Regioselective synthesis and crystal structure of ethyl-4-acetyl-5-((2-ethoxy-2-oxoethyl)thio)-3-hydroxythiophene-2-carboxylate, $C_{13}H_{16}O_6S_2$

Y. N. Mabkhot[*, I], S. S. Al-Showiman[I], A. Barakat[I, II], S. Yousuf[III] and M. I. Choudhary[I, III]

[I] Department of Chemistry, College of Science, King Saud University, P. O. Box 2455, Riyadh-11451, Saudi Arabia
[II] Department of Chemistry, Faculty of Science, Alexandria University, P.O. Box 426, Ibrahimia- 21321 Alexandria, Egypt
[III] H.E.J. Research Institute of Chemistry, International Center for Chemical Sciences, University of Karachi, Karachi-75270, Pakistan

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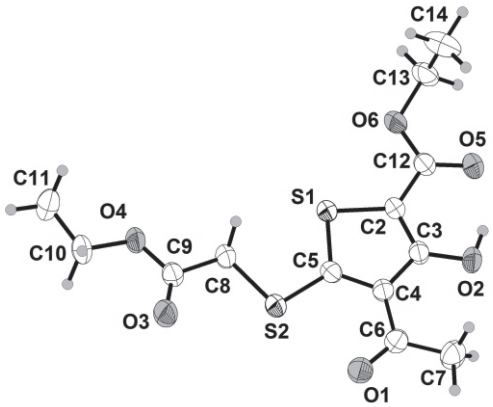

Abstract

$C_{13}H_{16}O_6S_2$, triclinic, $P\overline{1}$ (no. 2), a = 7.979(1) Å, b = 9.189(1) Å, c = 10.263(1) Å, α = 72.876(2)°, β = 71.485(2)°, γ = 76.655(2)°, V = 674.0 Å^3, Z = 2, $R_{gt}(F)$ = 0.0360, $wR_{ref}(F^2)$ = 0.0962, T = 273 K.

Table 1. Data collection and handling.

Crystal:	colourless blocks, size 0.50×0.50×0.55 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	4.21 cm^{-1}
Diffractometer, scan mode:	Bruker SMART APEX CCD, ω
$2\theta_{max}$:	50.98°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	7479, 2502
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2149
$N(param)_{refined}$:	195
Programs:	SHELX [10]

Source of material

The reagents and solvents used in this study are commercially available. A mixture of ethyl acetoacetate (13 g, 0.1 mol) and anhydrous potassium carbonate (25 g) in DMF (30 mL) was stirred vigorously at room temperature for 5 min, and then CS_2 (0.1 mol) was added with continued stirring for 30 min. The resulting reaction mixture was cooled in an ice bath, and ethyl 2-chloroacetate (0.1 mol) was added with continued stirring for 15 min. The cooling bath was subsequently removed, and the mixture was stirred for 2 h. The solid product was precipitated by addition of H_2O, collected by filtration, washed with water, and dried. Compound was recrystallized from EtOH to afford crystalline material. Yield: 92%; **m. p.** 95 °C. **IR** (KBr, cm^{-1}) ν_{max} = 3465, 1655, 1618, 1253; **^{1}H-NMR** (600 MHz, DMSO-d_6): δ 10.51 (brs, 1H, OH), 4.16 (q, 4H, J = 6.0 Hz, 2CH_2), 4.06 (s, 2H, CH_2), 2.48 (s, 3H, CH_3), 1.21 (t, 3H, J = 6.0 Hz, 2CH_3); **^{13}C-NMR** (100 MHz, DMSO-d_6): δ 14.5, 14.7, 36.6, 39.8, 61.5, 62.1, 101.6, 126.9, 167.6, 161.6, 163.4, 168.4, 192; **MS** m/z (%): 166.19 [M$^+$, 100%].

Discussion

Thiophene scaffolds have been reported to exhibit a wide variety of pharmacological properties, such as analgesic [1], antidepressant [2], anti-inflammatory [3], antimicrobial activities [4] and anticonvulsant [5–8]. Antiepileptic drugs (AEDs), such as tiagabine [7], etizolam [8], and brotizolam [9] also contain thiphene moieties in their structures. The title compound is composed of a planar thiophene ring (S1/C2-C5) with an ethyl acetyl (O5-O6/C12-C14), hydroxyl, carboxylate (O1/C6-C7), and thio 2-ethoxy-2-oxoethyl (S2/O3-O4/C8-C11), subtituants attached to C2, C3, C4 and C5 atoms, respectively. The S1 atom found to be deviated from the *r.m.s.* plane of the planar thiophene ring with a maximum value of 0.028(1) Å. The geometry of compound is stabilized by an intramoleuclar hydrogen bond to form a S(6) graph set motif. The crystal structure of compound is further stabilized by intermolecular C7–H7A···O5 interaction, that link the molecules to form dimers.

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(7A)	2*i*	–0.0920	0.0863	0.9418	0.083
H(7B)	2*i*	–0.1948	0.2284	0.8549	0.083
H(7C)	2*i*	–0.2120	0.2174	1.0139	0.083
H(8A)	2*i*	0.3804	0.6740	0.5991	0.051
H(8B)	2*i*	0.4148	0.6703	0.7426	0.051
H(10A)	2*i*	0.9029	0.6374	0.4154	0.052
H(10B)	2*i*	0.9493	0.6225	0.5573	0.052
H(11A)	2*i*	1.0504	0.8327	0.3913	0.087
H(11B)	2*i*	0.9017	0.8844	0.5184	0.087
H(11C)	2*i*	0.8559	0.8991	0.3770	0.087
H(13A)	2*i*	–0.5082	1.0337	0.8665	0.059
H(13B)	2*i*	–0.3763	1.1525	0.7780	0.059
H(14A)	2*i*	–0.5637	1.1488	0.6553	0.107
H(14B)	2*i*	–0.4977	0.9723	0.6662	0.107
H(14C)	2*i*	–0.3664	1.0913	0.5779	0.107
H(2A)	2*i*	–0.394(4)	0.573(3)	0.940(3)	0.07(1)

* Correspondence author (e-mail: yahia@ksu.edu.sa)

Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
S(1)	2*i*	0.06087(7)	0.70793(6)	0.77192(6)	0.0270(3)	0.0325(3)	0.0452(3)	–0.0035(2)	–0.0095(2)	–0.0056(2)
S(2)	2*i*	0.34356(7)	0.44321(6)	0.75204(6)	0.0275(3)	0.0354(3)	0.0480(3)	–0.0015(2)	–0.0067(2)	–0.0087(2)
O(1)	2*i*	0.1645(2)	0.2086(2)	0.8677(2)	0.041(1)	0.0353(9)	0.079(1)	–0.0009(7)	–0.0074(9)	–0.0130(8)
O(2)	2*i*	–0.3217(2)	0.4882(2)	0.9370(2)	0.0270(8)	0.042(1)	0.060(1)	–0.0085(7)	–0.0010(7)	–0.0082(8)
O(3)	2*i*	0.7033(2)	0.4531(2)	0.6060(2)	0.0342(9)	0.042(1)	0.084(1)	–0.0001(8)	–0.0016(9)	–0.0158(9)
O(4)	2*i*	0.6962(2)	0.6987(2)	0.5645(2)	0.0259(8)	0.0424(9)	0.0511(9)	–0.0057(7)	–0.0042(7)	–0.0120(7)
O(5)	2*i*	–0.4459(2)	0.7712(2)	0.8972(2)	0.0265(9)	0.048(1)	0.065(1)	–0.0012(7)	–0.0038(8)	–0.0059(8)
O(6)	2*i*	–0.2619(2)	0.9363(2)	0.7935(2)	0.0324(8)	0.0337(9)	0.065(1)	0.0014(6)	–0.0170(7)	–0.0089(7)
C(2)	2*i*	–0.1523(3)	0.6838(2)	0.8401(2)	0.027(1)	0.035(1)	0.038(1)	–0.0029(8)	–0.0096(9)	–0.0059(9)
C(3)	2*i*	–0.1684(3)	0.5364(3)	0.8808(2)	0.028(1)	0.040(1)	0.034(1)	–0.0062(9)	–0.0080(9)	–0.0070(9)
C(4)	2*i*	–0.0087(3)	0.4387(2)	0.8567(2)	0.031(1)	0.036(1)	0.033(1)	–0.0052(9)	–0.0083(9)	–0.0081(9)
C(5)	2*i*	0.1276(3)	0.5196(2)	0.7976(2)	0.030(1)	0.036(1)	0.033(1)	–0.0020(9)	–0.0102(9)	–0.0079(9)
C(6)	2*i*	0.0179(3)	0.2751(3)	0.8845(2)	0.039(1)	0.038(1)	0.039(1)	–0.007(1)	–0.008(1)	–0.010(1)
C(7)	2*i*	–0.1327(3)	0.1952(3)	0.9273(3)	0.050(2)	0.041(1)	0.077(2)	–0.013(1)	–0.011(1)	–0.017(1)
C(8)	2*i*	0.4363(3)	0.6115(3)	0.6728(3)	0.027(1)	0.037(1)	0.057(1)	–0.0039(9)	–0.008(1)	–0.008(1)
C(9)	2*i*	0.6267(3)	0.5750(3)	0.6124(2)	0.030(1)	0.043(1)	0.041(1)	–0.004(1)	–0.0084(9)	–0.010(1)
C(10)	2*i*	0.8792(3)	0.6854(3)	0.4931(2)	0.027(1)	0.056(2)	0.046(1)	–0.007(1)	–0.001(1)	–0.019(1)
C(11)	2*i*	0.9256(4)	0.8381(3)	0.4406(3)	0.047(2)	0.063(2)	0.061(2)	–0.023(1)	–0.001(1)	–0.014(1)
C(12)	2*i*	–0.2995(3)	0.7999(3)	0.8474(2)	0.031(1)	0.040(1)	0.039(1)	–0.0023(9)	–0.0112(9)	–0.007(1)
C(13)	2*i*	–0.4094(3)	1.0555(3)	0.7829(3)	0.041(1)	0.037(1)	0.070(2)	0.009(1)	–0.021(1)	–0.016(1)
C(14)	2*i*	–0.4637(4)	1.0680(3)	0.6607(3)	0.073(2)	0.062(2)	0.072(2)	0.024(2)	–0.036(2)	–0.017(2)

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