Condensation of αβ-Unsaturated Amines with Perfluoroarenes

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Condensation of αβ-unsaturated amines (enamines, keten *ON*-acetals, ynamines) with perfluoroarenes (perfluorobenzene, perfluorotoluene, bromopentafluorobenzene, perfluoropyridine) leads to the formation of ketones, esters, and amines α-substituted by a perfluoroaryl group. In the case of enamines, *C*-arylation can be followed by intramolecular *N*-arylation, giving fluorinated tetrahydrocarbazoles which can then be dehydrogenated by chloranil to give fluorinated carbazoles.

RADICAL addition of perfluoroalkyl iodides to enamines, ynamines, or keten *ON*-acetals leads to compounds substituted by a perfluoroalkyl chain at the α position.[1] In other reactions, such as the condensations of perfluoroalkenes with enamines [2] and ynamines,[3] which produce various polyfluorinated compounds, the unsaturated amines behave like nucleophilic species and are able to create a new carbon–carbon bond. We describe here their condensations with perfluoroarenes, compounds known to be susceptible to attack by nucleophiles.[4,5] These reactions result in the introduction of a perfluoroaryl nucleus α to a functional group. In the case of enamines the reaction can continue and form polyfluorinated indoles.[6]

Condensations with Enamines.—Condensation of the enamines (2) with perfluoroarenes (1) leads to compounds (4), (6), or (7) (Scheme 1). Reactions of *N*-cyclohex-1-enylpyrrolidine with perfluoropyridine or perfluorotoluene occur at room temperature without solvent. The fluorinated enamines (3; X = N, R = Me) and (3; X = C–CF_3, R = Me) formed by *C*-arylation of (2) (Scheme 1) can be detected by ^{19}F n.m.r. spectroscopy. Hydrolysis of the enamines produces the ketones (4; X = N, R = Me) (49%) and (4; X = C–CF_3, R = Me) (41%). The replacement of the fluorine atom *para* to the X substituent is in agreement with other nucleophilic substitutions.[7]

Perfluorobenzene does not react with enamines at room temperature. At 80 °C, however, fluorinated indole derivatives (6) are produced.[8] The mechanism involves an intramolecular *N*-arylation of the enamine (3) producing the quaternary ammonium salt (5) (Scheme 1), dealkylation of which by fluoride ion produces (6) and an alkyl fluoride.

Isolation of 5,6,7,8-tetrafluoro-9-(4-fluorobutyl)-1,2,3,4-tetrahydrocarbazole (6'a) † from *N*-cyclohex-1-enylpyrrolidine and perfluorobenzene gives proof of this mechanism (Scheme 1). A similar opening of a cyclic ammonium salt by a chloride ion has already been observed.[9] Dealkylation of (5') by a second enamine molecule is also possible and can lead to (6'b).

This synthesis of fluorinated tetrahydrocarbazoles can be applied to various enamines and perfluoroarenes. The results obtained with enamines (2) derived from cyclohexanone are listed in Table 1. The tetrafluoroindoles (9)—(17) prepared from other enamines and perfluorobenzene are summarized in Scheme 2.

The regioselectivity observed with perfluorotoluene, perfluoropyridine, and bromopentafluorobenzene is in agreement with an initial *C*-arylation; nucleophilic attack of the enamine *para* to the X group occurs leading to compounds (6f—h). We noticed that this initial *C*-arylation is in competition with an initial *N*-arylation producing *N*-dialkylaminopolyfluoroarenes (7). The *C-versus-N* initial arylation ratio is very dependent on the nature of the dialkylamino-portion of the enamine.

TABLE 1

Condensation of cyclohexanone enamines (2) with perfluoroarenes (1) at 80 °C

NR_2 of (2)	X of (1)	Reaction time/h	Fluorinated tetrahydrocarbazole	Nitrogen substituent R	Yield (%)
pyrrolidino	C–F	24	(6'a)	$[CH_2]_4F$	45
			(6'b)	$[CH_2]_4NR_2$	3
morpholino	C–F	240	(6'c)	$[CH_2]_2O-[CH_2]_2NR_2$	15
Me_2N	C–F	18	(6d)	Me	51
Et_2N	C–F	90	(6e)	Et	75
Et_2N	C–CF_3	36	(6f)	Et	86
Et_2N	N	24	(6g)	Et	61
Me_2N	C–Br	24	(6h)	Me	87

When perfluorobenzene is condensed with the enamine (2) this *C* : *N* ratio follows the order : dimethylamino (60 : 40), morpholino (75 : 25), 1-pyrrolidyl (80 : 20), diethylamino (100 : 0). This sequence does not obey the basicity order of the amines. A similar absence of correlation between basicity and reactivity has already been noticed in the case of amine condensations with perfluorobenzene.[10] Examination of the sequence shows that the rate per cent of *C*-arylation increases with the steric hindrance of the dialkylamino-group. On the other hand, the intramolecular *N*-arylation of the fluorinated enamine (3) does not seem very dependent on the substituents on the nitrogen atom.

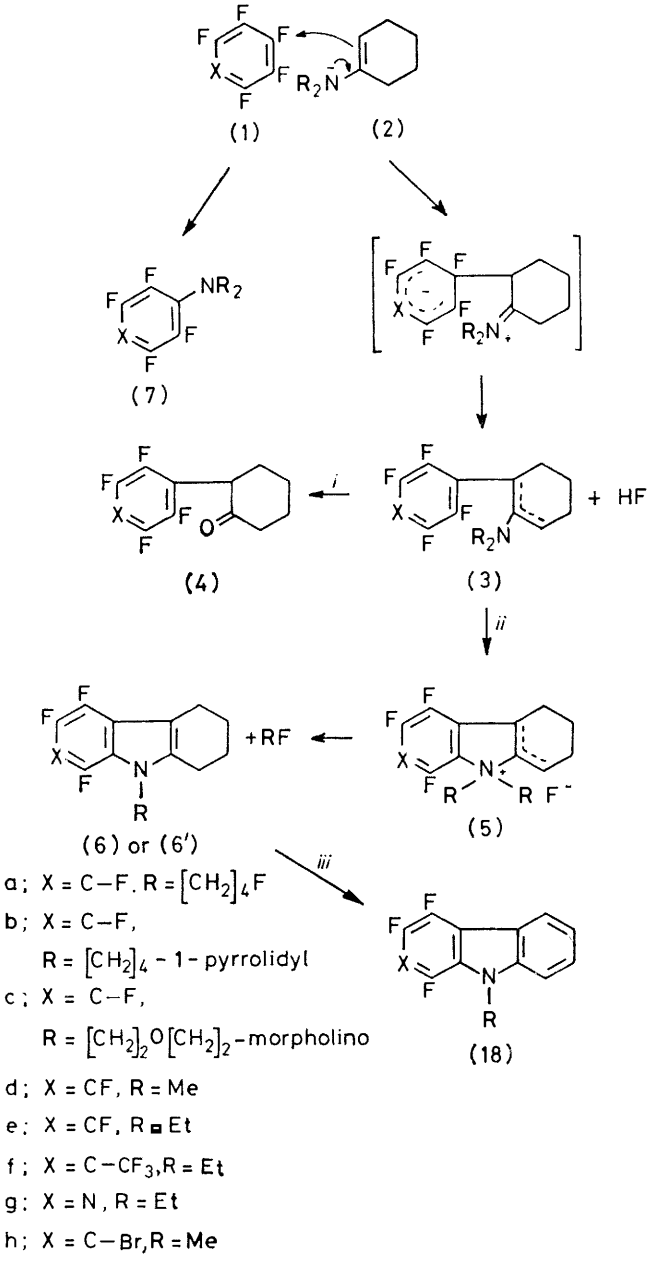
Fluorinated tetrahydrocarbazoles (6) or (6') can be dehydrogenated into fluorinated carbazoles (18) by chloranil in refluxing benzene (Table 2). This sequence constituted a convenient and short synthesis of 1,2,3,4-tetrafluorocarbazoles from readily available starting materials. Other syntheses involve the cyclisation of elaborated fluorinated compounds.[8b,c]

The photochemical transformation of *N*-methyl-*N*-

† Primed numbers refer to cases where the nitrogen substituent in compounds (6) is different from that in the original enamine (2).

(perfluorophenyl)aniline was described [8k] after publication of our preliminary communication.[6] A recent report shows that it is not possible to replace perfluoropyridine by perchloropyridine in such condensations with enamines.[11]

Condensation with Keten ON-*Acetals*.—Reaction of



SCHEME 1 Condensation of cyclohexanone enamines with perfluoroarenes (X = C–F, C–Br, C–CF_3, N). *Reagents*: *i*, H_3O^+; *ii*, reflux; *iii*, chloranil in refluxing benzene

1-ethoxy-*NN*-dimethyl vinylamine (19) with hexafluorobenzene at 80 °C only leads to *O* and *N*-arylation products. Pentafluoropyridine, the more reactive, condenses at 0 °C; hydrolysis leads to the ester (23) (Scheme 3).

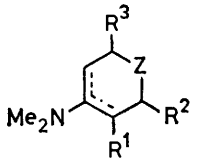
Condensation with Ynamines.—After hydrolysis, condensation of the perfluoroarenes with *NN*-diethylprop-1-ynylamine (24) leads to the amides (25) (Scheme 4). As far as we know this reaction is the first example of an ynamine arylation. Until now, attempts to alkylate ynamines have produced complex mixtures because the intermediate keten immonium compound is a very reactive species which condenses with a second ynamine molecule.[12] In the case of the arylation of (24) by perfluoroarenes, the keten immonium compound (26)

TABLE 2

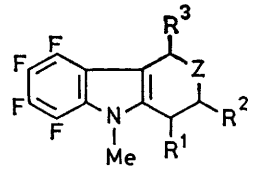
1,2,3,4-Tetrafluorocarbazoles (18)

Compound	Yield (%)	M.p. (°C)	Found (%)				Required (%)			
			C	H	F	N	C	H	F	N
(18a)	81	58–58.5	61.3	3.9	30.3	4.5	61.3	3.9	30.3	4.5
(18b)	87	126–127 [a]	61.9	2.8	29.5	5.4	61.7	2.8	30.0	5.5
(18c)	82	80–81	62.9	3.5	28.4	5.2	62.9	3.4	28.4	5.2

[a] Lit.,[8k] 110–112 °C.



(8) R^1=Me, R^2=R^3=H, Z = CH_2
(10a) R^1=R^3=H, R^2=Me, Z = CH_2
(10b) R^1=R^2=H, R^3=Me, Z = CH_2
(12) R^1=R^2=R^3=H, Z = NMe

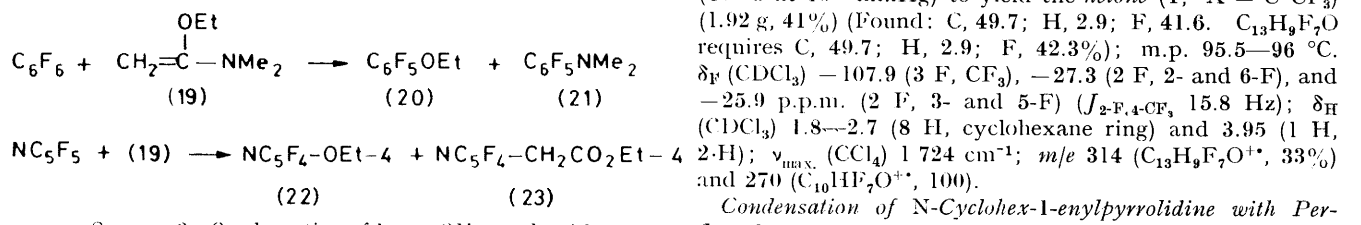


(9) R^1= Me, R^2=R^3=H, Z = CH_2
(11a) R^1=R^3=H, R^2=Me, Z = CH_2
(11b) R^1=R^2=H, R^3=Me, Z = CH_2
(13) R^1=R^2=R^3=H, Z = NMe.

(14) R^1 = Me, R^2 = Et
(15) R^1=Me, R^2= Et
(16) R^1 = Et, R^2 = H
(17) R^1=Et, R^2 = H

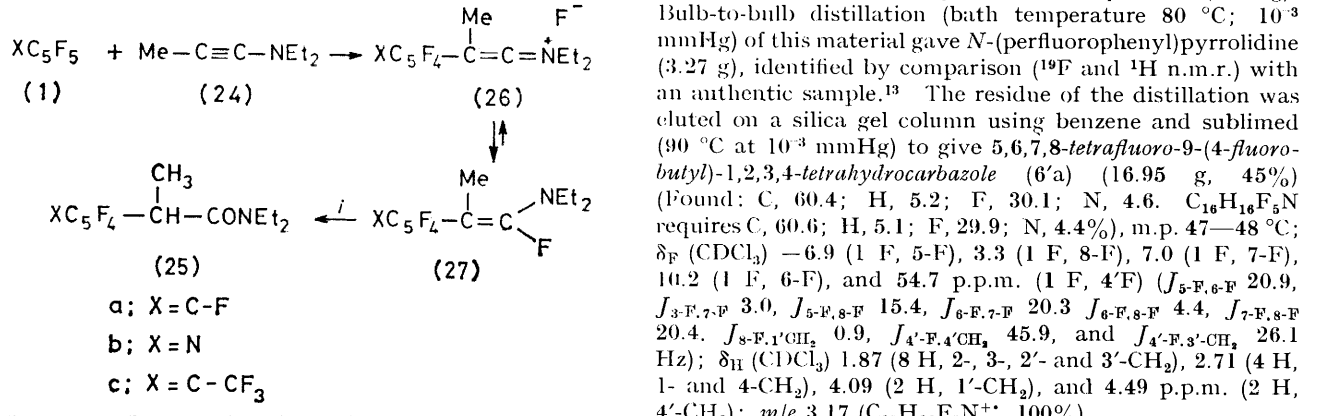
SCHEME 2 Condensation of various enamines with perfluorobenzene. *a*: Compounds (11a) and (11b) are obtained in the ratio 4 : 1

is efficiently captured by a fluoride ion to give the α-fluoro-enamine (27) (Scheme 4). Deplacement of the equilibrium towards (27) can be explained by the presence of an electronegative substituent on the β-enaminic



SCHEME 3 Condensation of keten *ON*-acetals with perfluoroarenes

carbon atom and by the high nucleophilicity of the fluoride ion. In the case of perfluorobenzene, a *para*-disubstituted product is also obtained.



SCHEME 4 Condensation of ynamines with perfluoroarenes. *Reagent: i*, H_3O^+

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded on Perkin-Elmer R 24 A or JEOL C 60 HL spectrometers. ^{19}F N.m.r. spectra were recorded on JEOL C 60 HL or Bruker WH90 instruments with perfluorobenzene as internal reference. I.r. spectra were recorded on a Perkin-Elmer 167 spectrometer. G.l.c. was performed on a Varian Aerograph 920 chromatograph (10 ft × 3/8 in column of 30% SE 30 on Chromosorb PAW 45—60 mesh at 180 °C). Mass spectra were taken on AEI MS 30 or VG Micromass 70-70F spectrometers.

2-(*Perfluoro-4-pyridyl*)*cyclohexanone* (4; X = N).—*N*-Cyclohex-1-enylpyrrolidine (8.6 g, 57 mmol) was added dropwise with stirring to perfluoropyridine (4.3 g, 25 mmol). The mixtnre was extracted using n-pentane to give a crude product (10.7 g). After hydrolysis [10N-H_2SO_4 (20 ml)], extraction (Et_2O), and drying ($MgSO_4$), the product was eluted on a silica gel column using benzene. Sublimation of the residue (40 °C at 10^{-3} mmHg) gave the *ketone* (4; X = N) (3.1 g, 49%) (Found: C, 53.5; H, 3.7; F, 30.5; N, 5.7. $C_{11}H_9F_4NO$ requires C, 53.4; H, 3.7; F, 30.7; N, 5.7%), m.p. 81—81.5 °C; δ_F ($CDCl_3$) −70.9 (2 F, 2- and 6-F) and 21.3 p.p.m. (2 F, 3- and 5-F); δ_H 1.8—2.6 (8 H, cyclohexane ring) and 4.2 (1 H, 2-H); $\nu_{max.}$ (CCl_4) 1 642 and 1 727 cm^{-1}; *m/e* 247 ($C_{11}H_9F_4NO^{+\cdot}$, 100%).

2-(*Perfluoro*-p-*tolyl*)*cyclohexanone* (4; X = C–CF_3).—A mixture of perfluorotoluene (3.5 g, 15 mmol) and *N*-cyclohex-1-enylpyrrolidine (4.5 g, 30 mmol) was stirred at room temperature for 1 h and then hydrolysed [3N-HCl (30 ml)]. The oily precipitate was isolated by decantation, washed with distilled water, and dried ($MgSO_4$) in n-pentane. After removal of the solvent *in vacuo*, the residue was eluted with benzene on a silica gel column and sublimed (40 °C at 10^{-3} mmHg) to yield the *ketone* (4; X = C–CF_3) (1.92 g, 41%) (Found: C, 49.7; H, 2.9; F, 41.6. $C_{13}H_9F_7O$ requires C, 49.7; H, 2.9; F, 42.3%); m.p. 95.5—96 °C. δ_F ($CDCl_3$) −107.9 (3 F, CF_3), −27.3 (2 F, 2- and 6-F), and −25.9 p.p.m. (2 F, 3- and 5-F) ($J_{2\text{-F},4\text{-}CF_3}$ 15.8 Hz); δ_H ($CDCl_3$) 1.8—2.7 (8 H, cyclohexane ring) and 3.95 (1 H, 2-H); $\nu_{max.}$ (CCl_4) 1 724 cm^{-1}; *m/e* 314 ($C_{13}H_9F_7O^{+\cdot}$, 33%) and 270 ($C_{10}HF_7O^{+\cdot}$, 100).

Condensation of N-*Cyclohex-1-enylpyrrolidine with Perfluorobenzene*.—A mixture of *N*-cyclohex-1-enylpyrrolidine (37 g, 245 mmol) and perfluorobenzene (22.3 g, 120 mol) was refluxed and stirred for 24 h. After cooling to room temperature, the mixture was hydrolysed [10N-H_2SO_4 (100 ml)], extracted (Et_2O), and dried ($MgSO_4$). Removal of the solvent *in vacuo* yielded crude product (26.7 g). Bulb-to-bulb distillation (bath temperature 80 °C; 10^{-3} mmHg) of this material gave *N*-(perfluorophenyl)pyrrolidine (3.27 g), identified by comparison (^{19}F and ^{1}H n.m.r.) with an authentic sample.[13] The residue of the distillation was eluted on a silica gel column using benzene and sublimed (90 °C at 10^{-3} mmHg) to give 5,6,7,8-*tetrafluoro*-9-(4-*fluorobutyl*)-1,2,3,4-*tetrahydrocarbazole* (6′a) (16.95 g, 45%) (Found: C, 60.4; H, 5.2; F, 30.1; N, 4.6. $C_{16}H_{16}F_5N$ requires C, 60.6; H, 5.1; F, 29.9; N, 4.4%), m.p. 47—48 °C; δ_F ($CDCl_3$) −6.9 (1 F, 5-F), 3.3 (1 F, 8-F), 7.0 (1 F, 7-F), 10.2 (1 F, 6-F), and 54.7 p.p.m. (1 F, 4′F) ($J_{5\text{-F},6\text{-F}}$ 20.9, $J_{3\text{-F},7\text{-F}}$ 3.0, $J_{5\text{-F},8\text{-F}}$ 15.4, $J_{6\text{-F},7\text{-F}}$ 20.3 $J_{6\text{-F},8\text{-F}}$ 4.4, $J_{7\text{-F},8\text{-F}}$ 20.4. $J_{8\text{-F},1'CH_2}$ 0.9, $J_{4'\text{-F},4'CH_2}$ 45.9, and $J_{4'\text{-F},3'\text{-}CH_2}$ 26.1 Hz); δ_H ($CDCl_3$) 1.87 (8 H, 2-, 3-, 2′- and 3′-CH_2), 2.71 (4 H, 1- and 4-CH_2), 4.09 (2 H, 1′-CH_2), and 4.49 p.p.m. (2 H, 4′-CH_2); *m/e* 317 ($C_{16}H_{16}F_5N^{+\cdot}$, 100%).

The aqueous phase was saturated with sodium carbonate and continuously extracted using n-hexane to give a basic fraction (11.84 g). Bulb-to-bulb distillation (bath temperature 70 °C; 10^{-3} mmHg) of the material gave unidentified non-fluorinated products (2.77 g), which had a strong amine odour. The residue from the distillation was first eluted with dichloromethane from an alumina column and then treated with a 50% solution of perchloric acid in absolute methanol. Several recrystallisations (−20 °C) in 1 : 1 : 1 methanol–diethyl ether–n-pentane gave 5,6,7,8-*tetrafluoro*-9-[4-(1-*pyrrolidylbutyl*)]-1,2,3,4-*tetrahydrocarbozolium perchlorate* (6′b; perchlorate) (1.5 g, 2.7%) (Found: C, 51.7; H, 5.3; F, 15.8; N, 6.0. $C_{20}H_{25}ClF_4N_2O_4$ requires C, 51.2; H, 5.4; F, 16.2; N, 6.0%); m.p. 165—166 °C (decomp.); δ_F for this compound and all other tetrafluoro-tetrahydro carbazoles very similar to δ_F for (6′a); δ_H (CD_3COCD_3) 1.8—2.2 (12 H, 2- and 3-CH_2, butyl CH_2CH_2, and pyrrolidyl), 2.77 (4 H, 1- and 4-CH_2), 3.56 (6 H, butyl NCH_2 and pyrrolidyl), 4.24 (2 H, NCH_2), and 5.13 (1 H, NH^+); *m/e* 368 ($C_{20}H_{24}F_4N_2^{+\cdot}$, 100%).

2-(6,7,8,9-*Tetrafluoro*-2,3,4,5-*tetrahydro*-9-*carbazolyl*)*ethyl* 2-*Morpholinoethyl Ether* (6′c). *Procedure A*.—A mixture of *N*-cyclohex-1-enylmorpholine (11 g, 66 mmol) and perfluorobenzene (5.58 g, 30 mmol) was refluxed and stirred for 24 h. After cooling to room temperature, the mixture was hydrolysed with 10N-H_2SO_4 (50 ml) extracted (diethyl ether), and the ethereal layer discarded. The aqueous layer was basified ($NaHCO_3$) and extracted with dichloromethane. Drying of the organic extract ($MgSO_4$) and removal of the solvent gave the crude product (2.25 g).

Sublimation (80 °C at 10^{-3} mmHg) gave the *ether* (1.82 g, 15%) (Found: C, 59.9; H, 5.9; F, 19.0; N, 6.8. $C_{20}H_{24}F_4N_2O_2$ requires C, 60.0; H, 6.0; F, 18.9; N, 7.0%), m.p. 91—92 °C; δ_H ($CDCl_3$) 1.86 (4 H, carbazolyl 3- and 4-CH_2), 2.42 (6 H, ether and morphilino OCH_2), 2.75 (4 H, carbazolyl 2- and 5-CH_2), 3.50 (2 H, ether OCH_2), 3.65 (6 H, ether and morpholino NCH_2), and 4.27 (2 H, N-CH_2); *m/e* 400 ($C_{20}H_{24}F_4N_2O_2^{+\bullet}$, 5%) and 100 ($C_5H_{10}NO^{+\bullet}$, 100).

5,6,7,8-*Tetrafluoro*-9-*methyl*-1,2,3,4-*tetrahydrocarbazole* (6d). *Procedure B.*—A mixture of *NN*-dimethylcyclohex-1-enylamine (7.5 g, 0.061 mol) and perfluorobenzene (5.69 g, 0.030 6 mmol) was refluxed and stirred for 18 h. After cooling to room temperature, the mixture was poured into 10N-H_2SO_4 (20 ml) when crystals were precipitated. These were filtered off and then dissolved in diethyl ether, washed with distilled water, and dried ($MgSO_4$). Removal of the solvent and sublimation (80 °C at 10^{-3} mmHg) gave the *carbazole* (6d) (4.82 g, 61%) (Found: C, 61.0; H, 4.3; F, 29.5; N, 5.3. $C_{13}H_{11}F_4N$ requires C, 60.7; H, 4.3; F, 29.5; N, 5.4%); m.p. 119—119.5 °C; δ_H ($CDCl_3$) 1.85 (4 H, 2- and 3-CH_2), 2.65 (4 H, 1- and 4-CH_2), and 3.67 (3 H, 9-CH_3); *m/e* 257 ($C_{13}H_{11}F_4N^{+\bullet}$, 80%) and 229 ($C_{11}H_7F_4N^{+\bullet}$, 100).

9-*Ethyl*-5,6,7,8-*tetrafluoro*-1,2,3,4-*tetrahydrocarbazole* (6e). —Using Procedure B, *NN*-diethylcyclohex-1-enylamine and hexafluorobenzene, refluxed for 90 h, gave the *carbazole* (6e) (75%) (Found: C, 62.2; H, 4.8; F, 28.1; N, 5.0. $C_{14}H_{13}F_4N$ requires C, 62.0; H, 4.8; F, 28.0; N, 5.2%); m.p. 120—121 °C; δ_H ($CDCl_3$) 1.32 (3 H, NCH_2CH_3), 1.87 (4 H, 2- and 3-CH_2), 2.72 (4 H, 1- and 4-CH_2), and 4.14 (2 H, NCH_2CH_3); *m/e* 271 ($C_{14}H_{13}F_4N^{+\bullet}$, 98%), 243 ($C_{12}H_9F_4N^{+\bullet}$, 89), and 215 ($C_{10}H_5F_4N^{+\bullet}$, 100).

9-*Ethyl*-5,6,8-*trifluoro*-7-*trifluoromethyl*-1,2,3,4-*tetrahydrocarbazole* (6f).—Prepared in 86% yield from perfluorotoluene and *NN*-diethylcyclohex-1-enylamine using Procedure B, except that the crystals were dissolved in $CHCl_3$, (reflux time, 36 h), the *carbazole* (6f) (Found: C, 6.0; H, 4.1; F, 35.4; N, 4.4. $C_{15}H_{13}F_6N$ requires C, 56.1; H, 4.1; F, 35.5; N, 4.4%) had m.p. 77—77.5 °C; δ_F ($CDCl_3$) −107.7 (3 F, 7-CF_3), −14.3 (1 F, 8-F), −7.7 (1 F, 6-F), and −6.5 p.p.m. (1 F, 5-F) ($J_{5\text{-F},6\text{-F}}$ 21.7, $J_{5\text{-F},8\text{-F}}$ 17.3, $J_{5\text{-F},CF_3}$ 21.7, $J_{6\text{-F},8\text{-F}}$ 6.2, $J_{6\text{-F},CF_3}$ 21.7, and $J_{8\text{-F},CF_3}$ 24.3 Hz); δ_H ($CDCl_3$) 1.33 (3 H, NCH_2CH_3), 1.88 (4 H, 2- and 3-CH_2), 2.75 (4 H, 1- and 4-CH_2), and 4.19 (2 H, NCH_2CH_3); *m/e* 321 ($C_{15}H_{13}F_6N^{+\bullet}$, 28%), 306 ($C_{14}H_{10}F_6N^+$, 48) 302 ($C_{15}H_{13}F_5N^+$, 31), 293 ($C_{13}H_9F_6N^{+\bullet}$, 97), and 265 ($C_{11}H_5F_6N^{+\bullet}$, 100).

9-*Ethyl*-1,3,4-*trifluoro*-5,6,7,8-*tetrahydro*-β-*carboline* (6g).—Prepared in 61% from perfluoropyridine and *NN*-diethylcyclohex-1-enylamine using Procedure B, except that the mixture was kept for 1 h at room temperature before refluxing (24 h), the crystals were dissolved in $CHCl_3$, and the product was eluted on silica gel (benzene) prior to sublimation at 100 °C and 5×10^{-3} mmHg; the β-*carboline* had m.p. 154.5—155 °C (Found: C, 61.1; H, 5.2; F, 22.4; N, 11.1. $C_{13}H_{13}F_3N_2$ requires: C, 61.4; H, 5.1; F, 22.4; N, 11.0%); δ_F ($CDCl_3$) −70.0 (1 F, 1-F), −48.7 (1 F, 3-F), and 0.3 p.p.m. (1 F, 4-F), ($J_{1\text{-F},3\text{-F}}$ 13.4, $J_{1\text{-F},4\text{-F}}$ 30.1, and $J_{3\text{-F},4\text{-F}}$ 20.6 Hz); δ_H ($CDCl_3$) 1.32 (3 H, NCH_2CH_3), 1.85 (4 H, 6- and 7-CH_2), 2.7 (4 H, 5- and 8-CH_2), and 4.08 (2 H, NCH_2CH_3); *m/e* 254 ($C_{13}H_{13}F_3N_2^{+\bullet}$, 100%).

7-*Bromo*-5,6,8-*trifluoro*-9-*methyl*-1,2,3,4-*tetrahydrocarbazole* (6h). *Procedure C.*—A mixture of bromopentafluorobenzene (30 g, 0.10 mol) and *NN*-dimethylcyclohex-1-enylamine (30 g, 0.24 mol) was refluxed and stirred for 24 h. After cooling to room temperature, the mixture was hydrolysed with 10N-H_2SO_4 (100 ml), extracted ($CHCl_3$), dried ($MgSO_4$), and sublimed (80 °C at 10^{-3} mmHg) to give the *carbazole* (6h) (33.59 g, 87%) (Found: C, 49.2; H, 3.5; Br, 25.0; F, 18.0; N, 4.5. $C_{13}H_{11}BrF_3N$ requires C, 49.1; H, 3.5; Br, 25.1; F, 17.9; N, 4.4%), m.p. 141 °C (decomp.); δ_F ($CDCl_3$) −26.5 (1 F, 8-F), −15.8 (1 F, 6-F), and −7.2 p.p.m. (1 F, 5-F) ($J_{5\text{-F},6\text{-F}}$ 20.6, $J_{5\text{-F},8\text{-F}}$ 15.2, $J_{6\text{-F},8\text{-F}}$ 5.3 and $J_{8\text{-F},9\text{-}CH_3}$ 2.8 Hz; δ_H ($CDCl_3$) 1.83 (4 H, 2- and 3-CH_2), 2.63 (4 H, 1- and 4-CH_2), and 3.62 (3 H, 9-CH_3); *m/e* 317 ($C_{13}H_{11}{}^{79}BrF_3N^{+\bullet}$, 100%).

5,6,7,8-*Tetrafluoro*-1,9-*dimethyl*-1,2,3,4-*tetrahydrocarbazole* (9). Prepared from the enamine (8) by Procedure B (reflux time, 20 days; yield 28%), the *carbazole* (9) had m.p. 99—99.5 °C (Found: C, 62.1; H, 4.9; F, 27.6; N, 5.0. $C_{14}H_{13}F_4N$ requires: C, 62.0; H, 4.8; F, 28.0; N, 5.2%); δ_H ($CDCl_3$) 1.26 (3 H, 1-CH_3), 1.81 (4 H, 2- and 3-CH_2), 2.74 (3 H, 1-H and 4-CH_2), and 3.71 (3 H, 9-CH_3); *m/e* 271 ($C_{14}H_{13}F_4N^{+\bullet}$, 64%) and 286 ($C_{13}H_{10}F_4N^+$, 100).

5,6,7,8-*Tetrafluoro*-2,9- and -4,9-*dimethyl*-1,2,3,4-*tetrahydrocarbazole* (11a) and (11b).—Prepared from perfluorobenzene and the enamine (10) using Procedure C, except that the product was eluted on silica gel (benzene) prior to sublimation (reflux time 115 h; yield 76%), the two isomers were obtained as a 4 : 1 mixture (Found: C, 62.1; H, 4.9; F, 28.0; N, 5.1. $C_{14}H_{13}F_4N$ requires C, 2.0; H, 4.8; F, 28.0; N, 5.2%; *m/e* 271 ($C_{14}H_{13}F_4N^{+\bullet}$, 82%) and 256 ($C_{13}H_{10}F_4N^+$, 100). The isomer (11a) showed δ_H ($CDCl_3$) (3 H, 2-CH_3) and 3.67 (3 H, 9-CH_3); isomer (11b) showed δ_H ($CDCl_3$) δ 1.24 (3 H, 4-CH_3) and 3.64 (3 H, 9-CH_3).

5,6,7,8-*Tetrafluoro*-3,9-*dimethyl*-1,2,4-*trihydro*-3-*azacarbazole* (13).—Prepared from perfluorobenzene and the enamine (12) using Procedure A, except that the product was eluted on alumina (pentane) prior to sublimation (reflux time 170 h; yield 15%) the *aza-carbazole* had m.p. 100—101 °C (Found: C, 57.3; H, 4.4; F, 27.9; N, 10.3. $C_{13}H_{12}F_4N_2$ requires C, 57.1; H, 4.4; F, 27.5; N, 10.2%); δ_H ($CDCl_3$) 2.52 (3 H, 3-CH_3), 2.77 (4 H, 1- and 2-CH_2), 3.61 (2 H, 4-CH_2), and 3.70 (3 H, 9-CH_3); *m/e* 272 ($C_{13}H_{12}F_4N_2^{+\bullet}$, 24%) and 229 ($C_{11}H_7F_4N^{+\bullet}$, 100).

1,2-*Diethyl*-4,5,6,7-*tetrafluoro*-3-*methylindole* (15).—Prepared from perfluorobenzene and the enamine (14) using Procedure B, except that sublimation was carried out at 40 °C (reflux time 145 h; yield 58%) the *indole* had m.p. 59—59.5 °C (Found: C, 60.3; H, 5.1; F, 28.9; N, 5.5. $C_{13}H_{13}F_4N$ requires C, 60.2; H, 5.0; F, 29.3; N, 5.4%); δ_H ($CDCl_3$) 1.03 (3 H, 2-CH_2CH_3), 1.33 (3 H, NCH_2CH_3), 2.27 (3 H, 3-CH_3), 2.67 (2 H, 2-CH_2), and 4.13 (2 H, NCH_2); *m/e* 259 ($C_{13}H_{13}F_4N^{+\bullet}$, 65%) and 244 ($C_{12}H_{10}F_4N^{+\bullet}$, 100).

1,3-*Diethyl*-4,5,6,7-*tetrafluoroindole* (17).—A mixture of *NN*-diethylbut-1-enylamine (16) (5 g, 39 mmol) and perfluorobenzene (3.6 g, 19 mmol) was refluxed and stirred for 113 h. The mixture was cooled and extracted with pentane. After removal of the solvent, the remaining product (4.59 g) was heated at 150 °C for 120 h, then hydrolysed with 10N-H_2SO_4 (20 ml) and extracted with diethyl ether. After drying ($MgSO_4$) and removal of the solvent, the product was eluted on an alumina column (pentane) and sublimed (30 °C at 5.10^{-3} mmHg) to yield the *indole* (17) (0.33 g, 7%) (Found: C, 59.0; H, 4.6; F, 31.0; N, 5.8. $C_{12}H_{11}F_4N$ requires C, 58.8; H, 4.5; F, 30.9; N, 5.7%), m.p. 76—76.5 °C; δ_H ($CDCl_3$) 1.23 (3 H, 3-CH_2CH_3), 1.40 (3 H, 1-CH_2CH_3), 2.73 (2 H, 3-CH_2), 4.15 (2 H, 1-CH_2), and 6.70 (1 H, 2-H); *m/e* 245 ($C_{12}H_{11}F_4N^{+\bullet}$, 53%) and 230 ($C_{11}H_8F_4N^+$, 100).

9-*Alkyl*-1,2,3,4-*tetrafluorocarbazoles* (18).—Chloranil (9 g, 37 mmol) was added to a solution of compound (6) (11 mmol) in dry toluene (20 ml). The mixture was refluxed for 48 h, cooled to room temperature, and the precipitate was filtered off and washed with pentane. The filtrate and washings were then washed with 20% aqueous NaOH and distilled water. After drying ($MgSO_4$) and removal of the solvent, the residue was sublimed (80 °C at 10^{-3} mmHg) to yield the *carbazoles* (18) (Table 2). Compound (18a) showed δ_F ($CDCl_3$) [typical for all compounds (18)] −13.8 (1 F, 4-F), −1.4 (1 F, 2-F), 2.3 (1 F, 1-F), 8.0 (1 F, 3-F), and 56.0 p.p.m. (1 F, 4′-F) ($J_{1\text{-F},2\text{-F}}$ 19.8, $J_{1\text{-F},3\text{-F}}$ 4.6, $J_{1\text{-F},4\text{-F}}$ 15.2, $J_{2\text{-F},3\text{-F}}$ 21.1, $J_{3\text{-F},4\text{-F}}$ 20.8, $J_{4'\text{-F},4'\text{-CH}_2}$ 48.3, and $J_{4'\text{-F},3'\text{-CH}_2}$ 26.1 Hz); δ_H ($CDCl_3$) 1.2—2.0 (4 H, 2′- and 3′-CH_2), 4.2 (2 H, 1′-CH_2), 4.4 (2 H, 4′-CH_2), 6.9—7.6 (3 H, 5,6,7-H), and 7.9 (1 H, 8-H); *m/e* 313 ($C_{16}H_{12}F_5N^{+\bullet}$, 38%) and 252 ($C_{13}H_6F_4N^+$, 100); $\nu_{max.}$ (CCl_4) 1 610 and 3 030 cm^{-1}. Compound (18b) had δ_H ($CDCl_3$) 3.76 (3 H, 9-CH_3), 7—7.5 (3 H, 5-, 6-, and 7-H), and 7.87 (1 H, 4-H); *m/e* 253 ($C_{13}H_7F_4N^{+\bullet}$, 100%); $\nu_{max.}$ (CCl_4) 1 610 and 3 032 cm^{-1}. Compound (18c) had δ_H ($CDCl_3$) 1.34 (3 H, NCH_2CH_3), 4.23 (2 H, NCH_2), 7—7.6 (3 H, 5-, 6-, and 7-H), and 7.97 (1 H, 4-H); *m/e* 267 ($C_{14}H_9F_4N^{+\bullet}$, 64%) and 252 ($C_{13}H_6F_4N^+$, 100).

Condensation of 1-*Ethoxy*-NN-*dimethylvinylamine* (19).—(a) *With perfluorobenzene*. A mixture of perfluorobenzene (5 g, 0.027 mol) and (19) (6.18 g, 0.054 mol) was refluxed for 10 h. After cooling to room temperature, the mixture was extracted with pentane and the extract hydrolysed with 10N-H_2SO (20 ml). After extraction (Et_2O), drying ($MgSO_4$), and distillation (50—60 °C, 10 mmHg), the product was eluted on silica gel (pentane) to give 2,3,4,5,6-pentafluorophenetole (20) (3.3 g, 58%), identified by comparison (^{19}F and ^1H n.m.r.) with an authentic sample,[14] and *NN*-dimethylpentafluoroaniline (21) (1.2 g, 21%) identified by comparison of its spectral characteristics with those published.[15]

(b) *With perfluoropyridine*. Compound (19) (6.3 g, 0.056 mol) was added dropwise to perfluoropyridine (4.6 g, 0.027 mol), cooled in an ice-bath. The mixture was then extracted with pentane to give a crude product (7.9 g) which was hydrolysed by 10N-H_2SO_4 (20 ml). After extraction (Et_2O) and drying ($MgSO_4$), the product was distilled on a spinning band (Perkin-Elmer M 131 T) to give 4-ethoxy-2,3,5,6-tetrafluoropyridine (22) (0.3 g, 6%), b.p. 78—88°C at 28 mmHg, and 2,3,5,6-*tetrafluoro*-4-*pyridyl acetate* (23) (3.2 g, 50%), b.p. 110—112 °C at 28 mmHg (Found: C, 45.5; H, 3.1; F, 31.9; N, 6.0. $C_9H_7F_4NO_2$ requires C, 45.5; H, 3.0; F, 32.0; N, 5.9%); δ_F (CCl_4) −72.2 (2 F, 2- and 6-F) and −19.7 p.p.m. (2 F, 3- and 5-F); δ_H (CCl_4) 1.27 (3 H, $CO_2CH_2CH_3$), 3.75 (2 H, CH_2CO_2Et), and 4.13 (2 H, CO_2CH_2); *m/e* 237 ($C_9H_7F_4NO_2^+$, 35%), 209 ($C_7H_3F_4NO_2^{+\bullet}$, 9%), 192 ($C_7H_2F_4NO^+$, 39), 165 ($C_6H_3F_4N^{+\bullet}$, 85), and 164 ($C_6H_2F_4N^+$, 100); $\nu_{max.}$ (CCl_4) 1 647 and 1 747 cm^{-1}.

Condensation of NN-*diethylprop*-1-*ynylamine* (24).—(a) *With perfluorobenzene*. A mixture of hexafluorobenzene (5.58 g, 0.03 mol) and (24) (3.33 g, 0.03 mol) was refluxed for 2 h. After cooling to room temperature, the mixture was hydrolysed by 10N-H_2SO (20 ml), extracted (Et_2O), and dried ($MgSO_4$) to give a crude mixture (6.4 g) containing (^{19}F n.m.r.) 80% of NN-*diethyl*-2-(*perfluorophenyl*)*propionamide* (25a), an analytical samples of which was obtained by g.l.c. (Found: C, 52.5; H, 4.6; N, 4.5. $C_{13}H_{14}F_5NO$ requires C, 52.9; H, 4.8; N, 4.7%), δ_F (CCl_4) −23.0 (2 F, 2- and 6-F), −7.2 (1 F, 4-F) and −1.3 p.p.m. (2 F, 3- and 5-F); δ_H (CCl_4) 1.09 (6 H, NCH_2CH_3), 1.50 (3 H, CH_3), 3.30 (4 H, NCH_2) and 4.20 (1 H, 2-H) ($J_{2\text{-H},CH_3}$ 6.9 Hz); $\nu_{max.}$ (CCl_4) 1 662 cm^{-1}; *m/e* 295 ($C_{13}H_{14}F_4NO^{+\bullet}$, 23%), 294 ($C_{13}H_{13}F_5NO^+$, 29), 195 ($C_8H_4F_5^+$, 35), and 100 ($C_5H_{10}NO^+$, 100). A second compound showing a singlet in the ^{19}F n.m.r. spectrum (δ −20.5 p.p.m.) and presumed to be the bis-adduct was not isolated.

(b) *With perfluoropyridine*. A solution of (24) (1.11 g, 10 mmol) in CH_2Cl_2 (5 ml) was added dropwise to a cooled (0 °C) solution of perfluoropyridine (1.69 g, 10 mmol) in CH_2Cl_2 (5 ml). The solution was stirred at 0 °C for 15 min, then at room temperature for a further 15 min. After removal of the solvent the crude product (2.37 g) was hydrolysed by 10N-H_2SO (10 ml), extracted (Et_2O), and dried ($MgSO_4$). Distillation afforded NN-*diethyl*-2-(*perfluoro*-4-*pyridyl*)*propionamide* (25b) (1.73 g, 62%), b.p. 95—97 °C at 0.3 mmHg (Found: C, 49.8; H, 4.6; F, 28.1; N, 9.6. $C_{12}H_{14}F_4N_2O$ requires C, 51.8; H, 5.1; F, 27.3; N, 10.1%); δ_F (CCl_4) −69.1 (2 F, 2- and 6-F) and −19.2 p.p.m. (2 F, 3- and 5-F); δ_H (CCl_4) 1.15 (6 H, NCH_2CH_3), 1.60 (3 H, CH_3), 3.37 (4 H, NCH_2), and 4.40 p.p.m. (1 H, 2-H) ($J_{2\text{-H},CH_3}$ 6.8 Hz); $\nu_{max.}$ (CCl_4) 1 660 cm^{-1}; *m/e* 278 ($C_{12}H_{14}F_4N_2O^{+\bullet}$, 100%).

(c) *With octafluorotoluene*. A solution of perfluorotoluene (2 g, 8.5 mmol) in pentane (5 ml) was added to a solution of (24) (0.94 g, 8.5 mmol) in pentane (5 ml) and the solution refluxed for 56 h. After removal of the solvent the product was hydrolysed by 10N-H_2SO (20 ml), extracted (Et_2O), and dried ($MgSO_4$). Distillation afforded NN-*diethyl*-2-(*perfluoro*-p-*tolyl*)*propionamide* (25c) (1.80 g, 62%) b.p. 95—100 °C at 0.2 mmHg (Found: C, 47.7; H, 4.0; F, 38.3; N, 4.0. $C_{14}H_{14}F_7NO$ requires C, 48.7; H, 4.1; F, 38.5; N, 4.1%); δ_F (CCl_4) −104.2 (3 F, CF_3), −22.7 (2 F, 3- and 5-F), and −20.7 p.p.m. (2 F, 2- and 4-F) ($J_{2\text{-F},CF_3}$ 21.1 Hz); δ_H (CCl_4) 1.07 (6 H, NCH_2CH_3), 1.50 (3 H, CH_3), 3.22 (4 H, NCH_2), and 4.15 p.p.m. (1 H, 2-H) ($J_{2\text{-H},CH_3}$ 7.0 Hz); $\nu_{max.}$ (CCl_4) 1 655 cm^{-1}; *m/e* 345($C_{14}H_{14}F_7NO^{+\bullet}$, 61%), 245 ($C_9H_4F_7^+$, 56), and 100 ($C_5H_{10}NO^+$, 100).

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