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The $S_{RN}1$ chemistry of 4-iodo-1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane

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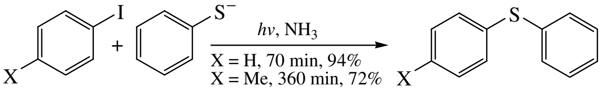
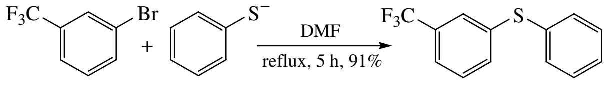
4-Iodo-1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane undergoes high-yield nucleophilic substitution by arene thiolates and the malonate anion *via* the $S_{RN}1$ mechanism.

Consistent with our interest in the mechanistic reactivity of octafluoro[2.2]paracyclophane (AF4) and its derivatives, with the ultimate goal of exploiting such knowledge to synthesize new materials, we have undertaken a preliminary examination of the $S_{RN}1$ reactivity of iodo-AF4.

The $S_{RN}1$ reactions are nucleophilic substitutions that proceed *via* chain reactions involving radical anion intermediates and where the key initiation step requires a single electron transfer from the nucleophile to the substrate.[1,2] One class of $S_{RN}1$ reactions that was pioneered by Bunnett and Yagupol'skii in the 1970s involves substitution of 'unactivated' haloaromatics by certain polarisable nucleophiles, which include aryl thiolates and enolates.[3] Many of these reactions have been carried out in liquid ammonia, with many requiring photoinitiation. A relative insensitivity of the reaction to what substituents are on the aromatic ring was found, as indicated in Scheme 1.[4] On the other hand, Yagupol'skii and co-authors indicated that trifluoromethyl substituents facilitated the reaction, such that no photochemical activation was necessary (Scheme 2),[5] a result also observed more recently in reactions of heteroarylthiolates with chloropyridines.[6] Looking at the more recent literature, it appears to now be much more common to use copper catalysis rather than $S_{RN}1$ conditions to accomplish this chemistry.[7]

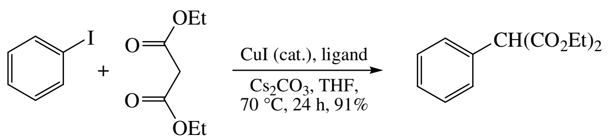


Scheme 1



Scheme 2

Although there is much literature on $S_{RN}1$ arylations of enolates, such as acetone enolate, mostly done in liquid ammonia,[3,8] efforts to utilise stabilised enolates of β-dicarbonyl compounds in a similar manner failed,[9] and arylation of enolates such as malonate anion has until now only been carried out using copper catalysis (Scheme 3).[7,10,11]



Scheme 3

Because the benzene rings of AF4 are highly electron deficient due to the presence of the fluorinated bridges, it was expected that iodo-AF4 would exhibit $S_{RN}1$ reactivity with appropriate $S_{RN}1$ nucleophiles. To our knowledge, no studies of the $S_{RN}1$ chemistry of any [2.2]paracyclophane have yet been reported.

Here, we report that iodo-AF4 **1** exhibits excellent $S_{RN}1$ reactivity with arene thiolates and, somewhat surprisingly, also with stabilised enolates, and these reactions provide ready access to a new group of AF4 derivatives (Scheme 4).[†] Both reactions required photochemical stimulation, with neither proceeding under simple thermal conditions, even at 120 °C, in the absence of irradiation with a sunlamp.[‡]

Consistent with the proposed $S_{RN}1$ mechanism for these reactions, addition of either 25% hydroquinone or 25% *m*-dinitrobenzene to the thiolate reaction led to a significant diminution of yield (30 and 21%, respectively).

Kornblum *et al.*[12] had demonstrated that nitronates, phenolates and other $S_{RN}1$ nucleophiles were quite effective in displacing nitro groups from electron deficient aromatics, such as 3,5-bis-

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[†] **2a**: white solid, mp 95–97 °C. ^{1}H NMR ($CDCl_3$) δ: 6.26 (s, 1H), 6.89 (d, 2H, *J* 12 Hz), 7.09 (d, 2H, *J* 12 Hz), 7.46–7.58 (m, 6H), 7.90 (d, 1H, *J* 6.9 Hz). ^{19}F NMR ($CDCl_3$) δ: 108.8 (d, 1F, J_{AB} 236.9 Hz), 110.3 (d, 1F, J_{AB} 239.7 Hz), 112.2 (d, 1F, J_{AB} 239.7 Hz), 114.0 (d, 1F, J_{AB} 236.9 Hz), 117.25 (d, 1F, J_{AB} 236.9 Hz), 118.1 (s, 2F), 118.4 (d, 1F, J_{AB} 236.9 Hz). MS, *m/z* (%): 460 (M^+, 78), 461 (18), 283 (93), 264 (100), 176 (30). HRMS: found, 460.0532; calc. for $C_{22}H_{12}F_8S$, 460.0532.

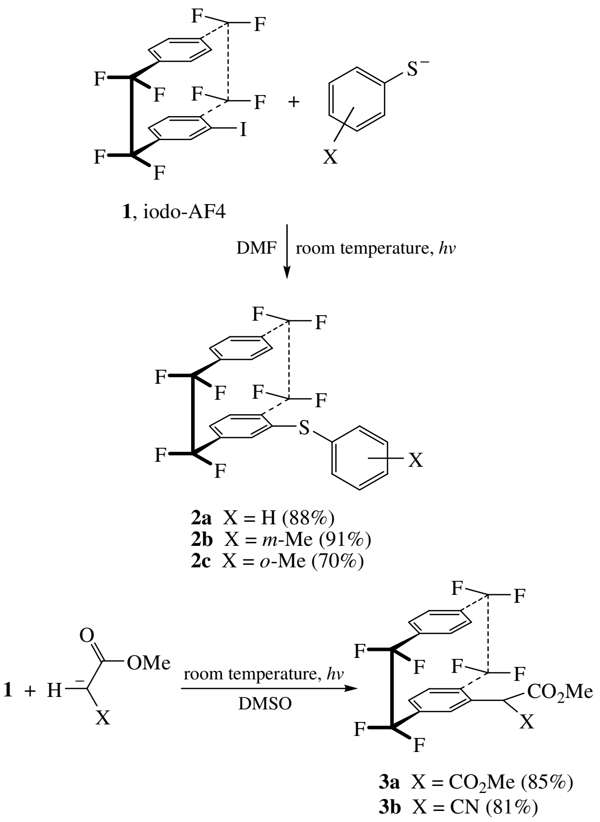
2b: white solid, mp 110–112 °C. ^{1}H NMR, δ: 2.40 (s, 3H, Ar*Me*), 6.21 (s, 1H), 6.80–6.90 (m, 1H), 7.07 (d, 1H, *J* 7.8 Hz), 7.01–7.42 (m, 7H), 7.91 (d, 1H, *J* 9 Hz). ^{19}F NMR, δ: 108.6 (d, 1F, J_{AB} 239.7 Hz), 110.0 (d, 1F, J_{AB} 234.1 Hz), 112.1 (d, 1F, J_{AB} 234.1 Hz), 113.85 (d, 1F, J_{AB} 239.7 Hz), 117.2 (d, 1F, J_{AB} 236.9 Hz), 117.9 (s, 2F), 118.4 (d, 1F, J_{AB} 236.9 Hz). MS, *m/z* (%): 474 (M^+, 67), 475 (17), 297 (90), 278 (100), 176 (63). Found (%): C, 58.03; H, 2.86. Calc. for $C_{23}H_{14}SF_8$ (%): C, 58.23, H, 2.97.

2c: white solid, mp 114–116 °C. ^{1}H NMR, δ: 2.42 (s, 3H, Ar*Me*), 6.20 (m, 2H), 6.88 (m, 2H), 7.06–7.44 (m, 6H), 7.89 (d, 1H, *J* 8.0 Hz). ^{19}F NMR, δ: 108.6 (d, 1F, J_{AB} 239.7 Hz), 110.0 (d, 1F, J_{AB} 236.9 Hz), 112.2 (d, 1F, J_{AB} 236.9 Hz), 113.95 (d, 1F, J_{AB} 239.7 Hz), 117.2 (d, 1F, J_{AB} 239.7 Hz), 118.0 (s, 2F), 118.4 (d, 1F, J_{AB} 239.7 Hz). ^{13}C NMR, δ: 21.64, 118.73, 119.11, 124.96, 125.02, 125.11, 125.18, 127.26, 128.91, 128.99, 129.29, 129.61, 129.72, 129.84, 131.50, 132.42, 134.79, 135.13, 135.66, 135.70, 141.14, 143.36, 143.42. MS, *m/z* (%): 474 (M^+, 98), 475 (27), 297 (84), 278 (100), 176 (21). Found (%): C, 57.86; H, 2.85. Calc. for $C_{23}H_{14}SF_8$ (%): C, 58.23; H, 2.97.

3a: white solid, mp 125–127 °C. ^{1}H NMR, AB system for OMe, δ: 3.61 (br. s, 3H) and 3.98 (br. s, 3H), 5.18 (s, 1H, CHX), 7.07–7.34 (m, 7H, ArH). ^{19}F NMR, δ: 110.3 (d, 1F, J_{AB} 236.8 Hz), 113.2 (d, 1F, J_{AB} 236.9 Hz), 116.5 (d, 1F, J_{AB} 242.5 Hz), 116.9 (d, 1F, J_{AB} 242.5 Hz), 117.3 (d, 1F, J_{AB} 242.5 Hz), 117.45 (d, 1F, J_{AB} 242.5 Hz), 120.25 (d, 1F, J_{AB} 242.5 Hz), 120.7 (d, 1F, J_{AB} 242.5 Hz). ^{13}C NMR, δ: 53.52, 53.78, 118.41, 128.87, 129.38, 129.79, 129.89, 130.38, 130.48, 132.26, 132.62, 132.82, 133.49, 133.82, 134.16, 134.83, 135.18, 135.53, 135.88, 167.64, 167.43. MS, *m/z* (%): 482 (M^+, 48), 454 (20), 423 (23), 306 (61), 176 (100). HRMS: found, 482.0764; calc. for $C_{21}H_{14}O_4F_8$, 482.0764.

3b: white solid, mp 136–138 °C. ^{1}H NMR, δ: 3.68 (s, 3H, OMe), 5.17 (s, 1H, CHX), 7.14–7.51 (m, 7H, ArH). ^{13}C NMR, δ: 40.45, 54.72, 114.99, 128.28, 129.46, 129.53, 130.05, 130.10, 130.51, 130.97, 132.07, 133.22, 133.39, 133.88, 135.06, 135.39, 136.22, 136.56, 136.90, 163.66. ^{19}F NMR, δ: 109.2 (d, 1F, J_{AB} 248.2 Hz), 114.7 (d, 1F, J_{AB} 248.2 Hz), 116.3 (d, 1F, J_{AB} 245.3 Hz), 116.4 (d, 1F, J_{AB} 245.3 Hz), 117.4 (d, 1F, J_{AB} 245.3 Hz), 117.5 (d, 1F, J_{AB} 245.3 Hz), 119.8 (d, 1F, J_{AB} 245.3 Hz), 119.8 (d, 1F, J_{AB} 245.3 Hz). MS, *m/z* (%): 449 (M^+, 46), 430 (14), 273 (11), 177 (16), 176 (100). Found (%): C, 53.21; H, 2.55; N, 2.81. Calc. for $C_{20}H_{11}F_8NO_2$ (%): C, 53.47; H, 2.55; N, 3.12.

[‡] *Typical procedure for the $S_{RN}1$ reactions of iodo-AF4*: 0.30 g of thiophenol (2.7 mmol) and NaH (60%, 0.11 g, 2.7 mmol) in DMF (5 ml) were stirred under N_2 at room temperature for 1 h. Iodo-AF4 (0.20 g, 0.42 mmol) was added and the reaction mixture was stirred overnight while being irradiated by a sunlamp under N_2 at room temperature. The reaction was then quenched with water (30 ml), extracted twice with diethyl ether (30 ml), and the organic layer dried (Na_2SO_4), evaporated, and the residue chromatographed (silica gel) to give product **2a** (88%).



Scheme 4

(trifluoromethylnitrobenzene). Nevertheless, the use of nitronates, such as $Me_2C{=}NO_2^-$, or phenolates in photoinitiated reactions with iodo-AF4 has led to complicated reaction mixtures that are synthetically useless.

In conclusion, on the basis of the above preliminary results, it appears that iodo-AF4 should be a versatile substrate in reactions with nucleophiles that can participate in aromatic substitution *via* the $S_{RN}1$ mechanism. Considering the wide variety of $S_{RN}1$ nucleophiles that are available, it should be possible to synthesise many new and potentially useful derivatives of octafluoro[2.2]paracyclophane using this methodology.

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