First Trapping of 5,5-Difluorocyclopentadiene

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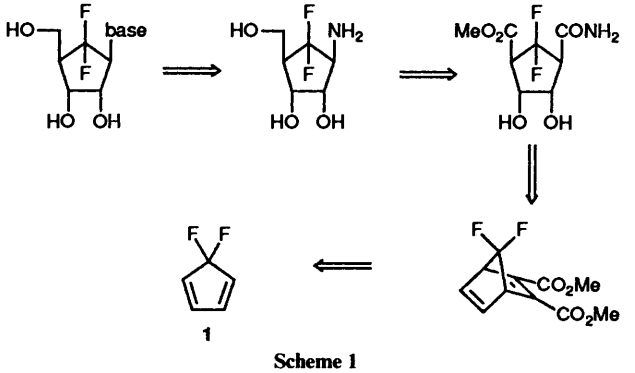
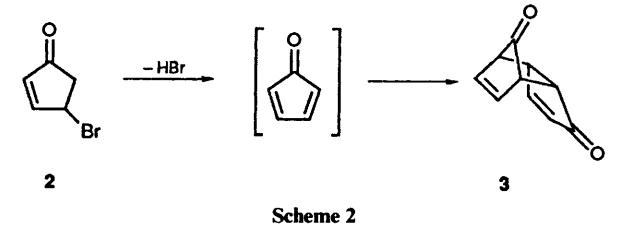
5,5-Difluorocyclopentadiene has been trapped for the first time by pyrolysis of 10,10-difluorotricyclo-[5.2.1.$0^{2,6}$]dec-8-en-3-ol.

The use of small fluorinated molecules as building blocks for more complex molecules has received a great deal of attention in recent years due to the success of specifically fluorinated compounds in the treatment of disease (*e.g.* the anti-cancer agent 5-fluorouracil; the anti-inflammatory agents flufenisal and diflunisal).[1] Biological activity is often associated with the fluorine atom or fluorinated substituent mimicking other functionalities such as hydroxy groups, ether linkages *etc.*[2] In particular, the potential use of the monofluoromethylene moiety as a replacement for the ring oxygen in furanoses,[3] led to the investigation into the preparation and synthetic utility of 5-fluorocyclopentadiene.[4] The possibility that the difluoromethylene moiety might also prove a useful mimic for the oxygen of furanose ring,[2] and therefore lead to new anti-viral agents, has prompted this study of 5,5-difluorocyclopentadiene (see Scheme 1). Like 5-fluorocyclopentadiene, 5,5-difluorocyclopentadiene has not previously been prepared and, therefore, it was first necessary to develop a suitable synthesis.

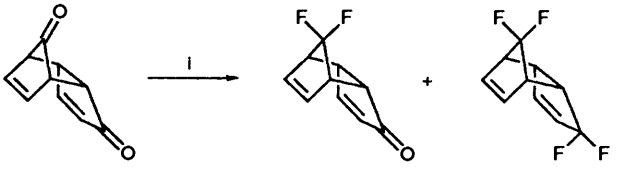


Scheme 1

The initial attempt to prepare **1** concentrated on methodology that had been successfully used to prepare cyclopentadienone.[5] Since this method utilised the elimination of hydrogen bromide from the suitably substituted cyclopentene **2** (see Scheme 2) it was first necessary to prepare 5-bromo-3,3-difluorocyclopentene. However, attempts to fluorinate either cyclopent-2-enone or **2** with diethylaminosulfur trifluoride (DAST) both failed to yield the desired compound, even under forcing conditions. Further, when tricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3,10-dione **3** was stirred for 3 days with excess DAST, the main product (57%) was 10,10-difluorotricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3-one **4*** with only trace quantities of 5,5,10,10-tetrafluorotricyclo[5.2.1.$0^{2,6}$]deca-3,8-diene **7** being observed (Scheme 3). These results, coupled with the scarcity of examples of enones reacting with DAST,[6] suggest that this reagent is reluctant to fluorinate carbonyl groups conjugated with double bonds.

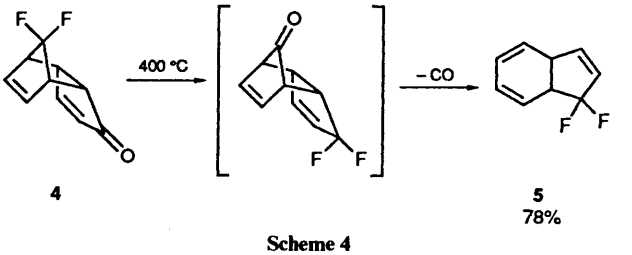


Scheme 2



Scheme 3 *Reagents and conditions:* i, DAST, CH_2Cl_2, room temp.

Since a number of dienes, including cyclopentadiene and cyclopentadienone,[7] are prepared by pyrolysis of a suitable Diels–Alder adduct, attempts were made to prepare **1** by this method. When **4** was passed through a furnace at 400 °C under vacuum, 9,9-difluorobicyclo[4.3.0]nona-2,4,7-triene, **5**† was produced instead of the desired diene (see Scheme 4).



Scheme 4

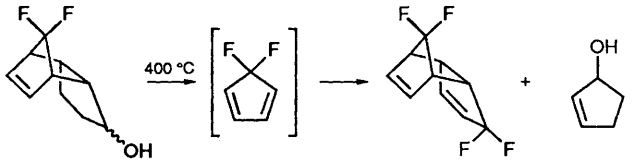
Presumably, this results from a Cope rearrangement,[8] which interconverts the allylic CO and the bridge CF_2 positions, followed by elimination of carbon monoxide.

Since the absence of products from the retro-Diels–Alder

* **4**: δ_H(250 MHz; $CDCl_3$) 7.34 (1 H, dd, *J* 5.0, 2.5), 6.13 (1 H, d, *J* 6), 6.03–5.84 (1 H, m), 5.84–5.71 (1 H, m), 3.78–3.63 (1 H, m), 3.55–3.37 (1 H, m), 3.37–3.03 (1 H, m) and 3.03–2.89 (1 H, m); δ_C(62.9 MHz; $CDCl_3$) 207.21 (d, *J* 1.5, C=O), 161.59 (d, *J* 0.8, CH), 139.70 (d, *J* 1.5, CH), 134.97 (dd, *J* 269.3, 271.6, CF_2), 129.94 (d, *J* 5.6, CH), 129.69 (d, *J* 5.7, CH), 48.29 (t, *J* 20.7, CH), 47.76 (dd, *J* 19.1, 19.9, CH), 45.51 (m, CH) and 43.31 (d, *J* 2.8, CH); δ_F(235.3 MHz; $CDCl_3$) −118.0 (1 F, dm, *J* 183) and −125.3 (1 F, d, *J* 183) (Found: M^+, 182.0543. $C_{10}H_8F_2O$ requires *M*, 182.0544).

† **5**: δ_H(300 MHz; $CDCl_3$) 6.29 (1 H, dd, *J* 5.9, 2.5), 6.03 (1 H, dd, *J* 5.9, 2.5), 5.96 (1 H, ddd, *J* 9.8, 5.7, 2.2 with extra long range allylic couplings of <0.2 Hz), 5.83 (1 H, ddd, 9.6, 5.7, 2.5), 5.73 (1 H, dd, *J* 9.8, 4.6), 5.59 (1 H, dd, *J* 9.6, 4.0), 3.78–3.66 (1 H, m) and 3.37–3.21 (1 H, m); δ_C(75.5 MHz; $CDCl_3$) 142.6 (t, *J* 10, CH), 133.5 (dd, *J* 246, 243, CF_2), 127.3 (t, *J* 28, CH), 123.8 (d, *J* 1, CH), 123.4 (dd, *J* 4, 2, CH), 121.5 (CH), 120.1 (dd, *J* 1, 7, CH), 43.6 (dd, *J* 27, 22, CH) and 41.9 (d, *J* 4, CH); δ_F(235.3 MHz, $CDCl_3$) −85.8 (1 F, ddd, *J* 251, 18, 3) and −91.1 (1 F, dt, *J* 251, 8) (Found: M^+, 154.0596. $C_9H_8F_2$ requires *M*, 154.0594).

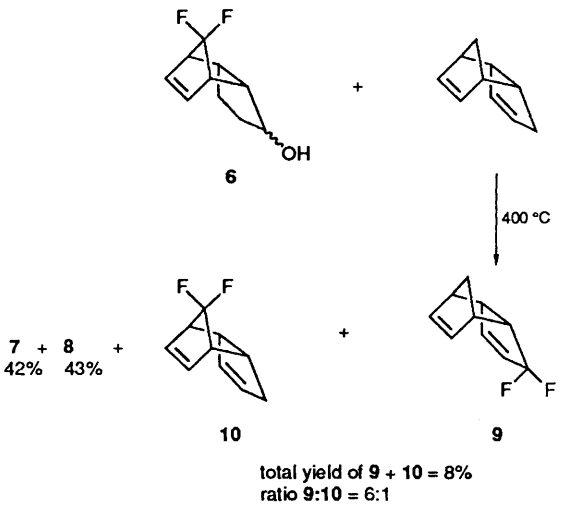
reaction in the pyrolysis of **4** may be due to the unfavourable co-formation of the unstable cyclopentadienone, it was decided to investigate the pyrolysis of a reduced derivative of **4**. Reaction of **4** with sodium borohydride provided 10,10-difluorotricyclo-[5.2.1.$0^{2,6}$]dec-8-en-3-ol **6*** in good yield (93%). Pyrolysis of this compound at 400 °C yielded, after column chromatography, a volatile solid identified as the deca-3,8-diene **7**† and cyclopent-2-enol **8** (see Scheme 5). Further, co-pyrolysis of **6** and



Scheme 5

dicyclopentadiene produced not only **7** and **8** but also the mixed Diels–Alder adducts **9**‡ and **10**§ as an inseparable mixture (see Scheme 6). The ratio of **9**:**10** was 6:1 (^{19}F NMR) indicating, as expected, the preference of **1** to act as the dienophile rather than a diene in the presence of cyclopentadiene. These results represent the first *in situ* trapping of 5,5-difluorocyclopentadiene **1**.

Our current studies are concentrating on trapping **1** with other dienophiles. However attempts to trap **1** using dimethyl



Scheme 6

acetylenedicarboxylate (DMAD) either by condensing the vapours from the pyrolysis tube onto DMAD at −78 °C or by passing DMAD through the furnace with **6** both failed to yield the desired adducts (only **7** and **8** were produced). Further studies are currently underway in order to develop methods of exploiting this new diene.

Acknowledgements

I wish to thank Professor S. M. Roberts and Dr. B. Ridge for helpful discussions and Dr. V. Sik and Dr. O Howarth for NMR spectra.

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Paper 2/03495F
Received 2nd *July* 1992
Accepted 10*th July* 1992

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* **6**: δ_H(250 MHz; $CDCl_3$), 6.41–6.32 (1 H, m), 6.18–6.09 (1 H, m), 4.33 (1 H, q, *J* 6), 3.19–2.59 (4 H, m), 1.94–1.46 (4 H, m) and 1.46–1.16 (1 H, m); δ_C(62.9 MHz; $CDCl_3$) 135.61 (dd, *J* 272, 270, CF_2), 134.91 (d, *J* 5, CH), 130.14 (d, *J* 6, CH), 74.33 (d, *J* 1, CH), 49.54 (dd, *J* 20, 18, CH), 48.48 (t, *J* 19, CH), 47.80 (d, *J* 2, CH), 42.26 (d, *J* 2, CH), 37.59 (CH_2) and 24.60 (d, *J* 1, CH_2); δ_F(235.3 MHz; $CDCl_3$) −116.8 (1 F, dm, *J* 182) and −132.2 (1 F, d, *J* 182) (Found: M^+, 186.0856. $C_{10}H_{12}F_2O$ requires *M*, 186.0857).

† **7**: δ_H(250 MHz; $CDCl_3$) 6.13–5.95 (2 H, m), 5.89–5.79 (2 H, m), 3.68–3.49 (1 H, m) and 3.26–3.03 (3 H, m); δ_C(62.9 MHz; $CDCl_3$), 140.28 (t, *J* 10.1, CH), 134.79 (t, *J* 269.8, CF_2), 131.81 (dd, *J* 29.8, 27.5, CH), 130.99 (dd, *J* 5.2, 2.7, CH), 129.20 (d, *J* 6.2, CH), 48.00 (ddd, *J* 20.1, 18.3, 4.9, CH), 47.50 (dd, *J* 23.2, 19.8, 3.3, CH), 47.23 (m, CH) and 45.47 (ddd, *J* 29.1, 19.9, 2.6, CH) (one CF_2 obscured by other signals); δ_F(235.3 MHz, $CDCl_3$) −65.7 (1 F, dm, *J* 263), −73.7 (1 H, dt, *J* 263, 4), −128.2 (1 F, dd, *J* 185 and 4) and −117.0 (1 F, dq, *J* 185, 2) (Found: M^+, 204.0557. $C_{10}H_8F_4$ requires *M*, 204.0562).

‡ **9**: δ_H(250 MHz; $CDCl_3$) 6.11–5.92 (2 H, m), 5.78 (1 H, dd, *J* 5.5, 3.0), 5.64 (1 H, d, *J* 5.5), 3.48–3.26 (1 H, m), 3.13–3.05 (1 H, m), 3.00–2.84 (2 H, m), 1.66 (1 H, d, *J* 9) and 1.48 (1 H, d, *J* 9); δ_C(75.5 MHz; $CDCl_3$) 143.5 (t, *J* 10.2, CH), 133.5 (d, *J* 2.5, CH), 132.5 (CH), 129.5 (dd, *J* 26.9, 19.0, CH), 51.9 (CH_2), 51.3 (t, *J* 3.8, CH), 49.6 (dd, *J* 26.6, 20.4, CH), 44.6 (d, *J* 5.8, CH) and 43.8 (t, *J* 3.7, CH) (CF_2 too weak to observe); δ_F(235.3 MHz; $CDCl_3$) −75.9 (1 F, ddd, *J* 260, 23, 3) and −99.3 (1 F, ddd, *J* 260, 14, 7) (Found: M^+, 168.0761. $C_{10}H_{10}F_2$ requires *M*, 168.0751).

§ **10**: δ_H(250 MHz) 6.11–5.92 (2 H, m), 5.61–5.58 (1 H, m), 5.48–5.40 (1 H, m), 3.48–3.26 (1 H, m) and 3.00–2.84 (3 H, m), CH_2 obscured by **9**; δ_C signals obscured by **9**; δ_F(235.3 MHz; $CDCl_3$) −120.3 (1 F, d, *J* 184) and −130.7 (1 F, d, *J* 184).