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Inter- and intra-molecular hydrogen-bonded trifluoromethylated alcohols: X-ray crystal structures of 2,5-bis(trifluoromethyl)hexane-2,5-diol, 1,1,1,4,4,4-hexafluoro-2-(3,4-methylenedioxyphenyl)butane-2,3-diol, and 1,1,1-trifluoro-2-oxo-3-(3,4-methylenedioxyphenyl)propane-2-ol

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Abstract

Trifluoromethylated alcohols, 2,5-bis(trifluoromethyl)hexane-2,5-diol (**1**), 1,1,1,4,4,4-hexafluoro-2-(3,4-methylenedioxyphenyl)butane 2,3-diol (**2**), and 1,1,1-trifluoro-2-oxo-3-(3,4-methylenedioxyphenyl)propane-2-ol (**3**) were prepared by direct nucleophilic trifluoromethylation of the corresponding diketo compounds, acetonylacetone and 3,4-methylenedioxyphenylglyoxal, respectively, with (trifluoromethyl)trimethylsilane. Their structures were confirmed by single crystal X-ray analyses. The presence of inter-molecular hydrogen bonding is observed in **1** and **3**, and a greater range of interactions, both inter- and intra-molecular, are seen in **2**.

Keywords: Diols; 2,5-Bis(trifluoromethyl)hexane-2,5-diol; 1,1,1,4,4,4-Hexafluoro-2-(3,4-methylenedioxyphenyl)butane-2,3-diol; 1,1,1-Trifluoro-2-oxo-3-(3,4-methylenedioxyphenyl)propane-2-ol; Intra- and inter-molecular hydrogen bonding

1. Introduction

Synthetic and structural aspects of organofluorine compounds have been the focal point of vigorous research [1–4]. Because fluorine is the most electronegative element and the van der Walls radius of fluorine is close to that of hydrogen, the introduction of a fluorine-containing group into organic molecules brings about some remarkable changes in the chemical and physical properties of the fluorinated products and also induces novel reactivities. These changes have been exploited in the fields of pharmaceutical, agrochemical and polymer chemistry [5–7].

Hydrogen bonding plays a very important role in stabilizing organic compounds and contributes to enhancing their suitability for medicinal purposes [8,9]. It is possible to predict the presence of hydrogen bonding in a molecule based on infrared spectroscopic studies but very difficult to predict the exact hydrogen-bonded structure of a molecule that has more than one hydroxyl group and contains a highly electronegative element, such as fluorine. Using single crystal X-ray analysis, the precise mode of hydrogen bonding in some trifluoromethylated diols and a monoalcohol has been elucidated.

2. Results and discussion

Nucleophilic trifluoromethylation of acetonylacetone with excess of (trifluoromethyl)trimethylsilane in monoglyme in the presence of a catalytic amount of CsF led to the formation of the corresponding trifluoromethylated silylether. Upon hydrolysis, 2,5-bis(trifluoromethyl)hexane-2,5-diol (**1**) was obtained [10]. Under similar reaction conditions, 3,4-methylenedioxyphenylglyoxal gave a mixture of 1,1,1,4,4,4-hexafluoro-2-(3,4-methylenedioxyphenyl)butane-2,3-diol (**2**) and 1,1,1-trifluoro-2-oxo-3-(3,4-methylenedioxyphenyl)propane-2-ol (**3**), which were separated by flash chromatography. They are colorless solids with sharp melting points, soluble in common organic solvents, and stable to air and moisture. They crystallize easily from a mixture of diethyl ether and hexane at room temperature.

The presence of hydroxyl groups and highly electronegative elements such as fluorine and oxygen in **1**–**3** gives rise to a variety of possible inter- and intra-molecular hydrogen-bonded structures. Spectroscopic data are not very helpful for predicting the exact structures of the molecules. A broad

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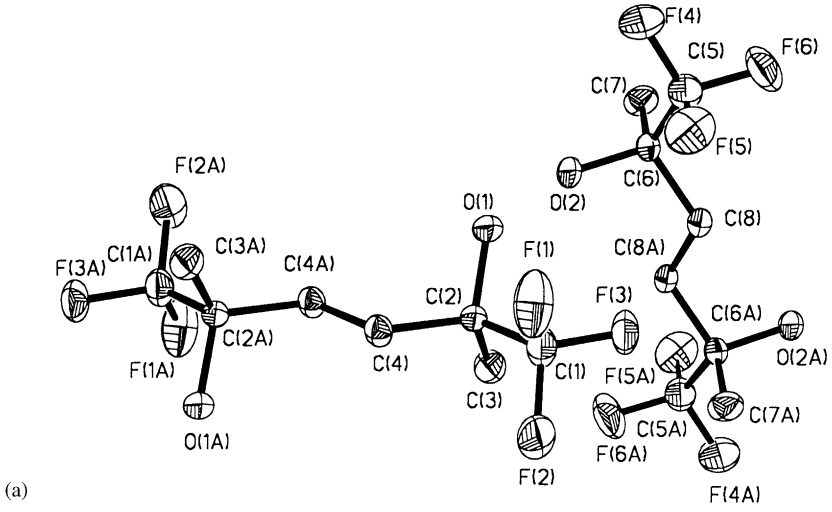
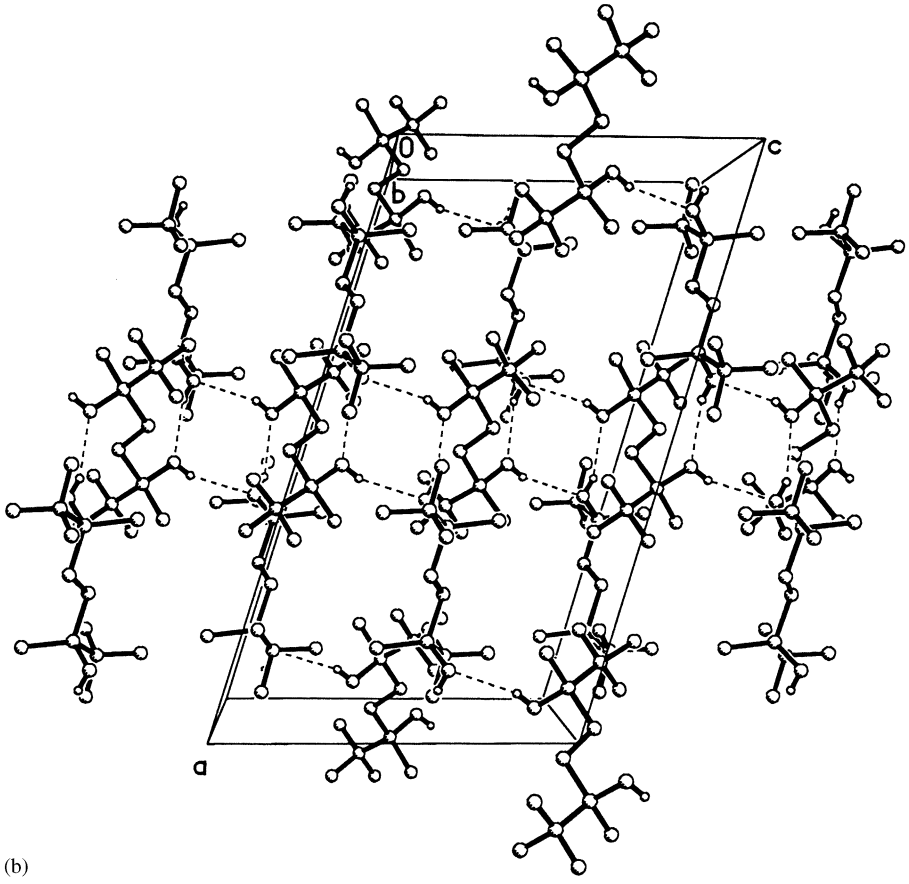
band is seen in the infrared spectra of **1**–**3** at ca. 3400 cm^{-1}. This has been assigned to the ν(OH) stretching frequency. A non-bonded hydroxyl group should give rise to an absorption band at ca. 3600 cm^{-1}. The shift of the band by ~200 cm^{-1} to lower energy in each of the above compounds strongly suggests the presence of hydrogen bonding. X-ray structural analyses have been used to determine the exact conformations of the molecules in the solid state.

X-ray quality crystals of compounds **1**–**3** were grown from a mixture of pentane and ether. Their structures are presented in Fig. 1(a) and (b), Fig. 2(a) and (b) and Fig. 3(a) and (b), respectively. Selected bond angles and bond lengths are given in Tables 1 and 2. They crystallize in the following respective monoclinic space groups: *C*2/*c*, *P*2(1)/*c* and *P*2(1)/*n*. All compounds form discrete molecular units; however, in the solid state, hydrogen

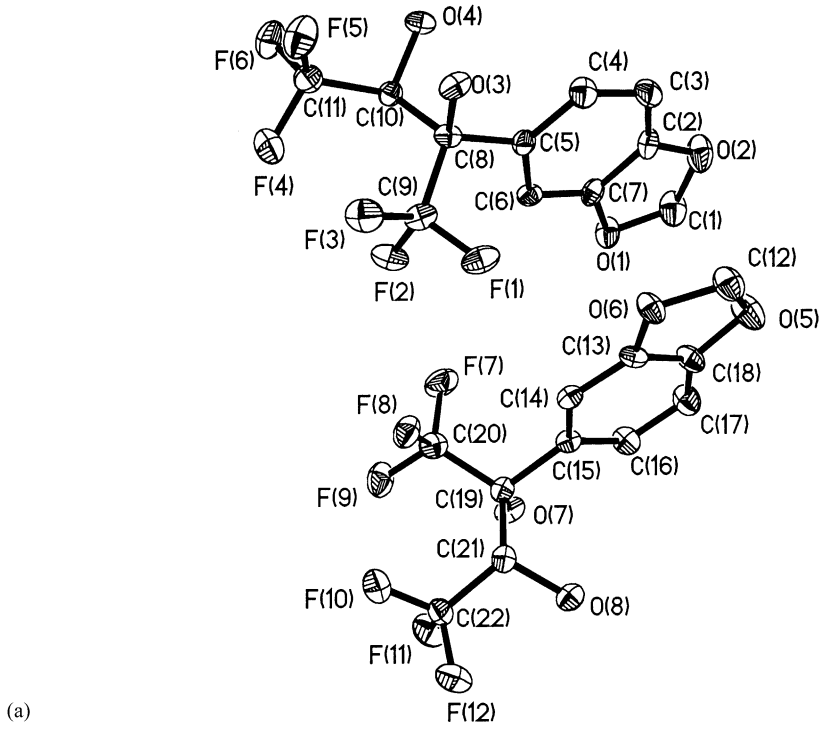


(a)

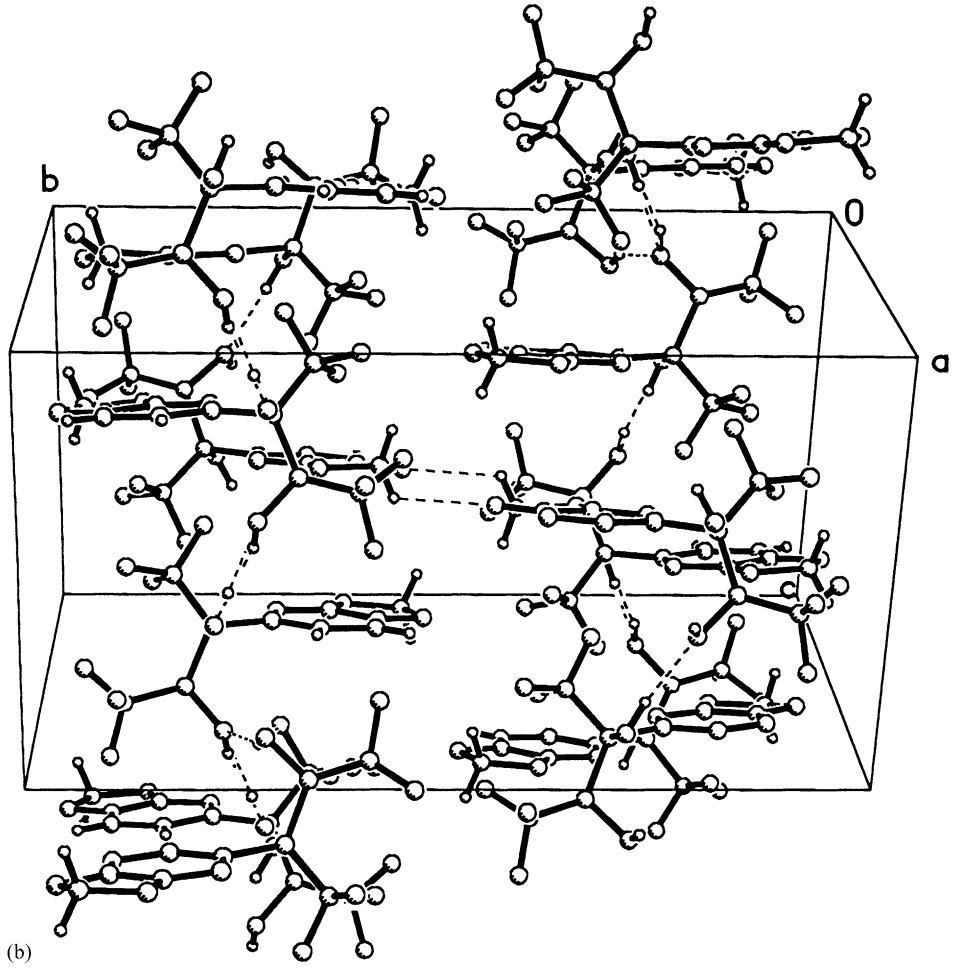


(b)

Fig. 1. (a) ORTEP drawing of **1** with thermal ellipsoids drawn at 30% probability level (H atoms omitted for clarity). (b) Crystal packing diagram of **1** viewed down the *b*-axis. Only the H atoms involved in hydrogen bonding are shown. The square synthon of H-bonded interactions is shown by a dashed line.

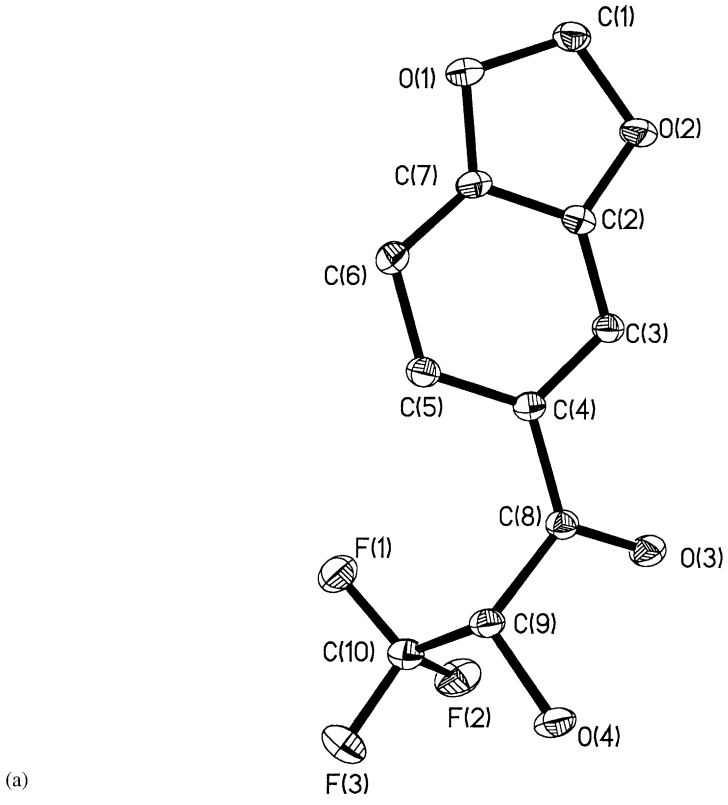


(a)

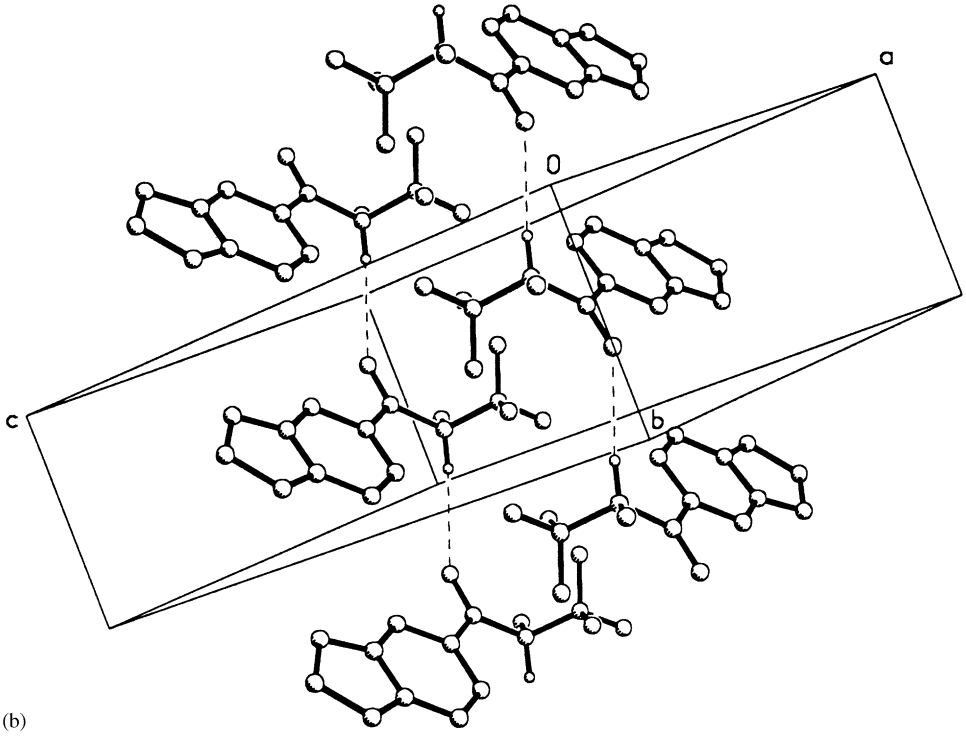


(b)

Fig. 2. (a) ORTEP drawing of **2** with thermal ellipsoids drawn at 30% probability level (H atoms omitted for clarity). (b) Crystal packing diagram of **2** along the *b*-axis. Only the H atoms involved in hydrogen bonding are shown. Inter-molecular interactions are indicated by a dashed line.



(a)



(b)

Fig. 3. (a) ORTEP drawing of **3** with thermal ellipsoids drawn at 30% probability level. (b) Crystal packing diagram of **3**. Only the H atoms involved in hydrogen bonding are shown. Inter-molecular interactions are indicated by a dashed line.

Table 1
Selected bond lengths (Å) for **1–3**

1			
F(1)–C(1)	1.323(3)	O(2)–C(6)	1.424(2)
F(4)–C(5)	1.332(3)	C(1)–C(2)	1.523(3)
O(1)–C(2)	1.416(2)	C(6)–C(8)	1.529(2)
2			
F(1)–C(9)	1.326(8)	O(1)–C(1)	1.417(9)
F(4)–C(11)	1.347(9)	O(2)–C(1)	1.437(9)
F(7)–C(20)	1.330(9)	O(7)–C(19)	1.412(8)
F(10)–C(22)	1.318(9)	C(8)–C(9)	1.528(10)
O(1)–C(7)	1.388(9)	C(19)–C(21)	1.568(10)
3			
O(1)–C(7)	1.3695(17)	O(4)–C(9)	1.4173(17)
O(1)–C(1)	1.443(2)	F(1)–C(10)	1.3428(19)
O(2)–C(2)	1.3770(17)	C(2)–C(3)	1.3726(19)
O(2)–C(1)	1.4419(19)	C(6)–C(7)	1.376(2)
O(3)–C(8)	1.2244(18)	C(9)–C(10)	1.527(2)

Table 2
Selected bond angles (°) for **1–3**

1			
F(1)–C(1)–F(3)	107.15(18)	O(1)–C(2)–C(3)	110.95(15)
F(3)–C(1)–F(2)	105.98(17)	O(1)–C(2)–C(1)	106.06(15)
F(1)–C(1)–C(2)	112.81(17)	C(3)–C(2)–C(1)	109.14(16)
O(2)–C(6)–C(5)	107.07(16)	C(8)–C(6)–C(7)	114.04(15)
2			
C(7)–O(1)–C(1)	105.7(6)	C(2)–O(2)–C(1)	105.4(5)
C(18)–O(5)–C(12)	105.1(6)	O(1)–C(1)–O(2)	108.8(6)
C(2)–C(3)–C(4)	116.6(8)	O(3)–C(8)–C(10)	104.6(5)
C(5)–C(8)–C(10)	108.4(5)	F(1)–C(9)–F(3)	106.6(6)
F(1)–C(9)–C(8)	111.0(7)	F(5)–C(11)–C(10)	114.4(7)
3			
C(7)–O(1)–C(1)	106.01(12)	C(2)–O(2)–C(1)	105.80(12)
O(2)–C(1)–O(1)	107.97(11)	C(3)–C(2)–O(2)	128.01(14)
O(2)–C(3)–C(7)	109.88(12)	C(2)–C(3)–C(4)	116.89(13)
O(1)–C(7)–C(6)	127.96(14)	F(2)–C(10)–F(1)	107.17(15)
F(2)–C(10)–C(9)	111.70(14)	F(3)–C(10)–C(9)	110.73(15)

bonding links many of the molecules forming supramolecular entities.

2.1. Crystal structures

Compound **1** (Fig. 1) is centro-symmetric with two-half molecules in the asymmetric unit. Both hydroxyl groups are involved in inter-molecular hydrogen bonding resulting in a distorted ''square'' of O−H···O interactions (2.7578(19) and 2.7086(18) Å) which are related by symmetry. The hydrogen-bonded squares are parallel to the *c*-axis and connect the molecules in three dimensions creating a supramolecular species. This hydrogen-bonded motif or synthon [11,12] is commonly found in many polyalcohols, e.g. pentaerythritol [13–16].

The structure of **2** shows the greatest range of interactions, both inter- and intra-molecular (Fig. 2). The latter is represented by the close proximity of C(4)–H(4B)···O(3) (2.755(9) Å). Each molecule also forms inter-molecular hydrogen bonds of 2.786(6) Å via the hydroxyl groups on each fluorinated chain. This forms a hydrogen-bonded sheet along the *a*- and *c*-axis with the piperonal aromatic moiety parallel to the *b*-axis. These sheets are joined by hydrogen bonding every fourth repeat unit along the *c*-axis by the methylene hydrogens of the piperonal moiety (3.024(10) Å). This complicated synthon links individual sheets via hydrogen bonding and causes the solid state structure to be three-dimensional.

Table 3
Crystallographic data for **1–3**

	Compound		
	1	**2**	**3**
Empirical formula	$C_8H_{12}F_6O_2$	$C_{11}H_8F_6O_4$	$C_{10}H_6F_3O4$
Formula weight	254.18	318.17	247.15
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	*C*2/*c*	*P*2(1)/*c*	*P*2(1)/*n*
a (Å)	18.022(2)	11.7029(7)	11.22160(10)
b (Å)	12.0302(14)	19.1585(12)	5.33550(10)
c (Å)	10.4922(12)	10.7623(7)	16.2074(3)
Bond angles (°)	106.675(2)	96.669(2)	98.2470(10)
V (Å^3)	2179.1(4)	2396.7(3)	960.35(3)
Z	8	8	4
ρ (Calculated) (mg/m^3)	1.549	1.764	1.709
F (000)	1040	1280	500
Crystal size	0.43 × 0.30 × 0.30	0.35 × 0.08 × 0.05	0.50 × 0.25 × 0.13
Reflection collected	7832	15033	9781
Independent reflections	1911	3051	2344
Data/parameters	1911/151	3051/379	2344/157
GOF on F^2	1.047	1.144	1.073
R_1 (wR_2 all data)	4.26(11.17)	8.84(17.59)	4.26(11.10)
Largest difference in peak and hole (electron Å^{-3})	0.242, −0.210	0.402, −0.432	0.518, −0.191

Compound **3** (Fig. 3) forms a weak hydrogen bond with only C9–H9a···O3 (3.4465(19) Å). This forms a one-dimensional chain along the *b*-axis. The hydrogen bonding synthon is a simple zig-zag chain. This alignment of the molecules along the *b*-axis brings the CF_3 groups into close proximity. The distance at closest approach between the nearest fluorine atoms is 2.84(2) Å. This is slightly longer than the sum of the van der Walls radii for fluorine (2.7 Å) [17].

3. Experimental details

3.1. Synthesis of *1–3*

All three compounds were prepared by direct nucleophilic trifluoromethylation of the corresponding diketo compounds, acetonylacetone and 3,4-methylenedioxyphenylglyoxal, respectively, with (trifluoromethyl)trimethylsilane in monoglyme in the presence of a catalytic amount of cesium fluoride. Details of the synthetic procedure, spectroscopic and analytical data were reported elsewhere [10].

3.2. X-ray crystallographic analysis of *1–3*

Crystallographic data are given in Table 3. The X-ray diffraction data for **1–3** were collected at 203(2) K on a Siemens SMART 1000 instrument (Mo Kα radiation, $\lambda = 0.71073$ Å) equipped with a Siemens LT-2A low temperature device. The SHELXTL version 5.10 program package was used for structure solution and refinement [18]. An absorption correction was applied to **1** and **2** using SADABS [19]. The structures were solved by direct methods and refined by using the SHELXS-97 program and full matrix least squares procedure using the SHELXTL version 5.10 program. All non-hydrogen atoms were refined anisotropically. Some details of the data collection and refinement are given in Table 3. Further details are provided in the supporting information.

Acknowledgements

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