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Reactions of 4,5-difluoro-1,2-dinitrobenzene with amines in dimethylformamide or EtOH

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Abstract

Substitution reactions of 1,2-difluoro-4,5-dinitrobenzene were explored in dimethylformamide alone and with KOH/H_2O, Hünig's base or Et_3N and with Me_2NHCl/Et_3N in EtOH. The fluorine atoms were always displaced in preference to the nitro groups. Three compounds were prepared from these studies and were characterised by X-ray single crystal structure determinations.

Keywords

4,5-difluoro-1,2-dinitrobenzene, fluoride, Hofmann elimination, Hünig's base, nucleophilic substitution

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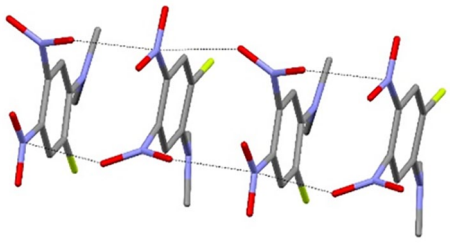

Introduction

The reaction of aniline with 2,4-difluoronitrobenzene **1** gives a low yield of 2,4-bis(phenylamino)nitrobenzene **2**[1,2] and 2,6-bis(phenylamino)-4-(iminophenyl)benzoquinone **3** (Scheme 1).[3] Compound **2** forms a crystalline host having hydrogen bonded hexamers enclosing large one-dimensional channels, which makes them organic zeolites. Using two different amines in sequence, butylamine then 1,4-diaminobutane, or butylamine then piperazine, a dimer **4** or **5** was formed, respectively. Dimer **4**, with a flexible spacer, crystallised with open framework channels of 10 Å in diameter,[4] whereas dimer **5**, with a more rigid spacer, was close packed.[5] The reaction of *N*-methyl-*o*-phenylenediamine **6** with 4,5-difluoro-1,2-dinitrobenzene **7** was studied as a potential iterative approach to 1,4-dihydro-*N*-heteroacenes, which may have interesting electronic properties.[6,7] The reaction of 2-fluoronitrobenzene **9** with enaminones gave aposafranones and their N-oxides, with butylamine and other amines gave 2-aminobenzimidazoles, with butylamine and other amines gave isoalloxazines and with aminomethylpyrazoles gave more complex medicinally active heterocycles[8–11] (Scheme 2). 4-Fluoronitrobenzene **10** has been used to explore the reactivity sequence of aromatic halides, to make *N*-alkyl-*p*-nitroanilines for second harmonic generation and in molecular recognition-based catalysis in nucleophilic aromatic substitution.[12–14] Compound **11** has been used in the synthesis and characterisation of isodiphenylfluorindone and isodiphenylfluorindinone.[15]

Discussion

4,5-Difluoro-1,2-dinitrobenzene **7**, has both activated fluorine atoms and also nitro groups, which activate each other.[16] 1,2-Dinitrobenzene reacts with butylamine to give 2-butylaminonitrobenzene. Our studies so far making phenazines have shown that the fluorine atoms displace in preference to a nitro group in EtOH.[6,7] Exploratory studies on reactions of compound **7** in dimethylformamide (DMF) with nucleophiles are reported here. DMF might be a better dipolar aprotic solvent for substitution reactions because it does not hydrogen bond to the nucleophile in the same

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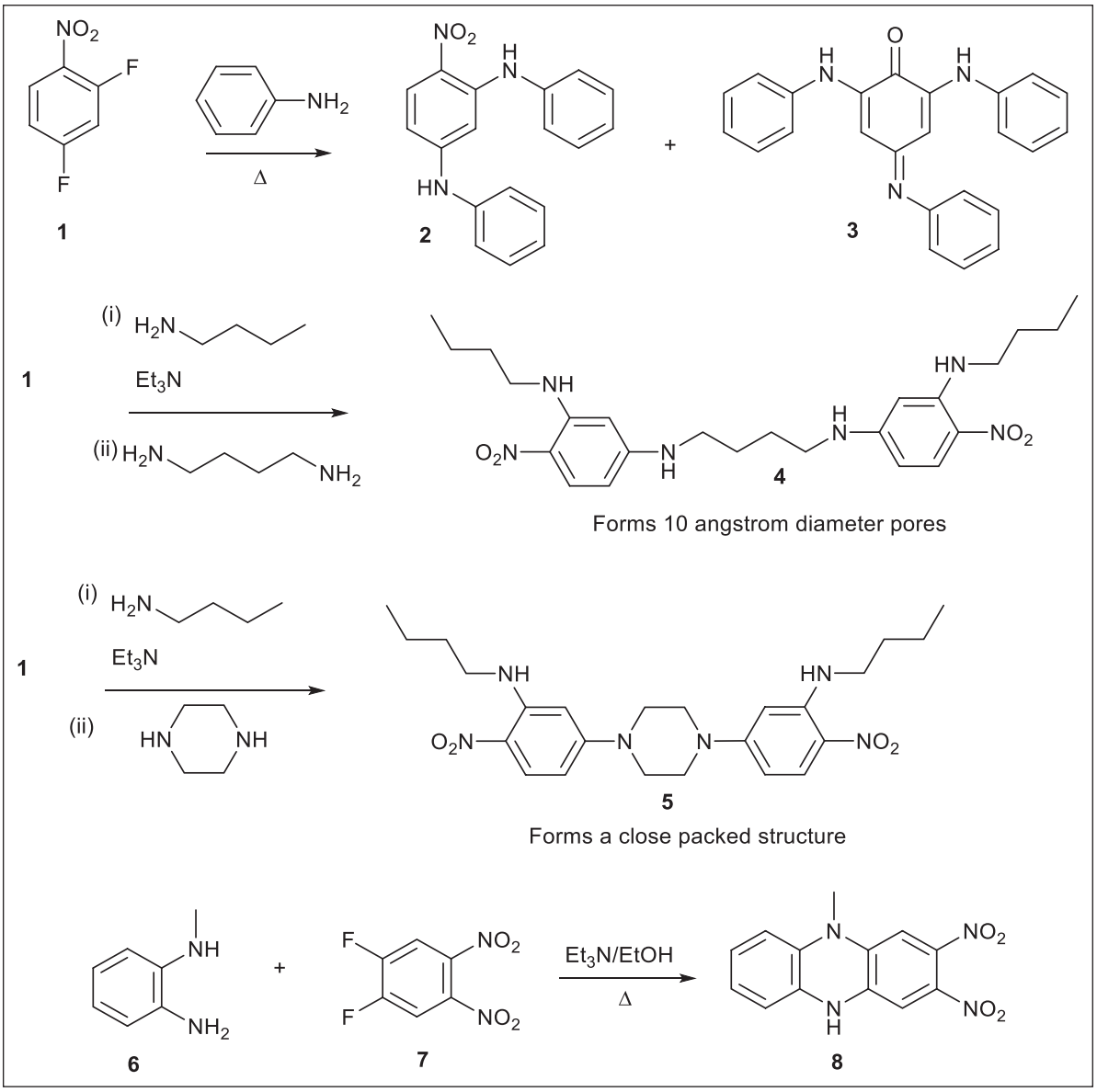
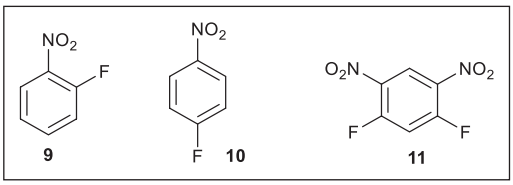
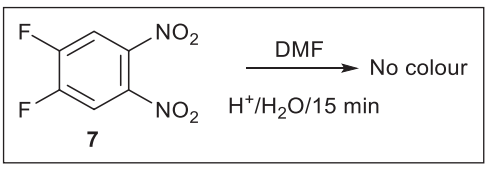


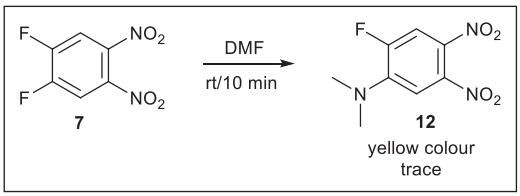
Scheme 1. A literature survey of some reactions of fluorinated and nitrated aromatic compounds with amines.[1–11]



Scheme 2. Some commercially available nitrated fluorobenzenes.

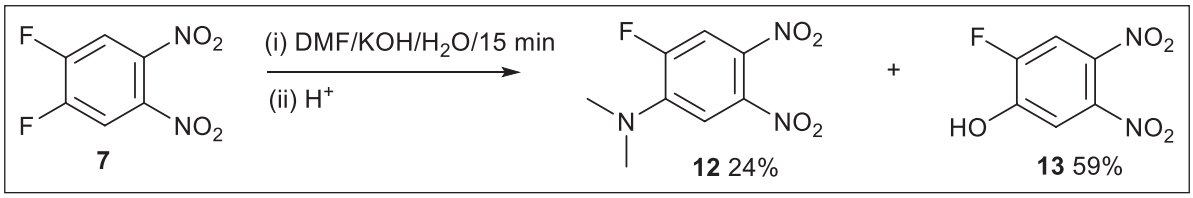


Scheme 3. Test 1: No yellow colour forms from compound **7** in acidified DMF. DMF: dimethylformamide.

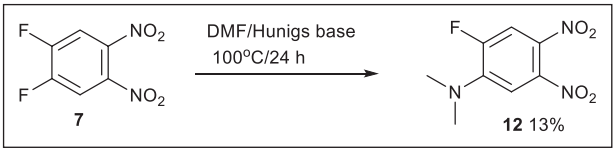


Scheme 4. Test 2: Yellow colouration forms from compound **7** in DMF. DMF: dimethylformamide.

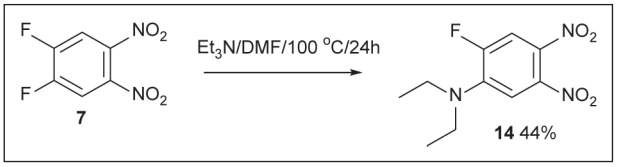
manner that it is a better solvent than methanol (MeOH) for certain nucleophilic substitution reactions.[17] It was of interest to see if tertiary amines reacted with compound **7**. In acidified DMF, compound **7** remains colourless (Scheme 3), but in fresh DMF, compound **7** rapidly turns pale yellow (Scheme 4). The trace of yellow compound was purified by



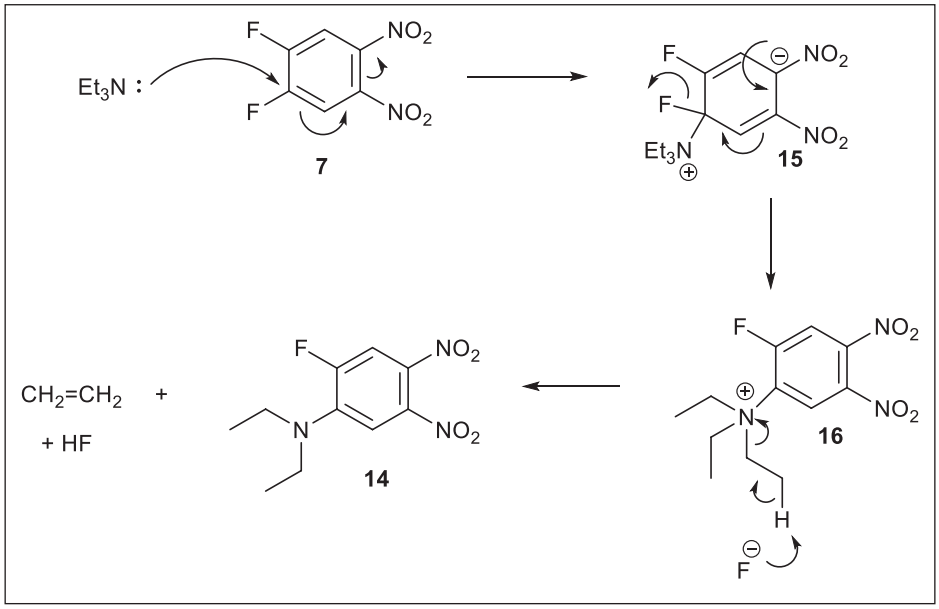
Scheme 5. Base catalysed generation of dimethylamine from DMF. DMF: dimethylformamide.



Scheme 6. Hünig's base catalysed reaction of compound **7** in DMF. DMF: dimethylformamide.



Scheme 7. Reaction of triethylamine with compound **7** in hot DMF.

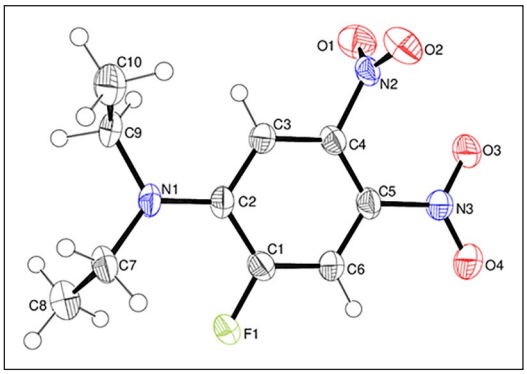


Scheme 8. A proposed mechanism for reacting compound **7** with triethylamine.

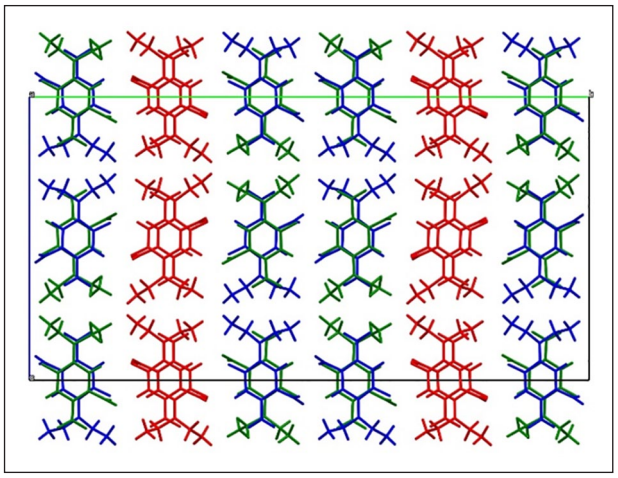
chromatography on silica and characterised by accurate mass spectrometry and by comparison of the R_f value with authentic material. DMF must have a very low concentration of dimethylamine in it from its decomposition.[1,18] This reaction can serve as a mild test for dimethylamine in DMF. In acid it will be protonated and does not react. DMF is decomposed by KOH/H_2O in a clean reaction to give substitution products **12** and **13**. (Scheme 5). The two products were easily characterised and both contained a fluorine atom as evidenced by peak splitting in the proton and carbon 400 MHz nuclear magnetic resonance (NMR) spectrum. The two nitro groups were not displaced. Hünig's base in hot DMF gave a low yield of compound **12** (Scheme 6). Hunig's base accelerates the reaction presumably by an acid–base reaction with residual water.

In contrast with Hünig's base, which is hindered to shield the basic nitrogen atom, Et_3N reacts with compound **7** in DMF to give the diethylamino substituted derivative **14** (Scheme 7). This reaction was not observed in EtOH so the tertiary amine is more nucleophilic in DMF. A mechanism is suggested in Scheme 8. Et_3N will attack and displace fluoride ions from compound **7** forming the quaternary salt **16**. Although many displacements of activated fluorine atoms have been performed, this is the first time the reactive 'naked' fluoride ion generated in the reaction has been utilised in this chemistry. A Hofmann elimination is most likely, rather than a more hindered substitution reaction, using the reactive fluoride counterion to give the product and ethene. Compound **14** was characterised by an X-Ray single crystal structure determination.

The asymmetric unit of compound **14** contains three molecules (containing C1, C11 and C21) with similar conformations (Scheme 9). In each case, the nitro group *para* to the amine group is close to coplanar with its attached



Scheme 9. The molecular structure of the C1 molecule in compound **14** showing 50% displacement ellipsoids.



Scheme 10. The unit-cell packing for compound **14** viewed down [100] with the C1, C11 and C21 molecules shown in red, blue and green, respectively.

aromatic ring [dihedral angles = 8.87 (11)°, 14.1 (2)° and 5.3 (2)° for the C1, C11 and C21 molecules, respectively]. Conversely, the nitro group *para* to the fluorine atom is substantially twisted with respect to the ring [dihedral angles = 82.7 (2)°, 72.0 (2)° and 82.3 (2)°, respectively]. The preference for the near-coplanarity of the former nitro group can be explained by the stabilisation gained by resonance with the amine nitrogen atom lone pair (i.e. the Et_2N^+=C quinoid form). In each molecule, one of the methyl groups is displaced above the plane of the aromatic ring and one below.

In the extended structure of compound **14**, the molecules stack in the [100] direction (Scheme 10) such that columns of C1 molecules occur along with alternating stacks of the C11 and C21 species; these motifs alternate in the [010] direction. The columns may be consolidated by very weak aromatic π–π stacking with centroid–centroid separations of 4.028 (3) Å for the C1 stacks and 3.770 (3)/4.197 (3) Å for the C11/C21 stacks. Two short intermolecular F···O contacts at 2.822 (5) Å and 2.884 (4) Å occur, compared to a van der Waals separation of 2.99 Å for these species and numerous weak C–H···O and C–H···F hydrogen bonds are also observed.

Finally dimethylamine was liberated in situ from dimethylamine hydrochloride in EtOH with Et_3N and reacted with compound **7** to give an unseparated mixture of a mono-substituted product **12** and a di-substituted product **17** (Scheme 11). The mixture was purified and the proton and carbon NMR data were analysed by subtraction of the data for the known compound **12**. Proton NMR integration gave an approximate product percentage ratio for compounds **12**:**17** of 57:43. This reaction showed that the nitro groups were not displaced.

Upon crystallisation, the crystallographer found and separated crystals for both compounds, which were characterised by X-ray single crystal structure determinations.

Compound **12** (yellow plate) contains one molecule in the asymmetric unit (Scheme 12). The N2/O1/O2 nitro group to the amine is close to coplanar with the C1–C6 ring [dihedral angle = 6.45 (5)°] whereas the N3/O3/O4 nitro group *para* to the F atom is substantially twisted away from the plane of the ring [dihedral angle = 73.38 (6)°]. As with compound **14**, the orientation of the N2 nitro group can be explained by a favourable resonance effect with N1 and the C4–N2 bond length of 1.4421 (15) Å is notably shorter than C5–N3 [1.4756 (15) Å]. It may also be noted that the mean separation of C2–C3 and C5–C6 [1.370 Å], which are double bonds in the quinoid resonance form is significantly shorter than the mean of the other carbon–carbon bond lengths [1.404 Å], which are single bonds in the quinoid form. The N1/C7/C8 grouping is twisted from the aromatic ring by 21.23 (11)°.

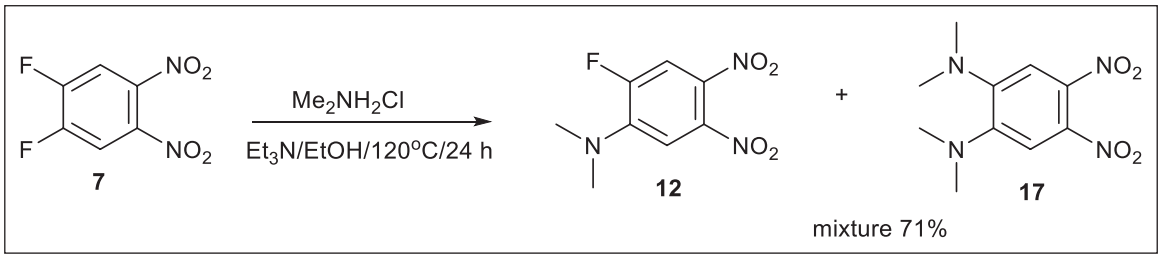
In the extended structure of compound **12**, unusual short N_n–O···N_n (n = nitro group) contacts[19] occur [O3···N2 = 2.8006 (14) Å; N3–O3···N2 = 156.13 (19)°; O4···N2 = 2.8902 (16) Å; N3–O4···N2 = 136.32 (9)°], which link the molecules into [001] chains (Scheme 13) with adjacent molecules related by *c*-glide symmetry; weak aromatic π–π stacking is also observed between adjacent rings in the chain [centroid–centroid separation = 3.9361 (8) Å]. Weak C–H···O and C–H···F hydrogen bonds crosslink the [001] chains.

Compound **17** (red lath) also crystallises with one molecule in the asymmetric unit (Scheme 14). In this case, the N4/O3/O4 nitro group (*para* to N2) is close to coplanar with the aromatic ring with a dihedral angle of 15.12 (19)° whereas N3/O1/O2 (*para* to N1) is substantially twisted [dihedral angle = 65.30 (8)°]. The presumed resonance from the N2 lone pair is manifested in the fact that the C2–N2 and C5–N4 bond distances [1.3665 (18) Å and 1.4457 (17) Å, respectively] are shorter than the C1–N1 and C4–N3 bonds [1.4066 (18) Å and 1.4775 (17) Å, respectively] and the mean length of C1–C6 and C3–C4 [1.380 Å] is significantly shorter than the other bonds in the ring [1.409 Å]. In the extended structure of compound **17**, some weak C–H···O and C–H···F hydrogen bonds may help to consolidate the packing.

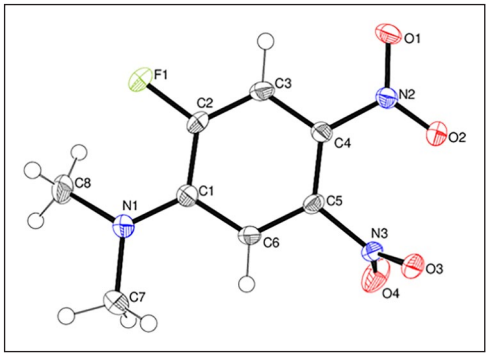
Experimental

Compounds **12–14** *and* **17** *are new compounds*

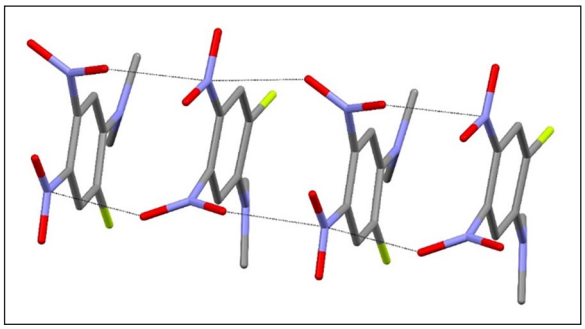
Infrared (IR) spectra were recorded on a diamond attenuated total reflection (ATR) Fourier transform infrared (FTIR) spectrometer. Ultraviolet (UV) spectra were



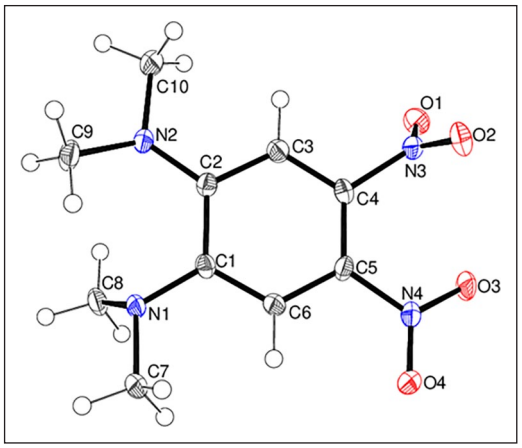
Scheme 11. Reaction of dimethylamine with compound **7** in EtOH.



Scheme 12. The molecular structure of compound **12** showing 50% displacement ellipsoids.



Scheme 13. Short N–O···N contacts (black dashed lines) generating [001] chains in the extended structure of compound **12**.



Scheme 14. The molecular structure of compound **17** showing 50% displacement ellipsoids.

recorded using a PerkinElmer Lambda 25 UV-VIS spectrometer with EtOH as the solvent. The term sh means shoulder. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100.5 MHz, respectively, using a Varian 400 spectrometer. Chemical shifts, δ, are given in ppm and measured by comparison with the residual solvent. Coupling constants, *J*, are given in Hz. High-resolution mass spectra were obtained at the University of Wales, Swansea, using an Atmospheric Solids Analysis Probe (ASAP; Positive mode) Instrument: Xevo G2-S ASAP. Melting points were determined on a Kofler hot-stage microscope.

For Tests 1 and 2 and Methods 1–4, the starting material was not recovered.

Test 1. DMF (5 mL) was treated with one drop of concentrated aqueous HCl and then treated with 1,2-difluoro-4,5-dinitrobenzene (20 mg, 0.098 mmol). The solution remained clear after 15 min. This is a control, which shows that the compound is not coloured in DMF and that it is a base-catalysed reaction, which turns the solution yellow.

Test 2. 1,2-Difluoro-4,5-dinitrobenzene (20 mg, mmol) was dissolved in DMF (5 mL) and left standing for 10 min. The solution turned pale yellow. The solution was diluted with water (250 mL), then extracted with dichloromethane (DCM; 50 mL). The pale yellow DCM layer was dried with $MgSO_4$ and decanted. After concentration a TLC plate eluted with 50:50 (DCM: light petrol) showed the single yellow product to have an identical R_f value to 2-(dimethylamino)-4,5-dinitrofluorobenzene **12**. *m/z* (Orbitrap ASAP) 230.0577 (M + H^+, 100%) $C_8H_9N_3O_4F$ requires 230.0578.

Method 1. 2-(Dimethylamino)-4,5-dinitrofluorobenzene 12 and 2-hydroxy-4,5-dinitrofluorobenzene 13. 1,2-Difluoro-4,5-dinitrobenzene **7** (50 mg, 0.25 mmol), in DMF (8 mL) and water (3 mL) were treated with an excess of dry KOH (100 mg, 1.9 mmol) and left at room temperature for 15 min. The mixture was diluted with dilute aqHCl (3M, 100 mL) and water (150 mL) and extracted with DCM (100 mL, ×2). The combined extracts were dried over $MgSO_4$ and decanted. The mixture was chromatographed on silica. The first yellow product was eluted with DCM to give the first compound, 2-(Dimethylamino)-4,5-dinitrofluorobenzene 12 (**12**, 14 mg, 24%) as a yellow solid, melting point (m.p.) 137°C –138°C (from DCM:light petroleum ether). λ_{max} (EtOH)/nm 390 (log ε 3.7) and 225 (3.6); λ_{max} (diamond; cm^{-1}) 3077w, 2923w, 2854w, 1729w, 1609vs, 1540vs, 1513vs, 1368s, 1314vs, 1259vs, 1233s, 1035vs, 892s, 848s, 806w, 749w, 719w, 661w, 571 and 453w; δ_H (400 MHz; $CDCl_3$) 3.10 (6H, d, J = 0.8), 6.78 (1H, d, J_{H-F} = 8.0) and 7.68 (1H, d, J_{H-F} = 14.0); δ_C (100.1 MHz; $CDCl_3$) 42.2, 42.3, 110.2, 110.3, 114.5, 114.7, 129.1(C–F), 142.6 (C–F),

144.2, 144.3, 148.9 and 151.5; *m/z* (Orbitrap ASAP) 230.0580 (M + H^+, 100%) $C_8H_9N_3O_4F$ requires 230.0577. The column was eluted with Et_2O: MeOH (95:5) then Et_2O:MeOH (50:50) which eluted the second compound, 2-hydroxy-4,5-dinitrofluorobenzene (**13**, 29 mg, 57%) as a yellow solid, m.p. 111°C –112°C (from DCM: MeOH). λ_{max} (EtOH)/nm 392 (log ε 3.8) and 210 (3.6); λ_{max} (diamond; cm^{-1}) 3637w, 3310w, 1594s, 1531vs, 1486s, 1455w, 1365w, 1309vs, 1223s, 1185s, 1038w, 884w, 857w, 818w, 785w, 751w, 624s and 586s; δ_H (400 MHz; CD_3OD) 6.64 (1H, d, J_{H-F} = 8.0) and 7.76 (1H, d, J_{H-F} = 12.0); δ_C (100.1 MHz; $CDCl_3$) 111.8, 112.1, 114.4, 114.6, 121.9 (C–F), 144.9 (C–F), 152.4, 154.8, 165.3 and 165.5; *m/z* (Orbitrap ASAP) 200.9953 (M − H^+, 100%) $C_6H_2FN_2O_5$ requires 200.9953.

Method 2. 2-(Dimethylamino)-4,5-dinitrofluorobenzene 12. 1,2-Difluoro-4,5-dinitrobenzene **7** (50 mg, 0.25 mmol) in DMF (20 mL) was treated with an excess of Hünig's base (0.5 mL) and heated at 100°C for 24 h. Upon cooling, the mixture was diluted with dilute aqHCl (3 M, 200 mL) and water (300 mL) and extracted with DCM (100 mL × 4). The combined extracts were dried over $MgSO_4$ and decanted. The mixture was purified by chromatography on silica. The yellow product was eluted with DCM to give the compound, 2-(Dimethylamino)-4,5-dinitrofluorobenzene 12 (7 mg, 12%) as a yellow solid, m.p. 137°C –138°C (from DCM:light petroleum ether) with identical spectroscopic properties to that reported in Method 1. A small amount of front running yellow product was characterised by *m/z* (Orbitrap ASAP) 230.0575 (M + H^+, 50%) $C_8H_9N_3O_4F$ requires 230.0577.

Method 3. 2-(Diethylamino)-4,5-dinitrofluorobenzene 14. 1,2-Difluoro-4,5-dinitrobenzene **7** (50 mg, 0.25 mmol) in DMF (20 mL) was treated with an excess of Et_3N (1 mL) and heated at 100°C for 24 h. Upon cooling, the mixture was diluted with dilute aqHCl (3 M, 200 mL) and water (300 mL) and extracted with DCM (100 mL × 4). The combined extracts were dried over $MgSO_4$, decanted and analysed by thin layer chromatography (TLC). Elution with DCM showed that both starting materials had been consumed leaving a front running (R_f = 0.9) pale yellow compound. The mixture was purified by chromatography on silica. DCM eluted the compound, 2-(Diethylamino)-4,5-dinitrofluorobenzene 14 (28 mg, 44%) as a yellow solid, m.p. 91°C –92°C (from DCM:light petroleum ether). λ_{max} (EtOH)/nm 392 (log ε 4.4) and 229 (4.2); λ_{max} (diamond; cm^{-1}) 2978w, 1609s, 1538vs, 1505vs, 1471w, 1445w, 1385s, 1313vs, 1219vs, 1138w, 1069s, 1039s, 892vs, 852vs, 795w, 696w, 610w and 574w; δ_H (400 MHz; $CDCl_3$) 1.29 (6H, t, *J* = 8.0), 3.51 (4H, q, *J* = 8.0), 6.84 (1H, d, J_{H-F} = 9.0) and 7.79 (1H, d, J_{H-F} = 15.0); δ_C (100.1 MHz; $CDCl_3$) 13.07, 46.8, 109.7, 114.9, 115.2, 127.9 (C–F), 142.3, 142.4 (C–F), 143.0, 148.1 and 150.7; *m/z* (Orbitrap ASAP) 258.0883 (M + H^+, 100%) $C_{10}H_{12}N_3O_4F$ requires 258.0885.

Method 4. Mixture of 2-(dimethylamino)-4,5-dinitrofluorobenzene 12 and 1,2-bis(dimethylamino)-4,5-dinitrobenzene 17. 1,2-Difluoro-4,5-dinitrobenzene **7** (50 mg, 0.25 mmol) in EtOH (10 mL) with dimethylammonium hydrochloride (40 mg, 0.48 mmol) and triethylamine (0.4 mL) were sealed in a Parr Teflon-lined vessel and heated at 120°C for 24 h. After cooling, the mixture was diluted with 2 M dil HCl (50 mL), extracted with DCM, dried with $MgSO_4$ and decanted. After evaporation the mixture was purified by chromatography on silica gel. Elution with 50:50 (light petroleum ether: DCM) gave the mixture of 2-(dimethylamino)-4,5-dinitrofluorobenzene 12 and 1,2-bis(dimethylamino)-4,5-dinitrobenzene 17 (43 mg, 71%) as yellow and red solids. λ_{max} (EtOH)/nm 389 (log ε 3.9); λ_{max} (diamond; cm^{-1}) 2957w, 1609m, 1507vs, 1367s, 1309vs, 1259s, 1136s, 1027s, 892s, 848s, 792s, 749s, 660s, 571s and 452s; 2-(dimethylamino)-4,5-dinitrofluorobenzene had the same NMR data as that reported in Method 1; 1,2-(dimethylamino)-4,5-dinitrobenzene gave δ_H (400 MHz; CD_3OD) 2.81 (12H, s), 7.16 (2H, s); δ_C (100.1 MHz; $CDCl_3$) 42.3, 113.5, 136.3 and 146.8; *m/z* (Orbitrap ASAP) 255.1090 (M + H^+, 100%) $C_{10}H_{15}N_4O_4$ requires 255.1093. Product ratio **12**:**17** = 57:43

Single-crystal diffraction

Yellow and red crystals were separated by the crystallographer. The crystal structure of compound **14** (yellow plate, 0.14 × 0.04 × 0.01 mm, recrystallised from DCM/light petroleum ether), compound **12** (yellow plate, 0.30 × 0.16 × 0.03 mm, recrystallised from DCM/light petroleum ether) and compound **17** (red lath 0.25 × 0.05 × 0.01 mm, recrystallised from DCM/light petroleum ether) were established using intensity data collected on a Rigaku CCD diffractometer (Cu Kα radiation, λ = 1.54178 Å) at 100 K. The structures were routinely solved by dual-space methods using SHELXT[20] and the structural models were completed and optimised by refinement against $|F|^2$ with SHELXL-2018.[21] The hydrogen atoms were placed geometrically (C–H = 0.95–0.98 Å) and refined as riding atoms; the methyl groups were allowed to rotate, but not to tip, to best fit the electron density. The constraint $U_{iso}(H) = 1.2U_{eq}$(carrier) or $1.5U_{eq}$(methyl carrier) was applied in all cases. Full details of the structures and refinements are available in the deposited cifs. The crystal quality of compound **14** is poor, resulting in rather high *R*-factors, but the structure has been unambiguously determined.

Crystal data for compound **14** ($C_{10}H_{12}FN_3O_4$): M_r = 257.23, orthorhombic, space group *Pbca* (No. 61), *a* = 7.9322 (2) Å, *b* = 41.3957 (10) Å, *c* = 20.9238 (4) Å, *V* = 6870.5 (3) $Å^3$, *Z* = 24, *T* = 100 K, μ = 1.097 mm^{-1}, ρ_{calc} = 1.412 g cm^{-3}, 46,655 reflections measured (4.3 ⩽ 2θ ⩽ 132.0°), 5980 unique (R_{int} = 0.051), *R*(*F*) = 0.110 [5091 reflections with $I > 2\sigma(I)$], *wR*(F^2) = 0.301 (all data), $\Delta\rho_{min,max}$ (*e* $Å^{-3}$) = −0.48, +1.03, CCDC deposition number 2225621.

Crystal data for compound **12** ($C_8H_8FN_3O_4$): M_r = 229.17 monoclinic, space group $P2_1/c$ (No. 14), *a* = 9.9153 (6) Å, *b* = 13.2473 (9) Å, *c* = 7.7815 (4) Å, β = 109.489 (6)°, *V* = 963.55 (11) $Å^3$, *Z* = 4, *T* = 100 K, μ = 1.228 mm^{-1}, ρ_{calc} = 1.580 g cm^{-3}, 13,876 reflections measured (9.5 ⩽ 2θ ⩽ 148.8°), 1921 unique (R_{int} = 0.038),

Table 1. Summary of the reaction data.

Entry	Substrate	Conditions	**12** (%)	**13** (%)	**14** (%)	**17** (%)
1	7	DMF/KOH/H_2O/15 min	24	59		
2	7	DMF/Hünigs base/100°C/24 h	13			
3	7	DMF/Et_3N/100°C/24 h			44	
4	7	EtOH/Me_2NH_2Cl/Et_3N/120°C /24 h	71 (mix)			71 (mix)

$R(F) = 0.035$ [1785 reflections with $I > 2\sigma(I)$], $wR(F^2) = 0.093$ (all data), $\Delta\rho_{min,max}$ (e Å^{-3}) = −0.26, +0.28, CCDC deposition number 2225622.

Crystal data for compound **17** ($C_{10}H_{14}N_4O_4$): M_r = 254.25, triclinic, space group $P\bar{1}$ (No. 2), a = 8.2303 (5) Å, b = 8.4946 (5) Å, c = 9.8922 (4) Å, α = 111.307 (5)°, β = 95.839 (4)°, γ = 111.405 (6)°, V = 577.57 (6) Å^3, Z = 2, T = 100 K, μ = 0.975 mm^{-1}, ρ_{calc} = 1.462 g cm^{-3}, 9924 reflections measured (10.0 ⩽ 2θ ⩽ 136.5°), 2109 unique (R_{int} = 0.063), $R(F)$ = 0.042 [1776 reflections with $I > 2\sigma(I)$], $wR(F^2)$ = 0.122 (all data), $\Delta\rho_{min,max}$ (e Å^{-3}) = −0.28, +0.25, CCDC deposition number 2225623 (Supplementary crystallographic material).

Conclusion

4,5-Difluoro-1,2-dinitrobenzene **7** quickly turns pale yellow in fresh DMF forming small, detectable amounts of 2-(dimethylamino)-4,5-dinitrofluorobenzene **12**. DMF with water and KOH forms 2-(dimethylamino)-4,5-dinitrofluorobenzene **12** and 2-hydroxy-4,5-dinitrofluorobenzene **13**. Reaction with triethylamine gives 2-(diethylamino)-4,5-dinitrofluorobenzene **14** via a quaternary ammonium fluoride salt. An unusual Hofmann elimination occurs with the fluoride counterion as base. Reaction with dimethylamine hydrochloride and triethylamine gives 2-(dimethylamino)-4,5-dinitrofluorobenzene **12** and 1,2-bis(dimethylamino)-4,5-dinitrobenzene **17**. Nucleophilic substitution of the second fluorine group requires higher temperatures and is a slower reaction in part because the product is sterically crowded. Table 1 summarises this data.

Entry 4 was sealed in a Parr vessel and the products were not separated, but the mixture **12**/**17** was purified.

These results show that DMF can be used in place of EtOH for nucleophilic substitution reactions of activated fluoride but some minor side reactions are introduced which may affect product purity. These studies are helpful for our ongoing work on an iterative approach to NOS-heteroacenes using 4,5-difluoro-1,2-dinitrobenzene **7** as a building block.[6,7]

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Supplemental material

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