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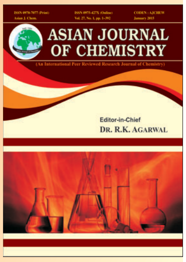

Synthesis, Crystal Structure and Biological Activity of Novel *N*-2-Chlorophenyl-*N′*-2-[3-phenoxymethyl-4-phenyl-[1,2,4]triazole-5-thio]acetyl Hydrazone

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N-2-Chlorophenyl-*N′*-2-[3-phenoxymethyl-4-phenyl[1,2,4]triazole-5-thio]acetyl hydrazone was synthesized by condensation reaction of 2-[3-phenoxymethyl-4-phenyl[1,2,4]triazole-5-thio]acethydrazide with 2-chlorobenzaldehyde under the conditions of microwave irradiation. The structure of the title compound was conformed by IR, ^{1}H NMR, ^{13}C NMR, elemental analysis and single crystal X-ray diffraction. In the crystal, the compound was assembled to one-dimensional chain-like supramolecular by three intermolecular hydrogen bonds. The promoting effects of the compound on rape growth was also tested preliminarily.

Keywords: Microwave synthesis, Hydrazone, Crystal structure, Biological activity.

INTRODUCTION

In recent years, a number of hydrazone derivatives having been claimed to possess a wide range of biological activities, such as antibacterial[1], antifungal[2], antimalarial[3] and antitumor[4]. In addition, owning to the strong coordination ability, hydrazone derivatives are extensively utilized as the collector for some transition metals[5]. Recently, these compounds have attracted considerable attention for their potential uses as in supramolecular chemistry because of their characteristic behaviours based on strong hydrogen-bond donors. In fact, the biological activity and the coordination ability of these kinds of compounds are closed related to their structure. Moreover, it has become an important means to study the supramolecular compounds from the crystallography view[6-8]. In view of this and as a part of our research, we synthesized *N*-2-chloro-phenyl-*N'*-2-[3-phenoxymethyl-4-phenyl[1,2,4]triazole-5-thio]acetyl hydrazone and studied the crystal structure which indicated that the compound was assembled to one-dimensional chain-like supramolecular. In addition, the preliminary biological activity tests showed that the title compound remarkably enhanced the root elongation of rape seedings, moreover, it possessed antibacterial activity against *bacillus subtilis*.

EXPERIMENTAL

Melting points were recorded using a digital model X-4 apparatus and are uncorrected. IR spectra were recorded on a digital FTS-3000 infrared spectrometer (KBr pellet). ^{1}H NMR and ^{13}C NMR spectra were determined as DMSO-d_6 solutions using a varian mercury plus-400 MHz spectrometer. Elemental analyses were determined using PE-2400 C H N elemental analyzer. Microwave irradiations were carried out in a Galanz domestic microwave oven in which a hole was made in the roof of the oven to permit a condenser to be fitted to the flask undergoing irradiation. In periods of irradiation, precautions were taken to avoid exposure to experimentalists.

All commercially available products were used without further purification; Phenoxyacetyl hydrazine (**2**), 1-phenoxyacetyl-4-phenylamino thiocarbamide (**3**) and 2-[3-phenoxymethyl-4-phenyl-1,2,4-triazole]-5-thione (**4**) were prepared according to literature procedures[10-13].

2-[3-Phenoxymethyl-4-phenyl[1,2,4]triazole-5-thio]ethyl acetate (5): A mixture of the 2-[3-phenoxymethyl-4-phenyl-1,2,4-triazole]-5-thione (20 mmol), ethyl chloroacetate (22 mmol) and anhydrous potassium carbonate (25 mmol) in acetone was mixtured, The solution was heated under reflux on a oil-bath for 8 h. Then the mixture was filtered off, the filtrate was evaporated and recrystallized from EtOH-H_2O.

2-[3-Phenoxymethyl-4-phenyl-[1,2,4]-triazole-5-thio]acethydrazide (6): 2-[3-Phenoxymethyl-4-phenyl-1,2,4-triazole-5-thio]ethyl acetate (**5**) (20 mmol) was added to a solution of ethanol (30 mL) and in 85 % hydrazine hydrate (20 mmol), The solution was heated under reflux on a oil-bath for 10 h. The mixture was filtered off and recrystallized from EtOH-DMF-H_2O.

***N*-2-chlorophenyl-*N*'-2-[3-phenoxymethyl-4-phenyl-[1,2,4]triazole-5-thio]acetyl hydrazone (7):** 2-[3-Phenoxymethyl-4-phenyl-1,2,4-triazole-5-thio]acethydrazide (**7**) (2 mmol), 2-chlorobenzaldehyde and DMF (6 mL) were placed in a dried round-bottomed flask and the reaction mixture was subjected to microwave irradiation (230 W) for 1 min periods up to a total of 5 min irradiation (400 W) again. The mixture was cooled to room temperature and then recrystallization from EtOH-DMF. The structure of the title compound has been elucidated by spectral (IR, ^{1}H NMR, ^{13}C NMR) and elemental analysis data.

Compound 7: Yield: 70 %, m.p. 175-177 ºC. IR (KBr, ν_{max}, cm^{-1}): ν = 3228 (N-H), 3066 (Ar-H), 1699 (C=O), 1597 (C=N), 1494 (C=N-N), 1214 (C-O-C), 690 (C-S-C). ^{1}H NMR (DMSO-*d*$_6$): δ_H = 12.01 (s, 1H, NH), 11.85 (s, 1H, NH), 8.39 (s, 1H, N=CH), 8.59 (s, 1H, N=CH), 4.09 (s, 2H, $SCH_2C=O$), 4.51 (s, 2H, $SCH_2C=O$), 5.07 (s, 2H, OCH_2), 6.84-7.95 (m, 14H, Ar-H); ^{13}C NMR (DMSO-*d*$_6$): δ_C = 34.6, 59.8, 115.0, 122.0, 124.5, 124.8, 127.8, 128.4, 128.6, 129.4, 129.9, 130.6, 130.8, 132.7, 132.8, 133.7, 133.9, 139.5, 142.8, 148.5, 152.6, 154.7, 157.1, 163.2, 168.4. Anal. Calcd for $C_{24}H_{20}N_5O_2SCl$: C: 60.31, H: 4.22, N: 14.65; found: C: 60.33, H: 4.20, N: 14.63.

From the data shown above, the spectroscopic data was in agreement with the crystal structure. In the ^{1}H NMR spectra, it was found out that the N-H proton peak of the title compound appeared in 12.01 and 11.85 ppm and the N-H proton peak shifted to low field, which was in accord with the strong hydrogen bond, N-H…N. Morever, the IR spectra exhibited the N-H stretching vibration absorption at 3228 cm^{-1}, which was also in accord with the intermolecular hydrogen bond N-H…N.

Crystal structure of 7: The single-crystal was obtained from the slow evaporation of EtOH solution of compound **7** at room temperature for one month. A suitable crystal was selected and mounted on the top of a glass fiber in a random orientation. All X-ray crystallographic data were collected on a Bruker SMART APEX II CCD diffractometer equipped with a graphite-monochromatized MoK$_\alpha$ radiation (λ = 0.71073 Å) radiation using φ/ω scan technique at 293 K. The structures were solved by a direct method and refined by a full-matrix least-squares procedure based on F^2 using the SHELXTL program package.The molecular structure of compound **7** is shown in Fig. 1 and a summary of the crystallographic data and refinement parameters are given in Table-1.

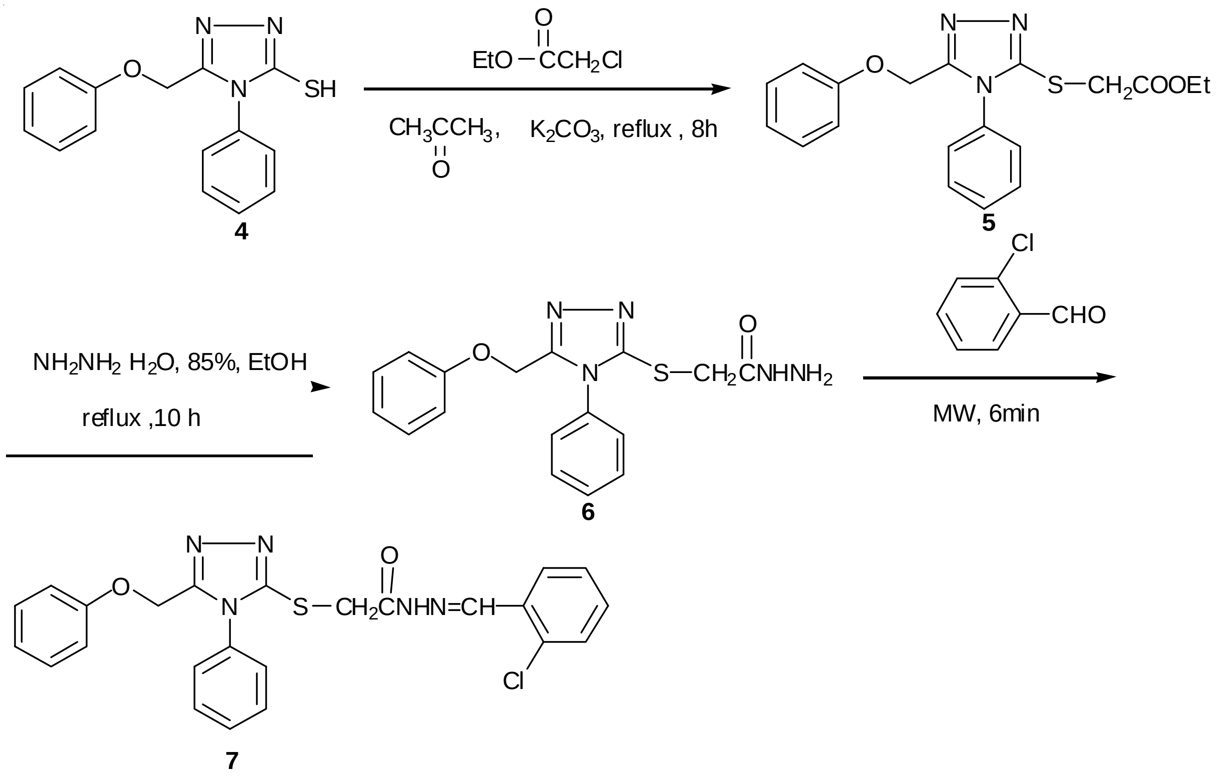
Bioactivity assay: The title compound was investigated for plant growth regulation activity. Method of plate culture was adopted and the compound solutions were prepared in the concentration of 100, 10, 1, 0.1, 0.01 and 0.001 ppm, whereafter, rape seeds were cultured in a 10 cm petri dish with 10 mL of different solution and a circular fiter paper. Then, the roots were allowed to grow at room temperature, the roots length was gained after 4 days, the percentage plant growth activity was calculated according to the following equation:

$$\text{Plant growth activity (\%)} = \frac{(N - N_1)}{N_1} \times 100$$

where N is the root length cultured in compound solution and N$_1$ is the length cultured in the distilled water under the same condition.

RESULTS AND DISCUSSION

The general synthesis routes of these compounds followed as (**Scheme-I**). The crystal structure of title compound atom-labelling scheme was shown in Fig. 1. The crystal data and structure refinement details for title compound was summarized in Table-1, selected bond distances and angles is listed in Table-2.



Scheme-I

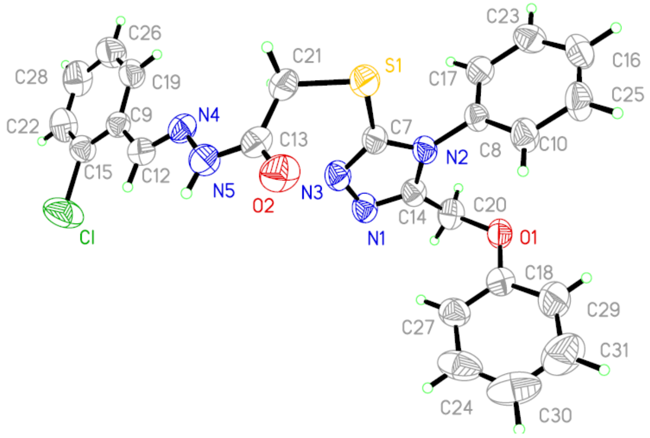


Fig. 1. Molecular structure of the title compound **7**

TABLE-1
CRYSTAL DATA AND STRUCTURE
REFINEMENT DETAILS FOR COMPOUND **7**

m.f.	$C_{96}H_{80}N_{20}O_8S_4Cl_4$
Formula weigh	1911.84
Crystal group	Triclnic
Space group	P21/c
a (Å)	1.6858(3)
b (Å)	9.988(2)
c (Å)	14.406(3)
α (°)	90.00
β (°)	112.61(9)
γ (°)	90.00
V (Å^3)	223.92 (8)
Z	1
Dcalcd (Mg m^{-3})	1.418
Absorption correction	Empirical
F (000)	992
Limiting indices	$-22 \leqq h \leqq 22$, $-12 \leqq k \leqq 13$, $-17 \leqq l \leqq 19$
Reflections collected	3321
Independent reflections	5383 [$R_{int} = 0.0304$]
Date/restraints/parameters	5383/0/298
Final R indices[I > 2σ(I)]	$R_1 = 0.0416$, $wR_2 = 0.0673$
R indices (all data)	$R_1 = 0.0792$, $wR_2 = 0.0723$
Refinement method	SHELXL
Goodness of fit on F^2	1.564
Crystal chromatography data deposited accession number	CCDC 739430

As shown in Fig. 2, the title compound contains a triazole ring and three benzene rings. Just as anticipation, the triazole ring is in one plane and the mean deviation from the best plane of the five non-H atoms is 0.0005 Å. In addition, from Fig. 3 we can find the parallel packing of the phenyl rings in the crystal of the compound. However, the distance between the centers of two parallel phenyl rings is 39.32 nm, which is out of the accepted range of the intermolecular π-π interaction[9]. There are three types hydrogen bonds in the crystal struchure as shown in Fig. 2. The first one is N(5C)-H(5AC)…N(3A), the other is O(2C)-H(23D)…C(23D) and the last one is N(3A)-

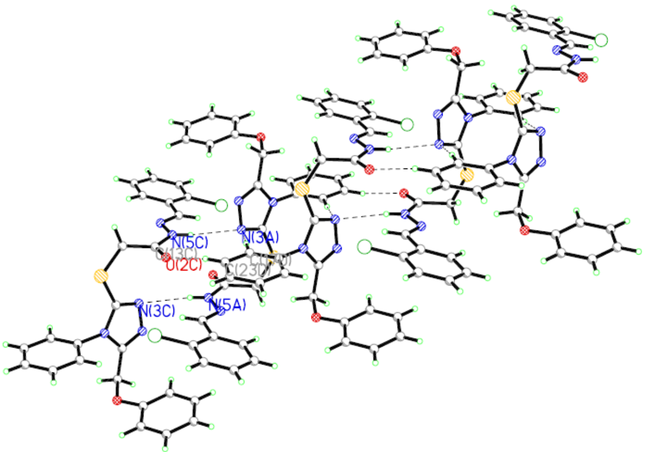


Fig. 2. C-H…O, N-H…C and N-H…N which link the supramolecule of the title compound with one-dimenisional chain superamolecule

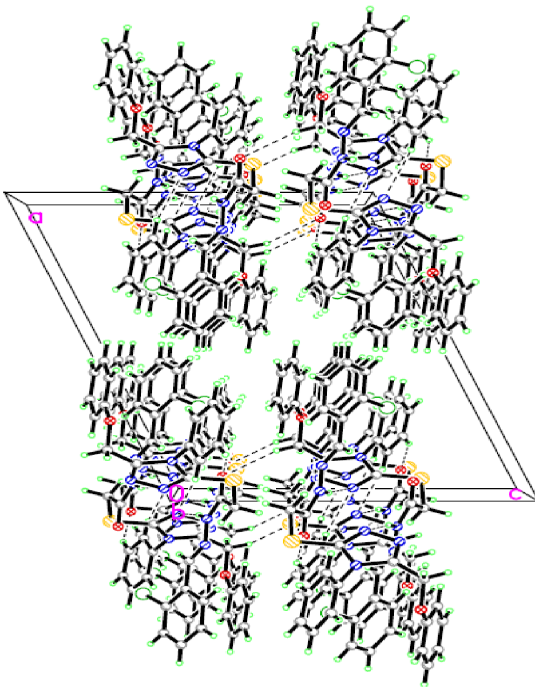


Fig. 3. Paking dingram of title compound

TABLE-2
SELECTED BOND LENGTHS (Å) AND BOND ANGLES (°) FOR COMPOUND **7**

C1-C15	1.7284(18)	S1-C7	1.7407(18)	S1-C21	1.7958(16)
O1-C18	1.3735(19)	O1-C20	1.4209(18)	O2-C13	1.2135(17)
N1-C14	1.3033(19)	N1-N3	1.3997(18)	N2-C7	1.3657(19)
N2-C14	1.3722(19)	N2-C8	1.4468(18)	N3-C7	1.3176(18)
N4-C12	1.2789(18)	N4-N5	1.3745(16)	N5-C13	1.3552(19)
C7-S1-C21	99.07(8)	C18-O1-C20	118.65(12)	C14-N1-N3	107.37(13)
C7-N2-C14	104.6(13)	C7-N2-C8	126.94(14)	C14-N2-C8	128.26(14)
C7-N3-N1	106.7(13)	C12-N4-N5	115.36(14)	C13-N5-N4	122.07(14)
N3-C7-N2	110.5(15)	N3-C7-S1	127.11(13)	N2-C7-S1	122.31(12)
C17-C8-N2	119.2(14)	C10-C8-N2	119.62(14)	N4-C12-C9	120.73(16)
O2-C13-N5	120.6(17)	N1-C14-N2	110.66(15)	N2-C14-C20	124.59(15)

TABLE-3
DATA OF HYDROGEN BOND FOR **3**

D-H…A	D-H (nm)	H…A (nm)	D…A (nm)	D-H…A (°)	Symmetry code
N(5C)-H(5AC)…N(3A)	0.086	0.2388	0.3236	168.78	-X, -Y, -Z
O(2C)-H(23D)…C(23D)	0.093	0.2464	0.1214	154.7	-
N(3A)-H(17D)…C(17D)	0.093	0.2598	0.1318	166.9	-

TABLE-4
PLANT GROWTH REGULATING ACTIVITY DATA

Compound	% Plant growth activity[a]					
	100 (ppm)	10 (ppm)	1 (ppm)	0.1 (ppm)	0.01 (ppm)	0.001 (ppm)
7	-100	-40.9	15.5	22.1	30.7	49.3
Heteroauxing	-100	-95.5	-88.9	-47.6	-46.1	-10.7

[a] Solution was prepared in the proportion of H_2O:DMF = 99.5:0.5, and 0.1 g Tween-100 was added to promote the compound to dissolved

H(17D)…C(17D). From Table-3, it is noted that the hydrogen bond N(5C)-H(5AC)…N(3A) is stronger than O(2C)-H(23D)…C(23D) and N(3A)-H(17D)…C(17D), because the hydrogen bond length of N(5C)---H(5AC)…N(3A) is shorter than the later two, respectively. Morever, it can also be seen that the crystals were linked to one-dimenisional chain-like superamolecule through three intermolecular hydrogen bonds, which form a nine-membered ring with C17D, C23D, H23D, O2C, C13C, N5C, H5AC, N3A, H17D. From Fig. 3, it can be seen that the supramolecular are connected by intermolecular hydrogen bond of O(2C)- H(23D)…C(23D) along the oc-axis direction and parallel packing along the ob-axis direction.

From the results summarized in Table-4, it is apparent that the title compound exhibit inhibition activity at high concentration of 100 and 10 ppm, while displayed enhancing root elongation activity at the low concentration. Also, compared with the hetero-auxing of isoconcentration, compound **7** remarkablely showed enhancement activity in low condition.

Conclusion

The synthesis and 1 D chain supramolecular structure of the title compound has been reported. The compound **7** is synthesized with the method of microwave-induced synthesis and this method has the advantages of mild conditions, simple operation, short reaction times and high yield. Interesting, there is an unusual NMR shift of the N-H is found. Finally, in the crystal of compound **7**, there are there types of hydrogen bonds in the crystal structure; and, with the help of them, the compound was assembled to 1 D chain supramolecular structure by these three types of intramolecular hydrogen bonds.

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