	123.4	146.3	76.9		
	anti-	140.1	126.0	121.3	144.4	78.2		
(11c)	*syn-*	141.4	149.7	110.5	133.8	74.4	55.6	
	anti-	139.8	147.2	110.5	132.4	75.1	55.6	
(11e)	*syn-*	141.2	b	b	b	74.3		
	anti-	139.9	b	b	b	74.5		
(12b)	*syn-*	24.0	127.2	121.7	144.3	72.8		
	anti-	24.0	126.9	119.9	142.4	71.9		
(12c)[c]	*syn-*	23.4	148.5	110.3	132.7	70.3	55.66	
	anti-	23.3	146.2	110.0	131.2	68.8	55.72	
(12e)	*syn-*	23.8	b	b	b	70.7		
	anti-	23.8	b	b	b	68.6		
(20)	*syn-*	23.4[d]	b	b	b	70.4		
	anti-	23.4[d]	b	b	b	68.5		
(14b)	*syn-*	31.3	126.6	118.2	146.9	75.2		16.2
	anti-	32.6	127.1	119.9	144.3	75.2		15.2
(14c)[c]	*syn-*	31.2	149.1	110.7	134.0	75.7	55.6	18.7
	anti-	32.6	147.2	110.7	132.0	75.5	55.8	17.2
(19c)[e]	*syn-*		149.1	110.9	135.4 ($C_{8a,10a}$)	74.1 ($C_{9,10}$)	56.2	

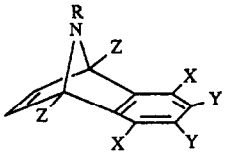
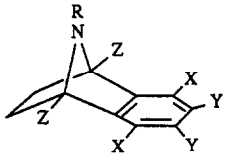
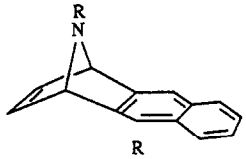
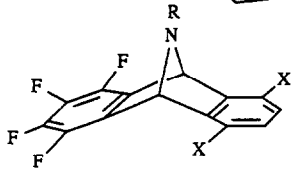
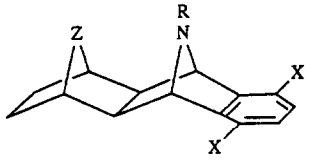
		$C_{5,8}$	$C_{6,7}$	$C_{13,14}$	$C_{9,10}$	OMe
(16)[b,f]	*syn-*	127.9	122.1	142.3	75.6	
	anti-	127.5	124.2	142.3	74.4	
(17)[b,f]	*syn-*	150.6	112.5	130.9	75.6	56.2
	anti-	147.8	112.5	130.9	71.9	56.2

a. Spectra recorded at the temperatures shown in table 3 unless indicated otherwise.[c]
b. The F-substituted ring showed complex signals due to ^{19}F ^{13}C coupling.
c. Measured at -23°C.
d. $C_{2,3}$ signals observed as a 1:1:1 triplet, J ≈ 85Hz.
e. Partial spectrum; a full summary of the ^{13}C NMR spectrum is given in the experimental section.
f. Assignment of chlorine *syn-* or *anti-* to the tetrafluoroaryl ring.

Low-temperature Chlorination at Nitrogen: Kinetic Control

Chlorination of the amines (**1**) at low temperature was found to occur predominantly from the *anti-* direction (table 3). However, there was a progressive increase in the amount of *syn-* attack (over the aryl ring) as the substituents in the aryl ring became more electronegative culminating in a preference for *syn-* attack in the case of the tetrafluoroaryl system (**1e**). This effect is not simply a reflection of the lone pair preferences in the starting amines since inversion is very rapid in the secondary amines and, in any case, a *syn-* lone pair is known to be favoured in (**1b**) and (**2b**).[11] The results for (**1a**) were very similar to those measured for (**1b**) and, in the absence of the substantial difference anticipated for the tetramethyl system, no further chlorination of tetramethyl derivatives was studied. Examination of the ratios measured at higher temperatures (under conditions of free inversion) shows a reversal of the invertomer ratio in almost every case; it is clear that the 'kinetic' ratios are contra-thermodynamic. The ratio of invertomers is therefore controlled neither by

Table 3. Kinetic and Thermodynamic Invertomer Ratios for N-Chloroamines

Substrate (R=H)	Compound	Product (R=Cl)	X	Y	Z	Low-temp chlorination Kinetic control[a] *syn-*[c]	*anti-*	Higher-temp equilibration Thermodynamic control[b] *syn-*[c]	*anti-*
(1a)		(11a)	Me	Me	H	31 :	69	63 :	37
(1b)		(11b)	H	H	H	28 :	72	60 :	40
(1c)		(11c)	OMe	H	H	34 :	66	67 :	33
(1d)		(11d)[h]	Cl	Cl	H	41 :	59	82 :	18
(1e)		(11e)	F	F	H	68 :	32	84 :	16
(3b)		(13b)[d]	H	H	Me	34 :	66	72 :	28[i]
(3c)		(13c)[e]	OMe	H	Me	40 :	60	80 :	20[i]
(2b)		(12b)	H	H	H	6 :	94	53 :	47
(2c)		(12c)	OMe	H	H	5 :	95	54 :	46
(2d)		(12d)[h]	Cl	Cl	H	18 :	82	71 :	29
(2e)		(12e)	F	F	H	20 :	80	80 :	20
(4b)		(14b)[d]	H	H	Me	5 :	95	52 :	48
(4c)		(14c)[f]	OMe	H	Me	21 :	79	71 :	29
(5)		(15)				33 :	67	87 :	13
					X				
(6)		(16)[c]			H	75 :	25	80 :	20
(7)		(17)[c]			OMe	61 :	39	77 :	23
			Z		X				
(8b)		(18b)	CH=CH		H	100 :	0	100 :	0
(9c)		(19c)[g]	CH_2CH_2		OMe	100 :	0	100 :	0

a. Measured in $CDCl_3$ at -50°C unless stated otherwise. Integration values ± 2%.
b. Measured at 25°C after complete thermal equilibration.
c. Assignments are shown as *syn-* or *anti-* to the aryl ring except for **(16)** and **(17)** where assignments are *syn-* or *anti-* to the tetrafluoroaryl ring.
d. Measured at -55°(±2)°C.
e. Measured at -36°C; a slightly higher temperature was necessary to overcome problems of low chloroamine solubility.
f. Measured at -36°C in d_8-toluene.
g. Measured at -40°C.
h. The tetrachloroaryl compounds were not obtained completely pure but there are no indications that invertomer ratios were affected.
i. We thank Dr. R.E. Moss for measuring these ratios.

ground-state considerations, nor by product stability. The 'kinetic' ratio must be a reflection of the relative energies of the two possible transition states and illustrates the balance of electronic, rather than steric, factors. The absolute preferences are difficult to rationalise; the key observation is that the balance shifts in favour of an increasing *syn-* preference as the electron density in the aryl ring is reduced by electron-withdrawing substituents. The results from chlorination of **(3b,c)** parallel closely the results with **(1b,c)**.[12] The result for **(5)** is not significantly different from that for **(1b)** although the small additional preference for *syn-* attack on **(5)** may be thought to be consistent with the lower electron density in the $C_{11}C_{12}$ bond resulting from 'partial bond fixation'.

The experiments with the ethano-bridged amines **(2)** show a heavy preference for *anti-* attack and emphasise that the approach of the electrophile is governed substantially by electronic factors, being contrary to expectations on purely steric grounds (where $H_{2,3\text{-exo}}$ would be expected to inhibit the *anti-* approach). The results again show a relative increase in *syn-* attack as the electron density in the aryl ring is reduced. The greater overall kinetic preference for *anti-* attack (over the ethano-bridge) in these cases emphasises the subsequent reversal of the preferred configuration at nitrogen which occurs in every case when inversion is allowed to take place freely. The presence of bridgehead methyl substituents in **(4b,c)** does not distort the picture substantially.

In the case of the 9,10-dihydro-9,10-iminoanthracenes, two aryl rings offer two sterically similar, but electronically different, approaches. Attack over the tetrafluorobenzo ring in **(6)** is preferred by a factor of 3:1 when compared to attack over the benzo itself in agreement with the earlier results and in close agreement with epoxidation studies on analogous alkenes (11-isopropylidenedibenzonorbornadienes)[13]. This preference is reduced slightly in **(7)** (61:39) as expected from the gradation seen in the series **(1b-e)**.

In work with 7-isopropylidenebenzonorbornenes **(21)**, Paquette has shown that the attack of electrophiles such as N-bromosuccinimide (NBS) and singlet oxygen on the alkene shows facial selectivity.[14] Selected results are shown in figure 2 where, significantly, the proportion of *syn-* attack during bromination

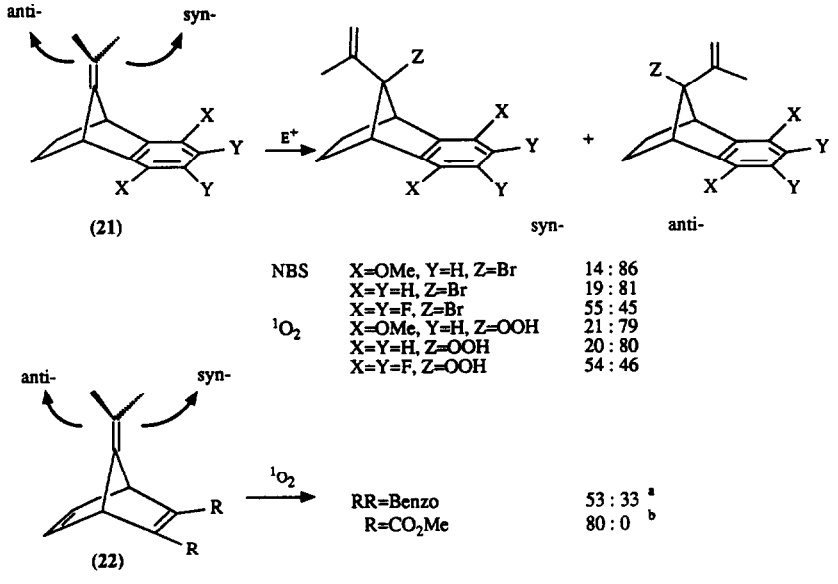
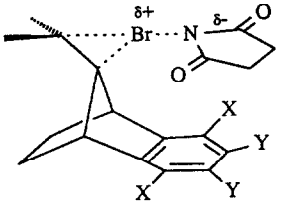


Figure 2. Facial selectivity in electrophilic addition to **(21)**[14] and **(22)**;[15] selected data.

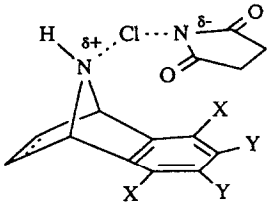
a. isolated yield of alcohol after reduction of hydroperoxide

b. isolated yield of hydroperoxide

increases from 14% to 58% as the aryl ring is made more electron-deficient by alteration of the ring substituents from dimethoxy- to tetrafluoro-. These results parallel the nitrogen work closely, although the products from the alkenes obviously do not allow for an assessment of the relative stabilities of the products since they cannot be equilibrated. Paquette proposed two influences to explain his results. Firstly, the exocyclic π bond in (**21**) is said to favour attack from the *anti-* face due to distortion of the π-orbital by mixing with a high-lying σ orbital. Secondly, when the electron density of the aromatic π cloud is decreased by electron-withdrawal, the aryl ring becomes better able to stabilise the transition state for *syn-* attack by means of an interaction with the trailing negatively-charged succinimide moiety of the brominating agent as shown in (**23**). This transition state model applies equally well to the other electrophiles in the alkene work[14] and to the amines in the present study, e.g. (**24**).

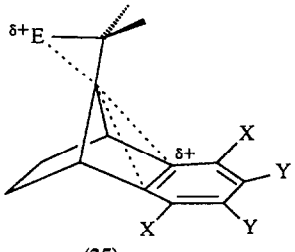


(23)



(24)

Mukai studied the reactions of singlet oxygen with 7-isopropylidenenorbornadienes (**22**), in which two π-systems are in competition.[15] The preference here, too, is for approach over the less electron-rich double bond as shown in figure 2. Mukai suggested a number of possible explanations including a repulsive secondary orbital interaction between the π-bond and the incoming electrophile. Paquette[14] has proposed an alternative hypothesis to explain the general preference for *anti-* attack in the ethano-bridged systems based on the development of a stabilising bishomoconjugative interaction as the system comes under the influence of the approaching electrophile, e.g. (**25**). However, such an explanation cannot apply to the nitrogen systems in which a quaternary nitrogen develops during the rate-limiting step.



(25)

The behaviour of the nitrogen and carbon (bridging amino- and isopropylideno-) systems nevertheless appear to be remarkably similar. First, there is a marked preference for *anti-* attack in the amines (**2**) corresponding to that observed for the alkenes (**21**). Superimposed upon that effect, is the *relative* favouring of attack over a π-system as the associated electron density is reduced, whether by changes within a family [e.g. (**21**) or (**2**)], by competition within the same molecule [e.g. (**22**), (**6**) or (**7**)], or by both effects [e.g. (**1a-e**)].

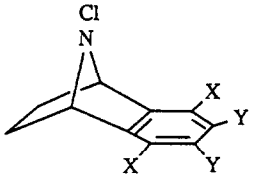
Thermodynamic Control of Invertomer Preferences at Nitrogen

The controversial question of substituent (lone pair) preferences in N-alkyl derivatives of the title ring system has been discussed earlier.[2] It is generally agreed that the nitrogen lone pair plays a minor role in determining configuration at nitrogen in secondary and tertiary amines and it is reasonable to assume that the influence of the lone pair in the N-chloroamines will be substantially less. In any case, the preferences shown under conditions of free inversion (table 3) are the reverse of expectations based on lone pair-π repulsions.[16] The gradual increase from 60% *syn*- to 84% *syn*- as the aryl ring becomes more electron-deficient in the series **(11b)** - **(11e)** is illustrative and shows a consistent preference for the chlorine to lie over the more electron-deficient π system. This is in keeping with a diminishing repulsion beween an $^{\delta+}$N-Cl$^{\delta-}$ dipole and the aryl ring as the π-electron density of the aryl ring is reduced. A similar picture emerges for the series **(12b)** - **(12e)** in which the *syn*- preference in each case is reduced marginally. This may result from a reduced destabilisation of the *anti*- configuration owing to the absence of the olefinic π-bond/N-Cl dipole repulsion in the series **(12)** although if this suggestion is correct, the effect may be attenuated by a slightly increased steric interaction between the *anti*-Cl and exo-$H_{2,3}$. In **(16)** and **(17)**, the chlorine is influenced by the two aryl groups and remains substantially *syn*- to the fluorinated aryl ring. The dimethoxybenzo ring (23%) again competes a little more effectively than the benzo (20%) when pitted against the more electron-deficient tetrafluorobenzo ring.

Variation in the Inversion Barrier at Nitrogen

During the course of these studies, it became clear that there was a progressive change in the barrier to inversion at nitrogen in this series of N-chloroamines. Variable-temperature NMR measurements of coalescence temperatures were not possible for the 1,4-dihydro-1,4-iminonaphthalenes because of the lack of thermal stability of many of the compounds even at moderate temperatures. The tetrahydro-systems were more stable; it was possible to gain some very approximate kinetic impressions for **(12b,c,e)** and to measure inversion barriers for **(12b)** and **(14bc)**. Table 4 shows measurements of the relative conversion of partially equilibrated mixtures of the amines **(12)** as each mixture progressed towards the equilibrium ratio at different temperatures.

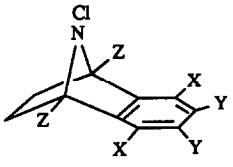
Table 4. Equilibration of *syn*-/*anti* Invertomer Mixtures

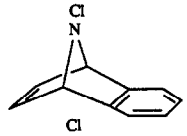
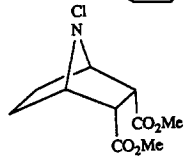
Compound	X	Y	Extent of Equilibration	Temp. °C	Equilibrium Ratio %
	OMe	H (12c)	39% → 54% *syn* (51 min)	28.5	54% *syn*
	H	H (12b)	15% → 33% *syn* (61 min)	18.0	53% *syn*
	F	F (12e)	30% → 49% *syn* (62 min)	0.8	80% *syn*

The extent of equilibration is similar in percentage terms (15 - 19%) but is obviously only approximately comparable because the starting ratios and ultimate equilibrium ratios vary. Nevertheless the differences between the temperatures necessary to achieve these changes establish a simple ranking **(12c)** > **(12b)** > **(12e)** for the inversion barriers.

The ^{13}C NMR spectra of **(14b)** and **(14c)** showed an unusually small frequency separation ($\Delta\nu$) between the signals for the bridgehead carbons ($C_{1,4}$). Coalescence could not be observed at 100MHz but ^{13}C NMR measurements at 15MHz brought the coalescence temperature T_c down to a reasonable level (table 5).

Table 5. Nitrogen Inversion Barriers for (14b) and (14c)

Compound	X	Y	Z		T_c[a] °C	$\Delta\nu$ Hz	$\Delta G^{\neq}_{anti\rightarrow syn}$[c] (kJmol^{-1})	$\Delta G^{\neq}_{syn\rightarrow anti}$[c] (kJmol^{-1})
	H	H	Me	**(14b)**[d]	45	0.49[b]	77.6	77.9
	OMe	H	Me	**(14c)**[e]	88	1.34[b]	84.6	87.2
	H	H	H	**(12b)**[f]	~170[g]		94.5	94.8

		$\Delta G^{\neq}_{inv}$
	**(11b)**[3]	98.2
	**(26)**[1]	87.8

a. ± 5°C **b.** for $C_{1,4}$; ± 0.02 Hz **c.** ± 1.5 kJmol^{-1} **d.** in d_6-DMSO
e. in chlorobenzene (using coaxial d_6-dmso lock) **f.** in *o*-dichlorobenzene; coalescence of $H_{2,3\text{-exo}}$
g. T_c estimated; coalescence was nearing completion at 159°C but **(12b)** decomposed at higher T.

The inversion barrier for **(14b)** is lower than might have been expected from comparison with the other available literature data in table 5, in particular the direct comparison with **(12b)**. Solvent effects may have had a small effect (although inversion barriers tend to be higher in more polar solvents for N-alkyl analogues[2]) but the use of DMSO was necessary for **(14b)** in order to achieve sufficient solubility for the low-field ^{13}C NMR work. The lower values for **(14b,c)** are consistent with the wider than usual CNC bond angles [97.3° for **(14c)** c.f. 95.7° for **(12c)**[4]]. This probably results from the effect of the methyl substituents, increasing the electron density in the bridgehead orbitals leading to increased mutual repulsion.[17] The wider bond angles would explain the reduction of the inversion barriers but the fact that they are still very substantial suggests that the intrinsic 'bicyclic effect' remains.

The higher value for the fully unsaturated systems **(11b)** [when compared with results for **(12b)** and **(26)**] suggests that unsaturation in the 2-carbon bridges raises the barrier and is a cumulative effect, in agreement with observations for the N-methyl analogues.[2] This effect can also be seen indirectly in the 1,4-dimethyl-1,4-iminonaphthalenes **(13b)** **(13c)**. Whilst it was not possible to measure inversion barriers by VT NMR in these examples, the observation that thermal equilibration of these N-chloroamines from low-temperature chlorination experiments was slow and that temperatures of 40-50°C were required to achieve rapid interconversion certainly suggests that two flanking π-systems can counter substantially the

barrier-lowering effect of the bridgehead methyl groups. However, the equilibration of the systems **(11)** having bridgehead hydrogens seemed somewhat easier in practice than for **(13)** so the picture is not simple.

Repulsions between the nitrogen p-orbital and the π-system (or systems) at the transition-state for inversion were proposed originally by Lehn when first discussing the 'bicyclic effect'.[1] Such interactions would be expected to increase as the aryl ring becomes more electron-rich in the present systems. The observation that inversion for **(12b)** is less rapid than for **(12e)** is in agreement with this idea. However, the position of **(12c)** as the slowest of the trio suggests that the dimethoxybenzo ring is behaving as relatively electron-rich in comparison with the benzo[12b] and the observed higher $\Delta G^{\neq}_{inv}$ value for **(14c)** compared with that for **(14b)** (table 5) confirms this. We feel that this transition-state effect is an additional factor which affects *relative* inversion barriers but that the major cause of the 'bicyclic effect' lies in unusual ground-state stabilisation.[18]

Summary

The barriers to inversion at nitrogen in the title compounds are uniquely high due to the combined influence of the 'bicyclic' effect and the presence of an electronegative atom on the bridging nitrogen.

This work has demonstrated that the products from reaction of these amines with an electrophile at low temperatures are unable to invert under the reaction conditions and variable stereoselectivity has been demonstrated. The two 'faces' of the amino-nitrogen are effectively non-equivalent under conditions of rapid inversion and the facial selectivity is controlled by electronic, rather than steric, factors. The work provides a good analogy with work on closely related alkenes where the two faces of the π-bond are effectively non-equivalent. The general preference for attack *anti-* to a bridging π-system in the 7-azabicyclo[2.2.1]heptyl system parallels work with the corresponding 7-isopropylideno analogues as does the tendency for an increase in attack over an aryl ring as the electron density in that ring is reduced. The stereoselectivity is defined during the approach of the electrophile; the product ratios are not a function of the invertomer ratio in the substrate (secondary amine). More importantly, the amine studies offer a unique demonstration that the initial product ratios are indeed the result of kinetic control and are not decided by product stability since equilibration of the primary products occurs on warming and leads to quite different product ratios in most cases.

The flanking π-systems in these N-chloroamines also exert an influence on the thermodynamic invertomer ratios (where the chlorine prefers to lie *syn-* to electron-deficient π-systems), and on inversion barriers (where electron-rich π-systems lead to an increase in the inversion barrier). Methyl substituents at the bridgehead positions of the azabicyclic system lead to a lowering of the inversion barrier.

Overall, a consistent picture emerges from this study of a range of compounds but the influences are relatively subtle. An overwhelming invertomer preference was seen only in highly hindered cases where one face of the amino-nitrogen was shielded sterically. Nevertheless, a substantial measure of control over invertomer ratios was possible by manipulation of reaction conditions and this provided an essential basis for subsequent reactivity studies.[5]

Experimental

Reactions were performed under dry nitrogen using solvents dried by standard methods. Magnesium sulphate was used to dry organic extracts prior to evaporation of solvent. Kugelrohr distillation was performed using a Büchi GKR 50 apparatus; a Leybold Hereaus single stage short path distillation plant, type KDL 1, was used for 'falling-film' distillation of sensitive liquids.

IR spectra were recorded in CH_2Cl_2 unless indicated otherwise. NMR spectra were measured in $CDCl_3$ with tetramethylsilane (TMS) as reference unless indicated otherwise.

^1H NMR spectra were recorded on Varian T 60 (60 MHz), EM 390 (90 MHz), Jeol PS 100 (100 MHz), Bruker AM 300 (300 MHz) or Bruker AM 400 (400 MHz) spectrometers.

^{13}C NMR spectra were recorded on Jeol FX 60 (15 MHz), Bruker AM 300 (75 MHz) or Bruker AM 400 (100 MHz) spectrometers. Chemical shift values are in ppm relative to TMS.

Temperature measurements on the NMR instruments used for the VT work were found to be accurate to within ± 1 K over the range used.

Mass spectra were measured routinely on a VG Micromass 14 spectrometer; base peaks are indicated by an asterisk. Accurate mass measurements were obtained through the SERC service at Harwell and, subsequently, Swansea.

Melting point measurements were made using a Kofler hot stage apparatus and are uncorrected.

Combustion Analyses were performed by CHN Analysis Ltd. of South Wigston, Leicester.

1,4-Dihydro-1,4-iminonaphthalenes and 1,2,3,4-tetrahydro-1,4-iminonaphthalenes

The routes to amines (**1a-e**) and (**2a-e**) are described in reference 2 together with full spectroscopic data.

1,4-Dimethyl-1,4-iminonaphthalenes and 1,4-dimethyl-2,3-dihydro-1,4-iminonaphthalenes

1-Trimethylsilyl-2,5-dimethylpyrrole

To a stirred solution of 2,5-dimethylpyrrole (37.56 g; 0.40mol) in dry diethyl ether (130 ml) and dry benzene (55 ml) under nitrogen was added potassium (14.20 g; 0.36 g atom) in small pieces over 20 min. The reaction mixture was stirred for 1 h and heated under reflux for a further 6 h. The potassiopyrrole slurry was cooled to 0°C and trimethylsilyl chloride (39.40 g; 0.36 mol) was added dropwise over 20 min. The reaction mixture was stirred overnight, filtered, and concentrated under reduced pressure. Fractional distillation of the residue afforded 1-trimethylsilyl-2,5-dimethylpyrrole (36.70 g; 61%), b.p. 94-97°C (18 mm Hg); lit.[19] 95-97°C (15 mm Hg). ^1H NMR δ 5.90 (s, 2H), 2.38 (s, 6H), 0.50 (s, 9H).

1,4-Dimethyl-1-4-iminonaphthalene (3b) and 1,4-dimethyl-2,3-dihydro-1,4-iminonaphthalene (4b)

A solution of bromofluorobenzene (6.28 g; 0.036 mol) in dry diethyl ether (25 ml) was stirred vigorously under nitrogen and cooled to -78°C. n-Butyllithium (0.09M in hexane; 40 ml) was added over 20 min. 1-Trimethylsilyl-2,5-dimethylpyrrole (6.96 g; 0.042 mol) was added and the mixture was allowed to warm to ambient temperature overnight with stirring. The reaction mixture was poured into water (50 ml) and extracted with dichloromethane (3 x 50 ml). The organic extracts were combined, dried over anhydrous $MgSO_4$, and evaporated under reduced pressure to afford (**3b**) as a pale yellow oil (3.23 g; 53%). ^1H NMR δ 6.90 - 7.25 (complex, 4H, aryl), 6.78 (s, 2H, $H_{2,3}$), 3.02 (brs, NH, exch.), 1.80 (s, 6H, CH_3).

A solution of (**3b**) (2.66 g; 0.0156 mol) in ethanol (40 ml) was hydrogenated at atmospheric pressure for

24 h over 10% Pd/C (79 mg). The reaction mixture was filtered through Celite and the solvent removed under reduced pressure to afford **(4b)** (2.44 g; 91%) as a yellow oil which was pure as shown by NMR spectroscopy and was used without further purification. ^{1}H NMR δ 7.19 (s, 4H, aryl), 2.50 (brs, NH, exch.), 1.96 (s, 6H, CH_3), 2.16-1.58 (brm, 2H, $H_{2,3}$exo-), 1.49-1.16 (brm, 2H, $H_{2,3}$endo-); MS ^{m}/z 145*(100%)[M^+- CH_2=CH_2], 144(48), 132(26), 128(9), 115(13), 94(28), 91(12), 77(12), 57(10), 55(9), 51(8); observed accurate ^{m}/z (M^+- CH_2=CH_2) 145.0894, calculated for $C_{10}H_{11}N$ 145.0892.

1,4-Dimethyl-5,8-dimethoxy-1-4-iminonaphthalene (3c) and
1,4-dimethyl-2,3-dihydro-5,8-dimethoxy-1,4-iminonaphthalene (4c)

A solution of n-butyllithium (1.57M in hexane; 58.5 ml) was added over 20 min to a stirred solution of 1,4-dimethoxy-2-chlorobenzene (15.83 g; 91.7 mmol) in dry diethyl ether (40 ml) at -78°C under nitrogen. 1-Trimethylsilyl-2,5-dimethylpyrrole (15.30 g; 91.7 mmol) was added over a 10 min period and the reaction mixture was allowed to warm to ambient temperature overnight, with stirring. Water (100 ml) was added and the product extracted with dichloromethane (3 x 60 ml). The combined organic extracts were dried over anhydrous $MgSO_4$ and and the solvent removed under reduced pressure. The resulting yellow oil was triturated with cold hexane to afford **(3c)** as a crystalline solid (7.22 g; 34 %), m.p. 112-117°C (with sublimation). IR (CH_2Cl_2) 3240w, 3100-2850brs, 2835s, 1605m, 1570w, 1490-1410brs, 1380m, 1355s, 1240s, 1175s, 1130m, 1075-1005brs, 860s cm^{-1}; ^{1}H NMR δ 6.70 (s, 2H, $H_{2,3}$), 6.42 (s, 2H, $H_{6,7}$), 3.68 (s, 6H, OCH_3), 2.78 (brs, NH, exch.), 1.90 (s, 6H, 1,4-CH_3); ^{13}C δ 148.7 ($C_{6,7}$), 146.8 ($C_{5,8/9,10}$), 143.1 ($C_{5,8/9,10}$), 111.6 ($C_{2,3}$), 73.1 ($C_{1,4}$), 56.4 (OCH_3), 17.8 (1,4-CH_3); MS ^{m}/z 231 (47%)[M^+], 216(37), 205*(100), 200(10), 191(14), 176(12), 115(10); observed accurate ^{m}/z 231.1262, calculated for $C_{14}H_{17}NO_2$ 231.1259.

A solution of **(3c)** (1.00 g; 4.35 mmol) in ethanol (20 ml) was hydrogenated at atmospheric pressure over 10% Pc/C (0.104 g) for 18 h. The reaction mixture was filtered through Celite and the solvent removed under reduced pressure to give **(4c)** (0.91 g; 90%) as a white amorphous solid m.p. 144°C (with sublimation). IR (CH_2Cl_2), 3270w, 3090-2850brm, 2835m, 1600w, 1490s, 1450brm, 1380m, 1350m, 1290-1245brm, 1210m, 1175m, 1120m, 1090m, 1050s, 870m cm^{-1}; ^{1}H NMR δ 6.56 (s, 2H, $H_{6,7}$), 3.72 (s, 6H, OCH_3), 2.30 (brs, NH, exch.), 1.80 (s, 6H, 1,4-CH_3), 2.00-1.20 (m, 4H, $H_{2,3}$); ^{m}/z 205*(100%)[M^+- CH_2=CH_2], 190(84), 175(17), 174(4), 118(2), 77(2); observed accurate ^{m}/z (M^+- CH_2=CH_2) 205.1107, calculated for $C_{12}H_{15}NO_2$ 205.1102.

***Exo,exo*-2,3-dideuterio-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydro-1,4-iminonaphthalene (10)**

The method applied by Marchand and Allen to compound **(1b)** was used.[8] To a solution of **(1e)** (200 mg; 0.9 mmol) in dry diethyl ether (23 ml) was added $LiAlD_4$ (39 mg; 0.9 mmol) as a slurry in dry ether (2 ml). The mixture was stirred under dry nitrogen for 20 hours at ambient temperature and quenched carefully with D_2O. The mixture was filtered and the filtrate was dried and evaporated. The crude product was subjected to preparative TLC (silica, 50:50 diethyl ether:petrol) and extraction of the band having Rf 0.4 gave the product **(10)** as a colourless oil (40 mg; 20%). ^{1}H NMR δ 4.87 (s, 2H), 2.32 (bs, NH), 1.26 (s, 2H).

N-Chlorination of secondary amines - General Methods

^{1}H and ^{13}C NMR data for the N-chloroamines are given in tables 1 and 2.

N-Chloroamines were usually made on a small scale in an NMR tube to allow measurement of invertomer ratios. A typical procedure is described for **(11c)**: A solution of **(1c)** (60 mg; 0.3 mmol) was dissolved in $CDCl_3$ (0.4 ml) in a 5 mm NMR tube and the solution was cooled to -50°C. Finely powdered

N-chlorosuccinimide (43 mg; 0.33 mmol) was added slowly, the contents mixed with the aid of a small glass paddle drawn from glass calillary tubing, and the tube was stoppered. The tube was kept at this temperature for 2 hours, agitating occasionally, then transferred without warming to the probe of an NMR spectrometer precooled to -50°C, and the ratio of invertomers produced under these conditions of 'kinetic control' was determined by direct integration of the areas under the respective peaks. In all cases, these ratios remained constant below O°C. The N-chloroamine solutions were warmed to 35°C and the equilibration monitored; when the ratio had stabilised, the 'thermodynamic' invertomer ratio was obtained by direct integration.

The other N-chloroamines were prepared in a similar manner. The time necessary for complete chlorination varied slightly, for example chlorination of **(2c)** to give **(12c)** required 4 hours. All chlorinations gave quantitative yields as judged by NMR spectroscopy. The pure N-chloroamines could be separated from excess N-chlorosuccinimide and succinimide by evaporation of solvent under vacuum and trituration with cold (0-10°C) $CFCl_3$. On evaporation of solvent, a 98% yield of **(11b)** was obtained by this method. In general, the unsaturated N-chloroamines **(11)** and **(13)** were reactive and decomposed thermally during handling at ambient temperatures; they were prepared in solution and used immediately for spectroscopic measurements or reactivity studies.

Certain N-chloroamines crystallised from solution as single invertomers. Such samples could be dissolved in $CDCl_3$ (pre-cooled in an NMR tube at -50°C) and their identity confirmed; on warming, equilibration occurred giving the 'thermodynamic' invertomer ratio.

In certain cases, particularly for the less-reactive N-chloroamines, larger-scale chlorinations with NCS were performed using dichloromethane as solvent, products were isolated and, where possible, analytical data obtained. The N-chloroamines **(12)** and **(14)** were more stable than their unsaturated counterparts **(11)** and **(13)** and preparative procedures are described below. Samples of the more stable N-chloroamines which had equilibrated thermally (partially or completely depending on the conditions) could also be obtained simply by treatment of the secondary amine with sodium hypochlorite:

N-Chloro-1,4-dihydro-1,4-iminonaphthalene (12b)

The hydrochloride salt of **(2b)** (250 mg; 1.4 mmol) in water (5 ml) was stirred with dichloromethane (5 ml) at 0°C. Commercial sodium hypochlorite solution was added dropwise until no further precipitate appeared, and the mixture was stirred for a further 3 minutes. The layers were separated and the aqueous layer washed with dichloromethane (2 x 5 ml). The combined organic layers were dried and evaporated giving crude **(12b)** in quantitative yield as a white solid. This was purified by sublimation (60°C/ 0.2 mm Hg) giving a pure sample of syn-/anti-**(12b)** in 90% yield as a white crystalline solid, m.p. 87 - 90°C. NMR (25°C) δ 7.22 (m, 4H), 4.53 (m, 2H), 2.46(m) & 2.17(m) (2H total), 1.35 (m, 2H).

N-Chloro-5,8-dimethoxy-1,2,3,4-tetrahydro-1,4-iminonaphthalene (12c)

A solution of **(2c)** (904 mg; 4.41 mmol) in dichloromethane (10 ml) was treated with NCS (660 mg; 4.9 mmol) and stirred in the dark under nitrogen for 2.5 h. The reaction mixture was flash chromatographed using dichloromethane eluant and the N-chloroamine **(12c)** (733 mg; 73%) was isolated as an off-white crystalline solid. A small sample was recrystallised from methanol to give colourless needles, m.p. 122.5-123.5°C (with sublimation). Analysis. Found: C, 60.13; H, 5.92; N, 5.83%. $C_{12}H_{14}NO_2Cl$ requires C, 60.13; H, 5.89; N, 5.84%.

N-Chloro-1,4-dimethyl-2,3-dihydro-1,4-iminonaphthalene (14b)

To a stirred solution of **(4b)** (1.92 g; 11 mmol) in dichloromethane (25 ml) under nitrogen was added N-chlorosuccinimide (1.78 g; 13.4 mmol). The mixture was stired for 1.5 h and the reaction mixture was flash

chromatographed over silica using dichloromethane as eluant. The N-chloroamine (**14b**) was isolated as a yellow oil. ; MS m/z 181/179 (9/30%)[M^+- CH_2=CH_2], 144*(100), 143(4), 115(6), 103(10), 102(4), 77(6), 51(4); observed accurate m/z 181.0476; calculated for (M^+- CH_2=CH_2) $C_{10}H_{10}N^{37}Cl$ 181.0472.

N-Chloro-1,4-dimethyl-2,3-dihydro-5,8-dimethoxy-1,4-iminonaphthalene (14c)

A stirred solution of (**4c**) (1.52 g; 6.50 mmol) in dry dichloromethane (20 ml) under nitrogen, was treated with N-chlorosuccinimide (1.00 6; 7.50 mmol) and the reaction mixture was stirred for 2.5 h. Flash chromatography of the reaction mixture on silica using dichloromethane eluant afforded (**14c**) as a pale yellow solid (1.66 g; 96%). A small sample was recrystallised several times from dry methanol to give an analytical sample, m.p. 120-121°C (with sublimation). Found: C, 62.89; H, 6.75; N, 5.24%. $C_{14}H_{18}NO_2Cl$ requires C, 62.80; H, 6.78; N, 5.23%. IR (CH_2Cl_2), 3100-2850m, 2840m, 1610m, 1500s, 1460m, 1440m, 1285-1250m, 1090s, 1010m, 970m; MS m/z 269/267 (1/4%)[M^+], 241/239(8/31), 240/238(9/31), 250(27), 204*(100), 190(10), 189(8), 175(5), 174(12).

N-Chloro-1,4-dihydro-1,4-iminoanthracene (15)

The amine (**5**)[2] (408 mg; 2.1 mmol) was stirred at 0°C in 1:1 diethyl ether:dichloromethane with NCS (350 mg; 2.6 mmol) for 2h. The solvents were evaporated under vacuum and, in attempting to extract the N-chloroamine (**15**) into $CFCl_3$, it was found that partial separation occurred because of the greater solubility of the syn-invertomer. The $CFCl_3$ extracts were combined and evaporated to give a mixture of syn- and anti-(**15**) (ratio 67:33) as an orange solid (275 mg) [m/z 229/227 (1:3) M^+]. The residue (216 mg) consisted of anti-(**15**) (ca. 60 mg) together with succinimide as shown by NMR spectroscopy. This sample of anti-(**15**) was kept cold and was used for solvolysis studies.[5]

9,10-Dihydro-9,10-iminonaphthalenes

N-Chloro-1,2,3,4-tetrafluoro-9,10-dihydro-9,10-iminoanthracene (16)

A solution containing (**6**)[2] (193 mg; 0.73 mmol) in dry chloroform (13 ml) was treated with NCS (97 mg; 0.73 mmol) and stirred in the dark under nitrogen for 1h. The solvent was removed under reduced pressure and the residue was flash-chromatographed over silica using dichloromethane to afford (**16**) (189 mg; 86%) as a white solid. Recrystallisation from hexane gave colourless crystals, m.p. 98-99.5°C. Analysis. Found: C, 56.32; H, 2.16; N, 4.57%. $C_{14}H_6NClF_4$ requires C, 56.12; H, 2.02; N, 4.67%. MS m/z 301/299(1/3%)[M^+], 266(38), 265(83), 251(25), 250*(100), 244(15), 237(25), 219(9), 125(19).

N-Chloro-1,2,3,4-tetrafluoro-5,8-dimethoxy-9,10-dihydro-9,10-iminoanthracene (17)

Amine (**7**)[2] (108 mg; 0.33 mmol) was treated with NCS (88 mg; 0.66 mmol) as described for (**6**) above to yield (**17**) (103 mg; 87%) as a white solid after flash chromatography. Recrystallisation from hexane afforded colourless crystals, m.p. 151-152.5°C. Analysis. Found: C, 53.54, H, 2.88; N, 3.92%. $C_{16}H_{10}NO_2ClF_4$ requires C, 53.43; H, 2.80; N, 3.89%. MS m/z 361/359(6/2%)[M^+], 324(32), 310*(100), 295*(100), 280(21), 267(14), 252(18), 224(21), 198(14), 155(9), 44(21).

Multicyclic amines

1,4-Etheno-1,2,3,4,9,10-hexahydro-9,10-iminoanthracene (8b)

The amine (**1b**) (750 mg; 5.2 mmol) and cyclohexa-1,3-diene (2.09 g; 26 mmol) were introduced into a thick-walled pyrex tube which was sealed and heated in an oil bath at 155°C for 23h. After cooling, colourless needle-like crystals formed. The product was dissolved in dichloromethane and the amine extracted into

dilute acid (2M HCl, 4 x 10 ml). The combined acid extracts were then made basic and the product extracted with dichloromethane (4 x 25 ml). The combined organic extracts were dried and evaporated to dryness under vacuum. The solid residue sublimed at 130°C/0.3 mm Hg to give **(8b)** (560 mg, 48%). A small portion was recrystallised from diethyl ether to provide an analytically pure sample, m.p. 118-120°C. Analysis. Found: C, 86.16,; H, 7.71; N, 6.25%. $C_{16}H_{17}N$ requires C, 86.05; H, 7.67; N, 6.27%. IR (CH_2Cl_2) 3300w, 3020m, 2920s, 2850m, 1620w, 1450m, 1375m, 1035m, 895m, 835m, 815s cm^{-1}; ^1H NMR δ 7.32-9.96 (m, 2H, aryl), 6.32 (m, 2H, $H_{12,13}$), 4.22 (s, 2H, $H_{9,10}$), 3.24 (brs, NH), 2.80 (m, 2H, $H_{1,4}$), 1.80 (s, 2H, $H_{4a,9a}$), 1.52-1.00 (m, 4H, $H_{2,3}$); MS $^m/z$ 223 [M^+], 206, 194, 178, 165, 143, 117*, 89.

1,4-Etheno-5,8-dimethoxy-1,2,3,4,9,10-hexahydro-9,10-iminoanthracene (8c)

A mixture of **(1c)** (200 mg; 1 mmol) and 1,3-cyclohexadiene (150 mg; 1.9 mmol) was heated in a sealed tube at 140°C for 12 hours. The tube was cooled and opened and the contents dissolved in diethyl ether. The ethereal solution was added to a solution of fumaric acid (230 mg; 2 mmol) in warm isopropanol (5 ml). The mixture was cooled in ice and the precipitated salt was filtered and dried. The precipitate was freed from solvent, dissolved in water (20 ml), the solution was basified with 2N K_2CO_3, and the product was extracted into diethyl ether (2 x 20 ml). The combined extracts were dried and evaporated to give a brown oil (150 mg) containing ca. 87% of **(8c)** and 13% of **(1c)**. The mixture was separated by preparative TLC (Kieselgel 80F, diethyl ether) and extraction of the fraction having R_f = 0.8 gave pure **(8c)** (60 mg; 23%) as a colourless oil. ^1H NMR δ 6.58 (s, 2H), 6.36 (m, 2H), 4.48 (s, 2H), 3.77 (s, 6H), 3.49 (brs, NH), 2.86 (brs, 2H), 1.86 (s, 2H), 1.30 (m, 4H).

1,4-Ethano-5,8-dimethoxy-1,2,3,4,9,10-hexahydro-9,10-iminoanthracene (9c)

A solution of **(8c)** (60 mg; 0.21 mmol) in dry diethyl ether (20 ml) was hydrogenated at 20 psi over 10% Pd/C for 30 min. The solution was filtered through Celite and evaporated to give a quantitative yield of pure **(9c)** as a colourless oil. ^1H NMR δ 6.59 (2H), 4.54 (s, 2H), 3.83 (s, 6H), 2.3-1.1 (complex, 13H); ^{13}C NMR (CD_2Cl_2) δ 146.84 ($C_{5,8}$), 140.61 ($C_{8a,10a}$), 109.96 ($C_{6,7}$), 62.04 ($C_{9,10}$), 56.20 (OMe), 41.91 ($C_{4a,9a}$), 28.41 ($C_{1,4}$), 27.63 ($C_{12,13}$), 22.67 ($C_{2,3}$) n.b. an off-resonance spectrum was not obtained owing to the small quantity of material available; some assignments are tentative.

N-Chloro-1,4-etheno-1,2,3,4,9,10-hexahydro-9,10-iminoanthracene (18b)

The amine **(8b)** (150 mg; 0.67 mmol) was treated with NCS (122 mg) in $CDCl_3$ (0.4 ml) in an NMR tube at -60°C as described above. The tube was placed in the probe of an NMR spectrometer, pre-cooled to -50°C, and the consumption of amine was monitored by following the disappearance of the signal at δ 4.22. The chloroamine **(18b)** gave the following ^1H NMR spectrum: δ 7.24 (m, 4H, aryl), 6.34 (m, 2H, $H_{12,13}$), 4.44 (s, 2H, $H_{9,10}$), 2.84 (m, 2H, $H_{1,4}$), 1.92 (m,2H, $H_{4a,9a}$), 1.28 (m, 4H, $H_{2,3}$). The amine decomposed thermally when warmed in solution.[20]

N-Chloro-1,4-ethano-5,8-dimethoxy-1,2,3,4,9,10-hexahydro-9,10-iminoanthracene (19c)

A solution of **(9c)** (30 mg; 0.1 mmol) in $CDCl_3$ in an NMR tube was cooled to -50°C. Finely powdered NCS (15 mg; 0.11 mmol) was added and the mixture held at -40°C with occasional agitation. The NMR tube was transferred to the probe of an NMR spectrometer pre-cooled to -40°C in order to estimate the invertomer ratio for **(19c)**. ^1H NMR δ 6.73 (s, 2H), 4.63 (s, 2H), 3.85 (s, 6H), 2.46-1.12 (complex, 12H); ^{13}C NMR (CD_2Cl_2) δ 149.05 ($C_{5,8}$), 135.41 ($C_{8a,10a}$), 110.87 ($C_{6,7}$), 74.12 ($C_{9,10}$), 56.20 (OMe), 41.13 ($C_{4a,9a}$), 28.02 ($C_{1,4}$), 27.37 ($C_{12,13}$), 22.69 ($C_{2,3}$) n.b. an off-resonance spectrum was not obtained owing to the small quantity of material available; some assignments are tentative. Accurate mass measurement of molecular ion: $^m/z$ 319.1339, $C_{18}H_{22}NO_2{}^{35}Cl$ requires 319.1340.

References and Footnotes

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