Tetrahedron Vol. 48, No. 5, pp. 861-884, 1992
Printed in Great Britain

0040-4020/92 $3.00+.00

Preparation and Spectroscopic Studies of the 1,4-Dihydro-1,4-iminonaphthalene (7-Azabenzonorbornadiene) Ring System

John W. Davies, Michael L. Durrant, Matthew P. Walker, Djaballah Belkacemi and John R. Malpass*

Department of Chemistry, University of Leicester, Leicester LE1 7RH, UK.

(*Received in UK* 8 *November* 1991)

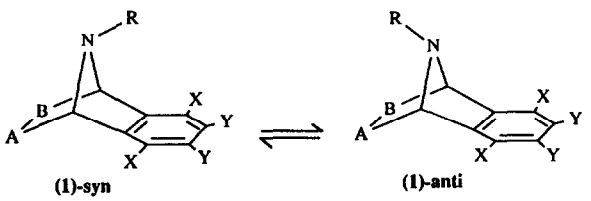
Key Words: 7-azanorbornyl derivatives, nitrogen inversion, inversion barriers, invertomer preferences.

Abstract *The synthesis of a range of N-alkyl 1,4-dihydro-1,4-iminonaphthalenes (7-azabenzonorbornadienes) and reduced derivatives is described together with 1,4-dihydro-1,4- and 9,10-dihydro-9,10- iminoanthracenes. VT NMR studies lead to unambiguous assignment of invertomer preferences; changes in the invertomer ratios and nitrogen inversion barriers are investigated as the electronic and steric environment is modified by variation of substituents in the carbon skeleton and at nitrogen.*

Introduction

Derivatives of the 7-azabicyclo[2.2.1]heptane, hept-2-ene and hepta-2,5-diene ring systems are the only cyclic amines in which the barrier to inversion at nitrogen approaches the high values observed in aziridines.[1] We have been interested in the origins of the unusually high barriers,[2] the question of invertomer preferences at nitrogen,[2a,3] and also stereochemical control in the formation[3] and reactions[4] of diastereoisomeric invertomers at nitrogen.

A number of derivatives of the title ring system have been studied earlier[5-9] but there has been no systematic quantitative investigation of the effect of substituents on invertomer preferences or nitrogen inversion barriers. We report here the preparation of a number of substituted 1,4-dihydro-1,4-iminonaphthalene and 1,2,3,4-tetrahydro-1,4-iminonaphthalene ring systems (**1**) (together with examples of corresponding iminoanthracene analogues) and we record detailed spectroscopic data.



(1)-syn **(1)-anti**

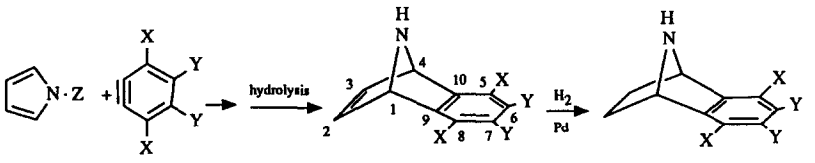
AB = CH_2-CH_2, CH=CH, $MeO_2CC{=}CCO_2Me$, substituted benzo-
R = H, Me, Et, CH_2Ph
X = H, Cl, F, Me, OMe
Y = H, Cl, F, Me, YY=benzo

^{13}C NMR correlations are particularly helpful in assigning configuration at nitrogen under conditions of slow inversion. Earlier work on proposed invertomer assignments and the importance of n-π bishomoallylic interactions in determining lone-pair preferences are assessed critically in the light of this direct evidence.[10]

Nitrogen inversion barriers have been measured for a number of N-methyl and N-benzyl derivatives of these ring systems in order to probe the effects of variation of the 2-carbon bridges on the inversion process.

Preparative Methods

The amines used in this study are shown in schemes 1 - 3; preparative methods are based largely on aryne additions to derivatives of pyrrole and isoindole and follow established general procedures, although many of the compounds are new. Routes to the secondary 1,4-dihydro-1,4-iminonaphthalenes and 1,2,3,4-tetrahydro-1,4-iminonaphthalenes are summarised in scheme 1.



(7a-7e) (8a-8e)

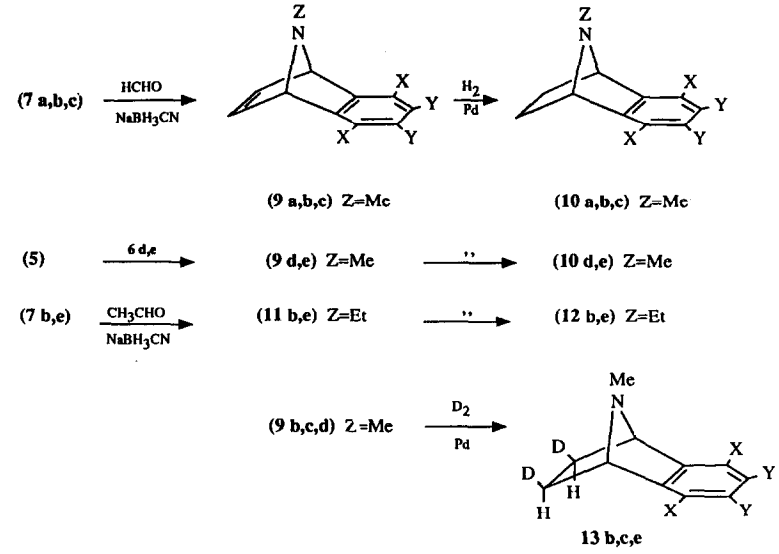
(2) Z=H
(3) Z=CO_2Et
(4) X=$SiMe_3$
(5) Z=Me

(6a) X=Y=Me
(6b) X=Y=H
(6c) X=OMe; Y=H
(6d) X=Y=Cl
(6e) X=Y=F

[a-e refer to the same substituents throughout this paper]

SCHEME 1

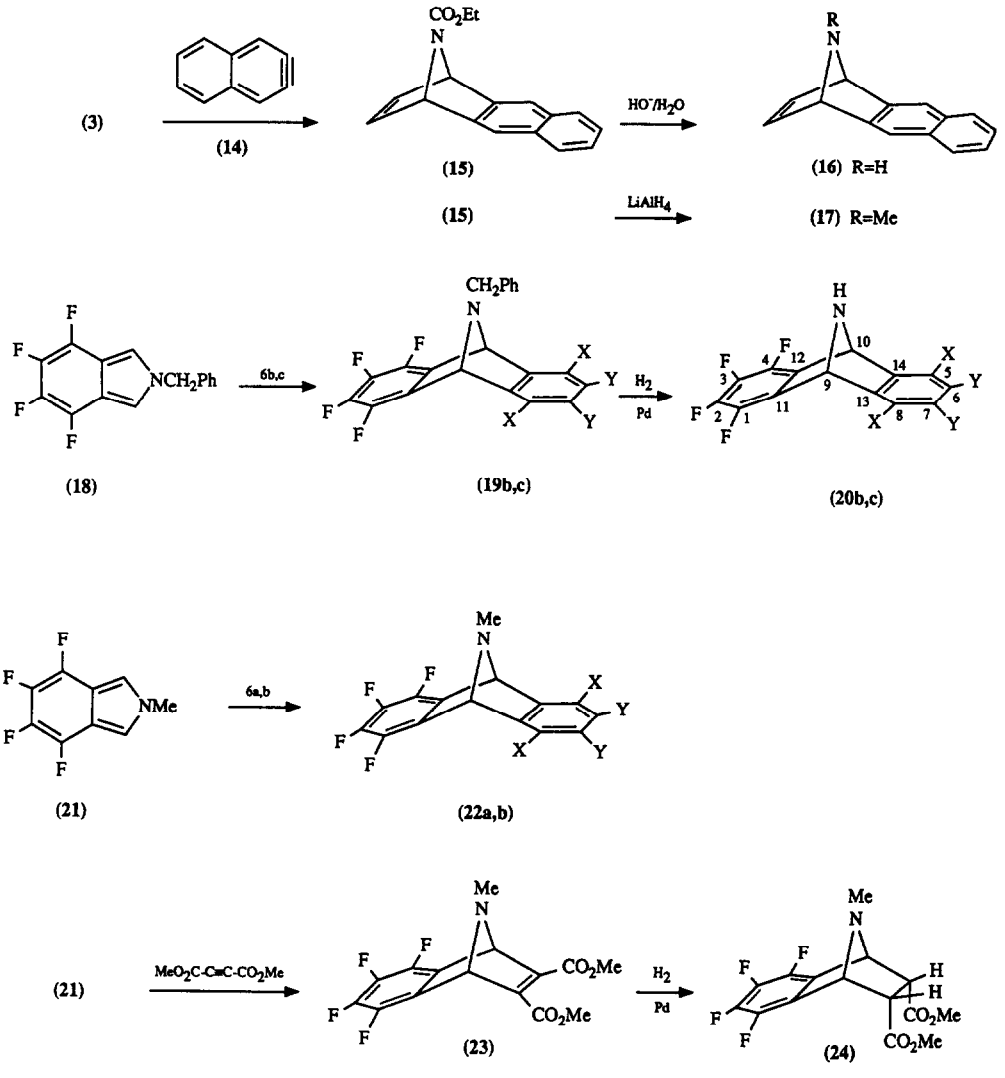
The corresponding tertiary amines were made by reductive amination (using the general method of Borch and Hassid[11] or were prepared directly from N-methylpyrrole[12] (scheme 2).



13 b,c,e

SCHEME 2

Scheme 3 summarises the synthesis of novel 1,4-dihydro-1,4-iminoanthracenes by addition of pyrroles to naphthalyne and of 9,10-dihydro-9,10-imino- anthracenes by benzyne addition to isoindoles[13]; the addition of dimethylacetylenedicarboxylate (DMAD) to 2-methyl-4,5,6,7-tetrafluoroisoindole **(21)** is included in scheme 3.[23] Hydrogenation of the etheno-bridges in **(7)**, **(9)**, **(11)**, **(15)** and **(23)** was straightforward; hydrogenolysis of the N-benzyl derivatives **(19b,c)** to give **(20b,c)** was achieved only with difficulty.



SCHEME 3

Measurement of Invertomer Preferences

Direct observation of syn- and anti-invertomers of the secondary amines **(7)**, **(8)** and **(20)** using ^{1}H and ^{13}C NMR spectroscopy at low temperature was not possible due to rapid inversion or proton exchange (or both); time-averaged ^{13}C NMR chemical shifts for these compounds are shown in table 1 and ^{1}H NMR data for new compounds are included in the experimental section.

At ambient temperature, inversion at nitrogen also led to varying degrees of broadening of signals due to the tertiary amines but on cooling to ca. -50°C, pairs of signals were resolved. Invertomer ratios are shown in table 2; the assignments shown will be justified in due course.

Table 1. ^{13}C NMR Data for Secondary Amines[b]

Compound	Aryl		$C_{2,3}$	$C_{1,4}$	Methyl
(7a)	146.2	($C_{9,10}$)	144.0	65.2	16.2
	130.7	($C_{5,8}$)			15.7
	126.7	($C_{6,7}$)			
(7b)[c]	151.1 s	($C_{9,10}$)	144.3 d	66.2 d	
	124.3 d	($C_{5,8}$)			
	120.5 d	($C_{6,7}$)			
(7c)	148.1 d	($C_{5,8}$)	144.1	63.8	56.2 (OMe)
	140.1 s	($C_{9,10}$)			
	110.8 d	($C_{6,7}$)			
(7e)	complex[a]		144.2 d	63.9	
(8a)	143.8	($C_{9,10}$)	26.0	60.0	16.1
	132.3	($C_{5,8}$)			15.7
	124.8	($C_{6,7}$)			
(8b)[b,c]	150.4 s	($C_{9,10}$)	28.6 t	63.0 d	
	127.7 d	($C_{5,8}$)			
	120.9 d	($C_{6,7}$)			
(8c)	146.8 d	($C_{5,8}$)	26.0 t	58.5 d	56.0 q (OMe)
	137.7 s	($C_{9,10}$)			
	110.2 d	($C_{6,7}$)			
(8e)	complex[a]			26.1	58.9
(20b)	126.4	($C_{5,8}$)	a	61.0	
	121.4	($C_{6,7}$)		($C_{9,10}$)	
	147.7	($C_{13,14}$)			
(20c)	148.2	($C_{5,8}$)	a	61.4	56.4 (OMe)
	112.1	($C_{6,7}$)		($C_{9,10}$)	
	136.6	($C_{13,14}$)			

a: The F-substituted ring showed complex signals due to $^{13}C^{19}F$ coupling.
b: Spectra measured in $CDCl_3$ (except for **(8b)** in CD_2Cl_2) and at ambient temperature.
c: Data for compounds **(7b)** and **(8b)** appear to have been reversed in ref. 6a [compounds **(4)** and **(5)** respectively]. Chemical shift values for **(7b)** are in good agreement with those quoted in ref. 6; slight differences in the values for **(8b)** are presumably due to the difference in solvent. We have also reversed the assignments of signals due to $C_{5,8}$ and $C_{6,7}$ (numbered $C_{8,11}$ and $C_{9,10}$ respectively in ref. 6a) on the basis of substituent shift calculations.

Table 2. Invertomer Ratios for Tertiary Amines

(measured in $CDCl_3$ at -50°C unless stated otherwise).[a]

Compound		Invertomer ratio by ^1H nmr (δ for N-Me) syn-Me : anti-Me[b]		Invertomer ratio by ^{13}C nmr syn-Me : anti-Me[b]
(9a)		70 : 30		
(9b)[e]		71(2.10) : 29(2.36)		69 : 31
(9b)	in CD_3OD (-20°C)	61 : 39		
(9c)		80(2.18) : 20(2.36)		80 : 20
(9d)		82(2.22) : 18(2.36)[d]		77 : 23
(9e)		88(2.18) : 12(2.36)[d]		84 : 16
(9e)	in CD_3OD (-55°C)	82 : 18		
(10a)	(-40°C)	f		95 : 5
(10b)[e]	(-55°C)			94 : 6[24]
(13b)	(-55°C)	94 : 6	(c.f. 93:7[9])	
(10c)	(-55°C)	f		97 : 3
(13c)	(-55°C)	f		97 : 3
(10d)	(-55°C)	f		97 : 3
(10e)	(-62°C)	f		98 : 2
(12e)	(-40°C)	f		88 : 12
(17)		86(2.10) : 14(2.40)		
(19b)		68 : 32[c]		
(19c)		60 : 40[c]		
(22b)		71(2.38) : 29[c](2.10)	(c.f. 73:27[5a])	
(23)	(-40°C)	66(2.18) : 34(2.46)		65 : 35
(24)	(-63°C)	~100(2.08) : 0		~100 : 0

a. **Errors.** Reproducibility in our hands was better than ±3%, usually based on integration of a number of pairs of signals. We recognise that errors may arise in principle in the ^{13}C n.m.r. integrations as a result of possible differences in relaxation rates between a pair of invertomers but the good agreement between the ^1H and ^{13}C values in table 2 is reassuring. The effect of solvent polarity on inversion barriers and ratios has been noted earlier[32] and is illustrated in table 2 by measurements for **(9b)** and **(9e)** in two solvents.

b. Syn-/anti- methyl with respect to the aryl ring.

c. Syn-/anti- methyl with respect to the tetrafluoroaryl ring.

d. These ratios differ slightly from those reported in ref. 5 but were reproducible using freshly purified materials. The ratios measured by ^{13}C n.m.r. were closer to these earlier values but are averages of ratios which varied more widely (±6%) between the sets of resonances; integration of the aryl carbon signals in **(9e)** was not possible due to C-F coupling. The ratio differences from the earlier work are not energetically significant but we have reversed the assignments for the preferred invertomer suggested in ref. 5.

e. The invertomer ratios for these compounds are not clearly reported in ref. 6. The ratios for compounds **(10b)** [2 in ref. 6] and **(9b)** [3 in ref. 6] appear to be reversed in table 1. in that paper; we assume that the authors measured a ratio of 80:20 for **(9b)** in $CDCl_3$ (71:29 in our hands). The quoted ratio for **(10b)** is 94:6 but we agree with the observation of Underwood[8] that the two N-methyl signals for the free amine are not separated at ambient temperature and the δ values quoted in ref. 6 [e.g. for **(9b)**, δ 2.60 and 2.36] are unreasonable. These results refer to solution in $CDCl_3$ but are more consistent with the spectra to be expected if the amine had been protonated.

f. The signals due to the minor invertomer could not be integrated accurately using ^1H NMR.

Selected signals in the ^1H NMR spectra of many of the compounds in table 2. were sufficiently well separated to allow integration at low temperature, e.g **(9a-e)**. Corresponding integration of pairs of signals in low-temperature ^{13}C spectra agreed well. Marchand[9a] has already recognised the heavily biased invertomer ratios for compound **(10b)** from ^1H NMR spectra and used the dideuterio- analogue **(13b)** to allow integration; kinetic protonation studies confirmed the 94:6 ratio. We were also able to see signals due to major and minor invertomers in the low-temperature ^1H NMR spectra of the dideuterio-compounds **(13b,c,e)** but accurate integration was only possible for **(13b)**. Measurement by ^{13}C NMR was possible, however, and there is good agreement between values obtained for **(10b)/(13b)** and for **(10c)/(13c)** showing that the substitution of D for H has no measurable effect on the invertomer ratio. We have obtained reasonable agreement between ratios for amines **(9)**, **(13)** using the kinetic protonation technique[10b] and low-temperature ^{13}C NMR measurements but found the latter method to be more convenient and reliable. Two sets of signals were observed at low temperature for all the latter entries in the table with the exception of **(24)**.

Given the controversy over the effects controlling invertomer preferences[6,7,8] in the few compounds for which direct measurements had been made[5,6,9] and the implication that substituents in an aryl ring could have a major effect on preferences [e.g. 80% syn-Me for **(9b)**[6] versus the suggested 83% anti-methyl for **(9e)**[5]], we felt it important to assign invertomer preferences clearly and consistently in this family of compounds. A knowledge of preferred invertomers was also necessary in order to attempt any investigation of stereoelectronic control in reactions at an inverting nitrogen atom[3,4,10]. We used the following approaches.

Assignment of Stereochemistry

1) ^1H NMR results

The minor resonance of the two N-methyl signals in the ^1H NMR spectra of each of the amines **(9)** at low temperature was at lower field than the major (table 2). The fact that the chemical shift of the minor N-methyl signal remained constant at δ 2.36 in these amines, despite the changing electronic character of the aryl ring, was consistent with its placement over the etheno-bridge (i.e. anti- to the aryl ring). The higher field position and greater variation in the δ value observed for the major signal was consistent with placement of the N-methyl group over the aryl ring; it thus experienced the greater shielding effect which varied as a function of aryl substitution. A similar pattern was observed for compounds **(17)** and **(23)** where the major, downfield signal was assigned to the anti- invertomer in each case.

The distinction between the methyl group syn-to the F_4-aryl ring (δ 2.38) in **(22b)** and that syn- to the H_4-aryl ring (δ 2.30) was based on a comparison between the values for the N-methyl group syn- to the aryl ring in **(9e)** (δ 2.18) and **(9b)** (δ 2.10) respectively. The chemical shift values are not directly comparable but the Δδ value is 0.08 ppm in each case, with the resonance for the N-Me over the tetrafluorinated ring being at lower field as expected in view of the reduced shielding. A similar Δδ value of 0.09 ppm was measured for the two benzyl CH_2 signals observed for **(19b)** (CH_2 syn- to F_4-aryl = δ 3.53; CH_2 syn- to H_4-aryl = δ 3.44).

In the case of **(24)** no minor signals were visible in the ^1H NMR spectrum even at -63°C; the observation of single resonances for $C_{1,4}$, $C_{2,3}$ and the N-methyl carbon confirmed the overwhelming syn-preference.

In related studies, the quaternisation of amines **(9)** and **(10)** with CD_3I[10b] has yielded two diastereoisomeric quaternary ammonium salts; the pattern of methyl signals here was also entirely consistent with the anti-N-methyl signal being at lower field and relatively insensitive to aryl substitution. In the case of **(10b)** the correspondence of the values for proposed syn-**(25)** and the value actually observed by other workers[25] for the salt **(26)** (where only syn-methylation is possible) is gratifying.

Table 3. ^{13}C NMR Data for Tertiary Amines[a]

Compound		$C_{1,4}$	$C_{2,3}$	$C_{5,8}$	$C_{6,7}$	$C_{9,10}$	NMe	CMe/OMe
(9a)	maj. syn-	70.2 d	143.5 d	130.1 s	132.0 s	140.7 s	36.4 q	16.8, 16.1 q
	min. anti-	70.8 d	138.1 d	127.0 s	131.4 s	144.1 s	35.4 q	17.3, 16.3 q
	Δδ	-0.6	5.4	3.1	0.6	-3.4	1.0	
(9b)	maj. syn-	71.4 d	143.8 d	123.5 d	124.7 d	147.4 s	36.9 q	
	min. anti-	72.2 d	138.4 d	120.1 d	124.1 d	149.7 s	35.9 q	
	Δδ	-0.8	5.4	3.4	0.6	-2.3	1.0	
(9c)	maj. syn-	69.1 d	143.9 d	150.3 s	109.9 d	135.2 s	37.1 q	55.6 q
	min. anti-	69.5 d	138.4 d	146.8 s	109.4 d	138.4 s	36.1 q	55.8 q
	Δδ	-0.4	5.5	3.5	0.5	-3.2	1.0	
(9d)[b]	maj. syn-	72.4	143.4	127.8	128.8	147.1	36.8	
	min. anti-	72.5	138.8	126.9	128.2	148.9	35.1	
	Δδ	-0.1	4.6	0.9	0.6	-1.8	1.7	
(9e)	maj. syn-	69.4 d	143.4 d	138.0m[c]	144.1m[c]	128.6m[d]	37.1 q	
	min. anti-	69.4 d	138.4 d	e	e	131.0m[d]	35.5 q	
	Δδ	0.0	5.0			-2.4	1.6	
(10a)[f]	maj. syn-	66.2	27.0	127.5	132.9	139.3	35.5	16.6, 16.1
	min. anti-	64.5	22.0	124.3	131.9	142.4	35.9	16.5, 16.0
	Δδ	1.7	5.0	3.2	1.0	-3.1	-0.4	
(13b)[bg]	maj. syn-	66.4	26.2	121.5	125.7	143.5	35.0	
	min. anti-	64.8	21.3	118.6	125.1	146.2	35.3	
	Δδ	1.6	4.9	2.9	0.6	-2.7	-0.3	
(10c)[b]	maj. syn-	64.2	26.3	148.8	109.0	132.0	35.2	
	min. anti-	62.2	21.4	145.7	108.5	135.2	35.6	
	Δδ	2.0	4.9	3.1	0.5	-2.8	-0.4	
(10d)[b]	maj. syn-	67.9	25.5	130.0	126.8	142.5	35.3	
	min. anti-	65.9	20.9	e	e	e	e	
	Δδ	2.0	4.6					
(10e)[h]	maj. syn-	64.6	25.9	138.8[c]	141.9[c]	125.4[d]	35.2	
	min. anti-	62.4	21.5	e	e	e	35.6	
	Δδ	2.2	4.4				-0.4	
(23)	maj. syn-[f]	71.7	150.8	i	[CO: 162.1]		36.1	52.9
	min. anti-	72.2	147.1	i	[CO: 163.3]		35.7	52.9
	Δδ	-0.5	3.7				0.4	
(24)[f]		67.7	47.0	i	[CO: 170.2]		34.6	52.1

		$C_{9,10}$	$C_{5,8}$	$C_{6,7}$	$C_{13,14}$	Benzyl	*(Methyl)*
(22a)	maj. syn-[j]	69.2	i	i	i		*(36.8 NMe; 16.5, 16.0)*
	min. anti-	68.6	i	i	i		*(36.0 NMe; 16.6, 16.0)*
(19b)	maj. syn-[j]	67.5	126.1	121.2	145.8	53.7,127.51,128.5,129.1,136.6	
	min. anti-	66.7	126.6	123.9	144.5	52.8,127.50,128.5,129.1,136.6	
(19c)	maj. syn-[j]	64.8	147.0	111.0	134.4	53.8,127.44,128.5,129.16,136.3	*(55.6)*
	min. anti-	64.4	150.1	111.3	132.4	53.0,127.36,128.5,129.12,136.6	

a: Spectra recorded in $CDCl_3$ at 75 MHz with TMS as internal standard and at -50°C unless otherwise stated; letters refer to multiplicities in off-resonance decoupling experiments. The assignment of signals due to the aryl carbons was based on simple calculations using substituent shift values[37]. Syn- and anti- denote stereochemistry of N-alkyl group with respect to the aryl ring.

b: This spectrum was measured at 100 MHz and at -55°C. We thank Dr. O.Howarth, SERC NMR Service, University of Warwick, for these spectra

c: $J_{C,F}$ = ca. 250 Hz; longer range CF coupling was not analysed.

d: CF coupling was not analysed.

e: Signals due to the minor invertomer were lost in baseline noise.

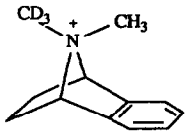
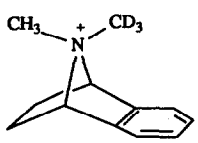
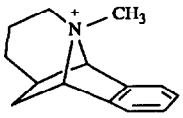
f: Spectrum measured at -40°C

g: Figures for **(13b)** are used in place of **(10b)**; deuteriation in **(10c)** led to differences in chemical shift of less than 0.1 ppm.

h: This spectrum was measured at 100 MHz and at -62°C.

i: The aryl signals were not clearly resolved due to CF coupling.

j: Syn-/anti- with respect to the tetrafluoroaryl ring; spectra recorded at -30°C.

(10b) ----> **syn-(25)** + **anti-(25)** **c.f. (26)**

δ_{Me} 3.10 δ_{Me} 3.10[25]

2) The χ -effect in ^{13}C NMR

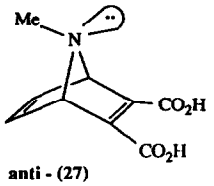
The chemical shift difference between the major and minor signals assigned to $C_{2,3}$ of compounds (**9a-e**) and (**10a-e**) was ca. 5 ± 0.5 ppm (table 3); the upfield signal was assigned to the invertomer suffering the compression effect of the proximate N-Me (anti- to the aryl ring) and was the minor invertomer in each case. The corresponding Δδ value for $C_{9,10}$ was smaller but significant; the major signal was found to be upfield in each case corresponding to the N-Me syn- to the aryl ring. The results for (**10a-e**) and (**13**) correspond closely. Morishima and Underwood working with (**9b,e**) and (**10b**) and Marchand with (**13b**) concluded that the major invertomer has the syn- methyl configuration. A crystalline sample of (**9b**) has been obtained and a crystal structure determination has shown it to have the methyl group syn-[26]; it is clear that the major invertomer crystallises preferentially (rather than the minor, as implied by the original, tentative assignment[5]).

Our work strengthens and extends the proposed syn-methyl preference to all of the amines (**9a-e**) and (**10a-e**) and encompasses the related systems (**12**), (**17**), (**22**), (**23**) and (**24**). A similar picture emerges for the N-benzyl compounds (**19**) where the smaller of the two signals due to $C_{13,14}$ is upfield of the larger; this shows that the minor invertomer has the benzyl group syn- to the non-fluorinated ring and hence the major invertomer has the benzyl syn- to the tetrafluoroaryl ring.

The consistency of the ^{13}C results and the invertomer preferences in this extended series adds to our confidence in the assignments and justifies the reassignments of the selected literature values referred to above.[27]

Invertomer preferences

Unequal invertomer ratios are a consequence of steric and/or electronic influences. Steric influences seem to be the predominant factor in determining invertomer preferences in a series of 2-azabicyclo-[2.2.2]octane/ene and [2.2.1]heptane/ene systems when the N-substituent is chlorine[31] and also in N-methyl-2-azabicyclo[2.2.2]oct- 5-ene.[6b] There are also systems in which electronic factors seem to be of significance, thus Morishima[6] observed that the invertomer ratio in the 7-azabicyclo[2.2.1]hepta-2,5-diene derivative (**27**) varied substantially according to the pH of the solution (76% anti-Me in dmso; 80% syn-Me in D_2O at pD 11). These observations were explained on the basis of a repulsive bis-homoallyl interaction between the nitrogen lone-pair and the π-bonds. Thus, a lone pair faced with interaction with either of two double bonds would prefer to interact with the less electron-rich of the two. In the case of (**27**), the difference was explained assuming a reduction of the electron density in the substituted π-bond by the



anti - (27)

electron-withdrawing (non-ionised) carboxylic acid groups versus an increase in electron density of the same π-bond by the carboxylate anions. It should be recognised, however, that the role of differential solvation was not considered and Nelsen has pointed out in a different system[30] that such amino acids will presumably exist at least partially as the N-protonated zwitterion. Morishima developed the argument to compounds (**7b**) and (**8b**) together with the N-methyl compounds (**9b**) and (**10b**). However, both the proposed assignment of the preferred orientation of the N-H in the secondary amines and the overall conclusions were challenged by Grutzner[7] and Underwood[8] who decided from PES work and contact shift studies, respectively, that the stabilisation arising from bishomoconjugative delocalisation is extremely small. No clear rationale emerged to explain the limited number of reported invertomer ratios, beyond a recognition that steric factors can be important. Whilst we were unable to comment on the secondary amines (where invertomer ratios can only be obtained indirectly), we felt that direct measurement of invertomer preferences for a range of bicyclic tertiary amines (where the inversion barrier is substantially higher) would be valuable in exploring further the relative importance of electronic effects. Variation of substituents in the aryl ring in each family of compounds would allow alteration of the electronic situation with minimal steric change and provide a simple, empirical test of the importance of π-lone pair interactions in this ring system.[40]

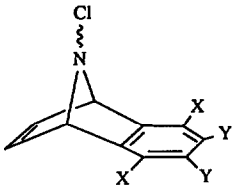
Two significant observations emerged from our results.

The first is the very small change in the invertomer ratio along the series (**9a-e**) [table 2] despite the very substantial change in electronic character of the aryl ring. The difference between benzo- (**9b**) and naphthaleno- (**17**) is also small ($\Delta\Delta G^{o}_{223K}$ = 1.7 kJ mol^{-1}); a major change in substituents on the etheno-bridge [c.f. (**9e**) and (**23**)] leads to a slightly larger difference in ratio but even this corresponds to a value for $\Delta\Delta G^{o}_{223K}$ of only 3.7 kJ mol^{-1}. Interestingly, the relative effects of differently substituted aryl rings, though small, seem to operate consistently. Thus, average invertomer ratios for (**9b**) [70:30] and (**9e**) [86:14] give ΔG^{o}_{223} values of ~1.6 and 3.4 kJmol^{-1} respectively and hence a difference of ~1.8 kJmol^{-1} which reflects the greater amount of the syn-methyl invertomer in the F_4-benzo rather than the H_4- case. This matches the observed preference shown by the N-methyl in (**22b**) [$\Delta G^{o}_{223} \approx$ 1.7 kJ mol^{-1}] where the two aryl rings are in competition in the same molecule.

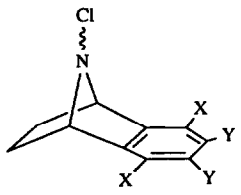
The observed ratios show a general increase in the proportion of the syn-methyl invertomer (a decrease in the proportion of anti-methyl/syn-lone pair) with an increase in the electronegativity of the substituents in the aryl ring.

Secondly, the values for the N-methyl compounds (**9a-e**) and (**17**) are remarkably similar to the ratios already recorded[3] for the corresponding N-chloro-analogues (**28a-f**) which are summarised in table 4.

Both of these observations are contrary to the predictions based on Morishima's model that the bishomoallylic interaction of the nitrogen lone pair is a destabilising one and that, when faced with overlap with two π-orbitals, the lone pair will interact with the less electron-rich of the two.



(28a) - (28f)



(29b) - (29e)

[a - e as in Scheme 1]

Table 4. syn-Cl : anti-Cl Ratios for N-Chloroamines (28) and (29)[3]

[values shown refer to Cl substituents respectively syn-/anti- to aryl ring]
[values for corresponding N-methyl compounds (9) and (10) are shown in brackets]

	(28)	(9)		(29)	(10)
a	63 : 37	[70 : 30]			
b	60 : 40	[71 : 29]	**b**	53 : 47	[94 : 6]
c	67 : 33	[80 : 20]	**c**	54 : 46	[97 : 3]
d	82 : 18	[82 : 18]	**d**	71 : 29	[97 : 3]
e	84 : 16	[88 : 12]	**e**	80 : 20	[98 : 2]
f	87 : 13	[86 : 14]*			

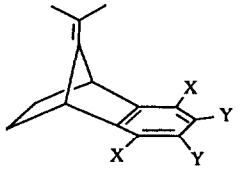
[**a-e** as in scheme 1; **f**: X = H; YY = benzo] ***(9f)** = **(17)** in scheme 3.

First, the energy of the HOMO of the aryl ring is expected to be lowered as the ring becomes substituted with electron-withdrawing groups. The gradation of the vertical ionisation potentials of a range of 1,4-dihydro-1,4-isopropylidene-naphthalenes **(30)**[28] illustrates the stabilisation of the HOMO by fluorine substitution (table 5), and provides a good analogy with the present work, showing the dramatic decrease in electron density above and below the benzene ring which results from halogen substitution, in particular. This shows itself in the stereoselectivity observed in the reactions of **(30)** with electrophiles[28] and is mirrored in the stereoselectivity shown in corresponding reactions of the nitrogen analogues **(7)**.[3] Given such an effect on the aryl π-system, any repulsive n-π interactions should be reduced and lead to an increase in the proportion of the anti-invertomer (syn- lone pair). This is contrary to the observed trend.

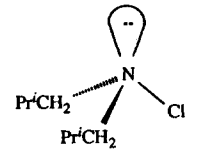
Table 5. Vertical ionisation potentials for (30) (eV)

	a′(π)	a″(π)	a′(π)
X = Y = H	8.20	8.70	8.85
X = OMe; Y = H	8.20	7.70	8.70
X = Y = F	9.03	8.75	9.03

(30)



Second, the lone pair of an N-chloroamine is expected to be much less diffuse than that of a teriary alkyl amine because of the increase in s-orbital character induced by the electronegative chlorine. An example of this effect has been found by Jennings who observed that the inversion barrier of the N-chloroamine **(31)** was insensitive to the polarity of the solvent used (ΔG = 39.71 kJmol^{-1} in $CHCl_2F$ and CD_3OD.[29] Thus, the replacement of methyl by chlorine in our systems would be expected to lead to an increase in the amount of the minor invertomer based on the



(31)

Morishima model since the degree of destabilisation would be lessened by the reduced n-π interactions. Very slight increases are observed in the amounts of anti-invertomer for (**28a,b,c,e**) compared to the corresponding amines (**9**) but (**28e,f**) do not change significantly. Thus the lone pair appears to play a minor role in determining the preferred configuration at nitrogen, as asserted earlier by Grutzner.[7]

In the 1,2,3,4-tetrahydro- systems (**10**) the proportion of the syn-methyl invertomer is increased relative to (**9**). However, this is presumably a consequence of the increase in steric congestion in the anti-configuration where the N-methyl encounters the exo- 2,3- protons of the ethano- bridge. The raising of the energy of one invertomer at nitrogen relative to its diastereomer as a result of steric congestion is a common phenomenon.[32] The heavy preference for the syn-methyl group in the amines (**10**) is hardly modified along the series despite substantial changes in the substitution of the aryl ring. The reduced syn- preference for the N-chloroamines (**29**) relative to the N-methyl analogues (**10**) (table 4) is presumably a reflection of the smaller size of the chlorine. The trend along the series (**29b**) - (**29e**) shows an increased tendency for the chlorine to lie over the aryl ring as the electron density in the ring is reduced; this would fit with simple expectations based on the demands of the N-Cl dipole.

Finally, it should be observed that the differences in invertomer ratio between the series of N-chloroamines (**28**) and the corresponding N-methyl amines (**29**) are very small. Indeed, with the exception of the steric factor in the case of series (**10**), there is little significant variation shown by the figures for each of the horizontal entries in table 4., emphasising that, whilst homoconjugative effects between neutral, closed shell systems are destabilising,[41] systems suffering such an interaction will distort to minimise the repulsive effects.[7]

Table 6. Nitrogen Inversion Barriers in Selected Bicyclic Tertiary Amines[a]

Compd	signal	solv.	T_c (°C)	Δυ (Hz)	$\Delta G^{\neq}_{inv}$[b] (kJ mol^{-1})		$\Delta G^{\neq}_{anti \rightarrow syn}$[c] (kJ mol^{-1})		$\Delta G^{\neq}_{syn \rightarrow anti}$[c] (kJ mol^{-1})	
					at T_c	25°C[f]	at T_c	25°C[f]	at T_c	25°C[f]
(**9a**)	(C=CH)	$CDCl_3$	44 ±2	32 ±2	66.5	66.9	65.7	66.1	67.9	68.3
(**9b**)	(N-Me)	$CDCl_3$	34 ±2	31 ±2	64.4	64.6	63.6	63.8	65.9	66.1
(**9b**)		CD_3OD					68.8		70.0	
(**9c**)	(N-Me)	$CDCl_3$	32 ±2	18 ±2	65.3	65.5	64.3	64.4	67.8	67.9
(**9d**)	(N-Me)	$CDCl_3$	5 ±2	16 ±2	59.6	59.2	58.6	58.2	62.1	61.7
(**9d**)[e]	(N-Me)	$CDCl_3$	-2 ±2	7.5	58.5					
(**9e**)	(N-Me)	$CDCl_3$	6 ±2	20 ±2	59.3	58.9	58.1	57.7	62.7	62.3
(**9e**)[e]		$CDCl_3$	1 ±2	10.4	58.5					
(**9e**)		CD_3OD					59.8		63.4	
(**13b**)	(N-Me)	$CDCl_3$	-5 ±4	24 ±2	56.5	55.8	55.2	54.6	61.3	60.7
(**13b**)[9a]	(N-Me)	$CDCl_3$	-40	21	54.3					
(**17**)	(N-Me)	$CDCl_3$	29 ±2	30 ±2	63.4	63.5	62.1	62.2	66.7	66.8
(**19b**)[d]			1 ±2	36 ±2	56.9	56.4	56.2	55.7	57.9	57.4
(**19c**)[d]			-7 ±2	12 ±2	57.6	56.9	57.1	56.4	58.0	57.3
(**22b**)	(N-Me)	$CDCl_3$	-6 ±2	8 ±2	58.7	58.0	58.0	57.4	60.0	59.4
(**22b**)[de]	(N-Me)	$CDCl_3$	-27	5.4	54.3					
(**23**)	(N-Me)	$CDCl_3$	-3 ±2	28 ±2	56.6	56.0	56.2	55.6	57.2	56.6

a. ^{1}H n.m.r. spectra measured at 100 MHz except where indicated[e].
b. Calculated directly from the Gutowsky-Holm equation assuming equal ratios of the two invertomers; quoted literature comparisons were also obtained in this way.
c. Syn-/anti- with respect to the aryl ring;[d] calculated using equilibrium constants from table 2.
d. In the case of (**19**), syn-/anti- with respect to the tetrafluoroaryl ring.
e. Measured at 60 MHz (ref. 5).
f. Extrapolation of $\Delta G^{\neq}$ value from T_C to 25°C using an estimated value of $\Delta S^{\neq}$ of 5 eu.[30,1]

Barriers to Inversion at Nitrogen

We[2b] and others[1,30] have discussed the unusually high barriers to inversion at nitrogen which characterise derivatives of the 7-azabicyclo[2.2.1]heptyl system. Lehn's suggestion of a 'bicyclic effect'[1] has yet to be fully explained although recent work by Nelsen has explored the phenomenon more deeply and has led to better estimates of the size of the effect.[30]

Until recently, inversion barriers for N-alkyl derivatives of the 7-azabicyclo[2.2.1]heptyl system have been available only for the N-methyl amines **(9d,e)**, **(22b)** and the N-benzyl series **(32)** - **(34)**.[33] Values have since been reported for N-methyl **(35)** and N-ethyl **(36)** derivatives of the parent system.[30] An estimate of 76.9 kJmol^{-1} was made some time ago[34] for the N-methyl amine **(9b)** using the known value of 98.0 kJ mol^{-1} for the N-chloro analogue **(28b)**[36] and the empirically derived relationship $\Delta G^{\neq}_{Cl} + \Delta G^{\neq}_{Me} \approx 1.28$. Whilst this relationship has been used successfully by Anet in work on piperidines,[35] our results (table 6) show that the relationship is not applicable to the title ring system, presumably due to operation of the 'bicyclic' effect. The measurement of inversion barriers was not the prime objective of this work but the present results (with literature comparisons where available) are summarised in table 6 and provide an opportunity to consider the relative effects of ethano-, etheno-, substituted etheno-, benzo- and substituted benzo- groups on the nitrogen inversion barrier in this ring system.

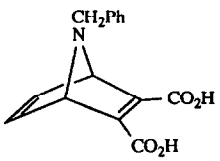
The nitrogen inversion barriers are measured at different coalescence temperatures and table 6 therefore includes values extrapolated to 25°C using the estimate for $\Delta S^{\neq}$ of 5 eu used by others.[30,1]

The values of $\Delta G^{\neq}_{anti \rightarrow syn}$ and $\Delta G^{\neq}_{syn \rightarrow anti}$ shown in table 6 have been calculated using equilibrium constants measured at -50°C (ratios in table 2). The extrapolation to 25°C is, again, included for reference. We recognise that these values are necessarily approximate although invertomer ratios did not appear to vary significantly over the limited temperature range available. We believe that it is possible to make some useful empirical observations (table 7).

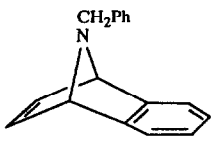
Table 7. Selected Nitrogen Inversion Barriers

[kJ mol^{-1}; 25°C]

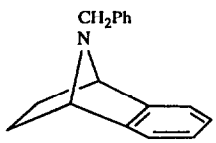
Compound	$\Delta G^{\neq}_{inv}$	$\Delta G^{\neq}_{syn \rightarrow anti}$	Compound	$\Delta G^{\neq}_{inv}$
(9b)	64.6	66.1	**(9a)**	66.9
(13b)	55.8	60.7	**(9b)**	64.6
(35)[30]	57.4	57.4	**(17)**	63.5
(36)[30]	54.9	54.9	**(9c)**	65.5
			(9d)	59.2
(32)[33]	59.8		**(9e)**	58.9
(33)[33]	61.9		**(22b)**	58.0
(34)[33]	52.7		**(23)**	56.0
(19b)	56.4			
(19c)	56.9			



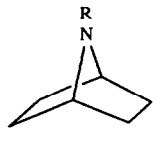
(32)



(33)



(34)



(35) R=CH_3

(36) R=CH_2CH_3

If interactions between the bridging π-systems and the N p-orbital are important at the transition state for N inversion, we would expect to see changes as the unsaturated bridges are saturated sequentially. On the basis of the data available, it was suggested recently that 2,3:5,6-unsaturation does not have a very large effect on 7-azanorbornane N inversion barriers.[30] However, comparison of $\Delta G^{\neq}_{syn\rightarrow anti}$ values for **(9b)** and **(13b)** shows a barrier reduction (5.4 kJ mol^{-1}) as the etheno- bridge is saturated and there is a further drop (3.3 kJ mol^{-1}) to the totally saturated **(35)**. Use of $\Delta G^{\neq}_{syn\rightarrow anti}$ values for **(9b)** and **(13b)** is justified here since they provide the best estimate of the energy difference between the two similar ground states (N-Me syn- to a benzo- ring in each case) and the corresponding transition states. In contrast, comparison of average ($\Delta G^{\neq}_{inv}$) values would suggest a larger difference (8.8 kJ mol^{-1}) between **(9b)** and **(13b)** but this is an exaggeration brought about by the higher ground state energy of the anti-Me invertomer of **(13b)**.

These figures suggest that the inversion barrier is lowered by saturation of one or more of the bridging π-bonds but also imply that a major factor here is the ground state destabilisation of the anti- N-Me invertomer (discussed earlier in the section on invertomer preferences). This is supported by the further reduction of the barrier of **(35)** by 2.5 kJ mol^{-1} on replacement of the N-Me by the slightly more bulky ethyl group.[30] Earlier work on the N-benzyl compounds **(33)** and **(34)** shows lower values than for the N-methyl compounds; there is a substantial drop on saturation of the etheno-bridge but the effect is probably exaggerated here, also.

Ground state effects caused by steric factors are less important in the other cases in table 7. A reduction in $\Delta G^{\neq}_{inv}$ of 5.5 kJ mol^{-1} is seen on replacement of the etheno- bridge in **(33)** by a tetrafluoroaryl ring in **(19b)**, consistent with a reduction of π-electron density. The effect is repeated for **(9b)** → **(22b)** (-6.6 kJ mol^{-1}) and is significant here in view of the even balance of ground state effects indicated by an identical invertomer ratio (71:29) for each amine.

The series **(9a-e)**, **(17)** provides an interesting comparison of the effect on $\Delta G^{\neq}_{inv}$ values of systematic changes in the electronic character of the benzene ring. The trend is clear: the most electron-rich aryl ring (tetramethyl) is associated with the highest inversion barrier, the all-hydrogen analogue is lower by 2.3 kJ mol^{-1}, and the dimethoxyaryl ring sits between these two. There is a substantial change for the two electron-deficient systems which show barriers which are lower by >6 kJ mol^{-1}. The slightly lower inversion barrier for the naphthaleno- bridged system **(17)** when compared to the benzo analogue **(9b)** may be associated with the reduced naphthalene 2,3-double bond character which results from partial bond fixation.

Comparison of etheno-, benzo- and carbomethoxy-substituted etheno- bridges is possible using $\Delta G^{\neq}_{inv}$ for **(9e)**, **(22b)** and **(23)** which share a common tetrafluorobenzo- ring as the second 'bridge'. Barriers are very similar for etheno- and benzo- but the reduction of electron density which results from introduction of methoxycarbonyl groups in **(23)** leads to a lowering of the inversion barrier in this case.

Conclusions

The barriers to inversion at nitrogen in the title compounds are uniformly high due to operation of the 'bicyclic effect'. The inversion barriers in N-alkyl derivatives of 7-azanorbornanes, -enes and 7-azanorbornadienes are sensitive to the effect of substituents in the ethano-, etheno- and benzo- bridges and at nitrogen. The barrier is highest when the nitrogen is flanked by electron-rich π-bonds; electron-withdrawing groups in bridging etheno- or benzo- groups lead to a lowering of the barrier. This is consistent with the idea of a reduction in destabilising interactions between the bridging π-bonds and the nitrogen p-orbital at the transition state for inversion but such a rationalisation may be an over-simplification since it does not take into account more complex orbital interactions in the rigid bicyclic framework or possible changes in ground-state energy. Indeed, an increase in the size of the substituent on nitrogen or the presence of exo-substituents in a saturated two-atom bridge (such as the exo-hydrogens in an ethano-bridge) leads to a lowering of the inversion barrier consistent with a simple destabilisation of the ground state due to steric interactions. It is not possible to separate ground state and transition state effects, both of which clearly influence $\Delta G^{\neq}_{inv}$.

Systematic comparison of the variation of invertomer ratios as a function of change in electronic character of etheno- and substituted benzo- bridges shows clear but small effects. The results contradict the earlier suggestion[6] that the nitrogen lone pair suffers a destabilising interaction with bridging π-bonds and, when given the choice, will prefer to interact with the less electron-rich of the two; the proportion of lone-pair syn- to a benzo- group actually increases as the aryl ring becomes more electron-rich. The electronic effects are relatively small, however and invertomer ratios vary relatively little even when the substituent at nitrogen changes from alkyl to chloro. These results support the assertion[7,8] that the nitrogen lone pair plays a minor role in determining the preferred configuration at nitrogen.

The largest displacement of the invertomer ratio is seen in systems having a saturated (ethano-) bridge where destabilising steric interactions are paramount.

Experimental

Experimental details are included for new compounds and also for known compounds where these were prepared by a different method to that reported previously.

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 with 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 run 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 and letters in brackets refer to observed multiplicities in off-resonance proton-decoupling experiments, where applicable.

Temperature measurements on the Bruker AM 300 instrument 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 Swansea.

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

N-Ethoxycarbonylpyrrole (3) was prepared according to the method of Ciamician and Dennstedt[14] in 55% yield, b.p. 69 - 72°C/ 17 mm Hg (lit.[14] 180°C).

N-Trimethylsilylpyrrole (4) was prepared from pyrrole and hexamethyldisilazane by the method of Fessenden and Crowe[15] in 73% yield, b.p. 72-76°C/60 mm Hg (lit.[15] 150 - 151°C). ^1H NMR δ 6.75 (m, 2H), 6.25 (m, 2H), 0.5 (s, 9H).

1,4-Dihydro-1,4-iminonaphthalene Derivatives

5,6,7,8-Tetramethyl-1,4-dihydro-1,4-iminonaphthalene (7a)

Following the general procedure of Hart and Teuerstein,[16] a stirred mixture of 1,2-dibromo-3,4,5,6-tetramethylbenzene (25.0 g; 0.09 mole) and N-trimethylsilylpyrrole (23.0 g; 0.17 mole) in dry THF (285 ml) was cooled to -78°C under nitrogen. The addition of n-butyllithium (1.6 M solution in hexane, 60 ml) in six portions from a syringe caused the solid to dissolve and the solution to turn cherry red. After stirring at -78°C for 1 h, the solution was allowed to warm to room temperature over 1 - 2 h and left overnight. The reaction mixture was poured into water (350 ml) and the organic phase separated. The aqueous layer was extracted further with diethyl ether (3 × 100 ml). The combined organic extracts were dried and evaporated under vacuum. The resultant dark red oil was treated with fumaric acid (10.5 g; 0.095 mole) in hot propan-2-ol (150 ml). On cooling, buff-coloured crystals of the fumarate salt of **(7a)** were precipitated (8.6 g; 32%).

The free amine was liberated by treatment with 2M NaOH solution and was extracted into dichloromethane. After drying and evaporation, the amine **(7a)** was obtained as a white solid. Vacuum sublimation gave fine, white crystals, m.p. 77-79°C. IR (CH_2Cl_2) 3260w, 3000m, 2920m, 2860m, 1450m, 1350m, 1190m, 1095m, 1055m, 1025m, 860s, 835s cm^{-1}; ^1H NMR δ 6.96 (m, 2H, $H_{2,3}$), 5.06 (m, 2H, $H_{1,4}$), 3.00 (br.s, NH), 2.22 (s, 6H, Me), 2.10 (s, 6H, Me); ^{13}C NMR see table 1; MS $^m/z$ 199 (M^+), 184, 173, 157; observed accurate $^m/z$ 199.136, calculated for $C_{14}H_{17}N$ 199.1361.

1,4-Dihydro-1,4-iminonaphthalene (7b)

The N-ethoxycarbonyl derivative of **(7b)** was obtained from **(3)** according to the method described in reference 9b; 'falling-film' distillation (80°C/0.2 mbar) gave a sample which, after washing with cold petrol, had m.p. 53.5-55°C. Hydrolysis of this purified sample using excess 17% aqueous NaOH was monitored by ^1H NMR. The reaction was approximately 74% complete after 21 h and 88% complete after 45 h at which time the product was extracted into diethyl ether, dried and concentrated under vacuum. Distillation (Kugelrohr; 120°C/0.2 mm Hg) gave **(7b)** in 78% yield from the N-ethoxycarbonyl compound. Spectroscopic data were in agreement with literature data[19]; for ^{13}C data, see table 1.

A more convenient approach to **(7b)** involved direct hydrolysis of the N-ethoxycarbonyl compound after removal of solvent but without any further purification. After heating under reflux with aqueous NaOH as described above, extraction into diethyl ether followed by drying, evaporation and distillation gave **(7b)**, b.p. 88-92°C/ 0.4 mm Hg, in 52% overall yield from **(3)**.

The amine was converted into the tetrafluoroborate salt for longer-term storage. This was prepared by treatment of a solution of **(7b)** in ether with an excess of HBF_4 (40% solution). The solid was filtered off, washed with cold diethyl ether and dried under vacuum over P_2O_5. The free amine was regenerated by treatment of the salt with aqueous base and extraction into the solvent of choice.

5,8-Dimethoxy-1,4-dihydro-1,4-iminonaphthalene (7c)

The amine **(7c)** was prepared from **(4)** in 16 - 25% yield using the general method of Anderson *et al.*.[17] It crystallised from diethyl ether, m.p. 84-85°C. Analysis. Found: C, 70.84; H, 6.51: N, 6.83%; $C_{12}H_{13}NO_2$ requires C, 70.86; H, 6.44; N, 6.89%. IR (CH_2Cl_2), 2940, 2830, 1610, 1495, 1465, 1435, 1345, 1240, 1070, 995, 965, 855, 930 cm^{-1}; ^1H NMR δ 6.96 (m, 2H, $H_{2,3}$), 6.45 (s, 2H, $H_{6,7}$), 5.20 (m, 2H, $H_{1,4}$), 3.73 (s, 6H, OMe), 2.77 (br s, NH); ^{13}C NMR data see table 1; MS $^m/z$ 203 (M^+), 188, 177, 162*.

The amine **(7c)** has also been prepared by Cragg *et al.*,[18] m.p. 80 - 81°C from **(3)** [using 1-amino-4,7-dimethoxybenzotriazole and lead tetra-acetate or 2-amino-3,6-dimethoxybenzoic acid and pentyl nitrite for production of 3,6-dimethoxybenzyne] followed by sequential chromatography and hydrolysis of the N-ethoxycarbonyl amine. This method led to higher reported overall yields but was less convenient.

5,6,7,8-Tetrachloro-1,4-dihydro-1,4-iminonaphthalene (7d) and
5,6,7,8-Tetrafluoro-1,4-dihydro-1,4-iminonaphthalene (7e)

These compounds were prepared using the method described for (**7c**) but using pentachlorobenzene and pentafluorobenzene respectively.

Amine (**7d**) was obtained in 29% yield but could not be purified completely. ^{1}H NMR δ 7.04 (s, 2H, $H_{2,3}$), 5.12 (s, 2H, $H_{1,4}$), 3.03 (bs, NH).

Amine (**7e**)[17] was obtained as a colourless oil which crystallised below 0°C after Kugelrohr distillation (142°C/0.2 mm Hg).^{1}H NMR δ 7.00 (m, 2H, $H_{2,3}$), 5.30 (m, 2H, $H_{1,4}$), 2.87 (br s, NH); ^{13}C NMR see table 1; MS 215 (M^+), 189*, 162.

1,2,3,4-Tetrahydro-1,4-iminonaphthalene derivatives

The hydrogenation of amines (**7**) to give (**8**) followed the basic method of Carpino and Barr;[19] any slight variations are indicated below.

5,6,7,8-Tetramethyl-1,2,3,4-tetrahydro-1,4-iminonaphthalene (8a)
Hydrogenation of (**7a**) in absolute ethanol over 10% palladium on charcoal (Pd/C) at 20 psi for 2 h gave (**8a**) in quantitative yield. ^{1}H NMR δ 4.62 (dd J=2.6, 1.7 Hz, 2H, $H_{1,4}$), 2.70 (bs, NH), 2.24 (s, 6H, Me), 2.17 (s, 6H, Me), 2.02 (m, 2H, *exo*-$H_{2,3}$), 1.2 (m, 2H, *endo*-$H_{2,3}$). ^{13}C NMR see table 1.

1,2,3,4-Tetrahydro-1,4-iminonaphthalene (8b)
Hydrogenation of the hydrochloride salt of (**7b**) in absolute ethanol over 10% Pd/C at 60 psi for 2 h gave the hydrochloride salt of (**8b**) in quantitative yield. Recrystallisation from EtOH/Et_2O gave (**8b:HCl**) as a white solid, m.p. 240-242°C dec. (lit. m.p. 241-242°C dec.[19]). Analysis. Found: C, 65.90; H, 6.62; N, 7.83%; $C_{10}H_{12}ClN$ requires C, 66.12; H, 6.66; N, 7.71%. Amine (**8b**) was stored as the hydrochloride salt and was regenerated as follows. To an aqueous solution of (**8b:HCl**) and an equal volume of diethyl ether was added 2N K_2CO_3 until the aqueous layer was basic. Separation of the ether layers followed by drying and evaporation gave the free amine (**8b**) as a white crystalline solid, m.p. 95-97°C (lit.[19] m.p. 96-98°C) which sublimed rapidly above 60°C at atmospheric pressure. For ^{13}C NMR data see table 1.

5,8-Dimethoxy-1,2,3,4-tetrahydro-1,4-iminonaphthalene (8c)
A solution of (**7c**) in absolute ethanol was hydrogenated over 10% Pd/C at 10 psi for 15 min. giving crude (**8c**) as a white solid. Kugelrohr distillation (200°C/0.8 mm Hg) gave pure (**8c**) as an amorphous white solid, m.p. 95-96°C, in 80% yield. Analysis. Found: C, 70.26, H, 7.45, N, 6.82%. $C_{12}H_{15}NO_2$ requires C, 70.23; H, 7.36; N, 6.82% ^{1}H NMR δ 6.50 (s, 2H, aryl), 4.68 (m, 2H, $H_{1,4}$), 3.70 (s, 6H, OMe), 2.43 (bs, NH), 1.20-2.10 (m, 4H, $H_{2,3}$); ^{13}C NMR see table 1; MS ^{m}/z 205 (M^+), 189, 177, 162.

5,6,7,8-Tetrachloro-1,2,3,4-tetrahydro-1,4-iminonaphthalene (8d)
Hydrogenation of (**7d**) under the conditions described for (**8c**) was unsuccessful; hydrogenolysis occurred giving (**8b**). Amine (**8d**) was therefore prepared by hydrogenation of (**7d**) over PtO_2 in absolute ethanol at atmospheric pressure for 15 min. ^{1}H NMR δ 4.71 (m, 2H, $H_{1,4}$), 2.51 (bs, NH), 2.05 and 1.26 (2H,2H, AA'BB' system, $H_{2,3}$exo,endo).

5,6,7,8-Tetrafluoro-1,2,3,4-tetrahydro-1,4-iminonaphthalene (8e)

Amine (**8e**) was prepared using the method as described above for (**8c**) rather than the method of Underwood.[8] It was obtained as a colourless oil after Kugelrohr distillation. ^{1}H NMR δ 4.83 (2H, m, $H_{1,4}$), 2.22 (1H, bs, NH), 2.09 and 1.26 (2H,2H, AA'BB' system, $H_{2,3}$exo,endo), ^{13}C NMR see table 1.

N-Methyl-1,4-dihydro-1,4-iminonaphthalene derivatives

N-Methyl-5,6,7,8-tetramethyl-1,4-dihydro-1,4-iminonaphthalene (9a)

N-Methyl-1,4-dihydro-1,4-iminonaphthalene (9b)

N-Methyl-5,8-dimethoxy-1,4-dihydro-1,4-iminonaphthalene (9c)

These amines were prepared from the corresponding secondary amines using the general methylation procedure of Borch and Hassid.[11] In a typical procedure, sodium cyanoborohydride (400 mg; 6.4 mmol), the fumarate salt of (**7c**) (927 mg; 2.9 mmol) and 40% formaldehyde solution (1.1 ml; 14.7 mmol) were stirred overnight in acetonitrile (35 ml). Diethyl ether was then added to the reaction mixture and the flask contents were washed with acid (0.6 M HCl; 3 × 30 ml). The combined aqueous acid extracts were made basic (2M NaOH, 40 ml) and the basic aqueous layer extracted with dichloromethane (4 × 50 ml). The combined organic extracts were dried and concentrated under reduced pressure to give crude (**9c**) which was recrystallised from light petroleum/diethyl ether to give the product (450 mg; 71%). Vacuum sublimation (0.4 mm Hg/ bath temperature 100°C) gave white crystals of (**9c**), m.p. 83-84°C (lit.[18] m.p. 84-86°C). Analysis. Found, C, 72.03, H, 6.98, N, 6.50%. $C_{13}H_{15}NO_2$ requires C, 71.87; H, 6.97; N, 6.45% IR (CH_2Cl_2), 2940s, 2830s, 2780m, 1610m, 1490s, 1460s, 1240s, 1215s, 1175m, 1105m, 1065s, 985s, 965m, 785s cm^{-1}; ^{1}H NMR δ 6.92 (m, 2H, $H_{2,3}$), 6.83 (s, 2H, aryl), 4.70 (m, 2H, $H_{1,4}$), 3.71 (s, 6H, OMe), 2.11 (br s, NH); ^{13}C NMR data are listed in table 3; MS ^{m}/z 217*(M^+), 202, 191, 177, 128.

The amines (**9a**) and (**9b**) were prepared in similar fashion.

(**9a**): 22% yield, m.p. 95-98°C. IR (CH_2Cl_2), 2940m, 2850m, 1440m, 1250m, 1105m, 805s cm^{-1}; ^{1}H NMR δ 6.80 (br, 2H, $H_{2,3}$), 4.56 (br, 2H, $H_{1,4}$), 2.16 and 2.10 (br, s, 15H); ^{13}C NMR data are listed in table 3; MS ^{m}/z 213*(M^+), 198, 187, 172; accurate ^{m}/z 213.152, calculated for $C_{15}H_{19}N$ 213.1517.

(**9b**):[8] 54% yield, b.p. 142°C/0.2 mm Hg. ^{13}C NMR data are listed in table 3.

N-Methyl-5,6,7,8-tetrachloro-1,4-dihydro-1,4-iminonaphthalene (9d)

N-Methyl-5,6,7,8-tetrafluoro-1,4-dihydro-1,4-iminonaphthalene (9e)

These amines[5b] were prepared by direct cycloaddition of the appropriate tetrahalogenobenzyne to N-methylpyrrole (**5**). ^{13}C NMR data are listed in table 3.

N-Alkyl-1,2,3,4-tetrahydro-1,4-iminonaphthalene derivatives

N-Methyl-5,6,7,8-tetramethyl-1,2,3,4-tetrahydro-1,4-iminonaphthalene (10a)

N-Methyl-1,2,3,4-tetrahydro-1,4-iminonaphthalene (10b)

N-Methyl-5,8-dimethoxy-1,2,3,4-tetrahydro-1,4-iminonaphthalene (10c)

N-Methyl-5,6,7,8-tetrachloro-1,2,3,4-tetrahydro-1,4-iminonaphthalene (10d)

N-Methyl-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydro-1,4-iminonaphthalene (10e)

In a typical procedure, amine (**9e**) (1.3 g; 5.7 mmol) was dissolved in methanol (30 ml) and hydrogenated over 10% Pd/C in a Parr apparatus for 2 h at a pressure of 20 psi. The catalyst was removed by filtration through celite and washed with more solvent. Evaporation under reduced pressure gave (**10e**) (1.23 g; 93%), m.p. 76-79°C. The amine was characterised as the mono-methyl sulphate, m.p. 160-161.5°C after recrystallisation from isopropanol. Analysis. Found: C, 43.67; H, 4.18; N, 3.88%. $C_{13}H_{15}NF_4SO_4$ requires: C, 43.70; H, 4.23; N, 3.92%. ^{13}C NMR data are listed in table 3.

Similarly prepared were the following N-methyl amines.

(10a): in 77% yield after acidification, washing with diethyl ether, rebasification, extraction into diethyl ether, drying and evaporation, m.p. 100-103°C. Found: C, 83.60; H, 9.78; N, 6.53%. $C_{15}H_{21}N$ requires C, 83.67; H, 9.83; N, 6.5%. IR (CH_2Cl_2) 2950s, 1450m, 1265m, 1195m, 1095m, 1005w, 840m cm^{-1}; ^1H NMR δ 4.10 (m, 2H, $H_{1,4}$), 2.15-2.00 (m, 15H + 2H, Me + $H_{2,3}$exo), 1.07 (m, 2H, $H_{2,3}$endo); MS $^m/z$ 215 (M^+), 200, 187*, 172.

(10b) was obtained as a yellow oil. Spectroscopic data were fully in accord with literature data[15]

(10c) m.p. 109-110.5°C after sublimation at 115°C/0.1 mm Hg. Analysis. Found: C, 71.14; H, 7.96: N, 6.28%. $C_{13}H_{17}NO_2$ requires C, 71.21; H, 7.81; N, 6.41%. IR 2945s, 2830sh, 1495s, 1460s, 1250s, 1200m, 1165m, 1090s, 1030m, 992m, 965m, 830m cm^{-1}; ^1H NMR δ 6.60 (s, 2H, aryl), 4.27 (m, 2H, $H_{1,4}$), 3.70 (s, 6H, OMe), 2.03 (m, 3H + 2H, NMe + $H_{2,3}$exo), 1.18 (m, 2H, $H_{2,3}$endo); ^{13}C NMR data are listed in table 3; MS $^m/z$ 219 (M^+), 204, 191*, 176, 148, 133.

(10d) Hydrogenolysis of the C-Cl bonds was avoided by the use of Adam's catalyst under 10 psi of hydrogen for 10 min., m.p. 134.5-136.5°C. IR (CH_2Cl_2) 2945m, 1360s, 1200m, 1135s, 1090m cm^{-1}; ^1H NMR δ 4.35 (m, 2H, $H_{1,4}$), 2.10 (M, 3H + 2H, NMe + $H_{2,3}$exo), 1.25 (m, 2H, $H_{2,3}$endo); MS $^m/z$ 297 (M^+), 282, 269,* 254, 235. ^{13}C NMR data are listed in table 3.

N-Ethyl-1,4-dihydro-1,4-iminonaphthalene (11b)
N-Ethyl-5,6,7,8-tetrafluoro-1,4-dihydro-1,4-iminonaphthalene (11e)

The fumarate salt of **(7b)** (1.25 g; 4.8 mmol), sodium borohydride (0.6 g; 9.6 mmol) and ethanal (2 ml; 36 mmol) were stirred in acetonit rile (50 ml) for 24 h. After column chromatography (basic alumina, diethyl ether), the N-ethyl amine **(11b)** was isolated as a yellow oil (199 mg; 23 %). Kugelrohr distillation (140°C/0.15 mm Hg) afforded a colourless oil. IR (CH_2Cl_2) 2960m, 2840w, 1670w, 1450m, 1375m, 1270w, 1120m, 1090m, 995w, 790s cm^{-1}; ^1H NMR δ 7.33-6.33 (m br, 6H, aryl & $H_{2,3}$), 4.57 (m, 2H, $H_{1,4}$), 2.27 (br, 2H, CH_2), 1.00 (t, 3H, Me); MS $^m/z$ 171*(M^+), 156, 145, 129.

The amine **(11e)** was prepared in a similar fashion from the fumarate salt of **(7e)** (908 mg; 2.74 mmol), sodium cyanoborohydride (0.5 g) and ethanal (1 ml) in acetonitrile (25 ml). The mixture was stirred overnight, excess diethyl ether was added and the basic product was extracted into 2M HCl (4 x 20 ml). The acidic layers were combined, basified with 2M NaOH and extracted into CH_2Cl_2 (4 x 30 ml). The organic extracts were dried, the solvent removed under vacuum and, after chromatography on alumina using diethyl ether, **(11e)** was isolated in 31% yield as a pale oil which crystallised from petrol (b.p. 40-60°C) as white needles. IR (CH_2Cl_2) 2960m, 2840w, 1490s, 1380m, 1355w, 1295m, 1200m, 1175m, 1120m, 1040s, 935s, 810s cm^{-1}; ^1H NMR δ 6.91 (m br, 2H, $H_{2,3}$), 4.96 (m, 2H, $H_{1,4}$), 2.26 (q br, 2H, CH_2), 1.00 (t, 3H, Me); MS $^m/z$ 243 (M^+), 217, 200,* 189. The amine was analysed as the tetrafluoroborate salt. Found: C, 43.57; H, 3.07, N, 4.40%. $C_{12}H_{10}NBF_8$ requires: C, 43.54; H, 3.05; N, 4.23%.

N-Ethyl-1,2,3,4-tetrahydro-1,4-iminonaphthalene (12b)

N-Ethyl-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydro-1,4-iminonaphthalene (12e)

The amines **(11b)** and **(11e)** were hydrogenated over Pd/C as described for the corresponding N-methyl analogues **(9b)** and **(9e)**.

Compound **(12b)** was isolated in 79% yield. IR (cm^{-1}, CH_2Cl_2), 2890s, 1450m, 1380m, 1340m, 1280br,m, 1200m, 1085m, 905s; ^1H NMR δ 7.13 (m, 4H, aryl), 4.17 (m, 2H, $H_{1,4}$), 2.33-1.93 (m, 4H, *exo*-$H_{2,3}$ & ethyl CH_2), 1.18 (m, 2H, *endo*-$H_{2,3}$), 1.00 (t, 3H, Me); MS $^m/z$ 173 M^+, 159, 145*,129, 117, 89.

Compound **(12e)** was isolated in 97% yield as a pale brown oil. Filtration over alumina in diethyl ether solution gave a clear oil which crystallised in the cold (75%) but was very soluble in cold petrol. IR (cm^{-1}, CH_2Cl_2), 2970s, 1490s, 1385s, 1293s, 1205m, 1135m, 1105m, 1090m, 1075m, 1035s, 1030s, 968m, 905s; ^1H NMR δ 4.52 (m, 2H, $H_{1,4}$), 2.33-2.00 (m, 4H, *exo*-$H_{2,3}$ & ethyl CH_2), 1.23 (m, 2H, *endo*-$H_{2,3}$), 1.00 (t, 3H, Me); MS $^m/z$ 245 (M^+), 218*, 207, 189, 162, 151, 143. The amine **(12e)** was analysed as the tetrafluoroborate salt. Analysis. Found: C, 42.94; H, 3.67; N, 4.25%. $C_{12}H_{12}NBF_8$ requires: C, 43.28; H, 3.63; N, 4.21%.

N-Methyl-*exo-exo*-2,3-dideuterio-1,2,3,4-tetrahydro-1,4-iminonaphthalene (13b)

N-Methyl-*exo-exo*-2,3-dideuterio-5,8-dimethoxy-1,2,3,4-tetrahydro-1,4-iminonaphthalene (13c)

N-Methyl-*exo-exo*-2,3-dideuterio-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydro-1,4-iminonaphthalene (13e)

The amines **(9b)**, **(9c)** and **(9e)** respectively were dissolved in methanol with 10% Pd/C catalyst and were stirred overnight under a balloon filled with deuterium gas. After filtration through Celite and evaporation of solvent, the corresponding amines **(13b)**, **(13c)** and **(13e)** were obtained.

Analysis of the mass spectra of these compounds revealed >97% incorporation of deuterium.

(13b): ^1H NMR δ 7.2 (m, 4H, aryl), 4,27 (s, 2H, $H_{1,4}$), 2.15 (s, 3H, NMe), 1.25 (s, 2H, *endo*-$H_{2,3}$); MS $^m/z$ 161 (M^+), 145, 131*, 116, 103, 90. ^{13}C NMR data are listed in table 3.

(13c): ^1H NMR δ 6.62 (s, 2H, aryl), 4.25 (s, 2H, $H_{1,4}$), 3.75 (s, 6H, OMe), 2.03 (s, 3H, NMe), 1.17 (s, 2H, *endo*-$H_{2,3}$); MS $^m/z$ 219 (M^+), 203, 191*, 176, 161, 148.

(13e): ^1H NMR δ 4.48 (s, 2H, $H_{1,4}$), 2.08 (s, 3H, NMe), 1.24 (s, 2H, *endo*-$H_{2,3}$); MS $^m/z$ 233 (M^+), 203*, 188, 162.

Dimethyl-5,6,7,8-tetrafluoro-9-methyl-1,4-dihydro-1,4-iminonaphthalene -2,3-dicarboxylate (23)

Dimethyl acetylenedicarboxylate (0.62 ml; 5 mmol) was added from a microsyringe to a stirred solution of **(21)** (1.02 g; 5 mmol) in dry dichloromethane (25 ml) and stirring was continued for 3 h. After this time, the solution was dried, filtered, and the solvent removed to give, after recrystallisation from diethyl ether/acetone, the 1:1 adduct **(23)** (0.89 g; 51%), m.p. 122-124°C. Analysis. Found: C, 52.04; H, 3.29; N, 4.03%. $C_{15}H_{11}NO_4F_4$ requires C, 52.18; H, 3.21; N, 4.06%. IR (cm^{-1}; CH_2Cl_2) 2950w, 1715s, 1630w, 1480s, 1430m, 1260m, 1225m, 1160m, 1105m, 1080m, 930w; ^1H NMR δ 5.18 (s, 2H, $H_{1,4}$), 3.80 (s, 6H, OMe), 2.23 (s, 3H, NMe); ^{13}C NMR data are recorded in table 3; MS $^m/z$ 345 (M^+), 315, 286, 272, 256, 203*, 189, 162.

Dimethyl-5,6,7,8-tetrafluoro-9-methyl-1,2,3,4-tetrahydro-1,4-iminonaphthalene-*endo-endo*-2,3-dicarboxylate (24)

The amine **(23)** (400 mg; 1.2 mmol) in ethyl ethanoate (40 ml) was hydrogenated over palladium/carbon for 2 h at 20 psi pressure. After filtration through Celite, the product **(24)** was obtained in quantitative

yield. Recrystallisation from diethyl ether/acetone gave colourless needles, m.p. 143-145°C. Analysis. Found: C, 51.86; H, 3.83; N, 4.08. $C_{15}H_{13}NO_4F_4$ requires C, 51.88; H, 3.77; N, 4.03%. IR (CH_2Cl_2) 2950w, 1745s, 1500s, 1435w, 1290m, 1200m, 1115m, 1040m, 950w, 820w cm^{-1}; ^1H NMR δ 4.58 (m, 2H, $H_{1,4}$), 3.67 (m, 2H, *exo*-$H_{2,3}$), 3.53 (s, 6H, OMe), 2.03 (s, 3H, NMe); ^{13}C NMR data are recorded in table 3; MS m/z 347 (M^+), 328, 316, 285, 273, 256, 228, 203*, 188, 162.

Iminoanthracene Derivatives

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

This was prepared (using the method described for (**7b**) above) from N-ethoxycarbonylpyrrole (**3**) (4.2 g, 0.03 mole) and naphthalyne (**14**), generated in dry dioxan at reflux from 2-amino-3-naphthoic acid (5.0 g; 0.027 mole) and isoamyl nitrite (3.5 g; 0.03 mole). The solvent was removed under reduced pressure to give a dark red oil (9.0 g) which was adsorbed onto basic alumina (Woelm, 30g) and then placed carefully on top of a column of 120g of basic alumina. The first compound eluted with diethyl ether was (**15**) (3.43 g; 49%). It was recrystallised from diethyl ether/acetone as colourless needles, m.p. 125-126°C. Analysis. Found: C, 77.25; H, 5.78; N, 5.28% $C_{17}H_{15}NO_2$ requires C, 76.96; H, 5.70; N, 5.28%. IR (CH_2Cl_2) 3040s, 2970w, 1710s, 1370m, 1325m, 1245m, 1095m, 870m cm^{-1}; ^1H NMR δ 7.78-7.21 (m, 6H, aryl), 6.88 (m, 2H, $H_{2,3}$), 5.62 (m, 2H, $H_{1,4}$), 4.03 (q, 2H, Et), 1.17 (t, 3H, Et); MS m/z 265 (M^+), 238, 236, 220, 192, 165*.

1,4-Dihydro-1,4-iminoanthracene (16)

The protected amine (**15**) (750 mg; 2.8 mmol) was hydrolysed by heating under reflux with NaOH (4.0 g) in 1:1 methanol-water (30 ml). The progress of the reaction was monitored by TLC and, after 8 h, the mixture was cooled and diluted with water. The aqueous layer was extracted with dichloromethane (4 x 30 ml) and the combined organic extracts were dried, combined and evaporated. The resultant yellow gum crystallised in the cold and was purified by Kugelrohr distillation (130°C/ 0.1 mm Hg) to give a pale yellow solid (425 mg; 78%). A small sample was recrystallised from diethyl ether, m.p. 111-113°C. IR (CH_2Cl_2) 3260w, 3000m, 1415w, 1355m, 1260w, 1085m, 1035m, 885m, 865s, 835s cm^{-1}; ^1H NMR δ 7.33-7.25 (m, 6H, aryl), 6.83 (m, 2H, $w_{1/2}$ 3 Hz, $H_{2,3}$), 4.95 (m, 2H, $w_{1/2}$ 3 Hz, $H_{1,4}$), 3.00 (br, s, NH); MS m/z 193 (M^+), 165, 144*, 128.

N-Methyl-1,4-dihydroanthracen-1,4-imine (17)

The amine (**17**) has been prepared in 13% yield by Bornstein[20] by addition of naphthalyne to N-methylpyrrole. However, (**17**) was obtained more conveniently and in higher overall yield in our work by hydride reduction of the N-ethoxycarbonyl compound (**16**):

Lithium tetrahydroaluminate (150 mg; 4 mmol) was slurried with dry ether (25 ml) and cooled to 0°C. A solution of (**16**) (300 mg; 1.1 mmol) in diethyl ether was added slowly to the slurry from a dropping funnel. The cooling bath was removed and the mixture was heated to reflux for 45 min. After cooling, the excess reducing agent was destroyed cautiously with water-saturated ether and then water. The mixture was filtered through Celite and the aqueous layer was separated and washed with more diethyl ether (2 x 25 ml). The combined organic extracts were washed with acid (2M HCl, 4 x 10 ml), the acid washings were made basic (2M NaOH) and the basic layer was extracted with dichloromethane (4 x 25 ml). The dichloromethane solution was dried and the solvent evaporated to yield crude (**17**) (177 mg; 78%). The solid was recrystallised from light petrol as white crystals, m.p. 91-94°C (lit.[20] 94.5-95.5°C). IR (CH_2Cl_2) 3040w, 2960w, 2750w, 1415w, 1100m, 880m, 805s cm^{-1}; ^1H NMR δ 7.75-7.30 (m, 6H, aryl), 6.80 (br s, 2H, $H_{2,3}$), 4.53 (br s, 2H, $H_{1,4}$), 2.15 (s, 3H, NMe); MS m/z 207* (M^+), 192, 178, 165.

2-Benzyl-4,5,6,7-tetrafluoroisoindole (18)

(i) 9-Benzyl-5,6,7,8-tetrafluoro-1,4-dihydronaphthalen-1,4-imine (**9e** Z = Me). A solution of n-butyllithium (1.1M in hexane; 87 ml) was added dropwise over a period of 10 mins to a stirred solution of pentafluorobenzene (16.15 g; 96 mmol) in dry diethyl ether (25 ml) under nitrogen at -78°C. Subsequently. a solution of 1-benzylpyrrole (15.16 g, 96 mmol) in dry ether (40 ml) was added over a further 10 mins. The reaction was allowed to warm to room temperature with continuous stirring and was left overnight; it was then poured into water (300 ml) and the product extracted into ether (2 x 150 ml); the combined organic extracts were washed with water and the amine product was extracted into cold 2M HCl (2 x 200 ml). The acidic extracts were combined and washed with diethyl ether (3 x 50 ml), cooled in an ice salt bath, and carefully basified with 2M NaOH solution. The free amine was extracted into diethyl ether (3 x 200 ml); the combined extracts were dried and the solvent removed under reduced pressure to affored a white amorphous solid (9.88 g, 34%) which was used without further purification.

(ii) The product from **(i)** (8.06 g; 26.8 mmol) was dissolved in dry dichloromethane (70 ml) and was added under nitrogen, to a stirred solution of 3,6-di(2-pyridyl)-1,2,4,5-tetrazine[38] (6.30 g, 26.8 mmol) in dry dichloromethane (60 ml). The addition was slightly exothermic and the progress of the reaction was monitored by observation of the evolved nitrogen. After 24h, the solvent was removed under reduced pressure to afford an off-white solid **(18)**, (7.15 g, 95%), m.p. 92-95°C (lit.[39] 96-97.5°C).

N-Benzyl-1,2,3,4-tetrafluoro-9,10-dihydroanthracen-9,10-imine (19b)

A solution of 2-bromofluorobenzene (1.75 g; 10 mmol) in dry tetrahydrofuran (7 ml) was added slowly to magnesium (0.304 g; $13x10^{-3}$ g atom) under nitrogen in a flask which was immersed in an ultrasonic bath. The dissolution of the magnesium was complete within 30 min. The isoindole derivative **(18)** (2.23 g; 8 mmol) was added slowly to the reaction mixture with stirring and the mixture was left to stir overnight. The reaction mixture was poured into water (200 ml), the organic layer was separated, and the aqueous layer extracted with diethyl ether (200 ml). The organic extracts were combined and dried over magnesium sulphate. The solvents were reduced under reduced pressure to give a dark oil which after flash chromatography on silica (9:1 40-60° b.p. petrol:diethyl ether) afforded a light yellow oil **(19b)**, 1.92 g; 67%. Further purification proved difficult and the product was used directly for subsequent reactions. ^{1}H NMR δ 7.38-7.19m; 7.07brs (9H, aryl), 5.27 (s, 2H, $H_{9,10}$), 3.50 (s, 2H, benzylic CH_2); ^{13}C NMR data are recorded in table 3; MS ^{m}/z 355 (M^+), 264, 251, 250, 91*, 65, metastable peak ^{m}/z 46.4 (91→65); observed accurate ^{m}/z 355.0980, calculated for $C_{21}H_{13}NF_4$ 355.0984.

N-Benzyl-1,2,3,4-tetrafluoro-5,8-dimethoxy-9,10-dihydroanthracene-9,10-imine (19c)

A solution of n-butyllithium (1.27M in hexane; 11 ml) was added over 15 min to a stirred solution of 2,2,6,6-tetramethylpiperidine (2.40 g; 18 mmol) in dry diethyl ether (25 ml) under nitrogen. After a further 10 min this lithium tetramethylpiperidide solution was added over a period of 20 min to a stirred solution of **(18)** (4.00 g; 14 mmol) and 2-chloro-1,4-dimethoxybenzene[21] (2.42 g; 14 mmol) in dry diethyl ether (80 ml) under nitrogen. The reaction mixture was left stirring overnight, then poured into water (300 ml) and extracted with diethyl ether (2 x 200 ml). The organic extracts were washed with water (25 ml) and dried. The solvents were removed under reduced pressure and the dark red residue was purified by flash chromatography on silica using dichloromethane, to afford a yellow oil. Trituration with n-hexane gave **(19c)** as a white crystalline solid (1.70 g; 30%) of sufficient purity for use in later work. A small sample was recrystallised several times from n-hexane to provide an analytically pure sample as white plates, m.p. 139°C. Analysis. Found: C, 66.63; H, 4.22; N, 3.37%. $C_{23}H_{17}NO_2F_4$ requires C, 66.51; H, 4.13; N, 3.37%. ^{1}H NMR δ 7.25 (m, 5H, benzyl), 6.58 (s, 2H, $H_{6,7}$), 5.44 (s, 2H, $H_{9,10}$), 3.75 (s, 6H, OMe), 3.45 (s, 2H, benzylic CH_2); ^{13}C NMR data are recorded in table 3.; MS ^{m}/z 415 (M^+), 384, 325, 324, 310, 295, 280, 267, 252, 224, 199, 91*, 65, 42.

1,2,3,4-Tetrafluoro-9,10-dihydro-9,10-iminoanthracene (20b)

A solution of **(19b)** (1.519 g; 4.28 mmol) was dissolved in glacial ethanoic acid (20 ml) and hydrogenated at 1 atm. over 10% palladium on carbon (0.138 g) for 48 h. The reaction mixture was then filtered through Celite and the solvent removed under reduced pressure. The residual oil was dissolved in dry diethyl ether (20 ml) and HCl gas was bubbled through until no further precipitation was observed. The precipitate was filtered off and dried under reduced pressure to afford **(20b:HCl)** as a white amorphous powder (0.475 g), m.p. 183°C (dec.). MS m/z 266, 265 *(M - HCl), 264, 250, 238, 237, 219.

The free amine **(20b)** was liberated by basification with 2M aqueous sodium hydroxide and extraction into dichloromethane. ^{1}H NMR δ 7.14 (m, 4H, aryl), 5.61 (s, 2H, $H_{9,10}$), 2.86 (br s, NH); ^{13}C NMR data are summarised in table 1. The amine was analysed as the N-chloro-derivative[22].

1,2,3,4-Tetrafluoro-5,8-dimethoxy-9,10-dihydro-9,10-iminoanthracene (20c)

A solution of **(19c)** (0.408 g; 0.98 mmol) in glacial acetic acid (15 ml) was hydrogenated as described for **(19b)** above to give **(20c:HCl)** (0.324 g; 92%). A small quantity was recrystallised from methanol/diethyl ether to give a fine white powder, m.p. 173-174°C (dec.). MS m/z 325 (M - HCl), 324, 310, 295*, 280, 267, 252, 224, 163, 44.

The free amine **(20c)** was liberated as described for **(20b)**. IR (CH_2Cl_2) 3250w, 3040-2830br, 2840m, 1610w, 1500s, 1350m, 1280w, 1190m, 1120m, 1050br, 820s cm^{-1}; ^{1}H NMR 6.58 (s, 2H, aryl), 5.44 (s, $H_{9,10}$), 3.75 (s, 6H, OMe), 3.45 (br s, NH); ^{13}C NMR data are summarised in table 1. The amine was analysed as the N-chloro- derivative[22].

N-Methyl-1,2,3,4-tetrafluoro-5,6,7,8-tetramethyl-9,10-iminoanthracene (22a)

A stirred mixture of 1,2-dibromo-3,4,5,6-tetramethylbenzene (4.00 g; 13.70 mmol) and 2-methyl-4,5,6,7-tetrafluoroisoindole **(21)** (2.77 g; 13.64 mmol) in dry diethyl ether (70 ml) was cooled to -78°C under dry nitrogen. n-Butyllithium (1.6 M solution in hexane; 10.0 ml) was added slowly via a syringe and the pale yellow solution immediately became cherry red. The solution was stirred at -78°C for 1 h and then allowed to warm slowly to room temperature. The reaction mixture was washed with cold 2M HCl (4 x 20 ml) and the aqueous layers separated. The combined acidic extracts were basified in the cold with 2M NaOH and the product extracted into dichloromethane (4 x 40 ml). The combined organic layers were dried, filtered and evaporated to give a dark brown solid which was recrystallised from petrol/diethyl ether to give **(22a)**, 1.19 g (26%).

N-Methyl-1,2,3,4-tetrafluoro-9,10-iminoanthracene (22b)[5a]

To dry magnesium turnings (0.227 g; 9.4 mmol) in dry tetrahydrofuran (2 ml) under nitrogen was added a few drops of a solution of 2-bromofluorobenzene (1.52 g; 8.7 mmol) in tetrahydrofuran (2 ml). The reaction flask was cooled as the Grignard reaction began and the remaining solution was run in. When the metal had dissolved completely, 2-methyl-4,5,6,7-tetrafluoroisoindole **(21)** (1.74 g; 8.6 mmol) in dry tetrahydrofuran (15 ml) was added and the darkening solution was heated under reflux for 1 h. After cooling, the product was extracted with aqueous HCl (1 M; 4 x 10 ml) and the combined acid extracts were made basic with 2M sodium hydroxide solution. The basic layer was extracted with dichloromethane (5 x 50 ml) and the combined organic extracts were dried and evaporated to give **(22b)** which was recrystallised from light petrol (0.28 g; 12%), m.p. 83-86°C. IR (CH_2Cl_2) 2950w, 2870w, 2790w, 1500s, 1485s, 1330m, 1270m, 1115m, 1095m, 1045m, 995m, 955m, 925m cm^{-1}; NMR δ 7.43-6.93 (m, 4H, aryl), 5.21 (s, 2H, $H_{9,10}$), 2.25 (br s, 3H, N-Me); MS m/z 279*(M^+), 264, 250, 237, 203, 188, 162; observed accurate m/z 279.067, calculated for $C_{15}H_9NF_4$ 279.0671.

References and Notes

1. J.M.Lehn, *Fortschr. Chem. Forsch.*, **1970**, *15*, 311; J.B.Lambert, 'Topics in Stereochemistry', ed. N.L.Allinger and L.Eliel, Wiley-Interscience, New York, **1971**, Vol.6, W.B.Jennings and S.D.Worley, *J.Chem.Soc.Perkin Trans. 2*, **1980**, 1512 and references cited therein.
2a. J.W.Davies, J.R.Malpass, J.Fawcett, L.J.S.Prouse, R.Lindsay and D.R.Russell, *J.Chem.Soc.Chem. Commun.*, **1986**, 1135.
b. J.W.Davies, J.R.Malpass and R.E.Moss, *Tetrahedron Lett.*, **1985**, *26*, 4533.
3. J.R.Malpass and M.P.Walker, *J.Chem.Soc.Chem.Commun.*, **1979**, 585.
4. M.L.Durrant and J.R.Malpass, *J.Chem.Soc.Chem.Commun.*, **1981**, 1028.
J.W.Davies, J.R.Malpass and R.E.Moss, *Tetrahedron Lett.*, **1986**, *27*, 4071.
5a. G.W.Gribble, N.R.Easton and J.T.Eaton, *Tetrahedron Lett.*, **1970**, 1075.
b. G.W.Gribble, R.W.Allen, C.S.LeHoullier, J.T.Eaton, N.R.Easton Jr., R.I.Slayton and M.P.Sibi, *J.Org.Chem.*, **1981**, *46*, 1025.
6a. K.Yoshikawa, K.Bekki, M.Karatsu, K.Toyoda, T.Kamio and I Morishima, *J.Amer.Chem.Soc.*, **1976**, *98*, 3272.
b. I.Morishima, K.Yoshikawa, M.Hashimoto and K.Bekki, *ibid.*, **1975**, *97*, 4283.
7. J.B.Grutzner, *J.Amer.Chem.Soc.*, **1976**, *98*, 6385 and references cited therein.
8. G.R.Underwood and H.S.Friedman, *J.Amer.Chem.Soc.*, **1977**, *99*, 27.
9a. A.P.Marchand and R.W.Allen, *Tetrahedron Lett.*, **1977**, 619 and references cited therein.
b. M.J.O.Anteunis, F.A.Borremans, J.Gelan, A.P.Marchand and R.W.Allen, *J.Amer.Chem.Soc.*, **1978**, *100*, 4050.
10a. Studies of the corresponding N-chloroamines will be published separately.
b. Studies of quaternisation of the tertiary amines in this series will be published separately; kinetic protonation has not been applicable to all bicyclic amines in our hands.
11. R.F.Borch and A.I.Hassid, *J.Org.Chem.*, **1972**, *37*, 1673.
12. D.D.Callander, P.L.Coe, J.C.Tatlow and A.J.Uff, *Tetrahedron*, **1969**, *25*, 25.
13. The synthesis of N-methyl- and N-benzyl-9,10-dihydro-9,10-imino-anthracenes by this method has been investigated in detail by Anderson *et al.*, *J.Org.Chem.*, **1979**, *44*, 1519.
14. G.Ciamician and M.Dennstedt, *Chem. Ber.*, **1882**, *15*, 2579.
15. R.Fessenden and D.F.Crowe, *J.Org.Chem.*, **1960**, *25*, 598.
16. H.Hart and A.Teuerstein, *Synthesis*, **1979**, 693.
17. P.S.Anderson, M.E.Christy, E.L.Engelhardt, G.F.Lundell and G.S.Ponticello, *J.Heterocyclic Chem.*, **1977**, *14*, 213.
18. G.M.L.Cragg, R.G.F.Giles and G.H.P.Roos, *J.Chem.Soc.Perkin 1*, **1975**, 1339.
19. L.A.Carpino and D.E.Barr, *J.Org.Chem.*, **1966**, *31*, 764.
20. J.Bornstein, S.E.Hunt, J.D.Hunt and D.E.Remy, *J.Org.Chem.*, **1979**, *44*, 805.
21. G.N.Vyas and N.M.Shah, *Org.Syn.Coll.Vol.4*, 837.
22. J.W.Davies, M.L.Durrant, J.R.Malpass and M.P.Walker, to be published.
23. c.f. J.M.Vernon, M.Ahmed and L.J.Kricka, *J.Chem.Soc.Perkin 1*, **1978**, 837 for discussion of related reactions.
24. Independently of our work, ^{13}C NMR has also been used by Quin to confirm the value of 94:6[9] for (10b): L.D.Quin, K.C.Caster, B.G.Marsi and J.A.Miller, *J.Org.Chem.*, **1986**, *51*, 3724.
25. E.Ciganek, *J.Org.Chem.*, **1980**, *45*, 1512

26. M.P.Byrn, C.E.Strouse, G.W.Gribble and C.S.LeHoullier, *Acta Cryst.*, **1985**, *C41*, 238.
27. We have also used a similar approach for assigning N-chloroamine invertomers in the same ring system and obtained consistent results which have been confirmed by chemical methods[4] and by X-ray determinations in two cases[2a].
28. L.A.Paquette, L.W.Hertel, R.Gleiter and M.Böhm, *J.Amer.Chem.Soc.*, **1978**, *100*, 6510.
29. W.B.Jennings and R.Spratt, *J.Chem.Soc.Chem.Commun.*, **1971**, 54.
30. S.F.Nelsen, J.T.Ippoliti, T.B.Frigo and P.A.Petillo, *J.Amer.Chem.Soc.*, **1989**, *111*, 1776 and references cited therein.
31. J.R.Malpass and N.J.Tweddle, *J.Chem.Soc., Perkin Trans. II*, **1978**, 120.
32. M.Raban, F.B.Jones Jr., E.H.Carlson, E.Banucci and N.A.LeBel, *J.Org.Chem.*, **1970**, *35*, 1497.
33. W.J.Deloughry and I.O.Sutherland, *J.Chem.Soc.Chem.Commun.*, **1971**, 1104.
34. H.Kessler and D.Liebfritz, *Tetrahedron Lett.*, **1970**, 4289.
35. F.L.Anet and I.Yavari, *Tetrahedron Lett.*, **1977**, 3207.
36. V.Rautenstrauch, *J.Chem.Soc.Chem.Commun.*, **1969**, 1122.
37. E.Breitmaeyer and W.Voelter, ^{13}C NMR Spectroscopy, 2nd. Ed., Verlag Chemie, **1978**.
38. G.M.Priestley and R.N.Warrener, *Tetrahedron Lett.*, **1972**, 4295.
39. J.Bornstein, D.E.Remy and J.E.Shields, *Tetrahedron Lett.*, **1974**, 4247.
40. H-D.Martin and B.Mayer, *Angew.Chem.Internat.Ed.Engl.*, **1983**, *22*, 283.
41. K.N.Houk, R.W.Gandour, R.W.Strozier, N.G.Rondan and L.A.Paquette, *J.Amer.Chem.Soc.*, **1979**, *101*, 6797.

We thank the SERC for financial support and Mr. Michael Lee for assistance with the preparation of compound (**7b**).