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UNSATURATED NITROGEN COMPOUNDS CONTAINING FLUORINE.
PART 7[1]. THE REACTION OF 2,5-DICHLORO-1,1,1,6,6,6-
HEXAFLUORO-3,4-DIAZAHEXA-2,4-DIENE WITH PHENYL-LITHIUM

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SUMMARY

Treatment of the title azine (1) with phenyl-lithium results in initial replacement of chlorine by phenyl to give the monophenylazine (4) and then the diphenylazine (5), but this is followed by successive replacement of fluorine in one CF₃ group to afford first the 3,4-diazahexa-1,3-diene CF₃CPh₂N=NPh=CXY (6) (X=Y=F), then (7) (X=F, Y=Ph) and finally (8) (X=Y=Ph).

INTRODUCTION

It has been reported previously that treatment of the dichloroazine (1) with N- and O-centred nucleophiles results in displacement of chloride ion to afford the mono- or di-substituted azines, (2) and (3), respectively, depending on the reactant ratio employed and the reaction conditions [2].

RESULTS AND DISCUSSION

In a preliminary investigation of carbanion attack on azine (1) it was observed that reaction involving an excess of phenyl-lithium gave orange red crystalline material the mass spectrum of which indicated that it contained a pentaphenyltrifluoromethyl compound, but this was not isolated pure and positively identified [3].

This prompted a detailed investigation of the reaction of azine (1) with phenyl-lithium, the results of which are summarized in the Table.

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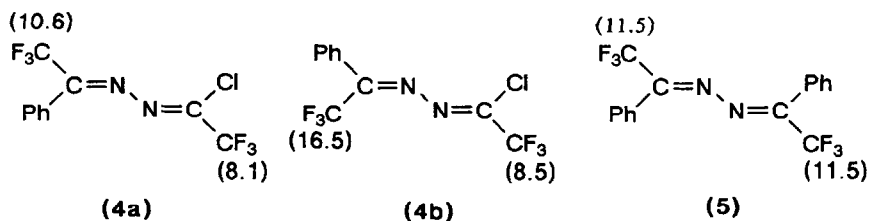
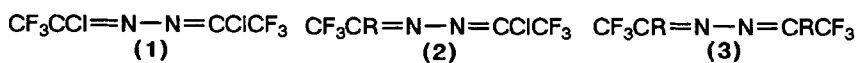
The mono- and di-phenylazines (**4**) and (**5**), respectively, are formed by addition of phenyl carbanion to a $\text{ClC}=\text{N}$ linkage followed by elimination of chloride ion. Use of a 1:1 reactant ratio in dilute or in concentrated solution did not result in exclusive or near exclusive formation of the monosubstituted azine as found with N- and O-centred nucleophiles, i.e. the second $\text{ClC}=\text{N}$ linkage was not deactivated appreciably to further carbanion attack. This is presumably because mesomeric electron release from a phenyl group is much less effective than release from a lone pair on nitrogen or oxygen. Such mesomeric release increases the electron density at carbon in the remaining $\text{ClC}=\text{N}$ linkage, i.e. $\text{CF}_3\text{CCl}=\text{N}=\text{N}=\text{C}(\text{CF}_3)-\text{X}(\text{R})_n \leftrightarrow \text{CF}_3\text{CCl}-\text{N}=\text{N}-\text{C}(\text{CF}_3)=\text{X}(\text{R})_n$ (where $\text{X}=\text{N}$, $n=2$ and $\text{X}=\text{O}$, $n=1$) and so nucleophilic attack on this linkage leading to the disubstituted azine is less favourable than initial attack on azine (**1**)

It was considered probable that the tetraphenyl- and pentaphenyl- compounds, (**7**) and (**8**), respectively, were formed via the diphenylazine (**5**). This was proved by reaction of azine (**1**) with two equivalents of phenyl-lithium at -78°C followed by treatment of the resulting product mixture [comprising mainly diphenylazine (**5**)] with a further three equivalents of phenyl-lithium at room temperature to afford mainly (**7**) (29%) and (**8**) (55%). The yields of these products were identical to those obtained by treatment of azine (**1**) with five equivalents of phenyl-lithium at room temperature.

The products are therefore considered to be formed by the pathway outlined in the Scheme. This is the first report of a nucleophilic displacement of fluoride ion from a trifluoromethyl group in a disubstituted azine of type (**2**) and may be attributed to (i) high electron deficiency at the azine carbons in the diphenylazine (**5**) due to $-I$ electron withdrawal by CF_3 and N not being counterbalanced to any extent by $+M$ electron release by phenyl and (ii) the nucleophilic strength of phenyl-lithium. The substitution is also noteworthy in that it involves loss of fluoride ion from an atom five removed from that attacked by the nucleophile

The difluorovinyl compound (**6**) was not detected in the products indicating that, as expected, it was more reactive towards nucleophilic attack than the other products. The ^{13}C and ^{19}F n.m.r. spectra of the tetraphenyl compound (**7**) indicated that it was formed as a single isomer, but the stereochemistry was not established.

One experiment, using a 1:1 ratio of reactants at -78°C , was carried out in air and not under nitrogen and a proportion of the phenyl-lithium was converted into lithium phenoxide. This resulted in the formation of a mixture of monophenylazine (**4**) (ca. 25%), monophenoxyazine (**9**) (ca. 12%) and diphenylazine (**5**) (19%) Compound (**9**) was identified by an accurate mass measurement and by a

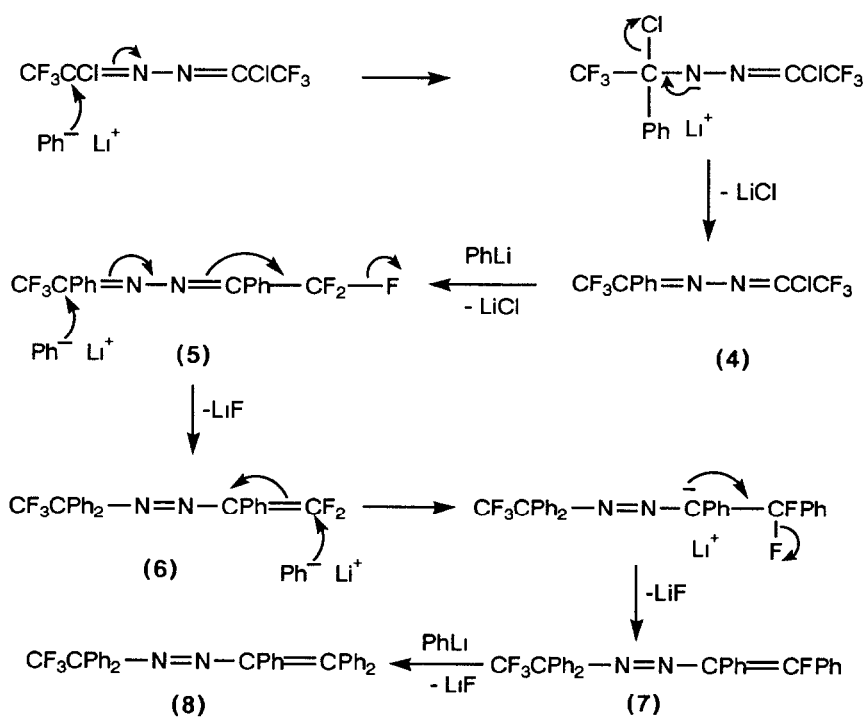
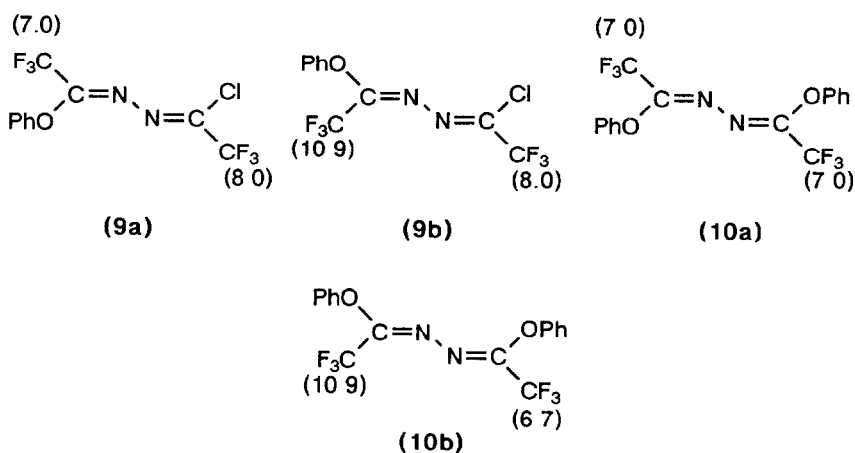


TABLE

Reaction of phenyl-lithium with azine (1) in diethyl ether ^a

Molar Ratio PhLi : (1)	Temp. (°C)	Products (%) ^b			
		(4) ^c	(5)	(7)	(8)
1 : 1	- 78 ^d	41	20	-	-
1 : 1	- 78 ^e	43	24	-	-
2 : 1	- 78	5	58	4	7
5 : 1	ca. + 20	-	-	29	55
2 : 1	- 78	-	4.5	29	55
3 : 1	ca. + 20				

^a Reactions carried out under nitrogen.^b Isolated yields based on reactant azine (1); biphenyl was also isolated from product mixture.^c Mixture of two isomers (4a) and (4b) in the ratio 18 : 1.^d Solvent volume 200 cm³.^e Solvent volume 30 cm³.



Scheme.

comparison of the ^{13}C and ^{19}F n.m.r. spectra of a mixture of compounds (4) and (9) with those of a pure sample of (9) synthesized in 73% yield by reaction of azine (1) with lithium phenoxide (1:1 molar ratio) in ether.

The azine (9) consisted of two isomers in the ratio 4:5:1.0 (^{19}F n.m.r.); cf. the diphenoxyazine (10) formed in 61% yield [from treatment of azine (1) with phenol (1:2 molar ratio) in the presence of triethylamine] as a mixture of two isomers in the ratio 7:4 [4]. The monophenylazine (4) was also formed as a mixture of two isomers.

The diphenylazine (5) has the (EE)-configuration as shown by an X-ray crystal study [5] and on steric grounds it is considered that the $\text{CF}_3\text{CCl}=\text{N}$ linkage in dichloroazine (1) and the monosubstituted azine isomers has the (Z)-configuration. The major isomers are therefore assigned structures (4a), (9a) and (10a) and are shown together with the observed ^{19}F n.m.r. chemical shifts (in parentheses) It is noteworthy that a *syn*- CF_3 group (*anti* to the nitrogen lone pair) absorbs to lower field than an *anti*- CF_3 group.

EXPERIMENTAL

Starting Materials

The dichloroazine (1) was synthesized from trifluoroacetic acid by the procedure reported [2] and phenyl-lithium [2.0M solution in cyclohexane and ether (70.30 v/v)] was purchased [Aldrich-Chemical Co. Ltd.].

General Techniques

Reactions involving phenyl-lithium were carried out under a nitrogen atmosphere in round-bottomed flasks fitted with either a cold finger ($-78\text{ }^\circ\text{C}$) or a water-cooled condenser with dropwise addition of the phenyl-lithium in anhydrous diethyl ether to a stirred solution of dichloroazine (1) in the same solvent at either $-78\text{ }^\circ\text{C}$ or room temperature. The resulting precipitate was filtered off at room temperature and the solvent was removed *in vacuo* from the filtrate at $-20\text{ }^\circ\text{C}$ to give crude product which was examined by TLC (SiO_2 , eluant $\text{C}_6\text{H}_{14}:\text{CH}_2\text{Cl}_2$ 4:1 v/v) and the components then separated by dry column flash chromatography (DCFC) using silica (Fluka 60 GF254 and a 30:1 w/w ratio of SiO_2 : product; eluant as above). Separated components were examined by i.r. (Perkin-Elmer 783 instrument) and n.m.r. {(solutions in CDCl_3); ^1H [Perkin-Elmer R32 (90 MHz),

Perkin-Elmer R34 (220 MHz) or Bruker AC 300 (300 MHz spectrometers using TMS as external reference], ^{19}F [Perkin-Elmer R32 (84.6 MHz) instrument with TFA as external reference and ^{13}C [Bruker WP80 (20.1 MHz) or AC 300 (75.0 MHz) spectrometers with broad band proton decoupling, D_2O as deuterium lock signal and TMS as external reference] with chemical shifts to low field of reference designated positive} spectroscopy and mass [Kratos MS25 instrument for low resolution spectra using electron impact (e.i.) or chemical ionisation (c i , NH_3) and Kratos Concept IS instrument for accurate mass measurement (e.i)] spectrometry

Reaction of Dichloroazine (1) with Phenyl-lithium

(a) Molar ratio 1:1

The addition of phenyl-lithium (5.75 cm^3 , 11.50 mmol) in ether (50 cm^3) to the azine (1) (3.00 g , 11.49 mmol) in ether (150 cm^3) at $-78\text{ }^\circ\text{C}$ over one hour followed by stirring at $-78\text{ }^\circ\text{C}$ for a further hour and then warming to room temperature gave lithium chloride (0.42 g , 10.0 mmol, 87%) and a dark yellow oil (3.01 g) the three components of which were separated (DCFC) and identified as (i) 2-chloro-5-phenyl-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (4) (nc) (R_F 0.60) (1.43 g , 4.73 mmol, 41%) (Found: C, 39.6; H, 1.9; N, 9.1; F, 37.4%; M^+ , 304 and 302. $\text{C}_{10}\text{H}_5\text{ClF}_6\text{N}_2$ requires C, 39.7; H, 1.7; N, 9.3, F, 37.7%; M , 302.5) as two isomers in the ratio 18:1; ν_{max} . 3075 w(arom. C-H str.), 1630s (C=N str.), 1200-1150s (C-F str.), 760s (CF_3 def.) and 740 and 710s (C-H out of plane def) cm^{-1} , δ_{H} 7.0 to 8.0 (mult., Ph); δ_{F} (major isomer) + 8.1 (CF_3CCl) and +10.6 (CF_3CPh) p.p.m. and δ_{F} (minor isomer) + 8.5 (CF_3CCl) and +16.5 (CF_3CPh), p.p.m.; δ_{C} 148.4 (q, $\text{PhC}=\text{N}$, ^2J 34.9 Hz), 131.8 (q, $\text{ClC}=\text{N}$, ^2J 36.0 Hz), 129.8 (s, ipso-Ph), 131.7, 128.9 and 127.7 (q-, m- and p-Ph), 119.7 (q, $\text{CF}_3\text{-CPh}$, ^1J 277.0Hz) and 116.9 (q, CF_3CCl , ^1J 275.3 Hz) p.p.m.; m/z (e.i.) 304 and 302 (35.7%, M^+), 267 [16.3; ($M\text{-Cl}$) $^+$], 247 [22.4, ($M\text{-HFCI}$) $^+$], 235 and 233 [53.0, ($M\text{-CF}_3$) $^+$], 197 (43.4, $\text{C}_9\text{H}_4\text{F}_3\text{N}_2^+$), 172 (49.5, $\text{C}_8\text{H}_5\text{F}_3\text{N}^+$), 140 and 138 (59.2, $\text{C}_7\text{H}_5\text{ClN}^+$), 103 (85.8, PhCN^+), 77 (100, C_6H_5^+) and 69 (98.7, CF_3^+), (ii) biphenyl ($R_F=0.54$) (0.21 g , 1.36 mmol) (Found: M^+ , 154. Calc. for $\text{C}_{12}\text{H}_{10}$ M , 154), m.p. and mixed m.p. $69\text{-}70\text{ }^\circ\text{C}$ and (iii) 2,5-diphenyl-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (5) (nc) (R_F 0.47) (0.78 g , 2.26 mmol, 20%) (Found: C, 56.1; H, 3.1; N, 7.8; F, 32.9%; M^+ , 344. $\text{C}_{16}\text{H}_{10}\text{F}_6\text{N}_2$ requires C, 55.8; H, 2.9; N, 8.1; F, 33.1%; M , 344), m.p. $40\text{-}42\text{ }^\circ\text{C}$, ν_{max} . 3110-3080w (arom. C-H str.), 1615s (C=N str.), 1200-1130s (C-F str.), 765s

(CF₃ def.) and 735 and 700s (C-H out of plane def.) cm⁻¹; δ_H 7.0 to 8.0 (mult., Ph) p.p.m.; δ_F + 11.5 (2 x CF₃) p.p.m.; δ_C 144.2 (q, C=N, ²J 34.5 Hz), 129.7 (ipso-Ph), 131.2, 128.7 and 128.1 (o-, m- and p-Ph), and 119.8 (q, CF₃, ¹J 276.7 Hz) p.p.m., m/z (e.i.) 344 (2.5%, M⁺), 275 [74.8, (M-CF₃⁺)], 172 (17.7, C₈H₅F₃N⁺), 103 (41.8, PhCN⁺), 77 (100, C₆H₅⁺) and 69 (42.1 (CF₃⁺)).

A second reaction, carried out under the same conditions except that the total solvent volume was reduced to 30 cm³, gave azine (4) (1.50 g, 4.97 mmol, 44%), azine (5) (0.95 g, 2.75 mmol, 24%) and biphenyl (0.20 g).

For a third reaction carried out at room temperature in ether (50 cm³) the ¹⁹F n.m.r. spectrum of the product mixture showed the presence of azines (4) and (5) and two components identified (see below) as the tetraphenyldiaza-1,3-diene (7) and the pentaphenyldiaza-1,3-diene (8) in the ratio 60:14:8:2.

(b) Molar ratio 1:2

The addition of phenyl-lithium (7.70 cm³, 15.40 mmol) in ether (15 cm³) to azine (1) (2.00 g, 7.66 mmol) in ether (50 cm³) at -78 °C over 30 minutes followed by stirring for two hours and then warming to room temperature gave a mixture (0.64 g) of lithium chloride and lithium fluoride and a yellow oil (2.51 g) the five components of which were separated (DCFC) and identified as (i) azine (4) (0.21 g, 0.39 mmol, 5%), (ii) biphenyl (0.25 g), (iii) azine (5) (1.53 g, 4.45 mmol, 58%), (iv) 1,2,5,5-tetraphenyl-1,6,6,6-tetrafluoro-3,4-diazahepta-1,3-diene (7) (nc) (R_F 0.38) (0.13 g, 0.28 mmol, 4%) (Found: C, 73.2; H, 4.3; N, 5.8; F, 16.6%, M⁺, 460 C₂₈H₂₀F₄N₂ requires C, 73.0; H, 4.4; N, 6.1; F, 16.5%, M, 460), m.p. 70-71 °C, ν_{max} . 3090-3040w (arom. C-H str.), 1620s (C=C str.), 1575w (N=N str.), 1200-1130, 1080 and 1070s (C-F str.), 780s (CF₃ def.) and 730 and 700s (C-H out of plane def.) cm⁻¹; δ_H 7.0-8.0 (mult., Ph) p.p.m., δ_F + 11.9 (s, 3F, CF₃) and -16.0 (s, 1F, =CF), p.p.m., δ_C 164.5 (d, =CF, ¹J 259.6 Hz), 140.4 (d, >C=CF, ²J 33.4 Hz), 138.3 to 127.8 (Ph), 125.0 (q, CF₃, ¹J 286.7 Hz) and 84.5 (q, >C-N, ²J 23.2 Hz) p.p.m.; m/z (c.i.) 460 (M⁺), (e.i.) 236 (18.4%, CF₃CHPh₂⁺), 235 (21.2, CF₃CPh₂⁺), 216 (28.7, CF₂CPh₂⁺), 215 (25.3, C₁₄H₉F₂⁺), 198 (44.9, C₁₄H₁₁F⁺), 197 (100, C₁₄H₁₀F⁺), 178 (36.6, C₁₄H₁₀⁺), 167 (38.6 C₁₃H₁₁F⁺), 165 (38.6, C₁₃H₉⁺), and (v) 1,1,2,5,5-pentaphenyl-6,6,6-trifluoro-3,4-diazahepta-1,3-diene (8) (nc) (R_F 0.32) (0.27 g, 0.52 mmol, 7%), (Found: C, 78.5; H, 4.8; N, 5.4; F, 11.5%. C₃₄H₂₅F₃N₂ requires C, 78.7; H, 4.8; N, 5.4; F, 11.0%), m.p. 125-127 °C, ν_{max} . 3080-3040w (arom. C-H str.), 1600w (C=C str.), 1580w (N=N str.), 1200-1100s (C-F str.), 770m (CF₃ def.), and 730 and 700s (C-H out of plane def.) cm⁻¹; δ_H 7.0-8.0 (mult. Ph)

p.p.m.; $\delta_F + 12.0$ (CF₃) p.p.m.; δ_C 151.7 (s, N-C=), 151.1 (s, Ph₂C=), 140.8 to 126.9 (Ph), 125.2 (q, CF₃ ¹J 286.6 Hz) and 83.7 (q, \rightarrow C-N, ²J 23.0 Hz) p.p.m.; m/z (e.i.) 490 [43.9%, (M-N₂)⁺], 470 (21.3, C₃₄H₂₄F₂⁺), 256 (76.5, Ph₃C₂H⁺), 255 (100, Ph₃C₂⁺) and 235 (18.7, CF₃CPh₂⁺).

(c) Molar ratio 1.5

The addition of phenyl-lithium (19.16 cm³, 38.32 mmol) in ether (10 cm³) to azine (1) (2.00 g, 7.66 mmol) in ether (15 cm³) at room temperature over a period of 40 minutes followed by stirring for sixteen hours gave a mixture (1.50 g) of lithium chloride and lithium fluoride and a dark orange solid (3.64 g) the three components of which were separated (DCFC) and identified as (i) biphenyl (0.35 g), (ii) compound (7) (1.01 g, 2.19 mmol, 29%) and (iii) compound (8) (2.21 g, 4.24 mmol, 55%).

In a second experiment addition of phenyl-lithium (3.83 cm³, 7.66 mmol) in ether (15 cm³) to azine (1) (1.00 g, 3.83 mmol) in ether (50 cm³) during thirty minutes at -78 °C followed by stirring at -78 °C for two hours and then warming to room temperature gave a mixture of compounds (4), (5), (7) and (8). The mixture was treated with a further quantity of phenyl-lithium (5.74 cm³, 11.49 mmol) in ether (10 cm³) during thirty minutes at room temperature and stirring was continued for sixteen hours. Work-up afforded a mixture (0.72 g) of lithium chloride and lithium fluoride and a dark orange solid (1.85 g) separation (DCFC) of which gave azine (5) (0.06 g, 0.17 mmol, 4.5%), biphenyl (0.15 g), compound (7) (0.52 g, 1.13 mmol, 29%) and compound (8) (1.10 g, 2.12 mmol, 55%).

(d) Molar ratio 1:1 in air

Dropwise addition of phenyl-lithium (5.75 cm³, 11.50 mmol) in ether (15 cm³) to azine (1) (3.00 g, 11.49 mmol) in ether (20 cm³) at -78 °C in air during fifty minutes and stirring continued at -78 °C for one hour gave lithium chloride (0.40 g, 9.5 mmol, 83%) and a dark yellow oil (2.53 g) separation (DCFC) of which gave (i) a mixture (1.35 g) of azine (4) (Found: M^+ , 302.0053. Calc. for C₁₀H₅³⁵ClF₆N₂: M , 302.0045) and 2-chloro-5-phenoxy-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (9) (Found: M^+ , 317.9989. Calc. for C₁₀H₅³⁵ClF₆N₂O: M , 317.9995 in the ratio 2.3:1.0 (¹⁹F n.m.r.)), (ii) biphenyl (0.21 g) and (iii) azine (5) (0.75 g, 2.18 mmol, 19%).

Reaction of Dichloroazine (1) with Lithium Phenoxide

Dropwise addition of an ethereal solution of lithium phenoxide [prepared from treatment of phenol (0.50 g, 5.31 mmol) in anhydrous diethyl ether (5 cm³) at 0 °C with n-butyl-lithium (3.4 cm³, 1.6M, 5.44 mmol) in ether (5 cm³)] to a stirred solution of azine (1) (1.40 g, 5.36 mmol) in ether (50 cm³) at -78 °C for half an hour, gave a precipitate of lithium chloride (0.21 g, 5.0 mmol, 93%). Removal of the solvent from the filtrate at -20 °C *in vacuo*, followed by purification (DCFC) of the residue afforded 2-chloro-5-phenoxy-1,1,1,6,6,6-hexafluoro-3,4-diazahexa-2,4-diene (9) (nc) (RF 0.60) (1.24 g, 3.89 mmol, 73%) (Found: C, 38.0; H, 1.8, N, 8.8%; M^+ , 320 and 318. C₁₀H₅ClF₆N₂O requires C, 37.7; H, 1.6; N, 8.8%; M , 318.5) as a mixture of two isomers in the ratio 4.5:1.0; ν_{\max} 3060w (arom C-H str.), 1670s (C=N str.), 1590 and 1480m (arom. C=C str.), 1290s (C-O str.), 1210-1125s (C-F str.) and 740s (arom. C-H out of plane def.) cm⁻¹; δ_H 6.8 (mult. 2H, *o*-C₆H₅) and 7.2 (mult., 3H, *m*- and *p*-C₆H₅) p.p.m.; δ_F (major isomer + 7.0 [s, CF₃C(OPh)=] and +8.0 (s, CF₃CCl=) p.p.m. and δ_F (minor isomer), +8.5 (s, CF₃CCl=) and +10.9 [s, CF₃C(OPh)=] p.p.m.; δ_C (major isomer) 152.8 (s, *ipso*-C₆H₅), 139.8 (q, PhOC=N, ²J 39.4 Hz), 130.8 (q, ClC=N, ²J 38.6 Hz), 116.9 (q, CF₃, ¹J 276.5 Hz) and 116.65 (q, CF₃, ¹J 275.2 Hz) p.p.m. and δ_C (minor isomer) 151.5 (s, *ipso*-C₆H₅), 150.4 (q, PhOC=N, ²J *ca.* 40 Hz), 133.9 (q, ClC=N, ²J *ca.* 40 Hz), 117.3 (q, CF₃, ¹J 275.4 Hz) and 116.2 (q, CF₃, ¹J 284.1 Hz) p.p.m. (*o*-, *m*- and *p*-C₆H₅ carbon absorptions for both isomers appeared between 129.8 and 119.5 p.p.m.); m/z (e.i.) 320 and 318 (22.0%; M^+), 283 [86.1, (M -Cl)⁺], 251 and 249 [22.8, (M -CF₃)⁺], 227 and 225 [44.7, (M -PhO)⁺], 77 (70.7, C₆H₅⁺) and 69 (100, CF₃⁺).

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