

Elemental fluorine. Part 6.[†] Fluorination of cyclic 1,3-diketones and related compounds

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Direct fluorination of cyclic 1,3-diones gives 2-mono- and 2,2-di-fluorinated products. The monofluorinated compounds crystallise in their enol forms and the difluorinated compounds form stable monohydrates whose crystal structures have been elucidated. Direct fluorination of phloroglucinol[‡] in formic acid yields 1,1,3,3,5,5-hexafluoro-2,2,4,4,6,6-hexahydroxycyclohexane.

Introduction

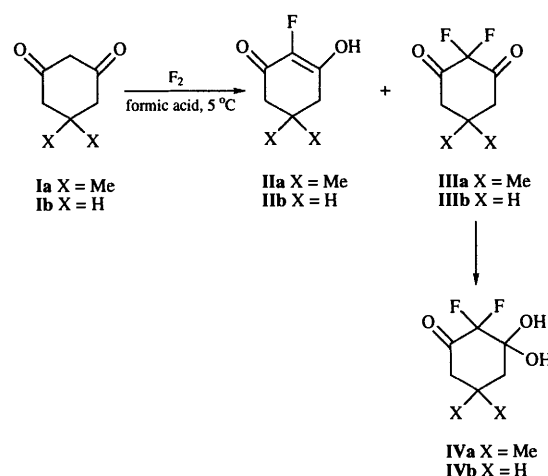
There is much interest in the preparation of fluorinated 1,3-dicarbonyl compounds, since they are useful building blocks for the synthesis of more complex molecules containing fluorine that are of potential value to both the pharmaceutical and agrochemical industries. Hitherto, most of the work on 1,3-diketones has been carried out on acyclic systems, but fluorinated derivatives of 5,5-dimethylcyclohexane-1,3-dione **Ia** have been prepared by Purrington² and Zajc³ with their respective co-workers. Purrington treated the trimethylsilyl ether derived from **Ia** with fluorine at $-78\text{ }^{\circ}\text{C}$ in CFCl_3 and obtained 2-fluoro-5,5-dimethylcyclohexane-1,3-dione **IIa** in 42% yield. Zajc treated **Ia** with xenon difluoride, in the presence of a mixture of cross-linked poly(styrene-4-vinylpyridine) and the boron trifluoride complex of this same copolymer, and claimed that 2,2-difluoro-5,5-dimethylcyclohexane-1,3-dione **IIIa** was obtained in high yield. We now believe that the compound isolated by Zajc was in fact the monohydrate of **IIIa**, i.e. **IVa** (*vide infra*).

Recently we reported that acyclic 1,3-diketones react with elemental fluorine to give mainly the corresponding 2-fluoro compounds in high yield.⁴ In the present paper, we describe the direct fluorination of cyclic 1,3-diketones and the related phloroglucinol, which can be regarded as a cyclic 1,3,5-triketone, where it will be noted that the products are significantly different from those produced in the fluorination of the acyclic systems described previously.

Results and discussion

When pentane-2,4-dione in formic acid was treated with fluorine, reaction occurred rapidly to give 3-fluoropentane-2,4-dione in high yield, but further fluorination was very slow. The slowness of this second fluorination was attributed to the fact that 3-fluoropentane-2,4-dione exists in its keto form in formic acid and to the fact that the rate of conversion to the reactive enol form is slow in this medium.⁴ In contrast to these earlier results, we have now found that, under similar conditions, the fluorination of the cyclic diketones **Ia** or **Ib** leads rapidly to the difluorinated compounds **IIIa** and **IIIb**. Thus, when **Ia** and **Ib** were treated with fluorine in formic acid at about $5\text{ }^{\circ}\text{C}$, both mono- and di-substituted compounds were obtained, with the

relative amounts of these fluorinated derivatives and starting material in the reaction product depending on the amount of fluorine used and the duration of the reaction (Scheme 1, Table



Scheme 1 Fluorination of cyclic 1,3-diketones

1). Reactions were worked up by removing solvent at reduced pressure, followed by reduced pressure distillation (entries 1 and 2) or sublimation (entries 3 and 4) of the residue. Zajc³ described the compound **IIIa** as a solid having a broad singlet at $\delta -124.3$ in its ^{19}F NMR spectrum (CFCl_3). For the following reasons, we now believe that the compound described by Zajc was in fact the monohydrate of **IIIa**, i.e. **IVa**. The distillate obtained from the fluorination of **Ia** with an excess of fluorine (entry 1) showed, in its ^{19}F NMR spectrum (dry $[\text{}^2\text{H}_6]\text{acetone}$), a sharp singlet at $\delta -121.4$ and a small broad singlet at $\delta -129.0$. Further purification by preparative scale GLC afforded **IIIa**, a liquid which showed only the sharp singlet in its ^{19}F NMR spectrum and resonances attributable to CO , CF_2 , CH_2 , $\text{C}(\text{CH}_3)_2$ and CH_3 in its ^{13}C NMR spectrum. Addition of water to a $[\text{}^2\text{H}_6]\text{acetone}$ solution of this liquid product caused the sharp singlet in the ^{19}F NMR spectrum almost to disappear and be replaced by a singlet at $\delta -129.0$. Furthermore, the ^{13}C NMR spectrum now had resonances attributable to $\text{C}(\text{OH})_2$ and $\text{CH}_2\text{C}(\text{OH})_2$ as well as CO , CF_2 , CH_2 , $\text{C}(\text{CH}_3)_2$ and CH_3 , i.e. a spectrum consistent with the monohydrate, **IVa**. The presence of a difluoromethylene group in **IVa** was confirmed when its ^{19}F NMR spectrum was measured at $-90\text{ }^{\circ}\text{C}$, a temperature at which ring interconversion was negligible, and

[†] Presented in part at the 211th ACS National Meeting, New Orleans, April, 1996.

[‡] IUPAC name 1,3,5-trihydroxybenzene.

Table 1 Fluorination of cyclic 1,3-diones^a

	Substrate	Molar ratio F ₂ :Substrate	t/h	Yield (%)		Conversion (%)
				II	III	
1	Ia	2.2:1	4.25	—	75	100
2	Ia	1.1:1	1.0	40	33	70
3	Ib	2.6:1	4	—	80	100
4	Ib	1.0:1	2	27	39	85

^a Temperature 0.6 °C. F₂ diluted to 10% v/v with nitrogen.

Table 2 Selected bond lengths in IVa and IVb

Bond	Length/Å	
	IVa	IVb
C(2)–F(22)	1.372(2)	1.374(2)
C(2)–F(21)	1.358(2)	1.359(2)
C(3)–O(32)	1.419(2)	1.421(2)
C(3)–O(31)	1.396(2)	1.410(2)
C(5)–C(52)	1.534(2)	—
C(5)–C(51)	1.531(2)	—

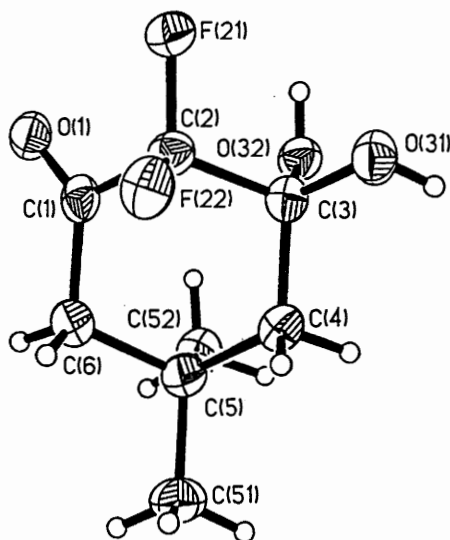


Fig. 1 ORTEP plot of IVa. Thermal ellipsoids are drawn at 50% probability level, the radius of the hydrogen atoms is chosen arbitrarily.

the broad singlet was resolved into two doublets (AX) at δ –112.0 and –147.2 ($J_{F,F}$ 239 Hz).

Hydrate IVa is stable at room temperature and crystals of this compound were obtained when a wet acetone solution of IIIa was slowly evaporated. A full single crystal X-ray analysis has been carried out and this confirmed the structure of IVa as being the monohydrate of the diketone IIIa. Molecule IVa adopts the expected chair conformation shown in Fig. 1, where the lengths of the axial bonds between carbon and the pairs of electronegative substituents F(21)/F(22) and O(31)/O(32) are longer by 0.014 and 0.023 Å, respectively, than the corresponding equatorial bonds. (These differences are more than three times the estimated standard deviation of the relevant bond length and are therefore considered to be significant). This is probably a manifestation of the anomeric effect where bond lengthening of the axial oxygen or halogen substituents has been observed for a variety of systems.⁵ The two methyl groups show no such axial–equatorial differences. These and selected bond lengths are given in Table 2. Analysis of non-bonded contacts reveals a network of hydrogen bonds

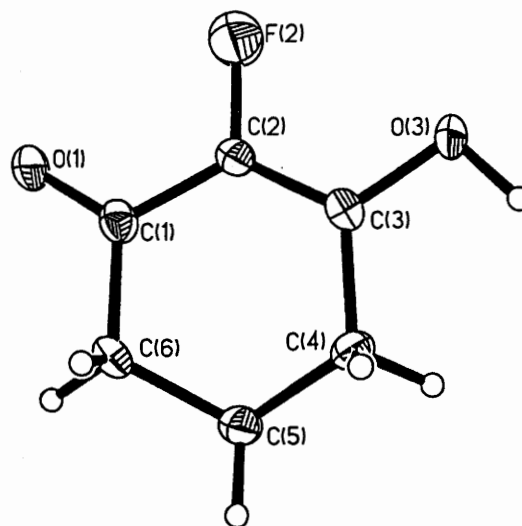


Fig. 2 ORTEP plot of IIb (for details see Fig. 1)

involving O–H...O (hydroxy) and O–H...O (keto) as well as O–H...F interactions. The O–H...O hydrogen bonds, which are considerably shorter than the O–H...F interactions (Table 3) form the basis of a two-dimensional hydrogen bond network.

Products obtained from the fluorination of 1,3-cyclohexanedione Ib, *i.e.* the mono- and di-fluorinated diketones IIb and IIIb and the hydrate IVb, correspond to those obtained from the fluorination of Ia. A crystal structure of IIb has been obtained (Fig. 2) which shows that this compound crystallises in its enol form, similar to the corresponding dimethyl compound IIa, which has been described by Purrington.² Structure IIb can be described as an envelope with the flap being formed by C(4), C(5) and C(6). The angle between the two planes is 42.3° and the atoms C(1), C(2), C(3), C(4), C(6), O(1), O(3) and F(2) deviate by no more than 0.09 Å from the main plane. Compound IIb is structurally similar to IIa, except for the carbon–carbon double bond, which is 0.025 Å shorter in IIa, and the flap angle in IIa of 44.2°. Hydrogen bonding is observed in both compounds, which for IIb involves O(3)–H(3)...O'(1), [O(3)...O'(1) 2.565 Å ($1+x, -y, \frac{1}{2}+z$), H(3)...O'(1) 1.57 Å, O(3)–H(3)...O'(1) 165°] but there is no evidence for any close O–H...F interactions.

Like IIIa, the difluoro compound IIIb readily formed a stable monohydrate IVb whose NMR spectra and crystal structure (Fig. 3) parallel those of IVa. The axial carbon–fluorine bond length in IVb is 0.015 Å longer than the equatorial (*i.e.* similar to IVa), but the difference between the two carbon–oxygen bonds, at 0.011 Å, is less pronounced (Table 2). Hydrogen bonding in this compound shows the rather unusual feature of two homodromic cycles with opposite sense of rotation in stacks along the *c*-axis (Fig. 4). Starting from O(32)–H(32)...O'(32) [O(32)...O'(32) 2.791 Å ($y, \frac{1}{2}-x, \frac{1}{2}-z$), H(32)...O'(32) 1.981 Å, O(32)–H(32)...O'(32) 162°] the cycle continues with the same bond parameters *via* ($\frac{1}{2}-x, \frac{1}{2}-y, z$) and ($\frac{1}{2}-y, x, \frac{3}{2}-z$) back to (x, y, z). The other cycle is formed by O(31)–

H(31)⋯O'(31) [O(31)⋯O'(31) 2.773 Å ($y, \frac{1}{2} - x, \frac{1}{2} - z$), H(31)⋯O'(31) 1.935 Å, O(31)–H(31)⋯O'(31) 165°]. The symmetry operators in this cycle are ($\frac{1}{2} - y, x, \frac{1}{2} - z$), ($\frac{1}{2} - x, \frac{1}{2} - y, z$), ($y, \frac{1}{2} - x, \frac{3}{2} - z$) and back to (x, y, z).

Hitherto, we have considered that phloroglucinol **V**, which can be regarded as the tri-enol of cyclohexane-1,3,5-trione, would be too reactive for controlled direct fluorination. Remarkably, when this compound was fluorinated in formic acid, the hexafluorohexahydroxy product **VI** (the trihydrate of the hexafluorotrione) was obtained in high yield (Scheme 2). The ^{19}F NMR spectrum [two doublets of equal intensity at $\delta -118.7$ ($J_{\text{F,F}}$ 266.9 Hz) and -140.3 ($J_{\text{F,F}}$ 266.8 Hz)] and the ^{13}C NMR spectrum [triplet at $\delta 115.3$ ($^1J_{\text{C,F}}$ 266 Hz, CF_2) and multiplet at $\delta 92.6$, $\text{C}(\text{OH})_2$] are consistent with the proposed structure being quite rigid. Further support for this structure

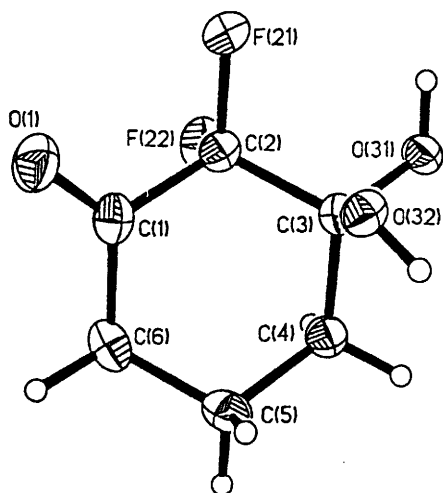


Fig. 3 ORTEP plot of **IVb** (for details see Fig. 1)

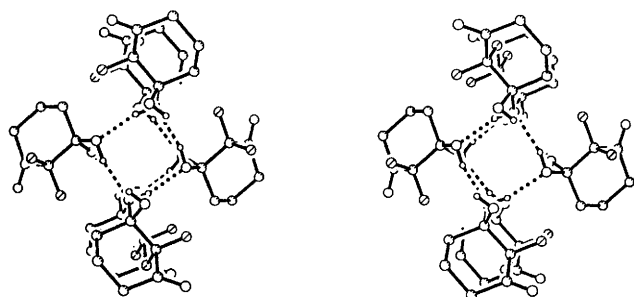
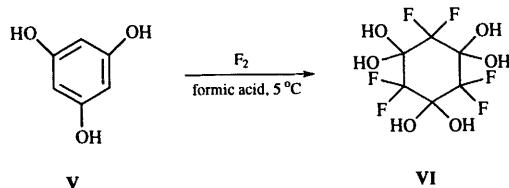


Fig. 4 Stereoview of the homodromic cycles of hydrogen bonds formed by **IVb**. The crystallographic c -axis is perpendicular to the drawing plane.



Scheme 2 Fluorination of phloroglucinol

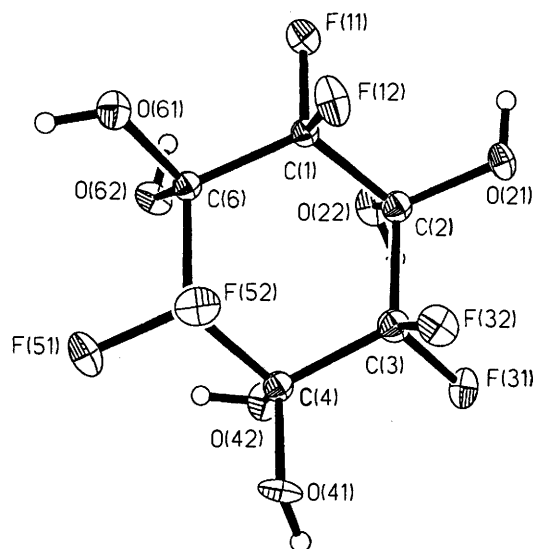


Fig. 5 ORTEP plot of **VI**. Carbon atoms refined with isotropic displacement parameters only (for further details, see Fig. 1).

comes from single crystal X-ray data (see Experimental section) which shows that average C–F and C–O bond lengths are 1.360(5) and 1.40(2) Å, respectively, and that the molecule crystallises with three molecules of water (Fig. 5).

An indication of the tenacity with which water is bound to **VI** was given by its vacuum sublimation at *ca.* 120 °C, which gave material whose ^{19}F and ^{13}C NMR spectra were consistent with the loss of only one molecular equivalent of water. The addition of water to an acetone solution of this material rapidly regenerated the trihydrate **VI**.

In conclusion, unlike the fluorination of acyclic 1,3-diones, where the formation of difluoro compounds is very slow, the fluorination of cyclic 1,3-diones leads to the rapid formation of 2,2-difluoro compounds. This is believed to be due to the monofluoro compounds **IIa** and **IIb** not only crystallising in their enol forms but also retaining this structure in formic acid where lone singlets in their ^{19}F NMR spectra are observed. The difluorinated compounds **IIIa** and **IIIb** have a high affinity for water and readily form stable hydrates, in common with other fluorinated carbonyl compounds.⁶

The chemistry of these novel fluorinated compounds is being investigated further.

Experimental

Generally, ^{19}F NMR spectra were recorded on a Bruker AC250 spectrometer operating at 250 MHz for hydrogen or 235 MHz for fluorine, with tetramethylsilane and fluorotrichloromethane as internal references. Chemical shifts (δ) are recorded in ppm and coupling constants (J) in Hz. For the low temperature ^{19}F NMR spectrum experiment, a Varian VXR 400 was used. ^{13}C NMR spectra were measured on a Varian Gemini 200 spectrometer. The spectra were recorded in dry $(\text{CD}_3)_2\text{CO}$. Except where stated otherwise, mass spectra were measured on a Fisons Trio 1000 mass spectrometer in the electron impact mode coupled to a Hewlett Packard 5890 II gas chromatograph fitted with a silicone elastomer coated column (SE 30; 25

Table 3 Hydrogen bonds found in **IVa**. The donor (D)–acceptor (A) distances as well as hydrogen–acceptor distances and corresponding angles are given. The position of the acceptor is generated by the symmetry operator given.

	D⋯A/Å	H⋯A/Å	D–H⋯A (°)	Symmetry operator
O(31)–H(31)⋯O(32)	2.814	2.00	169	$2 - x, 1 - y, 1 - z$
O(32)–H(32)⋯O(1)	2.854	2.04	169	$2 - x, -y, 1 - z$
O(32)–H(32)⋯F(21)	2.957	2.58	109	$2 - x, -y, 1 - z$
O(32)–H(32)⋯F(21)	2.763	2.43	105	x, y, z

m × 0.2 mm i.d.). Accurate mass measurements were determined at the EPSRC Mass Spectrometry Service Centre, Swansea.

General procedure for fluorination reactions

Reactions were carried out under the conditions outlined in Scheme 1. An FEP reaction vessel, fitted with a stirrer, was charged with a solution of the substrate in formic acid, purged with nitrogen and cooled so that the internal temperature was maintained at ca. 5 °C. A metered flow of 50% fluorine in nitrogen (v/v) was diluted further with nitrogen to 10% (v/v) before being passed through the solution. Exit gases were led to a soda lime-filled scrubbing tower. When reaction was complete, the vessel was purged with nitrogen before solvent was removed from the product at reduced pressure.

Fluorination of 5,5-dimethylcyclohexane-1,3-dione. Table 1, entry 1.—Removal of the solvent gave, on cooling, a light coloured solid which was shown by GLC to be mainly one compound. Its ¹⁹F NMR spectrum had a small sharp singlet (δ -121.4) and a large broad singlet (δ -129.0). This crude material was transferred to a short path distillation apparatus and distilled under reduced pressure to give a liquid whose ¹⁹F NMR spectrum now showed mainly the sharp singlet at δ -121.4. Preparative scale GLC was used to isolate the main product, 2,2-difluoro-5,5-dimethylcyclohexane-1,3-dione **IIIa** (Found: M^+ , 176.0649. C₈H₁₀F₂O₂ requires M , 176.0649); δ_F -121.4 (s); δ_H 1.09 (6 H, m, Me), 2.95 (4 H, m, CH₂); δ_C 28.8 (s, CH₃), 31.3 [s, C(CH₃)₂], 51.5 (s, CH₂), 109.6 (t, ¹J_{C,F} 260.5 CF₂), 195.5 (t, ²J_{C,F} 23.3, C=O).

A sample of **IIIa** was dissolved in aqueous acetone and slowly evaporated to give the crystalline 2,2-difluoro-5,5-dimethylcyclohexane-1,3-dione monohydrate **IVa**; δ_F -129.0 (br s) [at -90 °C; -112.0 (d, $J_{F,F}$ 239), -147.2 (d, $J_{F,F}$ 239)]; δ_H 1.08 (6 H, m, Me), 2.00 (2 H, m, CH₂), 2.46 (2 H, m, CH₂); δ_C 30.2 (s, CH₃), 32.5 [s, C(CH₃)₂], 47.9 [s, C(OH)₂CH₂], 51.3 (s,

COCH₂), 95.7 [t, ²J_{C,F} 22.6, C(OH)₂], 114.1 (t, ¹J_{C,F} 258.4, CF₂), 198.2 (t, ²J_{C,F} 24.7, C=O); m/z 176 (M^+ , 7%), 41 (100).

Table 1, entry 2.—Starting material was identified by GC-MS. 2-Fluoro-5,5-dimethylcyclohexane-1,3-dione **IIa** was identified by its ¹⁹F NMR spectrum [δ_F -169.6 (s), lit.,² -171 (s)] and mass spectrometry [m/z 158 (M^+ , 23%), 83 (100)]. The composition of the reaction product was estimated by GLC.

Fluorination of cyclohexane-1,3-dione. Table 1, entry 3.—Removal of the solvent gave, on cooling, a light coloured solid which had a small sharp singlet (δ_F -119.3) and a large broad singlet (δ_F -128.4) in its ¹⁹F NMR spectrum. This crude material was sublimed under vacuum to give a white solid which was further purified by preparative scale GLC to give 2,2-difluorocyclohexane-1,3-dione **IIIb**, mp 70 °C (Found: C, 48.0; H, 4.4; M^+ , 148.0336. C₆H₈F₂O₂ requires C, 48.6; H, 4.1%; M , 148.0336); δ_F -119.3 (s); δ_C 17.6 (s, CH₂CH₂CH₂), 38.2 (s, COCH₂), 114.7 (t, ¹J_{C,F} 259.4, CF₂); δ_C 195.8 (t, ²J_{C,F} 23.1, C=O). An aqueous acetone solution of **IIIb** gave, on slow evaporation, the crystalline 2,2-difluorocyclohexane-1,3-dione monohydrate **IVb** (Found: C, 42.9; H, 4.9. C₆H₈F₂O₃ requires C, 43.3; H, 4.9%; δ_F -128.4 (br s) [at -90 °C; -112.6 (d, $J_{F,F}$ 249.6), -145.7 (d, $J_{F,F}$ 249.6)]; δ_H 1.84 (2 H, m, CH₂), 2.06 (2 H, m, CH₂), 2.54 (2 H, m, CH₂); δ_C 19.5 (s, CH₂CH₂CH₂), 35.2 [s, CH₂C(OH)₂], 38.2 (s, COCH₂), 96.0 [t, ²J_{C,F} 22.9, C(OH)₂], 114.6 (t, ¹J_{C,F} 258.5, CF₂), 198.2 (t, ²J_{C,F} 25.0, C=O); m/z 148 (M^+ , 6%), 42 (100).

Table 1, entry 4.—Starting material and **IIIb** were identified by GC-MS. 2-Fluorocyclohexane-1,3-dione **IIb** was isolated by fractional sublimation and recrystallisation twice from ethyl acetate, mp 152–153 °C (Found: M^+ , 130.0430. C₆H₇FO₂ requires M , 130.0430); δ_F -167.4 (s); δ_C 20.9 (s, CH₂CH₂CH₂), 22.0 [s, CH₂C(OH)₂], 32.9 (s, CH₂C=O), 105.2 (s, COH), 140.7 (d, ¹J_{C,F} 236.0, CF), 199.1 (d, ²J_{C,F} 13.8, C=O). The composition of the reaction product was estimated by GLC.

Table 4 Crystal data for **IIb**, **IVa**, **IVb** and **VI**

	IIb	IVa	IVb	VI
Formula	C ₆ H ₇ FO ₂	C ₈ H ₁₂ F ₂ O ₃	C ₆ H ₈ F ₂ O ₃	C ₆ H ₁₂ F ₆ O ₉
M_r	130.12	194.18	166.12	392.16
Crystal system	Monoclinic	Monoclinic	Tetragonal	Monoclinic
Space group	<i>Cc</i>	<i>P2₁/c</i>	<i>P4₂/n</i>	<i>Cc</i>
<i>a</i> /Å	6.650(3)	7.8056(7)	15.746(2)	11.000(2)
<i>b</i> /Å	11.875(3)	7.5378(7)	15.746(2)	12.292(3)
<i>c</i> /Å	7.374(4)	15.558(1)	5.642(1)	8.244(2)
β (°)	102.98(4)	97.323(1)	—	99.5113
<i>V</i> /Å ³	567.4(4)	907.9(1)	1398.9(4)	1099.4(4)
<i>Z</i>	4	4	8	4
Temperature/K	150(2)	150(2)	150(2)	150(2)
No. reflections cell	25	512	442	25
θ_{min} , θ_{max} (°)	15, 20	12, 21	12, 23	15, 20
Crystal habit	Colourless prism	Colourless, irregular	Colourless prism	Colourless plates
Crystal dimensions/mm	0.225 × 0.15 × 0.075	0.4 × 0.6 × 1.0	0.40 × 0.15 × 0.15	0.45 × 0.4 × 0.15
D_x /Mg m ⁻³	1.523	1.421	1.578	2.067
<i>F</i> (000)	272	408	688	696
Radiation, λ /Å	Cu K α , 1.541 84	Mo K α , 0.710 73	Mo K α , 0.710 73	Cu K α , 1.541 84
μ /mm ⁻¹	1.163	0.132	0.157	2.282
Absorption corr.	Empirical	Empirical	None	None
Transmission min, max	0.9039, 1.0000	0.5538, 0.5816	—	—
θ_{max} (°)	75.06	25.40	25.66	74.89
No. reflections measured	1110	3635	5901	1098
Unique, obs. [<i>I</i> > 2 σ (<i>I</i>)]	1021, 948	1540, 1475	1227, 979	1038, 985
<i>R</i> _{int}	0.0160	0.0426	0.0422	0.0613
Weighting scheme ^a	0.1100, 0.1569	0.055, 0.3362	0.024, 0.93	0.1858, 5.9886
Extinction coefficient	0.0030(14)	0.0724(65)	0.0057(9)	0.0033(11)
No. parameters	85	129	133	163
<i>R</i> (<i>F</i>) observed	0.0495	0.0385	0.0338	0.0667
<i>R</i> (<i>F</i> ²) all	0.1428	0.1066	0.0859	0.2347
<i>S</i>	1.086	1.049	1.103	1.080
Max. Δ /σ	0.000	0.000	0.000	0.000
Min., max., $\Delta\rho$ /e Å ⁻³	-0.4, 0.3	-0.2, 0.3	-0.2, 0.2	-0.7, 0.6

^a The weighting scheme is of the form $w = \{\sigma^2(F_o^2) + [\frac{1}{3}m(F_o^2 + 2F_c^2)]^2 + \frac{1}{3}n\}^{-1}$.

Fluorination of phloroglucinol. Phloroglucinol (1.6 g, 125 mmol) in formic acid (50 ml) was treated with fluorine (0.08 ml) diluted to 10% v/v for 4 h at ca. 5 °C. Removal of the solvent under reduced pressure gave an off-white solid whose ^{19}F NMR spectrum showed two doublets of equal intensity at $\delta -118.7$ and -140.4 . Vacuum sublimation gave a white sublimate (2.1 g) which showed additional resonances at $\delta -123.4(2)$ and $-128.8(1)$. Slow evaporation of a solution of this material in aqueous acetone gave crystalline 1,1,3,3,5,5,-hexafluoro-2,2,4,4,6,6-hexahydroxycyclohexane; $\delta_{\text{F}} -118.7$, (d, $J_{\text{F,F}}$ 269.4), -140.4 , (d, $J_{\text{F,F}}$ 269.4); δ_{C} 115.3 (t, $^1J_{\text{C,F}}$ 266.5, CF_2), 92.6 [m, $\text{C}(\text{OH})_2$]; m/z (FAB $^-$), 287 (M - H $^-$).

Crystal structure analysis of IIb, IVa, IVb and VI

Data collection and data reduction. Data were collected on a Rigaku AFC6S four circle diffractometer (IIb, VI) and using a Siemens SMART-CCD system (IVa, IVb). Both diffractometers are equipped with Oxford CryoSystems low temperature attachments. All crystal data are given in Table 4. The data collection parameters for the Siemens SMART⁷ area detector system were selected in such a way as to cover at least a hemisphere of data. This was achieved by three ω -scans (total scan range 202, 143 and 77°) with ϕ -settings of 0, 88 and 180°. The crystal to detector distance was 61 mm, with a frame width of 0.3° ω and 10 s exposure time. Integrated intensities were obtained by using the SAINT⁸ program. Further data reduction, space group determination and graphics were carried out using SHELXTL.⁹

Structure solution and refinement. All crystal structures were determined by using the direct methods options from the SHELXS-86¹⁰ program. Least-squares refinement was carried out by minimising the function $w(F_o^2 - F_c^2)^2$ using SHELXL-93.¹¹ Atomic positions and anisotropic displacement parameters were refined for all non-hydrogen atoms. Hydrogen atoms were located by difference Fourier synthesis and their atom positions were refined with isotropic displacement parameters (IVb). In the case of IIb and IVa, hydrogen atoms were constrained to idealised positions and their isotropic displacement parameters were tied to 1.2 times the corresponding carbon atoms, except for hydroxy protons which were refined freely (only U_{iso} for IIb). Compound IIb crystallises as a racemic twin with a 2:1 ratio, which was included in the

refinement process, and no attempt was made to determine the absolute structure. The structure of VI is crystallographically more challenging since oxygen and fluorine have similar scattering power for X-rays. Assuming the alternating scheme of geminal difluoro and dihydroxy substituents on the cyclohexyl ring, two alternative models were tested which had F and OH interchanged. Both bond length and R -value (6.7 and 7.5%, respectively) criteria support the reported assignment. Additionally, it is possible to transform this unit cell setting into a pseudohexagonal cell with $a = 12.287$ and $c = 12.607$ Å. Consequently, data quality might be affected by the presence of a small twin contribution.

Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/40.

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