ELSEVIER

Journal of Fluorine Chemistry 74 (1995) 15–19

JOURNAL OF FLUORINE CHEMISTRY

Crystalline hydrogen-bonded adducts of dimethyl sulphoxide and 7-hydroxypolyfluoroquinolones (chromones)

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Received 22 June 1994; accepted 11 January 1995

Abstract

A stable crystalline hydrogen-bonded adduct of dimethyl sulphoxide (DMSO) and 7-hydroxy-5,6,8-trifluoro-2-carboxychromone has been prepared by the reaction of 2-carboxy-5,6,7,8-tetrafluorochromone with KOH/glycerol in DMSO. It has been found that pentafluorophenol and also 1-cyclohexyl-7-hydroxy-5,6,8-trifluoro-4(1*H*)-4-oxoquinoline-2-carboxylic acid form the corresponding crystalline hydrogen-bonded adducts with DMSO. The structure of the latter has been established from an X-ray crystallographic study.

Keywords: Hydrogen-bonded adducts; Dimethyl sulphoxide; Chromones; Quinolones; Pentafluorophenol; Single-crystal X-ray diffraction

1. Introduction

The capability of dimethyl sulphoxide (DMSO) for hydrogen bonding with various phenols is well known [1–4]. Although a great deal of work has been published concerning hydrogen-bonded complexes of DMSO and fluorine-containing phenols in solvents [1,2,4], none has been reported on crystalline adducts between DMSO and pentafluorophenol, to say nothing of 7-hydroxy polyfluoro-containing chromone(quinolone) systems.

In this paper, the interaction of 1-cyclohexyl-7-hydroxy-5,6,8-trifluoro-4(1*H*)-4-oxoquinoline-2-carboxylic acid and of 2-carboxy-7-hydroxy-5,6,8-trifluorochromone and pentafluorophenol with DMSO is described.

2. Experimental details

Melting points were measured in open capillaries and are reported uncorrected. Infrared spectra were measured on a Specord 75 IR spectrometer. ^{1}H NMR spectra were recorded on a Tesla BS-567 A instrument (^{1}H:100 MHz) using TMS as internal standard. ^{19}F NMR spectra were recorded on a Tesla BS-587 A instrument (^{19}F:75 MHz) using $CFCl_3$ as internal standard. All chemical shifts are reported in ppm and wavenumbers in cm^{-1}.

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SSDI 0022-1139(95)03249-5

2.1. Materials

Compounds **1** and **5** were prepared from pentafluorobenzoylpyruvic acid as described previously [5]. Compound **7** was prepared in a corresponding manner from pentafluorobenzoylpyruvic ester or pentafluorobenzoylpyruvic acid [5,6]. Compound **6** was made via our reported method [7].

2.2. X-Ray crystallographic study of compound 2

Crystal data: $C_{16}H_{14}F_3NO_4 \cdot (CH_3)_2SO$, M = 419.42, monoclinic; $a = 8.238(2)$, $b = 24.537(5)$, $c = 10.505(2)$ Å, $\beta = 115.27(2)°$, $V = 1920.2(7)$ Å^3, $P2_1/c$, $D_x = 1.459$ g cm^{-3}, $Z = 4$, μ(Cu Kα) = 2.00 mm^{-1}.

A crystal measuring $0.4 \times 0.3 \times 0.1$ mm was employed. All measurements were done on a Sinteks-PI diffractometer. Unit cell parameters were determined from automatic centring and refined by the least-squares method. Intensities were collected using graphite monochromatized Cu Kα radiation employing the $\theta/2\theta$ scan technique. A total of 2500 reflections were measured in the range $3 < 2\theta < 120°$, 2130 of which were assumed as being observed applying the condition $F^2 > 6\sigma(F^2)$. The structure was solved by direct methods and refined by the full-matrix least-squares method with an anisotropic temperature factor. The positions of all the H atoms were computed and refined with an isotropic temperature factor. The final R factor was 0.080 ($R_w = 0.089$) for all observed reflections (the molecules of DMSO are randomly distributed). Atomic scattering factors were taken from the *International Tables of X-ray Crystallography* [8].

2.3. Synthesis of the dimethylsulphoxide–7-hydroxy-1-cyclohexyl-5,6,8-trifluoro-4(1H)-oxoquinoline-2-carboxylic acid adduct (2) (nc)

Compound **1** (3.1 g, 9.08 mmol) was dissolved under reflux in a mixture of 100 ml of MeOH and 10 ml of DMSO. The reaction mixture was stored at room temperature for 75 h. The resulting precipitate was collected, washed with MeOH and dried at 70 °C to give 1.8 g (47%) of **2** [m.p. 172–175 °C (decomp.)]. ^{1}H NMR (DMF-d_7) δ: 0.97–2.2 (10H, m, $5CH_2$); 2.60 (6H, c, $2CH_3$); 3.95 (1H, w.s, NCH); 4.2 (w.s, COOH, OH); 6.3 (1H, s, CH) ppm. ^{19}F NMR (DMF-d_7) δ: −161.24 (1F, d-d, F-6); −147.43 (1F, d-d, F-5); −140.66 (1F, m, F-8) ppm; $J_{5-6}=J_{6-5}=20.0$; $J_{5-8}=11.7$; $J_{6-8}=7.8$ Hz. IR (cm^{-1}): 2800–2100 (OH, CO_2^-, NH^+); 1700 (C=O, acid); 1640 (C=O); 1600, 1520 (C=C); 1565 (CO_2^-); 1000–1070 (S=O); 970 (CF). Analysis: Found: C, 51.35; H, 5.15; F, 13.61; N, 3.19; S, 7.73%. Calc. for $C_{16}H_{14}F_3NO_4 \cdot C_2H_6OS$: C, 51.55; H, 4.81; F, 13.59; N, 3.34; S, 7.64%.

2.4. Synthesis of dimethylsulphoxide–2,3,4,5,6-pentafluorophenol adduct (4) (nc)

Pentafluorophenol (**3**) (5.6 g; 30.4 mmol) was heated at 30 °C and mixed with 3.0 g (38.4 mmol) of DMSO. The reaction mixture was stored at room temperature for 2 h. The resulting precipitate was collected and dried under reduced pressure under P_2O_5 to give 5.7 g (72%) of **4** (m.p. 37–39 °C). ^{1}H NMR ($CDCl_3$) δ: 2.74 (6H, c, $2CH_3$); 9.7 (1H, w.s, OH) ppm. ^{19}F NMR ($CDCl_3$) δ: −172.26 (1F, t-t, *para*-); −166.31 (2F, m, *meta*-); −163.13 (2F, m, *ortho*-) ppm. IR (cm^{-1}): 2650–2000 (OH); 1630, 1500 (C=C); 1050–900 (CF, S=O). Analysis: Found: C, 36.61; H, 2.98; F, 36.23; S, 12.09%. Calc. for $C_6HF_5O \cdot C_2H_6OS$: C, 36.65; H, 2.69; F, 36.23; S, 12.23%.

2.5. Synthesis of dimethylsulphoxide–7-hydroxy-5,6,8-trifluoro-2-carboxychromone adduct (8) (nc)

Method A

A mixture of compound **7** (10.0 g, 38.15 mmol), 27 g (195.0 mmol) of KOH and 10 g (108.0 mmol) of glycerin in 150 ml of DMSO was heated for 0.5 h at 100 °C. The reaction mixture was poured into a solution of concentrated HCl (60 ml) in 400 ml of water and extracted with ethyl acetate (500 ml). The organic layer was washed with 25 ml of water and concentrated to half its original volume. The residue was stored at room temperature overnight. The resulting precipitate was collected and dried at 70 °C to give 4.8 g (37%) of **8** [m.p. 250–254 °C (decomp.)]. ^{1}H NMR (CD_3OD) δ: 2.68 (6H, c, $2CH_3$); 5.0 (w.s, OH); 6.85 (1H, c, CH) ppm. ^{19}F NMR (CD_3OD) δ: −159.65 (1F, d-d, F-6, $J_{6-8}=6.7$; $J_{6-5}=18.5$ Hz); −158.19 (1F, d-d, F-8, $J_{8-6}=6.7$; $J_{8-5}=11.5$ Hz); −145.65 (1F, d-d, F-5, $J_{5-8}=11.5$; $J_{5-6}=18.5$ Hz) ppm. IR (cm^{-1}): 2750–2100 (OH); 1725 (C=O, acid); 1650 (C=O, chromone); 1590, 1520 (C=C); 1020–1000 (S=O); 980, 960 (CF). Analysis: Found: C, 42.70; H, 2.60; F, 17.04; S, 8.90%. Calc. for $C_{10}H_2F_3O_4 \cdot C_2H_6OS$: C, 42.61; H, 2.68; F, 16.85; S, 9.47%.

Method B

A mixture of compound **9** (0.12 g, 0.384 mmol) and 0.2 g (2.56 mmol) of DMSO in 4 ml of methanol was evaporated to half its original volume. After cooling to room temperature, the resulting precipitate was collected and dried at 70 °C to give 0.07 g (54%) of **8** [m.p. 250–254 °C (decomp.)]. The physicochemical data were identical to those listed above.

2.6. Synthesis of 7-hydroxy-5,6,8-trifluoro-2-carboxychromone (9) (nc)

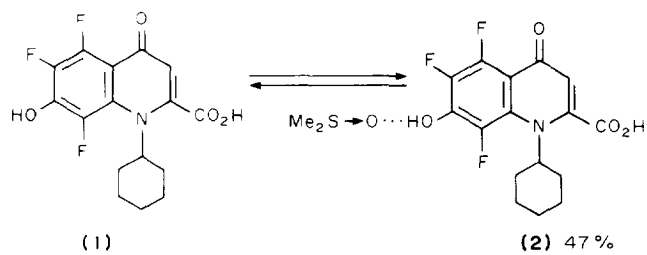
A mixture of compound **8** (0.9 g, 2.66 mmol) and (0.32 g, 3.02 mmol) of Na_2CO_3 in 10 ml of water was heated at 50 °C for 0.5 h. The mixture was neutralized with HCl until the pH value was 2, and then extracted twice with ethyl acetate (20 ml). The organic layer was concentrated to afford a precipitate which was collected and dried at 70 °C to give 0.5 g (72%) of **9** (m.p. 260–262 °C). ^{1}H NMR (CD_3OD) δ: 5.0 (w.s, OH); 6.87 (1H, c, CH) ppm. ^{19}F NMR (CD_3OD) δ: −159.72 (1F, d-d, F-6, $J_{6-8}=6.8$; $J_{6-5}=18.9$ Hz); −158.24 (1F, d-d, F-8, $J_{8-6}=6.7$; $J_{8-5}=11.8$ Hz); −145.68 (1F, d-d, F-5, $J_{5-8}=11.5$; $J_{5-6}=18.5$ Hz) ppm. IR (cm^{-1}): 3280 (OH); 1730 (C=O, acid); 1640 (C=O, chromone); 1610, 1520 (C=C); 980 (CF). Analysis: Found: C, 46.19; H, 1.36; F, 22.20%. Calc. for $C_{10}H_3F_3O_5$: C, 46.17; H, 1.16; F, 21.91%.

3. Results and discussion

3.1. Reaction of 1-cyclohexyl-7-hydroxy-5,6,8-trifluoro-4(1H)-4-oxoquinoline-2-carboxylic acid (1) with DMSO

In the present work, it has been found that interaction of 1-cyclohexyl-7-hydroxy-5,6,8-trifluoro-4(1*H*)-4-oxoquinoline-2-carboxylic acid (**1**) with dimethyl sulphoxide in MeOH gave product **2** (Scheme 1).

Compound **2** is stable when heated in methanol and water (or acidic water), but is destroyed by melting to give **1**. The ^{19}F NMR spectrum of **2** was almost identical to that for the starting compound **1** [5]. In the ^{1}H NMR spectrum of **2**, a resonance at δ 2.60 ppm was found for the CH_3 protons of



Scheme 1.

dimethyl sulphoxide. Consequently, in the IR spectrum of product **2** a powerful absorption band at ca. 1000–1070 cm^{-1} was attributed to sulphoxide.

3.2. X-Ray crystal structure of compound 2

Product **2** was subjected to single-crystal X-ray analysis with a view to finding its solid-state conformation. The bond lengths, bond angles, final atomic coordinates and thermal corrections for adduct **2** are listed in Tables 1–3, respectively. X-Ray crystallographic analysis demonstrated the solvate structure of **2** [$C_{16}H_{14}F_3NO_4 \cdot (CH_3)_2SO$] with strong hydrogen bonding between DMSO and fluoroquinolone (**1**). In the solid-state, the molecules of DMSO are randomly distributed and occupy two positions with populations 2/3 (atoms in this molecule are labelled by A) and 1/3 (label B). The structure of adduct **2**(A) determined by this study is shown in Fig. 1. The structural features of the hydrogen bond O(2)–H···O(DMSO) are as follows: the O···O distances are 2.55(3) Å for DMSO(A) and 2.43(6) Å for DMSO(B); the H···O distances are 1.8(1) Å (A) and 1.7(2) Å (B); the O–H···O angles are 141(7)° and 147(8)° for DMSO(A) and DMSO(B), respectively.

The quinoline fragment in **2** is virtually planar (with the angle between the benzene and the pyridine rings being 5.0°). The angle of the carboxy group arrangement around the C(3)–C(16) bond relating to the pyridine plane is 131.1°. The configuration of the pyridine nitrogen atom N(1) in the solvate is nearly trigonal planar. The bond length N(1)–C(10) is 1.52(1) Å. The cyclohexyl ring is in a chair conformation and essentially perpendicular to the quinoline ring plane.

Furthermore, the oxo group O(1) forms an intermolecular hydrogen bond O(1) (compound **2**) ···H–O(4) (compound **2'**) (x, $1/2-y$, $1/2+z$). The O···O distance is 2.516(8) Å, the H···O distance is 1.62(7) Å and the O–H···O angle 145(6)°. These hydrogen bonds form zigzag chains parallel to the c-axis.

3.3. Reaction of pentafluorophenol with DMSO

A similar reaction also occurs between pentafluorophenol (**3**) and DMSO leading to the stable crystalline adduct **4** (Scheme 2).

The OH stretching shifts ν_{OH} of compound **4** occur at ca. 2000–2650 cm^{-1} in the IR spectrum while the corresponding ν_{OH} stretches of pentafluorophenol are at 2450, 2670 and ca. 3100–3600 cm^{-1}.

Table 1
Bond lengths (Å) for adduct **2** [a]

F(1)–C(6)	1.314(8)	F(2)–C(7)	1.355(7)
F(3)–C(9)	1.352(7)	O(1)–C(1)	1.246(8)
O(2)–C(8)	1.331(7)	O(2)–H(O2)	0.87(7)
O(3)–C(16)	1.213(8)	O(4)–C(16)	1.287(7)
O(4)–H(O4)	1.01(6)	N(1)–C(3)	1.382(8)
N(1)–C(4)	1.413(7)	N(1)–C(10)	1.52(1)
C(1)–C(2)	1.425(8)	C(1)–C(5)	1.456(8)
C(2)–C(3)	1.34(1)	C(2)–H(2)	1.01(7)
C(3)–C(16)	1.512(8)	C(4)–C(5)	1.392(9)
C(4)–C(9)	1.395(8)	C(5)–C(6)	1.430(8)
C(6)–C(7)	1.387(9)	C(7)–C(8)	1.364(9)
C(8)–C(9)	1.378(8)	C(10)–C(11)	1.52(1)
C(10)–C(15)	1.51(1)	C(10)–H(10)	0.90(5)
C(11)–C(12)	1.54(2)	C(11)–H(111)	0.96(6)
C(11)–H(112)	0.88(7)	C(12)–C(13)	1.50(2)
C(12)–H(121)	0.95(7)	C(12)–H(122)	0.88(9)
C(13)–C(14)	1.48(2)	C(13)–H(131)	0.95(9)
C(13)–H(132)	0.9(1)	C(14)–C(15)	1.54(2)
C(14)–H(141)	1.01(7)	C(14)–H(142)	0.92(9)
C(15)–H(151)	0.94(7)	C(15)–H(152)	0.98(8)
SA–OA	1.54(3)	SA–CA(1)	1.68(2)
SA–CA(2)	1.57(5)		
SB–OB	1.55(7)		
SB–CB(1)	1.58(3)	SB–CB(2)	1.42(7)

[a] The H-atoms are labelled in relation to the corresponding O(2), O(4), C(2) and C(11)–C(15) atoms [thus the H-atoms labelled H(111)–H(152) are those connected to the C(11)–C(15) atoms].

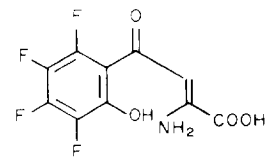
Table 2
Angles (°) for adduct **2**

C(8)–O(2)–H(O2)	104(5)	C(16)–O(4)–H(O4)	103(4)
C(3)–N(1)–C(4)	116.8(5)	C(3)–N(1)–C(10)	120.2(5)
C(4)–N(1)–C(10)	118.7(5)	O(1)–C(1)–C(2)	122.8(6)
O(1)–C(1)–C(5)	123.2(6)	C(2)–C(1)–C(5)	114.0(6)
C(1)–C(2)–C(3)	122.6(6)	C(1)–C(2)–H(2)	117(4)
C(3)–C(2)–H(2)	120(4)	N(1)–C(3)–C(2)	123.4(6)
N(1)–C(3)–C(16)	119.4(6)	C(2)–C(3)–C(16)	116.9(6)
N(1)–C(4)–C(5)	120.3(5)	N(1)–C(4)–C(9)	120.6(5)
C(5)–C(4)–C(9)	119.1(6)	C(1)–C(5)–C(4)	121.7(6)
C(1)–C(5)–C(6)	120.0(6)	C(4)–C(5)–C(6)	118.3(6)
F(1)–C(6)–C(5)	121.9(6)	F(1)–C(6)–C(7)	118.9(6)
C(5)–C(6)–C(7)	119.1(6)	F(2)–C(7)–C(6)	116.8(6)
F(2)–C(7)–C(8)	120.1(6)	C(6)–C(7)–C(8)	123.0(6)
O(2)–C(8)–C(7)	117.8(6)	O(2)–C(8)–C(9)	125.1(6)
C(7)–C(8)–C(9)	117.1(6)	F(3)–C(9)–C(4)	121.3(5)
F(3)–C(9)–C(8)	115.1(5)	C(4)–C(9)–C(8)	123.2(6)
N(1)–C(10)–C(11)	110.5(6)	N(1)–C(10)–C(15)	114.8(6)
N(1)–C(10)–H(10)	103(3)	C(11)–C(10)–C(15)	113.0(7)
C(11)–C(10)–H(10)	105(3)	C(15)–C(10)–H(10)	109(3)
C(10)–C(11)–C(12)	106.9(8)	C(10)–C(11)–H(111)	103(4)
C(10)–C(11)–H(112)	103(5)	C(12)–C(11)–H(111)	113(4)
C(12)–C(11)–H(112)	109(5)	H(111)–C(11)–H(112)	121(6)
C(11)–C(12)–C(13)	113(1)	C(11)–C(12)–H(121)	106(4)
C(11)–C(12)–H(122)	88(6)	C(13)–C(12)–H(121)	118(4)
C(13)–C(12)–H(122)	119(6)	H(121)–C(12)–H(122)	109(7)
C(12)–C(13)–C(14)	111(1)	C(12)–C(13)–H(131)	102(6)
C(12)–C(13)–H(132)	119(6)	C(14)–C(13)–H(131)	96(6)
C(14)–C(13)–H(132)	104(6)	H(131)–C(13)–H(132)	122(8)
C(13)–C(14)–C(15)	112(1)	C(13)–C(14)–H(141)	111(5)
C(13)–C(14)–H(142)	101(6)	C(15)–C(14)–H(141)	111(5)
C(15)–C(14)–H(142)	100(6)	H(141)–C(14)–H(142)	121(8)
C(10)–C(15)–C(14)	108.4(8)	C(10)–C(15)–H(151)	105(5)
C(10)–C(15)–H(152)	113(5)	C(14)–C(15)–H(151)	109(5)
C(14)–C(15)–H(152)	105(5)	H(151)–C(15)–H(152)	116(7)
O(3)–C(16)–O(4)	126.1(7)	O(3)–C(16)–C(3)	121.7(6)
O(4)–C(16)–C(3)	112.1(6)		
OA–SA–CA(1)	103(2)	OA–SA–CA(2)	113(2)
OB–SB–CB(1)	115(4)		
OB–SB–CB(2)	116(5)	CB(1)–SB–CB(2)	128(4)

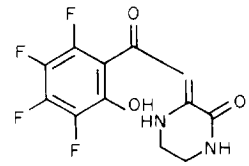
Table 3
Final atomic coordinates and thermal corrections U_{iso} and U_{eq} for adduct **2**

Atom	x	y	z	U_{iso}/U_{eq}
F(1)	0.1311(6)	0.0389(1)	1.2901(4)	0.082(2)
F(2)	0.2350(6)	−0.0530(1)	1.2182(4)	0.085(2)
F(3)	0.2498(6)	0.0286(1)	0.8229(4)	0.073(2)
O(1)	0.0625(8)	0.1433(2)	1.2460(5)	0.077(2)
O(2)	0.2955(7)	−0.0605(2)	0.9892(5)	0.074(2)
O(3)	−0.0530(7)	0.2161(2)	0.6988(4)	0.071(2)
O(4)	0.0850(7)	0.2708(2)	0.8832(5)	0.077(2)
N(1)	0.1753(7)	0.1323(2)	0.9014(5)	0.056(2)
C(1)	0.0858(9)	0.1383(2)	1.1369(6)	0.060(3)
C(2)	0.053(1)	0.1814(2)	1.0381(7)	0.062(3)
C(3)	0.0960(9)	0.1778(2)	0.9285(6)	0.057(3)
C(4)	0.1858(8)	0.0851(2)	0.9816(6)	0.053(3)
C(5)	0.1475(9)	0.0880(2)	1.0984(6)	0.058(3)
C(6)	0.166(1)	0.0396(2)	1.1791(7)	0.066(3)
C(7)	0.223(1)	−0.0081(2)	1.1396(6)	0.065(3)
C(8)	0.2525(9)	−0.0119(2)	1.0218(6)	0.061(3)
C(9)	0.2346(9)	0.0351(2)	0.9452(6)	0.058(3)
C(10)	0.307(1)	0.1387(2)	0.8357(7)	0.060(3)
C(11)	0.423(1)	0.1893(3)	0.893(1)	0.081(4)
C(12)	0.569(1)	0.1880(4)	0.838(1)	0.104(6)
C(13)	0.493(2)	0.1845(5)	0.681(2)	0.129(8)
C(14)	0.376(2)	0.1362(6)	0.629(1)	0.109(6)
C(15)	0.224(1)	0.1355(4)	0.6770(8)	0.079(4)
C(16)	0.036(1)	0.2241(2)	0.8235(7)	0.062(3)
SA	0.2531(5)	−0.0950(1)	0.6532(3)	0.094(2)
OA	0.402(4)	−0.083(2)	0.800(2)	0.088(7)
CA(1)	0.294(3)	−0.1600(9)	0.624(3)	0.14(1)
CA(2)	0.272(7)	−0.061(2)	0.534(4)	0.28(3)
SB	0.384(1)	−0.0907(4)	0.6547(9)	0.116(4)
OB	0.379(9)	−0.076(6)	0.796(5)	0.12(2)
CB(1)	0.395(7)	−0.154(1)	0.628(6)	0.15(3)
CB(2)	0.35(1)	−0.047(3)	0.557(6)	0.12(3)
H(O2)	0.30(1)	−0.056(3)	0.907(7)	0.08(3)
H(O4)	0.082(9)	0.295(3)	0.803(6)	0.15(2)
H(2)	0.01(1)	0.217(3)	1.058(7)	0.09(2)
H(10)	0.383(7)	0.110(2)	0.871(5)	0.05(1)
H(111)	0.471(9)	0.184(2)	0.993(6)	0.09(2)
H(112)	0.348(9)	0.216(3)	0.851(7)	0.08(2)
H(121)	0.652(9)	0.161(3)	0.892(7)	0.08(2)
H(122)	0.60(1)	0.220(3)	0.879(9)	0.13(3)
H(131)	0.40(1)	0.211(3)	0.653(8)	0.14(3)
H(132)	0.57(1)	0.182(4)	0.641(9)	0.13(4)
H(141)	0.33(1)	0.134(3)	0.522(7)	0.11(3)
H(142)	0.45(1)	0.109(3)	0.686(9)	0.11(4)
H(151)	0.16(1)	0.167(3)	0.646(7)	0.08(2)
H(152)	0.16(1)	0.101(3)	0.641(9)	0.15(3)

Interestingly, when the tetrafluorophenol derivatives **5** and **6** were investigated as proton donors for hydrogen-bond formation with DMSO, it was not possible to obtain crystalline adducts similar to **2** and **4**. This may result on the one hand from the fact that the hydrogen-bonding ability (or acidity) of compounds **1** and **3**, which contain two *ortho*-fluorine atoms, is stronger than that of compounds **5** and **6** which have bulky substituents in the *ortho*-position. These cause the hydroxyl group to twist out of the plane of the aromatic ring and thus prevent resonance stabilization. In addition, it is known from early investigations of structure–reactivity relationships [4] that *ortho*-substituted fluorophenols are more acidic in solution than the corresponding meta- and, especially, para-substituted compounds. On the other hand, compounds **5** and **6** may form strong intramolecular hydrogen bonds which cannot be ruptured in DMSO or MeOH as solvents, in contrast to the F···HO hydrogen bonds of **1** and **3**.



5



6

3.4. Reaction of 2-carboxy-5,6,7,8-tetrafluorochromone with KOH/glycerol in DMSO

Also of interest in the present discussion are the results obtained using 2-carboxy-5,6,7,8-tetrafluorochromone (**7**). Thus, chromone **7** forms a product **8** on refluxing with glycerol in DMSO in the presence of potash (Scheme 3). Adduct **8** is stable on heating in methanol, ethyl acetate and water (or acidic water), but the intermolecular hydrogen bond is ruptured on heating under alkaline conditions to give the 7-hydroxy derivative **9**. Treatment of **9** with a mixture of meth-

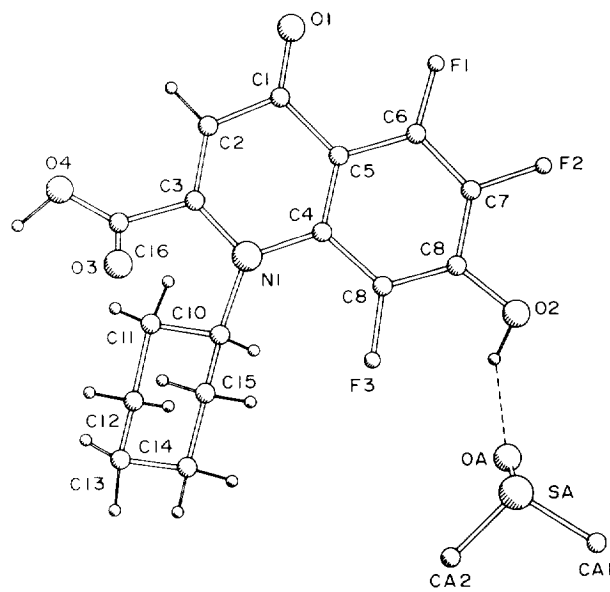
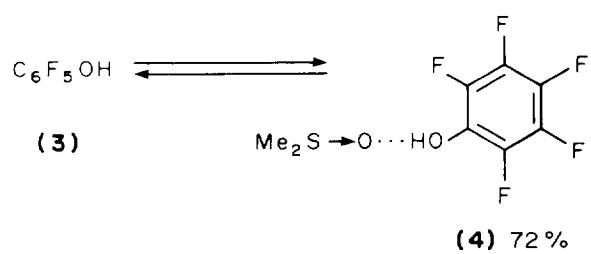
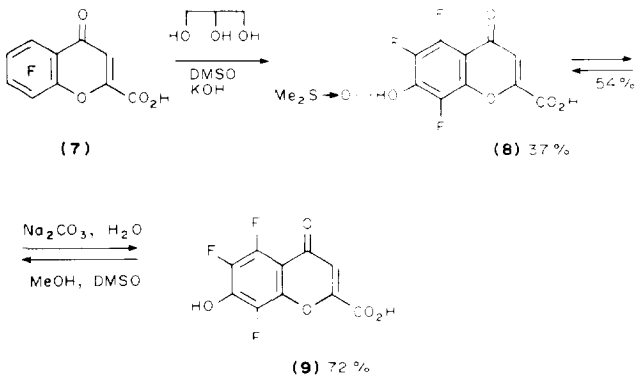


Fig. 1. The structure of adduct **2** (A).



(4) 72%

Scheme 2.



Scheme 3.

anol and DMSO afforded a good yield of solvate **8** (Scheme 3).

An alternative synthetic route to chromone **9** by treatment of **7** with $NaOH/H_2O$ (KOH/H_2O) was unsuccessful since the chromone ring is unstable to the hydroxide ion.

The structures of **8** and **9** have been assigned on the basis of their IR, ^1H and ^{19}F NMR spectra. In the ^{19}F NMR spectra of the compounds **8** and **9**, three resonance signals in the expected ratio were attributed to the C-5, C-6 and C-8 fluorine atoms of the C_6F_3 group. The IR shift ν_{SO} for compound **8** was found at ca. 1000–1020 cm^{-1}. Simultaneously the OH stretching band of compound **9** at 3280 cm^{-1} undergoes a remarkable shift to 2100–2650 cm^{-1} in product **8** (in the presence of DMSO). This clearly indicates that DMSO forms a strong hydrogen bond with the 7-hydroxychromone (**9**).

In conclusion, the reactions described demonstrate the strong hydrogen-bonding ability of hydroxybenzene derivatives containing two *ortho*-fluorine substituents.

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