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Functional tetrahydroquinoxalines from perfluoroaromatic precursors

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Abstract

A short series of bromo- and nitro-polyfluorobenzene derivatives gave the corresponding tetrahydroquinoxaline systems upon reaction with *N*,*N*′-dimethylethylene diamine. This annelation strategy gives useful quantities of functionalised tetrahydroquinoxaline systems which may be interesting scaffolds for the drug discovery arena.

Keywords: Fluoroaromatic; Nucleophilic aromatic substitution; Scaffold; Tetrahydroquinoxaline; Bicyclic nitrogen heterocycle

1. Introduction

Perfluorinated benzenoid systems are highly susceptible towards nucleophilic attack [1,2] and, since the first viable route to perfluoroarenes such as hexafluorobenzene was established around 50 years ago [3,4], many nucleophilic aromatic substitution reactions involving the functionalisation of fluoroarene systems using a wide range of nucleophilic species have been established [1,5,6]. This growing chemistry was recently comprehensively reviewed in this journal [1]. Surprisingly, however, reactions of perfluorobenzenoid systems with bidentate nucleophiles have not been explored in any detail [1] but a number of examples of such processes involving formation of a fused bicyclic ring system upon one-pot reactions of appropriate bidentate nucleophiles and hexafluorobenzene have been reported [7–10]. For example, formation of a tetrahydroquinoxaline ring upon a one-pot reaction of ethylenediamine with hexafluorobenzene (Scheme 1), has been described [7] and, in this context, related reactions of *N*,*N*-bidentate nucleophiles and pentafluoropyridine have recently been recorded [11–13].

In principle, the process outlined in Scheme 1 represents efficient methodology for the synthesis of functional quinoxaline derivatives and, potentially, a wider range of functional bicyclic heterocycles depending on the bidentate nucleophile used, if developed further.

The use of polyfunctional bicyclic nitrogen heterocycles as scaffolds for the parallel synthesis of libraries of structurally diverse receptor molecules for applications in drug design using the ‘privileged structures’ concept, is an increasingly important strategy in the life-science industries [14]. Consequently, there is a growing need in the drug discovery process for access to an ever wider range of low molecular weight, bicyclic heterocyclic scaffolds that bear different functionality such as bromine, aldehyde, ketone and nitro groups that may be used as effective starting materials in hit-to-lead generation [15–17].

In order to increase the functionality present on the tetrahydroquinoxaline scaffolds prepared by the methodology outlined in Scheme 1, we were interested in studying reactions of various polyfluorobenzenoid systems bearing bromine or nitro substituents which, in principle, could offer functional ‘handles’ for further derivitisation in parallel synthesis, e.g. palladium catalysed coupling reactions of the C–Br bond, etc.

In this paper, we report reactions of a model bidentate nitrogen nucleophile, *N*,*N*′-dimethylethylene diamine **1**, with several bromo- and nitro-polyfluorobenzene systems. Reactions of pentafluorobenzenoid systems with bidentate nucleophiles have not been described previously in the literature.

2. Results and discussion

Reactions between *N*,*N*′-dimethylethylene diamine **1** and several polyfluorobromobenzenes **2–4** were carried out in refluxing acetonitrile solution in the presence of sodium bicarbonate and the results are collected in Scheme 2.

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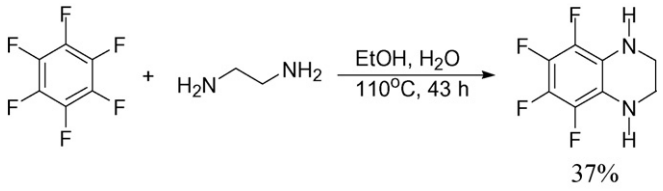


Scheme 1. From Reference [7].

Pentafluorobromobenzene **2** and **1** gave a mixture of tetrahydroquinoxaline derivatives **5** and **6** in the ratio 1:9.6 as determined by ^{19}F NMR spectroscopy of the crude product mixture. Similarly, 1,2-dibromotetrafluorobenzene **3** gave **7** and **8** as a mixture of isomers in the ratio 1:7.2 after prolonged reflux with **1** in acetonitrile. In each reaction, the identity of the major products, **6** and **8**, respectively, were identified by NMR spectroscopy. For **6**, no $^{3}J_{FF}$ *ortho* coupling (~20 Hz) is observed for the resonance attributed to the fluorine atom located at the 5-position and the symmetrical structure of **8** gives rise to only one resonance in the ^{19}F NMR spectrum.

For reactions of pentafluorophenyl derivatives (C_6F_5X), it is well established that, in general, the major product of reaction with monodentate nucleophiles is the *para* disubstituted system although several exceptions exist [1]. For example, reaction of dimethylamine with bromopentafluorobenzene gives a 5:1:94 *ortho*:*meta*:*para* isomer product ratio [18] although the ratio of isomers formed can be very dependent upon the nature of the nucleophile, substrate and solvent [1,19,20]. This orientation of substitution is reflected in the product distribution shown in Scheme 2. Here, reaction of **1** with **2** gives **6** as the major product which arises from initial substitution of the fluorine atom located at the site *para* to bromine followed by subsequent cyclisation *meta* to the bromine due to the geometry of the system. Similarly, **8** is formed by initial substitution *para* to bromine in **3** and subsequent cyclisation *para* to the second bromine substituent.

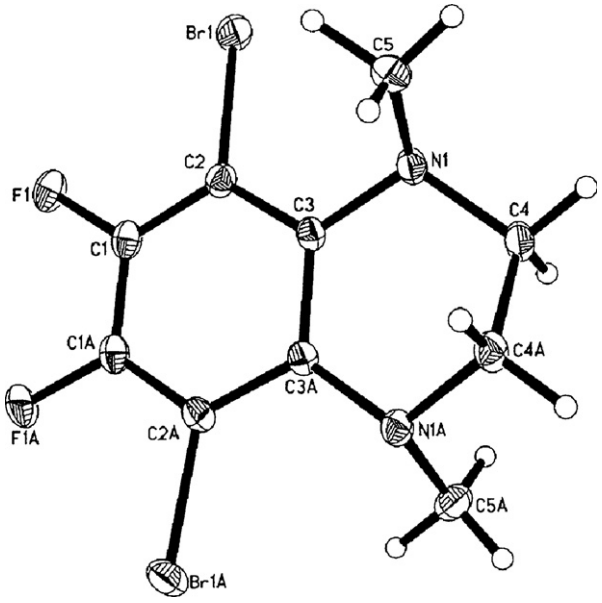
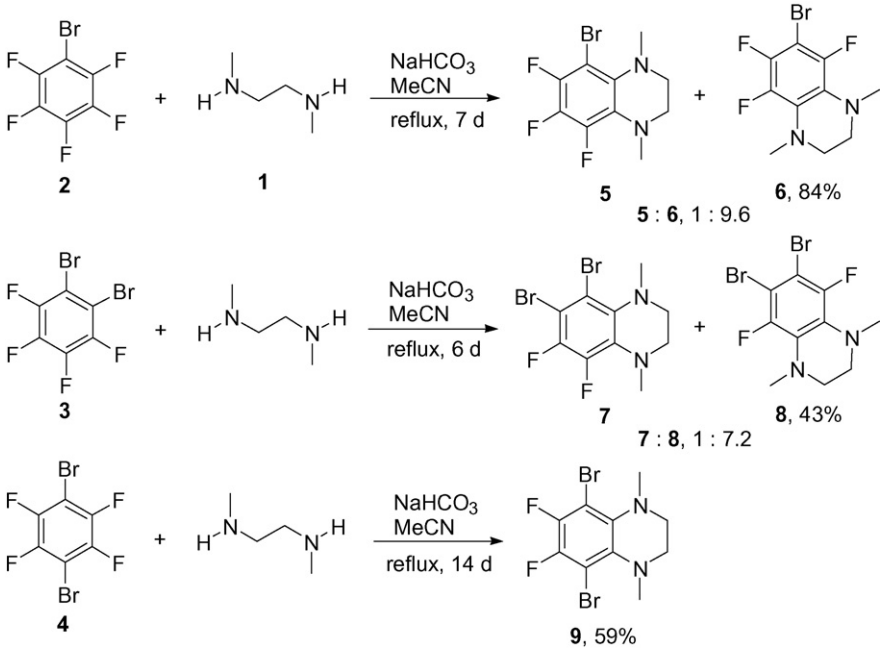


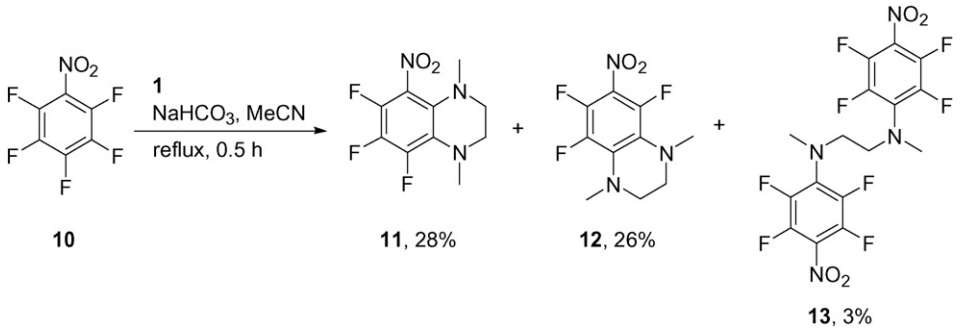
Fig. 1. X-ray structure of **9**. Displacement ellipsoids are shown at the 50% probability level.

Reaction of 1,4-dibromotetrafluorobenzene **4** gave **9** as the exclusive product arising from displacement of fluorine atoms *ortho* to the two bromine substituents. In this case, the reaction was very slow indeed and prolonged reflux was required to achieve a reasonable yield of product.

The molecular structure of compound **9** is shown in Fig. 1. The molecule is located in a special position on a two-fold axis whereby the heterocycle adopts the half-chair conformation



Scheme 2. Reactions of polybromofluorobenzene derivatives.



Scheme 3. Reaction of pentafluoronitrobenzene with **1**.

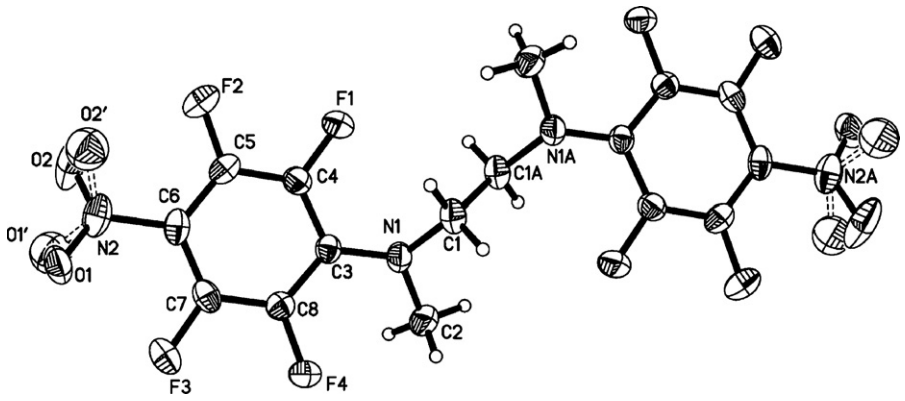


Fig. 2. The molecular structure of **13**. The nitro groups are disordered; displacement ellipsoids are shown at the 50% probability level.

with a pyramidal configuration for both nitrogen atoms. This conformation differs from that observed in closely related pyrido[2,3-*b*]pyrazine derivatives [11–13] and is probably caused by *peri*-type interactions with the bulky bromine substituents. The molecules **9** in the crystal are linked together by a number of CH···N interactions and the aromatic rings of adjacent molecules are parallel but do not overlap.

In contrast to the very long reaction times required for annelation of the bromofluorobenzenes **2–4** used above, pentafluoronitrobenzene **10** reacted very rapidly with **1** at reflux temperature in 30 min due to the presence of the strongly electron withdrawing nitro group that significantly activates the aromatic ring towards nucleophilic attack. A mixture of the products **11**, **12** and **13** were obtained in 28, 26 and 3% yield, respectively, after separation by column chromatography (Scheme 3).

Since the ratio of annelated products, **11**:**12**, is approximately 1:1, the relatively high proportion of **11** reflects the activating influence of the highly electron withdrawing nitro group on adjacent *ortho* atoms which enables initial substitution at the *ortho* position to compete effectively with substitution at the corresponding *para* position. This effect has been noted previously for other nitrogen nucleophiles in reactions of pentafluoronitrobenzenes in which hydrogen bonding between the nitro group and the incoming nitrogen nucleophile was also suggested to be a factor in enhanced *ortho* substitution [21]. A small amount of non-cyclised product **13** was obtained reflecting the lower reactivity of the *meta* position which allows intermolecular substitution to compete effectively with the intramolecular cyclisation process.

The structure of compound **13** was confirmed by X-ray crystallography (Fig. 2). The molecule **13** has a centre of symmetry and, therefore, adopts an *s*-trans configuration around the C1–C1a bond. In the crystal, layers in which the adjacent molecules are linked by CH···O and CH···F contacts are formed. No overlapping of the aromatic rings is observed but C–F bonds are arranged in an anti-parallel mode with the shortest C···F distance of 2.929 Å. The layers are packed in a herringbone pattern, typical for aromatic systems. It may be noted that ^{19}F NMR analysis of **13** shows four signals in a 1:1:1:1 ratio indicating some degree of restricted rotation of the N(Me)R group that is attached to the tetrafluorobenzenoid ring.

3. Conclusion

These few initial experiments indicate that bromo- and nitropolyfluoro benzene derivatives can act as useful starting materials for annelation processes involving reaction with a bidentate nucleophile such as **1**. Whilst mixtures of products are obtained in several cases due to the non-specific nucleophilic aromatic substitution processes, useful quantities of tetrahydroquinoxaline scaffolds bearing useful functionality other than fluorine can be accessed by this general strategy providing access to a range of polysubstituted tetrahydroquinoxaline derivatives.

4. Experimental

4.1. General

All starting materials were obtained commercially and used as received. NMR spectra unless stated otherwise were run in deuteriochloroform and recorded using a Bruker AMX 500 spectrometer operating at 400 MHz (^{1}H NMR), 376 MHz (^{19}F NMR) and 100 MHz (^{13}C NMR). Chemical shifts are measured in ppm from $CFCl_3$ (^{19}F) or $CDCl_3$ (^{1}H and ^{13}C) and coupling constants are given in Hz. Mass spectra were obtained using a Fisons VG Trio 1000 spectrometer linked to a Hewlett Packard 5890 Series II gas chromatograph fitted with a 25 m HP1 (methylsilicone) column. Carbon, hydrogen and nitrogen elemental analyses were obtained using an Exeter Analytical CE-440 elemental analyser.

4.2. General procedure for nucleophilic aromatic substitution reactions of perfluoroarenes with N,N′-dimethylethylene diamine *1*

A mixture consisting of the perfluoroarene, *N*,*N*′-dimethylethylene diamine **1**, sodium bicarbonate and acetonitrile was heated with stirring at reflux temperature until ^{19}F NMR analysis of the reaction mixture indicated high conversion. The solvent and excess **1** were evaporated to leave a solid. Dilute hydrochloric acid (1 M) was added to the solid and the product was extracted with ethyl acetate (4 × 60 ml). The combined extracts were dried ($MgSO_4$) and evaporated to leave a crude product which was analysed by ^{19}F NMR and GCMS. Chromatography of the crude product on silica gel as the eluent gave the pure products.

4.2.1. Reaction of pentafluorobromobenzene *2*

Pentafluorobromobenzene **2** (4.94 g, 20 mmol), **1** (3.53 g, 40 mmol), sodium hydrogencarbonate (6.72 g, 80 mmol) and acetonitrile (500 ml), after reflux for 7 d gave a mixture containing *5-bromo-6,7,8-trifluoro-1,4-dimethyl-1,2,3,4-tetrahydro-quinoxaline* **5**; δ_F −138.36 (1F, d, $^3J_{FF}$ 24.5, F-6), −146.43 (1F, dd, $^3J_{FF}$ 18.4, $^4J_{FF}$ 1.9, F-8), −165.03 (1F, dd, $^3J_{FF}$ 23.7, $^3J_{FF}$ 20.7, F-7); *m*/*z* (EI$^+$) 296 ([M]$^+$, 100%), 294 ([M]$^+$, 93), 281 (64), 279 (66), 267 (21), 266 (27), 265 (34), 264 (46), 225 (34), 223 (33), 200 (51), 199 (41), 185 (52), 171 (52), 158 (33); and, **6** as a mixture of isomers in the ratio 1:9.6. Column chromatography using hexane and dichloromethane (1:6) as the eluent, gave *6-bromo-5,7,8-trifluoro-1,4-dimethyl-1,2,3,4-tetrahydro-quinoxaline* **6** (4.95 g, 84%) as a yellow oil (Found: C, 40.66; H, 3.38; N, 9.73; F, 19.25. $C_{10}H_{10}BrF_3N_2$ requires C, 40.70; H, 3.42; N, 9.49; F, 19.31%); δ_H 2.79 (3H, d, $^5J_{HF}$ 1.2, CH_3), 2.98 and 3.05 (4H, AA′BB′, CH_2), 2.98 (3H, d, $^5J_{HF}$ 2.4, CH_3); δ_C 42.95 (m, N*C*H$_3$), 43.77 (m, N*C*H$_3$), 46.28 (s, CH_2), 47.39 (s, CH_2), 87.84 (ddd, $^2J_{CF}$ 26.2, $^2J_{CF}$ 22.1, $^3J_{CF}$ 1.9, C–Br), 124.67 (dt, $^2J_{CF}$ 13.8, $^3J_{CF}$ 3.0, C-9), 129.98 (m, C-10), 139.67 (ddd, $^1J_{CF}$ 243.4, $^2J_{CF}$ 15.8, $^4J_{CF}$ 6.5, C-8), 143.89 (ddd, $^1J_{CF}$ 239.4, $^2J_{CF}$ 15.6, $^3J_{CF}$ 7.4, C-7), 148.51 (ddd, $^1J_{CF}$ 240.8, $^3J_{CF}$ 4.5, $^4J_{CF}$ 3.1, C-5); δ_F −123.33 (1F, dd, $^5J_{FF}$ 7.9, $^4J_{FF}$ 3.4, F-5), −140.80 (1F, dd, $^3J_{FF}$ 22.2, $^5J_{FF}$ 7.8, F-8), −152.58 (1F, ddm, $^3J_{FF}$ 21.6, $^4J_{FF}$ 2.7, F-7); *m*/*z* (EI$^+$) 296 ([M]$^+$, 100%), 294 ([M]$^+$, 99), 281 (42), 279 (46), 266 (17), 265 (18), 264 (29), 225 (17), 223 (16), 200 (22), 171 (23).

4.2.2. Reaction of 1,2-dibromotetrafluorobenzene *3*

1,2-Dibromotetrafluorobenzene **3** (6.16 g, 20 mmol), **1** (3.53 g, 40 mmol), sodium hydrogencarbonate (6.72 g, 80 mmol) and acetonitrile (500 ml) after reflux for 6 d gave a mixture containing *5,6-dibromo-7,8-difluoro-1,4-dimethyl-1,2,3,4-tetrahydro-quinoxaline* **7**; δ_F −128.94 (1F, d, $^3J_{FF}$ 20.7, CF–CBr), −146.84 (1F, dq, $^3J_{FF}$ 21.45, $^5J_{HF}$ 3.7, FC–CN); *m*/*z* (EI$^+$) 358 ([M]$^+$, 55%), 356 ([M]$^+$, 100), 354 ([M]$^+$, 51), 343 (23), 341 (42), 339 (23); and **8** as a mixture of isomers in the ratio 1:7.2. Chromatography using ethyl acetate as the eluent gave *6,7-dibromo-5,8-difluoro-1,4-dimethyl-1,2,3,4-tetrahydro-quinoxaline* **8** (3.07 g, 43%) as a yellow oil (Found: C, 33.57; H, 2.74; N, 7.75; F, 10.34. $C_{10}H_{10}Br_2F_2N_2$ requires C, 33.74; H, 2.83; N, 7.87; F, 10.67%); δ_H 2.87 (3H, m, CH_3), 2.99 (2H, br s, CH_2); δ_C 43.29 (m, *C*H$_3$), 46.82 (s, *C*H$_2$), 102.99 (m, C–Br), 129.11 (dd, $^2J_{CF}$ 11.1, $^3J_{CF}$ 6.9, =C–N), 148.33 (dd, $^1J_{CF}$ 242.1, $^4J_{CF}$ 3.3, C–F); δ_F −115.00 (s); *m*/*z* (EI$^+$) 358 ([M]$^+$, 55%), 356 ([M]$^+$, 100), 354 ([M]$^+$, 52), 343 (22), 341 (42), 339 (23).

4.2.3. Reaction of 1,4-dibromotetrafluorobenzene *4*

1,4-Dibromotetrafluorobenzene **4** (6.16 g, 20 mmol), **1** (3.53 g, 40 mmol), sodium hydrogencarbonate (6.72 g, 80 mmol) and acetonitrile (500 ml) w after reflux for 14 d and chromatography using hexane and dichloromethane (1:6) as the eluent gave *5,8-dibromo-6,7-difluoro-1,4-dimethyl-1,2,3,4-tetrahydro-quinoxaline* **9** (4.21 g, 59%) as a pale yellow solid; mp 108–109.5 °C (Found: C, 33.48; H, 2.80; N, 7.88; F, 10.44. $C_{10}H_{10}Br_2F_2N_2$ requires C, 33.74; H, 2.83; N, 7.87; F, 10.67%); δ_H 2.84 (3H, s, CH_3), 3.02 (2H, s, CH_2); δ_C 44.62 (s, CH_3), 45.42 (s, CH_2), 105.20 (dd, $^2J_{CF}$ 11.9, $^3J_{CF}$ 8.4, C–Br), 137.41 (m, =C–N), 144.27 (dd, $^1J_{CF}$ 244.9, $^2J_{CF}$ 18.8, C–F); δ_F −132.07 (s); *m*/*z* (EI$^+$) 358 ([M]$^+$, 54%), 356 ([M]$^+$, 100), 354 ([M]$^+$, 51), 343 (21), 341 (40), 339 (22), 327 (22), 325 (20), 285 (19), 262 (18), 260 (20).

4.2.4. Reaction of pentafluoronitrobenzene *10*

Pentafluoronitrobenzene (2.13 g, 10 mmol), **1** (0.88 g, 10 mmol), sodium hydrogencarbonate (1.68 g, 20 mmol) and acetonitrile (100 ml) after reflux for 15 min and column chromatography using hexane and dichloromethane (1:6) as the eluent gave *5,6,7-trifluoro-1,4-dimethyl-8-nitro-1,2,3,4-tetrahydro-quinoxaline* **11** (0.72 g, 28%) as a red solid; mp 53–54 °C (Found: C, 45.80; H, 3.80; N, 15.89; F, 21.79. $C_{10}H_{10}F_3N_3O_2$ requires C, 45.98; H, 3.86; N, 16.09; F, 21.82%); δ_H 2.79 (3H, s, 1-NCH$_3$) 2.92 (3H, d, $^5J_{HF}$ 2.4, 4-NCH$_3$), 3.09 and 3.19 (4H, AA′BB′, CH_2); δ_C 42.77 (s, 1-NCH$_3$), 43.03 (d, $^4J_{CF}$ 8.0, 4-N*C*H$_3$), 47.25 (s, CH_2), 47.38 (s, CH_2), 125.49 (dd, $^2J_{CF}$ 9.1, $^3J_{CF}$ 3.2, C-10), 127.90 (m, C-8), 130.22 (d, $^3J_{CF}$ 5.4, C-9), 134.18 (ddd, $^1J_{CF}$ 244.2, $^2J_{CF}$ 16.3, $^2J_{CF}$ 14.7, C-6), 139.21 (ddd, $^1J_{CF}$ 252.3, $^2J_{CF}$ 13.7, $^3J_{CF}$ 5.3, C-5), 145.03 (ddd, $^1J_{CF}$ 251.0, $^2J_{CF}$ 12.1, $^3J_{CF}$ 4.2, C-7); δ_F −142.42 (1F, d, $^3J_{FF}$ 22.2, F-7), −155.49 (1F, dd, $^3J_{FF}$ 22.6, $^4J_{FF}$ 3.0, F-5), −170.30 (1F, t,

$^3J_{FF}$ 22.2, F-6); *m/z* (EI$^+$) 261 ([M]$^+$, 57%), 201 (38), 199 (56), 187 (81), 185 (67), 171 (73), 160 (39), 158 (40), 145 (100), 131 (40), 107 (38); and, *5,6,8-trifluoro-1,4-dimethyl-7-nitro-1,2,3,4-tetrahydro-quinoxaline* **12** (0.69 g, 26%) as a bright orange solid; mp 93–94 °C (Found: C, 45.80; H, 3.84; N, 15.94; F, 21.50. $C_{10}H_{10}F_3N_3O_2$ requires C, 45.98; H, 3.86; N, 16.09; F, 21.82%); δ_H 2.77 (3H, d, $^5J_{HF}$ 0.8, NCH_3), 3.02 and 3.25 (4H, AA′BB′, CH_2), 3.24 (3H, d, $^5J_{HF}$ 5.2, NCH_3); δ_C 42.37 (d, $^4J_{CF}$ 13.5, NCH_3), 43.70 (d, $^4J_{CF}$ 5.3, NCH_3), 46.48 (s, CH_2), 47.96 (s, CH_2), 119.80 (m, C-7), 121.94 (ddd, $^2J_{CF}$ 12.7, $^3J_{CF}$ 2.9, $^3J_{CF}$ 2.9, C-10), 134.93 (ddd, $^2J_{CF}$ 6.3, $^3J_{CF}$ 6.3, $^4J_{CF}$ 3.4, C-9), 136.75 (ddd, $^1J_{CF}$ 242.7, $^2J_{CF}$ 15.0, $^4J_{CF}$ 3.0, C-5), 141.58 (ddd, $^1J_{CF}$ 254.6, $^2J_{CF}$ 16.9, $^3J_{CF}$ 4.6, C-6), 145.39 (d, $^1J_{CF}$ 254.6, C-8); δ_F −136.14 (1F, dd, $^5J_{FF}$ 7.2, $^4J_{FF}$ 7.2, F-8), −151.72 (1F, dd, $^3J_{FF}$ 20.7, $^4J_{FF}$ 7.5, F-6), −156.74 (1F, dm, $^3J_{FF}$ 20.4, F-5); *m/z* (EI$^+$) 261 ([M]$^+$, 91%), 215 (88), 200 (34), 198 (38), 195 (41), 186 (30), 185 (36), 174 (58), 172 (100), 154 (32), 145 (40), 144 (44), 125 (34), 42 (67); and, *N,N′-dimethyl-N,N′-bis-(2,3,5,6-tetrafluoro-4-nitro-phenyl)-ethane-1,2-diamine* **13** (0.13 g, 3%) as a yellow solid, mp 73–74 °C (Found: C, 40.46; H, 2.09; N, 11.82. $C_{16}H_{10}F_8N_4O_4$ requires C, 40.52; H, 2.13; N, 11.81%); δ_H 2.80 (3H, d, $^5J_{HF}$ 1.2, 2, CH_3), 3.17 (2H, s, CH_2); δ_F −144.88 (1F, dd, $^3J_{FF}$ 20.7, $^5J_{FF}$ 8.3, F-2), −148.65 (1F, ddd, $^3J_{FF}$ 22.1, $^4J_{FF}$ 8.4, $^5J_{FF}$ 3.9, F-6), −150.93 (1F, ddd, $^3J_{FF}$ 21.0, $^4J_{FF}$ 21.0, $^5J_{FF}$ 3.6, F-3), −158.36 (1F, dd, $^3J_{FF}$ 21.3, $^5J_{FF}$ 21.3, F-5); *m/z* (EI$^+$) 237 (94), 221 (19), 206 (46), 191 (33), 190 (49), 178 (31), 176 (49), 163 (100), 149 (37), 137 (18), 99 (23), 42 (39).

4.3. X-ray crystal structure determination of **9** and **13**

The X-ray single crystal data for both compounds were collected at 120 K on a Bruker SMART CCD 6000 diffractometer (Mo Kα, λ = 0.71073 Å, ω-scan, 0.3°/frame) equipped with an Oxford Cryostream cooling device. Both structures were solved by direct method and refined by full-matrix least squares on F^2 for all data using SHELXTL software. All non-hydrogen atoms were refined with anisotropic displacement parameters, H-atoms were located on the difference map and refined isotropically.[1]

Crystal data for **9**: $C_{10}H_{10}Br_2F_2N_2$, M = 356.02, monoclinic, space group $C2/c$, a = 10.3825(2), b = 15.4013(3), c = 8.5490(2) Å, β = 124.15(1)°, U = 1131.25(4) Å^3, $F(0\,0\,0)$ = 688, Z = 4, D_c = 2.090 mg m^{-3}, μ = 7.165 mm^{-1}. 6318 reflections collected; 1640 unique data (R_{merg} = 0.019). SADABS absorption correction was applied. Final $wR_2(F^2) = 0.0422$ for all data (93 refined parameters), conventional $R(F)$ = 0.0165 for 1498 reflections with $I \geq 2\sigma$, GOF = 1.117.

Crystal data for **13**: $C_{16}H_{10}F_8N_4O_4$, M = 474.28, monoclinic, space group $P2_1/c$, a = 8.9004(2), b = 5.6928(1), c = 17.4069(4) Å, β = 102.21(1)°, U = 862.03(3) Å^3, $F(0\,0\,0)$ = 476, Z = 2, D_c = 1.827 mg m^{-3}, μ = 0.188 mm^{-1}. 6092 reflections collected; 1674 unique data (R_{merg} = 0.016). Final $wR_2(F^2) = 0.1319$ for all data (172 refined parameters), conventional $R(F)$ = 0.0501 for 1473 reflections with $I \geq 2\sigma$, GOF = 1.054.

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References

[1] G.M. Brooke, J. Fluorine Chem. 86 (1997) 1–76.
[2] R.D. Chambers, Fluorine in Organic Chemistry, Blackwell, Oxford, 2004.
[3] J.A. Godsell, M. Stacey, J.C. Tatlow, Nature 178 (1956) 199–200.
[4] J.A. Godsell, M. Stacey, J.C. Tatlow, Tetrahedron 2 (1968) 193–202.
[5] R.D. Chambers, C.R. Sargent, Adv. Heterocycl. Chem. 28 (1981) 1–71.
[6] M.J. Silvester, Adv. Heterocycl. Chem. 59 (1994) 1–37.
[7] J. Burdon, V.A. Damodaran, J.C. Tatlow, J. Chem. Soc. (1964) 763–765.
[8] T.N. Gerasimova, N.A. Orlova, J. Fluorine Chem. 28 (1985) 361–390.
[9] Y. Inukai, T. Sonoda, H. Kobayashi, Bull. Chem. Soc. Jpn. 52 (1979) 2657–2660.
[10] A.H. Haines, Tetrahedron Lett. 21 (1980) 285–286.
[11] G. Sandford, R. Slater, D.S. Yufit, J.A.K. Howard, A. Vong, J. Org. Chem. 70 (2005) 7208–7216.
[12] A. Baron, G. Sandford, R. Slater, D.S. Yufit, J.A.K. Howard, A. Vong, J. Org. Chem. 70 (2005) 9377–9381.
[13] C.A. Hargreaves, G. Sandford, R. Slater, D. Yufit, J.A.K. Howard, A. Vong, Tetrahedron 63 (2007) 5204–5211.
[14] D.A. Horton, G.T. Bourne, M.L. Smythe, Chem. Rev. 103 (2003) 893–930.
[15] I. Collins, J. Chem. Soc. Perkin Trans. 1 (2000) 2845–2861.
[16] I. Collins, J. Chem. Soc. Perkin Trans. 1 (2002) 1921–1940.
[17] S.J. Teague, A.M. Davis, P.D. Leeson, T. Oprea, Angew. Chem. Int. Ed. 38 (1999) 3743–3748.
[18] J. Burdon, P.L. Coe, C.R. Marsh, J.C. Tatlow, Tetrahedron 22 (1966) 1183–1188.
[19] J. Burdon, D. Fisher, D. King, J.C. Tatlow, J. Chem. Soc., Chem. Commun. (1965) 65–66.
[20] L.S. Kobrina, G.G. Furin, G.G. Yakobson, Zh. Org. Khim. 6 (1970) 512–520.
[21] J.G. Allen, J. Burdon, J.C. Tatlow, J. Chem. Soc. (1965) 1045–1049.

[1] CCDC 640452 and 640453 contain the supplementary crystallographic data for this paper. These data can be viewed free of charge via http://www.ccdc.cam.ac.uk/cont/retrieving.html or from the CCDC, 12 Union Road, Cambridge, CB2 1EZ; fax: +44 1223 336033. E-mail: deposit@ccdc.cam.ac.uk.