

# Synthesis, Structure and Biological Activities of *S*-[ $\alpha$ -(4-Methoxyphenylcarbonyl)-2-(1,2,4-triazole-1-yl)] ethyl-*N,N*-dimethyldithiocarbamate

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The title compound was prepared by reaction of *N,N*-dimethyldithiocarbamate sodium with 1-bromo-1-(4-methoxyphenylcarbonyl)-2-(1,2,4-triazole-1-yl) ethane. Its crystal structure has been determined by X-ray diffraction analysis.

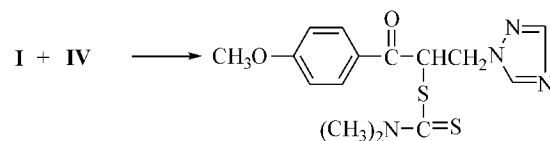
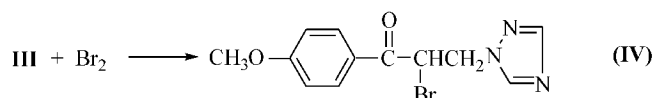
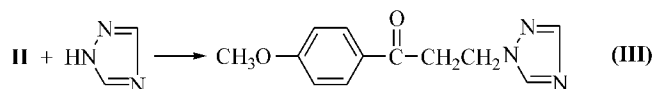
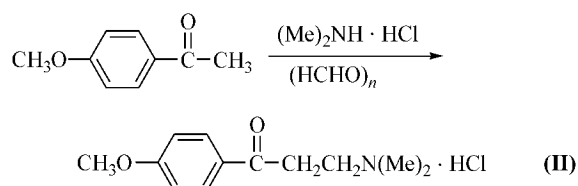
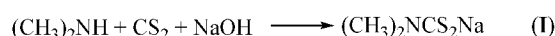
The crystal belongs to triclinic with space group  $P\bar{1}$ ,  $a = 0.7339(2)$  nm,  $b = 1.1032(2)$  nm,  $c = 1.1203(2)$  nm,  $\alpha = 90.27(3)^\circ$ ,  $\beta = 102.03(3)^\circ$ ,  $\gamma = 104.91(3)^\circ$ ,  $Z = 2$ ,  $V = 0.8556(3)$  nm<sup>3</sup>,  $D_c = 1.360$  g/cm<sup>3</sup>,  $\mu = 0.325$  mm<sup>-1</sup>,  $F(000) = 368$ , final  $R_1 = 0.0475$ . The planes of 4-methoxybenzyl group and triazole ring are nearly perpendicular to each other. The dihedral angle is  $83.97^\circ$ . There is an obvious  $\pi$ - $\pi$  stacking interaction between the molecules in the crystal lattice. The results of biological test show that the title compound has fungicidal and plant growth regulating activities.

**Keywords** *N,N*-dimethyldithiocarbamate, 1,2,4-triazole, crystal structure, biological activity

## Introduction

As an important type of fungicides, triazole compounds are highly efficient, low poisonous and inward absorbent.<sup>1-3</sup> At present, the studies on triazole derivatives are mainly concentrated on compounds with triazole as the only active group. There are few reports of triazole compounds that contain both triazole group and other active group in a single molecule. Dialkyl-substituted dithiocarbamate salts have also shown interesting biological effects.<sup>4</sup> *N,N*-Dialkyldithiocarbamate has been known as broad-range fungicides and having different fungicidal mechanism with triazole compounds.<sup>5</sup> But triazole compounds containing *N,N*-dimethyldithiocarbamate have rarely been reported. In order to search for new triazole compounds with higher bioactivity, the title compound was synthesized. The biological activities of the compound were tested. Also, its structure was determined by single crystal X-ray diffraction analysis. The synthetic route is described

as follows:



## Experimental

### Materials and general methods

All chemicals were commercially available sources and used without further purification. Elemental analyses were measured with a Perkin-Elmer 1400C analyzer. IR spectra ( $4000$ — $400$  cm<sup>-1</sup>), as KBr pellets, were recorded on a Nicolet FT-IR 170X spectrophotometer. <sup>1</sup>H NMR spectra were measured with a JEOL FX-90Q nuclear magnetic resonance spectrometer (CDCl<sub>3</sub> as solvent, TMS as internal standard).

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### Synthesis of the target compound

The intermediates **I**<sup>6</sup> and **II**<sup>7</sup> were prepared according to the reported methods. 4-Methoxyacetophenone, poly-formaldehyde and dimethyl-amine hydrochloride were refluxed with ethanol for 5 h, then the mixture was poured into acetone and intermediate **II** was obtained. Yield 83.7%, m.p. 178–180 °C. Intermediate **III** was prepared by reaction of triazole with intermediate **II** in water by reflux according to the method reported in literature.<sup>8</sup> Yield 54.8%, m.p. 60–61 °C. The synthesis of the title compound is described below.

To a 100 mL flask 15 mmol of intermediate **III**, 25 mL of acetic acid and 15 mmol of sodium acetate were added. Then 15 mmol of bromine was dropwise added with stirring at 50–55 °C. The reaction was maintained for about 2–3 h until the mixture was turned into colorless or light yellow. Then 50 mL of water and 40 mL of chloroform were added. The organic layer was successively washed with saturated sodium bicarbonate solution and brine, then dried over sodium sulfate and the chloroform solution containing about 15 mmol of intermediate **IV** was filtrated into a 100 mL flask. Cooled with ice-water, 30 mL of acetone solution of intermediate **I** was added under stirring and the mixture was stirred at room temperature (about 18 °C) for 1.5 h. The solution was filtered, concentrated and purified by flash chromatography (silica gel, using  $V_{\text{ethyl ethanoate}}:V_{\text{cyclohexane}} = 1:4$  as eluent) to afford the target compound. Single crystals suitable for X-ray measurements were obtained by recrystallization from ethyl ethanoate/cyclohexane ( $V:V = 1:3$ ) at room temperature. m.p. 120–122 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 80 MHz)  $\delta$ : 8.15 (s, 1H), 7.98 (s, 1H), 6.81–8.00 (m, 4H), 6.27 (dd,  $J_{12} = 4.88$ ,  $J_{13} = 11.11$  Hz, 1H), 4.88 (dd,  $J_{13} = 11.11$ ,  $J_{23} = 13.89$  Hz, 1H), 4.68 (dd,  $J_{12} = 4.88$ ,  $J_{23} = 13.89$  Hz, 1H), 3.82 (s, 3H), 3.55 (s, 3H), 3.32 (s, 3H); IR (KBr)  $\nu$ : 3138, 2934, 2841, 1666, 1602, 1568, 1505, 1460, 1245, 1177 cm<sup>-1</sup>. Anal. calcd for C<sub>15</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub>S<sub>2</sub> ( $M_r = 350.46$ ): C 51.41, H 5.18, N 15.99; found C 51.17, H 5.16, N 16.30.

### Determination of crystal structure

In the determination of the structure of the single crystal, X-ray intensities were recorded by Rigaku Raxis-IV diffractometer using graphite monochromated Mo K $\alpha$  radiation ( $\lambda = 0.071073$  nm). In the range of  $1.86^\circ < \theta < 26.49^\circ$ , 2998 independent reflections were obtained. Intensities were corrected for Lorentz and polarization effects and empirical absorption, and all data were corrected using SADABS program<sup>9</sup> with  $T_{\text{min}} = 0.9088$  and  $T_{\text{max}} = 0.9378$ .

The structure was solved by direct methods using SHELXS-97 program.<sup>10</sup> All the non-hydrogen atoms were refined on  $F^2$  anisotropically by full-matrix least squares method. Hydrogen atoms were located from the difference Fourier map and added to the structure calculations, but

their positions were not refined. The contributions of these hydrogen atoms were included in structure-factor calculations. The final least-square cycle gave  $R = 0.0475$ ,  $wR = 0.1258$  for 2581 reflections with  $I > 2\sigma(I)$ ; the weighting scheme,  $w = 1/[\sigma(F_o^2) + (0.0703P) + 0.2700P]$ , where  $P = (F_o^2 + 2F_c^2)/3$ . The maximum and minimum difference peaks and holes are 340 and  $-235$  e/nm<sup>3</sup>, respectively.  $S = 1.088$  and  $(\Delta/\sigma)_{\text{max}} = 0.003(7)$ . Atomic scattering factors and anomalous dispersion corrections were taken from *International Table for X-Ray Crystallography*.<sup>11</sup> A summary of the key crystallographic information is given in Table 1. The final position parameters of non-hydrogen atoms are given in Table 2.

**Table 1** Crystal data of the title compound

Empirical formula	C <sub>15</sub> H <sub>18</sub> N <sub>4</sub> O <sub>2</sub> S <sub>2</sub>
Formula weight	350.45
Temperature	29(2) K
Wavelength	0.071073 nm
Crystal system, space group	Triclinic, $P\bar{1}$
Unit cell dimensions	$a = 0.7339(2)$ nm, $b = 1.1032(2)$ nm, $c = 1.1203(2)$ nm, $\alpha = 90.27(3)^\circ$ , $\beta = 102.03(3)^\circ$ , $\gamma = 104.9(3)^\circ$
Volume	0.8556(3) nm <sup>3</sup>
$Z$ , Calculated density	2, 1.360 Mg/m <sup>3</sup>
Absorption coefficient	0.325 mm <sup>-1</sup>
$F(000)$	368
Crystal size	0.30 mm $\times$ 0.20 mm $\times$ 0.20 mm

**Table 2** Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement parameters (nm<sup>2</sup>  $\times 10$ ) for the title compound

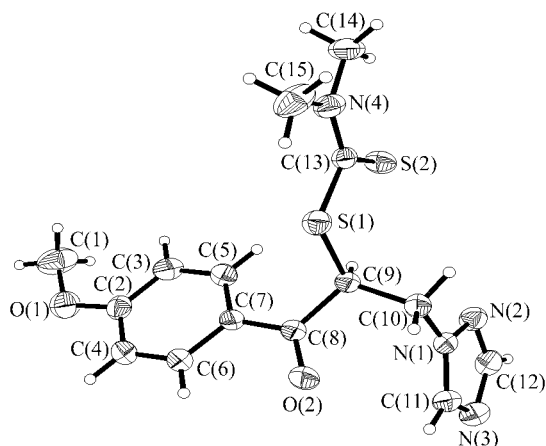
Atom	$x$	$y$	$z$	$U_{\text{eq}}^a$
S(1)	3805(1)	2411(1)	1816(1)	54(1)
S(2)	999(1)	2898(1)	-409(1)	63(1)
N(1)	-1281(2)	-23(1)	2035(1)	50(1)
N(2)	-2715(2)	100(1)	1096(1)	59(1)
N(3)	-3960(3)	-793(2)	2655(2)	73(1)
N(4)	4787(2)	3306(1)	-166(2)	63(1)
O(1)	2835(2)	7168(1)	5344(2)	83(1)
O(2)	1718(2)	1415(1)	4285(1)	77(1)
O(1)	2659(4)	8156(2)	4576(3)	106(1)
O(2)	2521(2)	5984(2)	4827(2)	59(1)
O(3)	1931(3)	5686(2)	3569(2)	64(1)
O(4)	2803(3)	5084(2)	5619(2)	65(1)
O(5)	1661(3)	4456(2)	3140(2)	58(1)
O(6)	2540(3)	3875(2)	5195(2)	60(1)
O(7)	1964(2)	3544(2)	3936(2)	51(1)
O(8)	1714(3)	2225(2)	3552(2)	52(1)
O(9)	1465(2)	1844(2)	2202(1)	46(1)
O(10)	717(3)	422(2)	1936(2)	52(1)
O(11)	-2061(3)	-546(2)	2943(2)	66(1)
O(12)	-4279(3)	-375(2)	1521(2)	63(1)
O(13)	3223(2)	2908(1)	308(2)	48(1)
O(14)	4638(4)	3768(2)	-1393(2)	87(1)
O(15)	6729(3)	3292(2)	477(3)	92(1)

<sup>a</sup>  $U_{\text{eq}}$  is defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

## Results and discussion

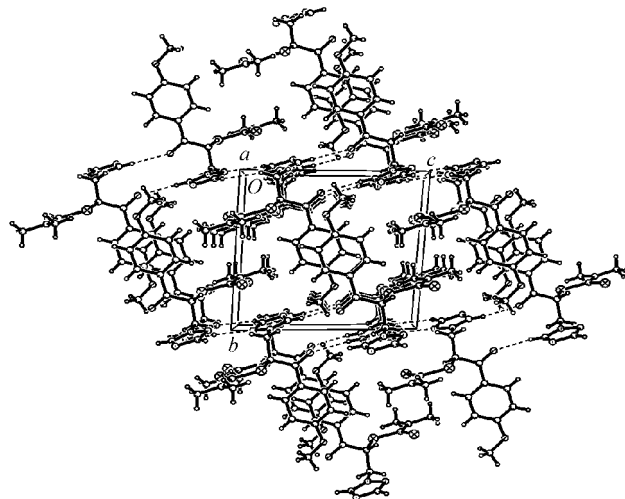
### Description of the structure

Fig. 1 shows a perspective view of the title compound



**Fig. 1** Molecular structure for the title compound with the atomic numbering scheme.

with atomic numbering scheme, and Fig. 2 shows a perspective view of the crystal packing in the unit cell. Selected bond lengths and angles are listed in Table 3. Hydrogen bonds and potentially weak intermolecular interactions are listed in Table 4.



**Fig. 2** A view of the crystal packing down the *a*-axis for the title compound.

**Table 3** Selected bond lengths (nm) and angles ( $^{\circ}$ ) for the title compound

S(1)—C(13)	0.178(2)	S(1)—C(9)	0.181(2)
S(2)—C(13)	0.165(2)	N(1)—C(11)	0.133(2)
N(1)—N(2)	0.135(2)	N(1)—C(10)	0.145(2)
N(2)—C(12)	0.131(3)	N(3)—C(11)	0.131(3)
N(3)—C(12)	0.134(3)	N(4)—C(13)	0.133(2)
N(4)—C(14)	0.146(3)	N(4)—C(15)	0.146(3)
C(1)—C(2)	0.137(2)	C(1)—C(1)	0.140(3)
C(2)—C(8)	0.121(2)	C(2)—C(4)	0.136(3)
C(13)—S(1)—C(9)	103.2(8)	C(11)—N(1)—N(2)	109.0(2)
C(11)—N(1)—C(10)	131.2(2)	N(2)—N(1)—C(10)	119.8(1)
C(12)—N(2)—N(1)	102.4(2)	C(11)—N(3)—C(12)	102.2(2)
C(13)—N(4)—C(14)	121.2(2)	C(13)—N(4)—C(15)	123.3(2)
C(14)—N(4)—C(15)	115.5(2)	C(2)—C(1)—C(1)	119.0(2)
C(4)—C(2)—C(1)	116.0(2)	C(4)—C(2)—C(3)	120.7(2)
C(1)—C(2)—C(3)	123.3(2)	C(5)—C(3)—C(2)	118.7(2)
C(2)—C(4)—C(6)	120.5(2)	C(7)—C(5)—C(3)	120.9(2)
C(4)—C(6)—C(7)	120.4(2)	C(5)—C(7)—C(6)	118.9(2)
C(5)—C(7)—C(8)	124.1(2)	C(6)—C(7)—C(8)	117.1(2)
C(2)—C(8)—C(7)	121.7(2)	C(2)—C(8)—C(9)	118.4(2)

**Table 4** Intermolecular interaction distances (nm) of the title compound

D—H...A	Symm.	D—H	H...A	D...A	D—H...A
C(11)—H(11A)...O(2)	$-x, -y, 1-z$	0.09300	0.24493	0.32326	141.91
C(12)—H(12A)...N(2)	$-1-x, -y, -z$	0.09300	0.25755	0.33482	140.80
C(15)—H(15C)...S(2)	$1+x, y, z$	0.09600	0.28715	0.36037	133.85

D: Donor; A: Acceptor; Symm.: Symmetry applied in acceptor.

For the title compound, the crystal structure consists of  $S[\alpha(4\text{-methoxyphenylcarbonyl})_2(1,2,4\text{-triazole-1-yl})]_2\text{ethyl-}N,N\text{-dimethyldithiocarbamate}$  and has an inversion symmetry center. Bond lengths and angles are generally normal in the phenyl ring and triazole ring of the title compound.<sup>12,13</sup> The bond lengths and angles in *N,N*-dimethyldithiocarbamate group are in good agreement with the previous report.<sup>14</sup> The triazole ring [N(1), N(2), N(3), C(11) and C(12)] with the conjunction carbon atom C(10) is fairly planar, and the deviation from the least squares plane through the ring atoms is smaller than 0.001(3) nm. Plane equation:  $-1.9725x + 10.1658y + 4.2659z = 1.1070$ . The phenyl ring [C(2), C(3), C(4), C(5), C(6) and C(7)] with the conjunction carbon atom C(8) and methoxy group [O(1) and C(9)] are also quite planar with plane equation:  $7.1646x - 0.5670y - 3.1279z = -0.0305$ , and the largest deviation from the least squares plane is 0.004(3) nm. The dihedral angle between the triazole ring moiety and the phenyl ring is 83.97(2)°. All atoms in *N,N*-dimethyldithiocarbamate group are also quite planar, and the largest deviation from the least squares plane is 0.0011(3) nm. Plane equation:  $-1.3219x + 10.1820y + 3.9686z = 2.6623$ . This plane is nearly perpendicular to the plane of *p*-methoxyphenyl ketone, with the dihedral angle of 89.26(2)°. The dihedral angle between the plane of *N,N*-dimethyl-dithiocarbamate group and the plane of triazole moiety is 5.29(2)°.

There are some potentially weak (C—H...Y hydrogen bonds, Y = O, N and S) intermolecular interactions.<sup>15,16</sup> The N(2), O(2) and S(2) with C atoms form potentially weak intermolecular interactions which are shown in Table 4. The other feature of intermolecular interaction is due to the two different types of  $\pi$ - $\pi$  stacking interactions between the molecules in the crystal lattice. The center-to-center distances between two adjacent phenyl rings are 0.3963 and 0.3902 nm, respectively. It is obvious that they form the stronger  $\pi$ - $\pi$  stacking interaction.<sup>17</sup> In the solid state, these intermolecular interactions stabilize the structure.

### Biological activity

The primary biological test showed that the title compound exhibits inhibiting activity towards fungi, such as stem wilt of asparagus, rape sclerotinose and tobacco virus, but not remarkably. Its inhibiting rates reach 11.1%, 8.9% and 18.8% at 50  $\mu\text{g/mL}$ , respectively. It shows promoting activity towards rooting of cucumber

cotyledon and growing of cucumber cotyledon, and the promoting rates reach 47.5% and 9.4% at 10  $\mu\text{g/mL}$ . It possesses lower inhibiting activity towards wheat coleoptile elongation and rape hypocotyledonary axis, and its inhibiting rates reach 2.3% and 3.6% at 10  $\mu\text{g/mL}$ , respectively.

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