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Aryl Participation in Methanolysis of N-Chloro-1,4-dihydro-1,4-iminonaphthalenes (7-Azabenzonorbornadienes) and Derivatives

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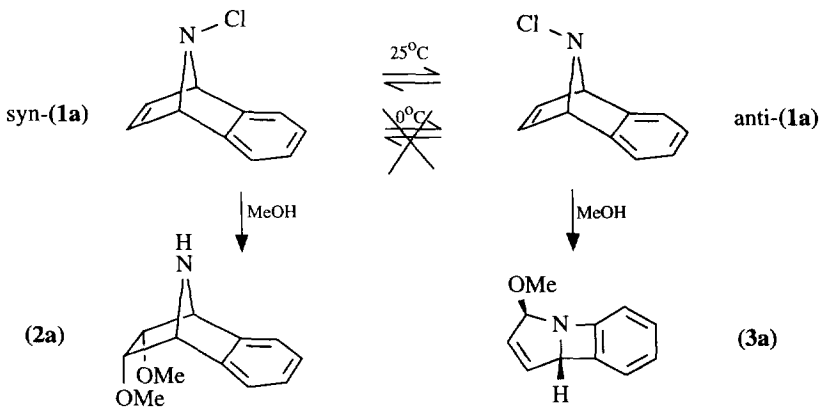
Abstract: Routes to derivatives of the 6,7-benzo-1-azabicyclo[3.2.0]heptyl ring system are described; the relative ability of substituted aryl rings to participate in selective reaction of the *anti*- invertomers of the title compounds during Ag(I)-catalysed methanolysis reactions is estimated qualitatively. The intrusion of N-Cl homolysis during methanolysis in some cases can be suppressed completely by the use of an Ag(I) salt together with a minimal quantity of methanol in a non-polar solvent, giving heterolysis products in excellent yield.

Introduction

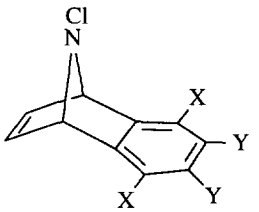
We have shown[1] that, in methanol at ambient temperature (under conditions of rapid inversion), the chloroamine (**1a**) gave the dimethoxy-compound (**2a**) as the major product (scheme 1); this compound was formed via participation of the π-electrons of the etheno- bridge in the loss of the *syn*- Cl as chloride ion. A small quantity of the secondary amine resulting from homolytic dechlorination of (**1a**) was also isolated under these conditions. In contrast, when the reaction was performed under conditions of slow inversion (below 0°C), it was possible to distinguish cleanly between the two pathways shown in scheme 1. Thus, *syn*- (**1a**) led, again, to formation of (**2a**) whilst the corresponding *anti*- invertomer of (**1a**) gave the rearrangement product (**3a**). Clearly, since inversion to *syn*-(**1a**) was now impossible, the *anti*-invertomer was constrained to follow the alternative, slower pathway which involved participation of the π-electrons of the benzene ring.

Scheme 1

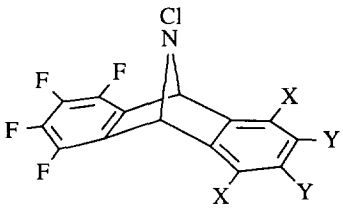


Conditions: MeOH / 25°C √ X
Ag^+ / MeOH / 0°C √ √

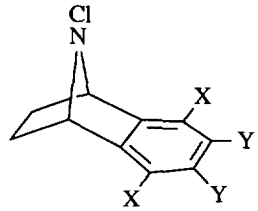
Broadly similar behaviour was observed[1] in the case of the dimethoxybenzo- analogue **(1b)**, but differences in reactivity have led us to extend our studies to include electron-deficient systems such as the tetrafluoroaryl compound **(1c)**. In addition, we have made a direct comparison of the behaviour of electron-rich and electron-deficient aryl rings using the 9,10-iminoanthracene derivatives **(4a)** and **(4b)**.



X=Y=H **(1a)**
X-OMe; Y=H **(1b)**
X=Y=F **(1c)**



(4a)
(4b)



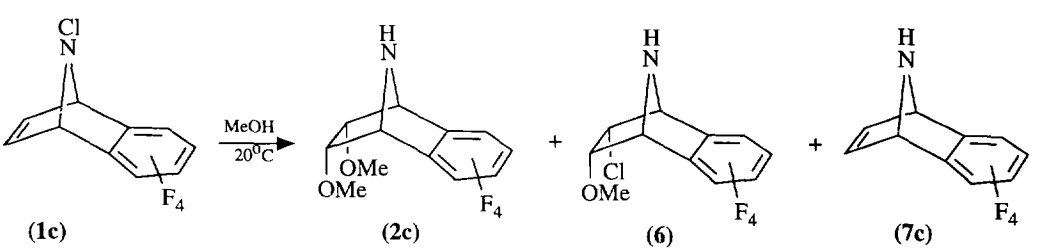
(5a)
(5b)
(5c)

We have also compared the reactivity of the ethano-bridged system **(5c)** containing a tetrafluoroaryl ring with that of the more electron-rich compounds **(5a)** and **(5b)**.[1] As part of our investigations into the rearrangement of derivatives of **(1)** and **(5)** bearing alkyl substituents at C_1 and C_4, we have developed conditions which encourage a substantial increase in the efficiency of the benzo-participation route, at the expense of the competing homolytic pathway.[2] Rearrangement of the relatively unreactive systems **(5a)** and **(5b)** under these conditions has led to dramatic improvements in the yields of 5,6-benzo-1-azabicyclo[3.2.0] heptane derivatives derived from the pathway involving benzo- participation.

Results and Discussion

The synthesis of the secondary amines and N-chloro-amines used in this work has been reported separately, together with studies of nitrogen inversion and invertomer preferences in the chloro-amines.[3a,b] The structures of the methanolysis products from **(1a)** and **(1b)** have been established.[1] By comparison, methanolysis of the tetrafluoro- analogue **(1c)** at 20°C (in the absence of silver salts) was sluggish; the products (scheme 2) were the expected dimethoxy-compound **(2c)** plus the chloromethoxy-compound **(6)** which was presumably formed by competition between the methanol and chloride ion in solution, a process observed only in this example. A small quantity of homolysis product **(7c)** was isolated from the room temperature reaction.

Scheme 2



(1c) **(2c)** **(6)** **(7c)**

An approximate indication of relative reactivity was obtained when the three N-chloroamines (**1**) were heated in methanol alone under similar conditions. The relative reaction times in table 1 show the marked effect of the fluoro- substituents in slowing the overall reaction rate.

Table 1 also summarises the product ratios in each case and this gives an additional indication of the relative reactivities of the *syn-* and *anti-* configurations. Each N-chloroamine is free to invert at 20°C and the *syn-* invertomers are consistently more reactive leading, *via* participation of the etheno- π-electrons, to the formation of (**2a,b,c**) as the major products. The formation of (**6**) occurs only in the case of (**1c**) but homolysis intrudes to some extent in each reaction giving (**7a,b,c**). The only system in which the aryl ring competes at all under conditions of free inversion is (**1b**) where the dimethoxybenzo ring is capable of assisting in the displacement of the *anti-* chloride ion giving a small amount of (**3b**).[1]

Table 1.
Methanolysis of N-Chloroamines (1) at 20°C in the absence of Ag^+

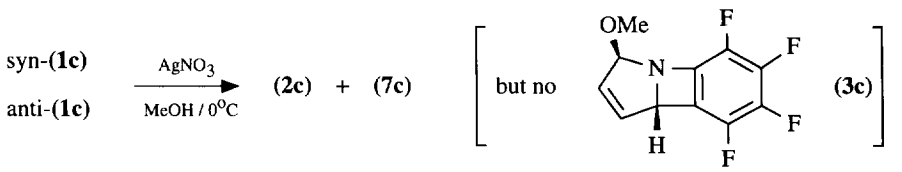
N-Chloroamine	Reaction time	Products (% yield)[a] (2)	(3)	(6)	(7)
(**1a**)	20 hours	32(27)	-	-	11(10)
(**1b**)	16 hours	47(37)	11(13)	-	25(16)
(**1c**)	2 weeks	55(23)	-	23(8)	8[b]

a. Two yields are quoted. The first is based on ^{1}H NMR integration of the crude reaction product relative to a known weight of an internal standard [p-dibromobenzene for (**1a**) and (**1c**); propanone for (**1b**)]. The yield in parenthesis is the isolated yield.

b. This amine could not be isolated in pure form from the mixture.

There was no evidence for heterolysis of *anti-* (**1c**) in any of the experiments performed in this study. For example, when a mixture of *syn- and anti-* (**1c**) was cooled to 0°C and treated with $AgNO_3$ in methanol, only (**2c**) and a small amount of (**7c**) were observed. No (**3c**) was produced even under these conditions, which were chosen to encourage heterolysis of the N-Cl bond whilst preventing inversion of the *anti-* (**1c**) to *syn-* (scheme 3).

Scheme 3



The relative reactivity of (**1a,b,c**) in the presence of silver ion was confirmed qualitatively by solvolysis of samples of these compounds (consisting of a defined ratio of invertomers) in CD_3OD on addition of small amounts of $AgClO_4$. The progress of the reactions was monitored against an internal standard in the probe of an NMR spectrometer maintained at low temperature (table 2). It was necessary to allow the temperature to rise to -6°C before (**1c**) reacted at a reasonable rate, in contrast to (**1a**) and (**1b**) which were consumed at

-55°C under similar conditions.[4] The relative rate of disappearance of the two invertomers was also monitored in each case. For both (**1a**) and (**1c**), the signal due to $H_{1,4}$ of the *syn-* invertomer disappeared more quickly than the *anti-* whilst for (**1b**), the corresponding signal of the *anti-* invertomer was reduced more rapidly, confirming the activating effect of the methoxy groups on aryl participation in loss of the *anti-* Cl, relative to hydrogen or fluorine.

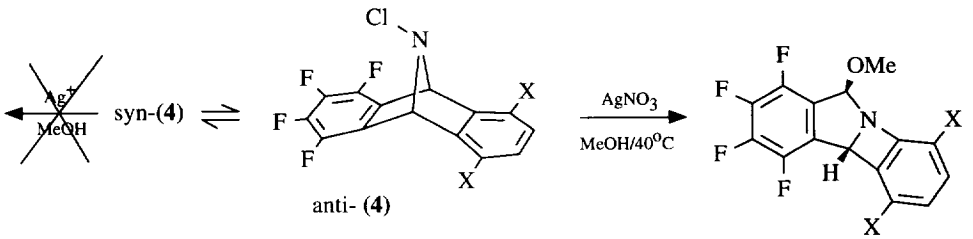
Table 2.
Ag(I)-Catalysed Reaction of N-Chloroamines (1) in d_4-Methanol at Low Temperature

N-Chloroamine	Initial ratio *syn- / anti-*	Temp. (°C)	Products (% yield)* d_6-(2)	d_3-(3)	(7)
(**1a**)	28 : 72	-55	16[a]	40[b]	10[a]
(**1b**)	37 : 63	-55	13[b]	43[c]	23[b]
(**1c**)	80 : 20	-6	45[c]	-	14[a]

* Internal standard: p-dioxan for (**1a**); p-dibromobenzene for (**1b**) and (**1c**).
Yields estimated by ^{1}H NMR to: a) ±2%; b) ±3%; c) ±5%

The bridged anthracenes (**4a**) and (**4b**) did not react with silver salts in methanol at low temperature, presumably due to the deactivating effect of the tetrafluorobenzo ring. It was necessary to heat to 40°C and, even under these conditions, the reaction proceeded slowly. Inevitably then, inversion occurred during the course of the reaction and the hoped-for kinetic separation of the less-reactive invertomers (having the chlorine *anti-* to the tetrafluoroaryl ring) was impossible. The results are summarised in scheme 4.

Scheme 4

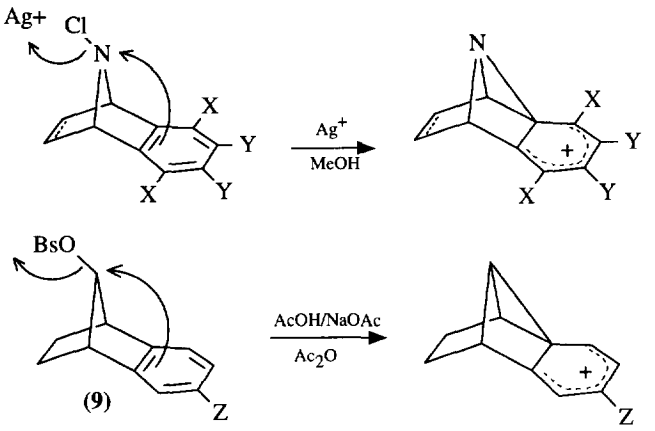


X=H	20%	80%	(**4a**)	6 days →	(**8a**) 80%	[+ (**4a**) 12%]
X=OMe	23%	77%	(**4b**)	2 days →	(**8b**) 90%	

The products derive entirely from participation of the more reactive aryl ring and the relative reaction times imply that the dimethoxybenzo- ring is more reactive than benzo- by a factor of more than three. The isolated yields of (**8a**) [accounting for recovered (**4a**)], and (**8b**) confirm that some of the product is derived from the less-reactive *syn-* invertomer (NCl *anti-* to the fluorinated ring) by prior inversion in each case.

The relative participatory abilities of the aryl rings follow the sequence shown in scheme 5; the intermediates are shown as localised carbocations for clarity but it is likely that symmetrical, non-classical intermediates are involved in the symmetrical systems chosen in our study. The pattern is very similar to that which emerged from the quantitative studies on the brosylates (**9**) reported by Tanida[5] and is entirely supportive of the heterolytic mechanism proposed earlier.[1]

Scheme 5



relative rates

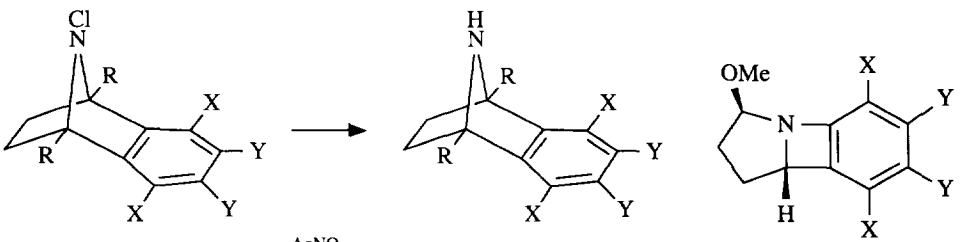
X = OMe, Y = H > X=Y=H >> X=Y=F

K_{rel} at 77.6°C

Z =	OMe	H	Cl
	53.7	1	0.045

The brosylate solvolyses were performed on systems having a saturated 2-carbon bridge and we have also explored the ethano-bridged compounds (**5**). The tetrafluorobenzo- compound (**5c**) failed to react at all, even under forcing conditions (scheme 6). This contrasts with the behaviour of (**5a**) which underwent homolysis under standard conditions, and (**5b**) which homolysed but also provided (**11b**) in low yield (23%) as a result of dimethoxybenzo- participation in loss of chloride.[1] The yield of (**11b**) in the latter example was raised to 53% by preparing a mixture rich in the *anti*- invertomer by chlorination at low temperature and then performing the solvolysis at low temperature, thus preventing loss of the *syn*- invertomer by inversion, and avoiding competition from the homolytic process.[1]

Scheme 6

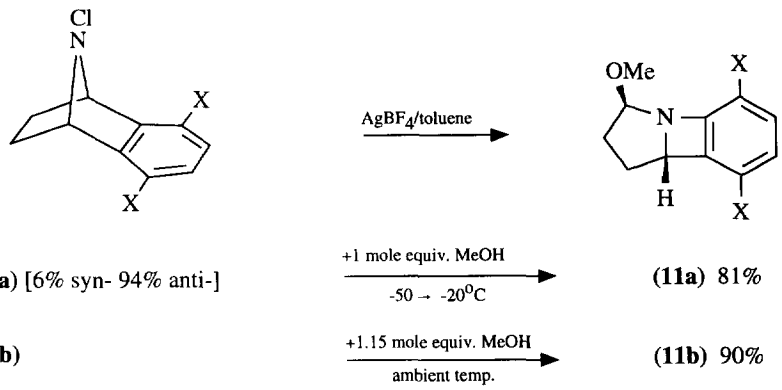


R=H; X=Y=F	(**5c**)	$AgNO_3$, MeOH/55°C	-		-
R=H; X=Y=H	(**5a**)	$AgNO_3$, MeOH	(**10a**)	(70%)	-
R=H; X=OMe; Y=H	(**5b**)	$AgNO_3$, MeOH/55°C	(**10b**)	(26%)	(**11b**) 23% [ref.1]
R=Me; X=OMe; Y=H	(**12**)	1) $AgNO_3$/toluene, 2) MeOH/$NaBH_4$	(**13**)	(96%)	-
R=H; X=Y=H	(**5a**)	$AgBF_4$/toluene	(**10a**)		-

We were surprised that benzo-participation was only observed in the case of (**5b**) and that the low reactivity of the benzo-group was allowing the balance to shift in favour of homolysis. Whilst using

N-chloroamines in the synthesis of pyrrolizidine ring systems, Schell[6] circumvented problems of homolysis by treating N-chloroamines with $AgBF_4$ in aprotic media and isolated products of ionic rearrangement. Unfortunately, we found that treatment of **(12)** with $AgBF_4$ in toluene gave only the homolysis product **(13)** and similar behaviour was observed for **(5a)**.[2] However, we found that the addition of a small amount (ca. 1 mole equivalent) of methanol changed the picture dramatically giving heterolysis products.[2] Application of these conditions to **(5a)** and **(5b)** led to a similar change of direction; the products corresponded to those expected for heterolysis of the N-Cl bond with aryl participation and they were isolated in high yield (scheme 7). Thus, in the case of **(5a)**, the combination of kinetically-controlled chlorination [giving a 6:94 ratio of *syn-* : *anti-* **(5a)**], a low reaction temperature (to prevent inversion), the presence of a *small amount* of methanol in toluene solvent, and the use of $AgBF_4$ led to clean heterolysis giving **(11a)** in a yield of 81% and *with no significant intrusion from the homolysis reaction* (scheme 7).

Scheme 7



In the case of **(5b)**, the use of similar conditions also encouraged clean heterolysis leading to production of **(11b)** in excellent yield (90%) even at room temperature and under conditions of free inversion.

The role of the methanol in suppressing competition from N-Cl bond homolysis is not clear. The methanol may alter the activity of the silver ion (whether in solution or on the surface of undissolved $AgBF_4$). Aromatic solvents are known to complex with silver ion and it is possible that small quantities of methanol disrupt these complexes and increase the effective ability of silver ion to promote the heterolytic pathway. Certainly, it is likely that the intimate relationship between substrate, silver ion and methanol will be different in toluene solvent than in a large excess of methanol.

The application of these empirical observations to the effective heterolysis of a range of 1-methyl- and 1,4-dimethyl- derivatives of the title ring system will be reported separately.[7]

Summary

A significant measure of control over the reactivity of these ring systems is possible. The more useful pathway, involving rearrangement to derivatives of the 1-azabicyclo[3.2.0]heptane ring system, proceeds via participation of the aryl π-electrons. This can be encouraged, except in the case of electron-deficient aryl rings, in each variant of the title ring system studied.

In compounds such as **(1)**, a preference for the benzo-participation route can be achieved by maximising the proportion of the *anti*-N-chloro invertomer in the substrate by control of chlorination conditions[3b] and by preventing subsequent nitrogen inversion during the reaction by maintaining the reaction temperature below 0°C during treatment with a Ag(I) salts.

Dibenzo- systems such as **(4)** involve the more electron-rich ring selectively and give rearrangement products in good yield, despite the need for higher temperatures and long reaction times.

In cases where there is no competition from another π-system, such as **(5)**, the use of silver salts in methanol leads to the formation of unacceptable quantities of homolysis products. Under these circumstances, a simple modification of the reaction conditions involving the use of minimal quantities of methanol together with silver salts in a non-polar solvent leads to the isolation of rearrangement products in high yield.

Experimental

Routine ^1H NMR spectra were recorded on Varian EM 390 (90 MHz) or Jeol JNM-PS100 (100 MHz) spectrometers and low field ^{13}C NMR spectra on a Jeol JNM FX60 spectrometer operating at 15.4 MHz. Higher field ^1H and ^{13}C NMR spectra were recorded on a Brucker AM 300 spectrometer. Spectra were measured in $CDCl_3$ with tetramethylsilane (TMS) as internal reference unless indicated otherwise. Signal characteristics are described using standard abbreviations: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), m (multiplet), br (broad); protons identified as NH or OH were shown to be exchangeable with D_2O. In the ^{13}C NMR spectra, C, CH, CH_2, CH_3 are used, where appropriate, to indicate quaternary, methine, methylene and methyl carbons respectively, as shown by off-resonance decoupling or DEPT experiments.

IR spectra were recorded on PE 1604 FT or PE 298 IR spectrometers as solutions in CH_2Cl_2 unless indicated otherwise. Band intensities are described using standard abbreviations: s (strong), m (medium), w (weak), br (broad), v (very).

Mass spectra were measured routinely on a VG Micromass 14 spectrometer and were obtained using ionisation by electron impact; the base peak is indicated by an asterisk. Accurate mass measurements were obtained through the SERC service at University College 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.

Reactions were performed under dry nitrogen using solvents dried by standard methods. Diethyl ether was dried over sodium wire and distilled from $LiAlH_4$. Dichloromethane and methanol were distilled from calcium hydride. Petroleum ether and ethyl ethanoate were distilled prior to use and toluene for small-scale reactions was distilled from sodium-benzophenone; petroleum ether refers to the fraction b.p. 40 - 60°C unless stated otherwise. Thin-layer chromatography (TLC) was conducted on standard commercial aluminium sheets pre-coated with a 0.2 mm layer of silica gel (Merck 60 - 254).

Methanolysis of 9-Chloro-1,4-dihydronaphthalen-1,4-imines (1a), (1b), and (1c) at Ambient Temperature General Procedure

The N-chloroamines (0.7 - 1.6 mmol) were dissolved in a minimum of dry methanol (5 - 10 ml) and allowed to stand at ambient temperature 20°C in the dark under dry nitrogen. The progress of each reaction was monitored by ^1H NMR spectroscopy. After completion, the solvent was evaporated and the residue taken into dichloromethane and then treated with 0.1M K_2CO_3 solution. The aqueous phase was washed further with portions of dichloromethane and the combined organic extracts were dried and the solvent removed under vacuum. The products and ratios are summarised in Table 1; the characterisation of the products from **(1a)** and **(1b)** has already been reported.[1]

The products from the solvolysis of **(1c)** were separated by flash chromatography on Kieselgel using ethyl ethanoate as solvent. During this latter separation, the novel amine 2-*endo*-chloro-3-*endo*-methoxy-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydronaphthalen-1,4-imine **(6)** was isolated in 8% yield (38 mg). Recrystallisation from diethyl ether - petroleum ether gave a sample of analytical purity, m.p. 132 - 133°C.

δ ($CDCl_3$): 4.96 (m, 2H, $w_{\frac{1}{2}}$ = 8Hz, $H_{1,4}$), 4.5 (dd, 1H, J = 7.5, 4.5Hz, H_3), 4.06 (dd, 1H, J = 7.5, 4.5Hz, H_2), 3.13 (br, s, NH). ν_{max} (CH_2Cl_2): 3300w, 2930w, 2830w, 1500s, 1385m, 1300m, 1200m, 1125s, 1075s, 1005m, 975m, 935s, 805s cm^{-1}. m/z: 283(M^+). 280, 246, 214, 203, 189*, 162. Found: C, 46.89; H, 2.96; N, 5.01; Cl, 12.69%. $C_{11}H_8NOF_4Cl$ requires: C, 46.91; H, 2.86; N, 4.97; Cl, 12.59%.

The major product (**2c**) was isolated in a yield of 23% and was shown to be identical to a sample produced by heterolysis in the presence of silver nitrate (below). The homolysis product (**7c**) was also identified by comparison of the ^1H NMR spectrum with that of an authentic sample.

Ag(I)-Promoted methanolysis of 9-chloro-5,6,7,8-tetrafluoro-1,4-dihydronaphthalen-1,4-imine (1c) at 0°C

The N-chloroamine (**1c**) (350 mg, 1.4 mmol) and finely ground silver nitrate (500 mg) were stirred for 40 min in dry methanol at 0°C in the dark under dry nitrogen; the N-chloroamine had been allowed to equilibrate prior to the reaction and the *syn-* : *anti-* ratio was 80 : 20. The mixture was then filtered, poured into 0.1M K_2CO_3 solution (50 ml) and the aqueous phase was extracted with dichloromethane (4 x 20 ml). The combined organic extracts were dried and the solvent removed under vacuum to give a yellow oil (344 mg) which crystallised in the cold. Repeated recrystallisation from diethyl ether/petroleum ether gave 2,3-bis-*endo*-methoxy-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydronaphthalen-1,4- imine (**2c**), m.p. 140 - 142.5°C (111 mg, 35%). δ ($CDCl_3$): 4.93 (m, 2H, $w_{\frac{1}{2}}$ = 5 Hz, $H_{1,4}$), 4.04 (m, 2H, $w_{\frac{1}{2}}$ = 5 Hz, $H_{2,3}$), 3.38 (s, 6H, OMe), 2.33 (br, s, NH, exchangeable with D_2O). ν_{max} (CH_2Cl_2): 3300w, 2930m, 2830m, 1500s, 1390m, 1200m, 1115m, 1075m, 1025m, 980m, 935m, 805m cm^{-1}. m/z: 277 (M^+), 262, 246, 215, 202, 189*, 162, 88. Found: C, 51.81; H, 3.96; N, 5.26%. $C_{12}H_{11}NO_2F_4$ requires: C, 51.99; H, 4.00; N, 5.05%.

The mother liquors from the recrystallisation were shown to contain further (**2c**) (25 mg, 8%) and (**7c**) (9 mg, 3%) by integration of the ^1H NMR spectrum of the mixture against an internal standard (p-dibromobenzene). These two amines could not be separated successfully by chromatography.

Ag(I)-Promoted methanolysis of 9-chloro-1,4-dihydronaphthalen-1,4-imines (1a), (1b), and (1c) at low temperature

In a typical procedure, the N-chloroamine (**1b**) (41 mg, 0.17 mmol) and p-dibromobenzene (16 mg, 0.067 mmol) were dissolved at 0°C in ice-cold d_4-MeOH (*ca.* 0.5 ml) and the solution transferred to an NMR tube which was maintained at -60°C. The ^1H NMR spectrum of the solution was recorded at -55°C and the initial ratio of *syn-* and *anti-* (**1b**) was calculated by integration of the signals due to $H_{1,4}$ at δ 5.08 and 5.24 respectively.

The spectra were recorded as small portions of silver perchlorate (*ca.* 35 mg) were added and the rate of loss of *syn-* and *anti-*invertomers measured by integration against the internal standard. After allowing the solution to warm to ambient temperature in the probe, the crude yields of the products d_6-(**2b**), d_3-(**3b**), and (**7b**), were calculated using the known weight of internal standard. Finally, the solution was diluted, made basic (K_2CO_3 solution) and then extracted with dichloromethane (2 x 2 ml). The extracts were combined, dried and evaporated. The NMR spectrum of this residue was compared against spectra of authentic (**2b**), (**3b**), and (**7b**) to confirm that these were the products of the solvolysis. The yields of products from the solvolyses of (**1a**), (**1b**), and (**1c**) are given in table 2 together with the temperatures at which the reactions were performed.

Ag(I)-Promoted methanolysis of 11-chloro-1,2,3,4-tetrafluoro-9,10-dihydro-9.10-iminoanthracene (4a)

The N-chloroamine (**4a**) (58 mg, 0.19 mmol) was dissolved in warm dry methanol (4 ml) and transferred to a 'Reacti-Vial' containing silver tetrafluoroborate (93 mg, 0.48 mmol) under nitrogen. The reaction mixture was stirred in the dark at 40°C for 6 days, after which TLC showed very little N-chloroamine remaining. The reaction mixture was filtered through Celite followed by further diethyl ether washings from the reaction vessel (6 ml). The filtrate was made up to 20 ml with water and basified with 1M (aq) K_2CO_3 solution, then refiltered through Celite and the organic layer separated. The filtrate was extracted with further

diethyl ether (3 x 15 ml); the combined organic extracts were washed with water and dried over anhydrous $MgSO_4$. Removal of solvent under reduced pressure afforded an off-white solid (53 mg).

The solid was examined by ^1H NMR spectroscopy and found to contain 2-methoxy-3,4-(tetrafluorobenzo)-6,7-benzo-1-azabicyclo[3.2.0]heptane (**8a**), (46 mg, 80%) and unchanged (**4a**), (7 mg, 12%) by integration relative to a known quantity of dichloromethane as an internal standard. δ_H (90 MHz; $CDCl_3$): 7.07 (4H, m, aryl), 6.30 (1H, brs), 5.66 (1H, brs), 3.58 (3H, s). δ_C (75 MHz; $CDCl_3$): 155.2, 136.4, 128.2, 122.2, 120.7, 111.5 (aryl; the tetrafluorobenzo signals were complex due to CF coupling), 93.7, 76.6, 53.6 (OMe). $^m/z$: 295 (M^+, 43%), 265(100), 264 (56), 252 (17), 237 (23) $C_{15}H_9NOF_4$ requires $^m/z$ 295.0620; found: 295.0615.

Ag(I)-Promoted methanolysis of 11-chloro-1,2,3,4-tetrafluoro-5,8-dimethoxy-9,10-dihydro-9.10-iminoanthracene (4b)

The N-chloroamine (**4b**) (96 mg, 0.26 mmol) was dissolved with warming in dry methanol (4 ml) and transferred by syringe to a Reacti-Vial containing silver tetrafluoroborate (192 mg, 0.98 mmol) under nitrogen. The reaction mixture was stirred in the dark at 40°C for 48h, after which time no starting N-chloroamine remained, as shown by TLC analysis. The contents of the reaction vessel were filtered through Celite and the vessel was rinsed with more diethyl ether (6 ml). The filtrate was then made up to 20 ml with water, basified with 1M (aq) K_2CO_3 solution and filtered again through Celite. The filtrate was made up to 40 ml with water, the organic layer separated, and the aqueous layer extracted further with diethyl ether (3 x 20 ml). The combined organic layers were dried over anhydrous $MgSO_4$ then evaporated under reduced pressure to afford 2-methoxy-3,4-(8,9,10,11-tetrafluorobenzo)-6,7-(12,15-dimethoxybenzo)-1-azabicyclo-[3.2.0]heptane (**8b**) as a white solid (82 mg, 90%).

A small amount of the solid was recrystallised several times from n-hexane to afford an analytically pure sample of (**8b**) as needles, m.p. 149 - 150°C. δ_H (90 MHz; $CDCl_3$): 6.56 (1H, d, J = 10 Hz, Aryl H), 6.44 (1H, d, J = 10 Hz, Aryl H), 6.33 (1H, brs), 5.85 (1H, brs), 3.82 (3H, s, ArOMe), 3.79 (3H, s, ArOMe), 3.59 (3H, s, OMe). δ_C (15 MHz; $CDCl_3$): 147.9, 142.7, 141.2, 122.5 (4 x s, aryl C), 114.2, 109.9 (2 x d, aryl CH), (the tetrafluorobenzo signals were complex due to CF coupling), 92.3 (d), 77.0 (d), 56.4 (q, 2 x aryl OMe), 54.9 (q, OMe). $^m/z$ (%) 355 (M^+, 100), 340(39), 325(31), 324(36), 310(36), 295(19), 294(11), 280(36), 44(14). Found: C, 57.44; H, 3.76: N, 3.97%. $C_{17}H_{13}NO_3F_4$ requires: C, 57.47; H, 3.69; N, 3.94%.

Ag(I)-Promoted methanolysis of 9-chloro-5,6,7,8-tetrafluoro-1,2,3,4-tetrahydronaphthalen-1,4-imine (5c)

The N-chloroamine (**5c**) (435 mg, 1.7 mmol) was dissolved in dry methanol (10 ml) and the solution was warmed in an oil bath at 55°C. Silver perchlorate (716 mg) was added and the mixture was stirred in the dark under N_2 for 3 h at the same temperature. The solvent was removed under vacuum and dichloromethane (50 ml) and water (30 ml) were added. The mixture was shaken and the two layers were separated. The aqueous layer was extracted with further dichloromethane (2 x 10 ml). The combined organic extracts were dried, evaporated and chromatographed on alumina using diethyl ether as the eluant. Unchanged starting material (276 mg, 65%) was recovered; ^1H NMR spectroscopy was used to confirm the absence of any other product.

Low-temperature preparation and Ag(I)-promoted rearrangement of 9-chloro-1,2,3,4-tetrahydro-1,4-iminonapthalene (5a) in toluene with minimum methanol

N-Chlorosuccinimide (276 mg, 2.07 mmol) was added to a solution of 1,2,3,4-tetrahydro-1,4-iminonaphthalene (**10a**) (250 mg, 1.72 mmol) in dry dichloromethane (10 ml) at -50°C under nitrogen. After stirring for 2.5 h, the solvent was evaporated at reduced pressure without allowing the temperature of the reaction mixture to rise above -20°C. The residue was dissolved in cold toluene (10 ml) and filtered at low temperature (to remove NCS and succinimide). The resulting solution of N-chloroamine (**5a**) was added to a mixture of silver tetrafluoroborate (400 mg, 2.06 mmol) and dry methanol (70 µl, 1.73 mmol) in dry toluene

(10 ml) at -50°C. The reaction mixture was allowed to warm to -20°C and stirred at that temperature for 4 h. After evaporation of the solvent at reduced pressure, brine (20 ml) and 2M (aq) sodium hydroxide solution (20 ml) were added, and the mixture subsequently filtered (to remove the silver salt residues). The product was extracted into dichloromethane (3 x 25 ml) and the organic layers were washed with water (20 ml). The combined organic extracts were dried over anhydrous magnesium sulphate and the solvent evaporated under reduced pressure. The residue was purified by flash chromatography (30 : 70 diethyl ether : petroleum ether) to afford a pale yellow oil which was identified as the rearrangement product **(11a)** (242 mg, 81%) by comparison of its ^{1}H NMR spectrum with that of an authentic sample prepared by hydrogenation of **(3a)**.[1]

Ag(I)-Promoted rearrangement of 9-chloro-5,8-dimethoxy-1,2,3,4-tetrahydro-1,4-iminonaphthalene (5b) in toluene with minimum methanol

The N-chloroamine **(5b)** (92 mg, 0.39 mmol) was added to a stirred mixture of silver tetrafluoroborate (97 mg, 0.50 mmol), dry methanol (18 µl, 0.45 mmol) and toluene (15 ml). The reaction mixture was stirred in the dark under nitrogen for 3 h during which time a white precipitate formed. The supernatant was removed and the precipitate dried under reduced pressure, treated with 2M (aq) NaOH solution (20 ml), then extracted with dichloromethane (3 x 20 ml). The organic extracts were combined, dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to afford **(11b)**, (86 mg, 90%) as a pale yellow solid, identified by direct comparison with an authentic sample.[1]

References and Footnotes

1. Durrant, M.L.; Malpass, J.R.; *Tetrahedron*, **1995**, *51*, 7063.
2. Davies, J.W.; Malpass, J.R.; Moss, R.E. *Tetrahedron Lett.*, **1986**, *27*, 4071.
3. **a.** N-Alkyl and NH derivatives: see Davies, J.W.; Durrant, M.L.; Walker, M.P.; Belkacemi, D.; Malpass, J.R. *Tetrahedron*, **1992**, *48*, 861, and references cited therein.

   b. N-Chloro derivatives: see Davies, J.W.; Durrant, M.L.; Walker, M.P.; Malpass, J.R. *Tetrahedron*, **1992**, *48*, 4379, and references to the work of others cited therein.
4. The temperatures in table 2 should be used as a useful but approximate guide to overall reactivity; it was not easy to reproduce the overall rates of reaction precisely in repeat runs due to the difficulty in mixing at low temperature following addition of solid silver perchlorate.
5. Tanida, H.; Tsuji, T.; Ishitobi, H. *J.Amer.Chem.Soc.*, **1964**, *86*, 4904.
6. Schell, F.M.; Ganguly, R.N. *J.Org.Chem.*, **1980**, *45*, 4069.
7. Davies, J.W.; Naylor, A.; Malpass, J.R.; Moss, R.E. manuscript in preparation. Some preliminary results in this area have been reported in reference 2.

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