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ORIGINAL PAPER

The Synthesis and Crystal Structure of 5-(4-Bromophenylamino)-2-methylsulfanylmethyl-2*H*-1,2,3-triazol-4-carboxylic Acid Ethyl Ester

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Abstract The 5-(4-bromophenylamino)-2-methylsulfanylmethyl-2*H*-1,2,3-triazol-4-carboxylic acid ethyl ester **6** was synthesized from *p*-bromoaniline. The yielded product **6** was investigated with X-ray crystallographic, NMR, MS, and IR techniques. Compound **6**, $C_{13}H_{15}BrN_4O_2S$, Mr = 371.26, crystallizes in the monoclinic space group $P2_1/n$ with unit cell parameters $a = 5.5220(1)$, $b = 26.996(5)$, $c = 10.596(2)$ Å, $\beta = 103.83(3)$. $V = 1533.8(5)$ Å^3, $Z = 4$, D$x = 1.608$ mg m^{-3}. The final R_1 was 0.0844; wR_2 was 0.1560. H-bond is discussed.

Keywords Crystal structure · DMSO · Synthesis · 2*H*-1,2,3-triazole · H-bond · Dimroth rearrangements · 2-Methylsulfanylmethyl-2*H*-1,2,3-triazol-4-carboxylic acid ethyl ester

Introduction

In recent years, the thio-function group compounds of 1,2,3-triazole derivatives have been attracting the attention of chemists and pharmacologists. Certain compounds having the 1,2,3-triazole nucleus have been reported as having antibacterial [1], antifungal [2], antiviral [3], anti-inflammatory, and analgesic [4] properties. Recently, some 1,2,3-triazole derivatives had been synthesized which inhibit tumor proliferation, invasion and metastasis [5], and anti-HIV [6, 7] properties. The 1,2,3-triazole compounds containing sulfur have been found to possess to a moderate degree fungicidal activity and better pesticidal activities [8]. The synthetic route for the intriguing reaction between 1,2,3-triazole and dimethylsulfoxide (DMSO) is shown in Scheme 1.

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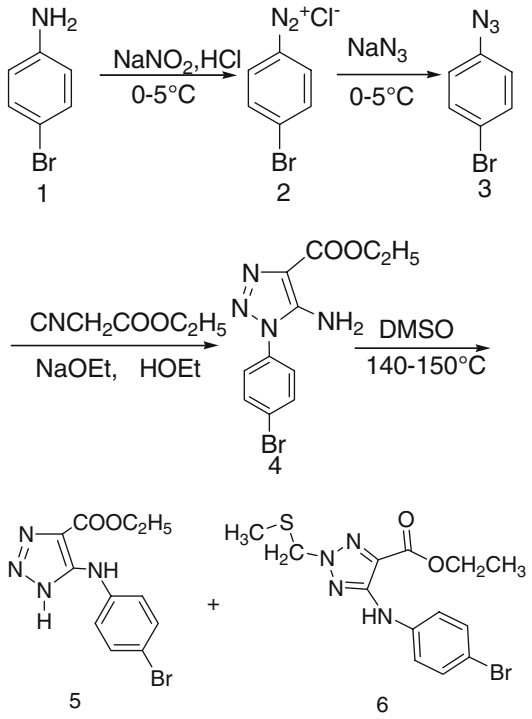
Experimental Section

All melting points were uncorrected and determined on an XT_4-100x microscopic melting point apparatus. IR spectra were obtained in KBr disks on a Nicolet NEXUS 670 FT-IR spectrometer. MS were performed on a HP-5988A spectrometer (EI at 70 eV). ^{1}H-NMR spectroscopy ($CDCl_3$) was recorded on Varian Mercury plus-300 instrument with TMS as an internal standard. Elemental analyses were carried out on a Yanaco CHN Corder MT-3 analyzer.

2.1 5-Amino-1-(4-bromophenyl)-1,2,3-triazol-4-carboxylic acid ethyl ester **4** was prepared following methods in the literature [1, 8], m.p. 168–169 °C.

2.2 Procedure of preparation of 5-(4-bromophenylamino)-2-methylsulfanylmethyl-2*H*-1,2,3-triazol-4-carboxylic acid ethyl ester **6.**

A mixture of 5-amino-1-(4-bromophenyl)-1,2,3-triazol-4-caroxylic acid ethyl ester **4** (0.5 g) and dimethyl sulfoxide (DMSO) 6.0 mL was heated under 140–150 °C for 10 h with stirring. The cooled reaction mixture was poured into 60 mL water and the thick and cloudy liquor was extracted with ethyl ether (20 × 5 mL) and then the resulting solution was dried with anhydrous sodium sulfate for 4 h. The sodium sulfate was removed by filtration. The extraction solution was concentrated. The solid was purified by chromatography



Scheme 1 The synthesis route of compound **6**

on a column of silica gel, was eluted successively with 1:8 ethyl acetate–petroleum ether to give white blocks of compound **5**, yield 30.5%, m.p. 164–165 °C. ^{1}H-NMR: 7.932(s, 1H,–NH–), 7.508–7.533(d, 2H, J = 7.5H$_Z$, Ar-3,5), 7.320–7.345(d, 2H, J = 7.5H$_Z$, Ar-2,6), 7.007(s, 1H, triazole ring-H), 4.471–4.533(q, 2H, J = 6.9H$_Z$, OCH$_2$–), 1.444–1.477(t, 3H, J = 6.9H$_Z$, –OCH$_2$CH$_3$). MS m/z: 312(M$^+$, 56), 282(3), 266(7), 238(2), 209(4), 198(3), 185(100), 171(4), 157(27), 149(13), 130(55), 117(3), 102(21), 91(7), 83(12), 76(23), 69(10), 63(8), 57(10), 50(14), 44(29). IR: 3378, 3164, 3070, 2996, 2929, 1699, 1610, 1571, 1490, 1464, 1400, 1346, 1315, 1274, 1216, 1176, 1113, 1076, 1015, 987, 909, 882, 844, 812, 783, 669, 552, 495. White needles of compound **6**, yield 62.5%, m.p. 102–103 °C. ^{1}H-NMR: 8.084(s, 1H, –NH–), 7.476–7.492(d, 2H, J = 4.8H$_Z$, Ar-3,5), 7.318–7.334(d, 2H, J = 4.8H$_Z$, Ar-2,6), 5.441(s, 2H, –CH$_2$S–), 4.500–4.571(q, 2H, J = 7.2 Hz, –OCH$_2$–), 2.391(s, 3H, –SCH$_3$), 1.481–1.529(t, 3H, J = 7.2 Hz, –OCH$_2$CH$_3$). MS m/z: 372(M$^+$, 25), 340(53), 325(14), 297(11), 267(1), 251(17), 223(11), 213(100), 196(26), 182(16), 172(46), 157(33), 145(18), 130(26), 117(8), 102(21), 90(13), 76(23), 61(50), 50(8), 43(6). IR: 3358, 3192, 3087, 2999, 2938, 2914, 1691, 1603, 1566, 1523, 1471, 1407, 1371, 1349, 1304, 1259, 1144, 1114, 1075, 1024, 998, 964, 908, 811, 783, 745, 693, 668, 646, 588, 502.

The purified product was dissolved in ethyl acetate and petroleum ether solvent. The crystal was obtained after 7 days by evaporation of the solvent.

Table 1 Crystal data and structure refinement details

Empirical formula	$C_{13}H_{15}BrN_4O_2S$
CCDC deposit number	286960
Formula weight	371.26
Temperature, K	293(2)
Wavelength, Å	0.71073
Reflections for cell determination	25
2θ range for above	10–20°
Crystal system	Monoclinic
Space group	$P2_1/n$
Cell dimensions	a = 5.5220(1)
	b = 26.996(5)
	c = 10.596(2) Å
	β = 103.83(3)
Volume, Å^3	1533.8(5)
Z	4
Density (calculated), mg m^{-3}	1.608
Absorption coefficient, mm^{-1}	2.826
Diffractometer/scan	Enraf-Nonius
	CAD-4 $\omega/2\theta$
F(000)	752.0
θ range for data collection, degree	0.98–24.98
Index ranges	$0 \le h \le 6$;
	$0 \le k \le 32$;
	$-12 \le l \le 12$
Reflections collected	2,664
Independent reflection	1,890
Data/restrains/parameters	2,664/0/191
Extinction coefficient	0.0000(2)
Goodness-of-fit on F^2	1.084
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0488,
	wR_2 = 0.1275
R indices	R_1 = 0.0844,
	wR_2 = 0.1560
Largest different peak and hole	0.747 and −0.636 eÅ^{-3}

Single crystals were selected and mounted on the tip of a glass fiber. Preliminary examination and data collection were performed with Mo$K\alpha$ radiation (λ = 0.71073 Å) on an Enraf-Nonius CAD4 computer controlled kappa axis diffractometer operating in the $\omega/2\theta$ scanning mode. The structure was determined by direct methods (SHELXS-86) and refined by full covariance matrix methods (SHELXL-97). The crystal data and the refinement details are given in Table 1.

The structure of the title compound is shown in Fig. 1. The selected bond lengths are given in Table 2, selected bond angles are given in Table 3. The geometric calculations were performed using the program SHELX-97.

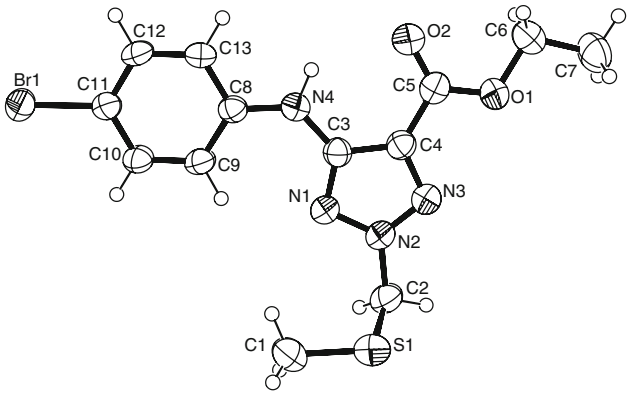


Fig. 1 ORTEP drawing of the title compound **6** showing the atom numbering scheme (Ellipsoids: 50% probability)

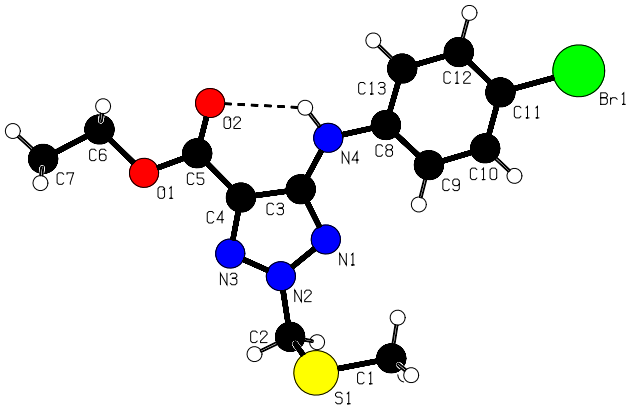


Fig. 2 The H-bond structure of the compound **6** (PWT drawing for the Platon)

Table 2 All non-hydrogen bond lengths (Å)

Atoms	Length	Atoms	Length
S1–C1	1.788(6)	N4–C8	1.377(6)
S1–C2	1.798(6)	Br1–C11	1.894(5)
O1–C5	1.321(6)	C3–C4	1.409(7)
O1–C6	1.450(6)	C4–C5	1.453(7)
O2–C5	1.216(6)	C6–C7	1.480(8)
N1–C3	1.330(6)	C8–C13	1.390(6)
N1–N2	1.354(5)	C8–C9	1.396(6)
N2–N3	1.304(6)	C9–C10	1.370(7)
N2–C2	1.443(6)	C10–C11	1.374(7)
N3–C4	1.343(6)	C11–C12	1.376(7)
N4–C3	1.367(6)	C12–C13	1.374(7)

Table 3 All non-hydrogen bond angles (°)

Atoms	Angle	Atoms	Angle
C1–S1–C2	100.1(3)	O2–C5–O1	124.7(5)
C5–O1–C6	115.4(4)	O2–C5–C4	121.2(4)
C3–N1–N2	102.9(4)	O1–C5–C4	114.1(4)
N3–N2–N1	116.0(4)	O1–C6–C7	108.1(5)
N3–N2–C2	123.4(4)	N4–C8–C13	117.5(4)
N1–N2–C2	120.5(4)	N4–C8–C9	124.4(4)
N2–N3–C4	104.2(4)	C13–C8–C9	118.0(4)
C3–N4–C8	130.0(4)	C10–C9–C8	120.2(4)
N2–C2–S1	113.4(4)	C9–C10–C11	120.8(5)
N1–C3–N4	125.7(4)	C10–C11–C12	120.1(4)
N1–C3–C4	109.0(4)	C10–C11–Br1	120.0(4)
N4–C3–C4	125.4(4)	C12–C11–Br1	119.9(4)
N3–C4–C3	107.9(4)	C13–C12–C11	119.4(4)
N3–C4–C5	124.8(4)	C12–C13–C8	121.5(4)
C3–C4–C5	126.9(4)		

Results and Discussion

The structure of the title compound is shown in Fig. 1. In recent years, the synthesis and characteristics of *s*-triazolo[3,4-b]-1,3,4-thiadiazoles have been investigated [9]. These heterocyclic compounds contain 1,2,3-triazole, 1,2,4-triazole, and 1,3,4-thiadiazole rings condensed through a C–N bond. In a continuation of our earlier studies [10], we now report the crystal structure of 5-(4-bromophenylamino)-2-methylsulfanylmethyl-2*H*-1,2,3-triazol-4-carboxylic acid ethyl ester **6**.

Compound **5** is obtained by Dimroth rearrangements. 5-Amino-1-(4-bromophenyl)-1,2,3-triazol-4-caroxylic acid ethyl ester **4** rearrange into ethyl 5-(4-bromophenylamino)-1*H*-1,2,3-triazole-4-carboxyate **5** when heated in DMSO. Then the reaction of compound **5** with DMSO gives title compound **6**.

The 2*H*-1,2,3-triazole ring system is planar. The bond lengths N1–N2 1.354(5), N2–N3 1.304(6) Å are in agreement with values reported for triazole, N–N 1.352 Å by earlier studies [11]. The bond lengths for C3–N1 and C4–N3, 1.330(6) Å and 1.343(6) Å, respectively, are between those expected for C=N and C–N.

In the crystal structure, there is an intramolecular N4–H(4)···O2 hydrogen bond involving the C=O O2 atom and the 5 position N–H. The molecular conformation and packing are stabilized by intramolecular N4–H(4)···O2 interactions. The bond length of Donor-H···Acceptor is 2.88Å (N–H 0.90; H···O2 2.22Å), the bond angle is 130°. The H-bond structure of the compound **6** is shown in Fig. 2.

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