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The crystal structure of 2,2,2-trifluoro-1-(isoquinolin-1-yl)ethane-1,1-diol, $C_{11}H_8F_3NO_2$

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	$0.22 \times 0.20 \times 0.18$ mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ :	0.15 mm^{-1}
Diffractometer, scan mode:	Smart, φ and ω
θ_{max} , completeness:	25.1° , >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	6371, 1799, 0.031
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 1410
$N(\text{param})_{\text{refined}}$:	160
Programs:	Bruker [1], SHELX [2, 3]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$).

Atom	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.7543(2)	0.63936(15)	0.40948(16)	0.0419(4)
H1	0.6487	0.6318	0.3888	0.050*
C2	0.8053(2)	0.70634(17)	0.51301(18)	0.0517(5)
H2	0.7340	0.7433	0.5637	0.062*
C3	0.9637(2)	0.72079(17)	0.54477(19)	0.0542(5)
H3	0.9963	0.7670	0.6163	0.065*
C4	1.0696(2)	0.66816(17)	0.47251(17)	0.0472(5)
H4	1.1745	0.6795	0.4937	0.057*
C5	1.02207(19)	0.59614(15)	0.36501(16)	0.0372(4)
C6	0.86168(18)	0.58065(14)	0.33255(15)	0.0331(4)
C7	0.82250(17)	0.50761(15)	0.22285(15)	0.0333(4)
C8	1.07828(19)	0.47062(18)	0.18714(18)	0.0458(5)
H8	1.1503	0.4326	0.1382	0.055*
C9	1.12923(19)	0.53837(16)	0.28880(17)	0.0440(5)
H9	1.2348	0.5470	0.3087	0.053*
C10	0.65706(18)	0.48042(15)	0.16748(15)	0.0371(4)
C11	0.5787(2)	0.38918(17)	0.25074(19)	0.0479(5)
F1	0.56076(14)	0.42381(12)	0.37518(12)	0.0675(4)
F2	0.43873(12)	0.36392(11)	0.19804(13)	0.0711(4)
F3	0.66016(14)	0.29235(11)	0.26025(13)	0.0690(4)
N1	0.92546(15)	0.45588(13)	0.15363(14)	0.0408(4)
O1	0.56888(14)	0.57972(11)	0.16272(12)	0.0467(4)
H10	0.4932(19)	0.5713(18)	0.1078(18)	0.056*
O2	0.66443(14)	0.43114(12)	0.04176(12)	0.0493(4)
H20	0.7599(18)	0.4182(19)	0.035(2)	0.059*

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Abstract

$C_{11}H_8F_3NO_2$, monoclinic, $P2_1/c$ (no. 14), $a = 8.6599(8)$ Å, $b = 11.6216(12)$ Å, $c = 10.0903(9)$ Å, $\beta = 93.393(2)^\circ$, $V = 1013.73(17)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0352$, $wR_{\text{ref}}(F^2) = 0.0984$, $T = 273(2)$ K.

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The asymmetric unit of the molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

All chemicals, reagents and solvents are of analytical grade and are commercially available. Preparation of 2,2,2-trifluoro-1-(isoquinolin-1-yl)ethane-1-ol: To a solution of

(trifluoromethyl)trimethylsilane (0.36 g, 0.32 mmol) and isoquinoline-1-carbaldehyde (3.6 g, 6.36 mmol) in 10 mL anhydrous tetrahydrofuran was added tetrabutylammonium fluoride (4 g, 7.63 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and warmed to room temperature to stir overnight. The reaction was quenched with dilute

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hydrochloric acid and was stirred for another 2.5 hours. The pH of the reaction mixture was adjusted to 8.0 and the separated aqueous layer was extracted with ethyl acetate. The organic phase was then dehydrated with anhydrous sodium sulfate and concentrated at reduced pressure to afford the product (1.24 g, 86%). Preparation of 2,2,2-trifluoro-1-(isoquinolin-1-yl)ethane-1,1-diol: to a solution of 2,2,2-trifluoro-1-(isoquinolin-1-yl)ethan-1-ol (1.24 g, 5.47 mmol) in anhydrous dichloromethane (10 mL) was added Dess-Martin periodinane (2.78 g, 6.56 mol). The reaction mixture was stirred at room temperature overnight and was quenched with water, followed by extracting with dichloromethane and concentrating at reduced pressure. The crude product was recrystallized from *n*-hexane (100 mL) twice to afford a crystalline solid (1.06 g, 81.4%). **¹H NMR** (400 MHz, DMSO-*d*₆) δ [ppm] 8.82 (d, *J* = 8.8 Hz, 1H), 8.57 (d, *J* = 5.6 Hz, 1H), 8.04 (d, *J* = 8.3 Hz, 1H), 7.98 (d, *J* = 5.6 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.74 (t, *J* = 8.4 Hz, 1H), 3.34–3.28 (m, 1H). **¹³C NMR** (101 MHz, DMSO-*d*₆) δ [ppm] 151.69, 140.62, 139.11, 132.16, 129.51, 128.61, 127.81, 127.61, 125.70, 125.40, 122.85. **MS** (ESI): *m/z* = 242 [M-H][−]. Crystals were grown in hexane/chloroform at room temperature.

Experimental details

All hydrogen atoms were placed in geometrically calculated positions. The *U*_{iso} values of the hydrogen atoms were set to 1.2 *U*_{eq}.

Comment

2,2,2-Trifluoro-1-(isoquinolin-1-yl)ethane-1,1-diol has a very broad application prospect as an important intermediate in pharmaceutical synthesis. The structure of isoquinoline-diol is an effective ingredient which is used preventing skin aging and wrinkles, for preventing hair loss, wherein 1,5-isoquinolinediol was developed as an agent to prolong life. In this application the collagenase can be inhibited to improve the wrinkles of the skin. It is also the main component of the synthesis of poly (ADP-ribose) polymerase (PARP) inhibitors [4]. In particular, the introduction of a CF₃ group into a drug candidate enhances the chemical and metabolic stability of the compound, improves lipophilicity and bioavailability, and even increases protein binding affinity [5–7].

The structure of the title compound was clarified by spectroscopy and X-ray diffraction. The crystal structure shows

that there is one molecule in the asymmetric unit (cf. the figure). The crystal structure shows that the molecules are stabilized by intermolecular hydrogen bonds: O2···H10-O1 (distance = 1.974 Å), O1-H10-O2 and the packing is stabilized by the van der Waals forces. All bond lengths and angles are comparable to those in the literature [8–10].

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