

Synthesis, Crystal Structure and Herbicidal Activity of a 1, 2, 4-triazol-5(4*H*)-one Derivative

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Summary: A new triazole compound, C₁₆H₁₁Cl₂N₃O, was synthesized and the crystal structure was determined by single crystal X-ray diffraction study. The crystal symmetry is monoclinic, space group P2(1)/c, with a = 15.710(10) Å, b = 9.969(6) Å, c = 10.800(7) Å, α = 90°, β = 103.271(11)°, γ = 90°. The herbicidal activity of the title compound was determined showing a good herbicidal activity.

Keywords: Crystal structure, Synthesis, 1,2,4-triazole, Herbicidal activity.

Introduction

In recent years, heterocycle compounds have received extensive attentions in medicinal and pesticidal chemistry field [1-5] owing to a wide range of biological activities. Notably, 1,2,4-triazole compounds play a crucial role due to their excellent pharmacological and pesticidal performances. Some of them have shown a variety of biological activities including fungicidal [6], insecticidal [7], herbicidal [8], KARI [9], anti-HIV [10] and anti-tumor activities [11], etc. The first triazolinone herbicide, namely azafenidin, was developed by Dupont in the 1970s[12], which evoked the successful invention and commercialization of a number of triazolinone derivatives for crop protections, such as amicarbazone[13], azafenidin [12], sulfentrazone[14] and carfentrazone-ethyl. These compounds are effective in being useful in [15, 16]. We are interested in developing the novel 1,2,4-triazole compounds for herbicidal applications. Here, we report the synthesis and bioactivity of a novel 1, 2, 4-triazole derivative, namely, 4-benzyl-1-(2,4-dichlorophenyl)-3-methyl-1*H*-1,2,4-triazol-5(4*H*)-one, which displays good herbicidal activity against monocotyledon.

Results and Discussion

Chemistry and Spectroscopic Properties

Compound **3** was synthesized at 0-5 °C. Compound **4** was prepared according to the known procedure [8]. The molecular structures of all the intermediates and target compounds were analyzed by ¹H NMR spectroscopy, infrared spectroscopy (FT-IR), elemental analysis as well as single crystal X-ray diffraction analysis. Based on the ¹H NMR spectrum of the title compound, the CH₂ proton signals appear

at as a singlet at 4.91 ppm. The two methyl groups appear as two singlets at δ 2.10 ppm and 2.37 ppm, respectively. The IR spectrum of the title compound shows an absorption band at 1711 cm⁻¹, which is assigned as the characteristic stretching vibration signal of the carbonyl (C=O) functional group. The signal of C=N double bonds appeared at a wave number of 1583 cm⁻¹.

Crystal Structure

The molecular structure and unit cell crystal packing of the compound are presented in Fig. 1 and 2 respectively. The atomic coordinates and equivalent isotropic displacement parameters are shown in Table-1. The selected bond lengths, bond angles and torsion angles of the title compound are listed in Table-2 and 3 respectively [17-19]

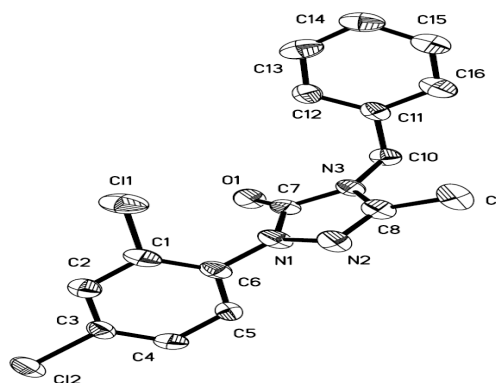


Fig. 1: Molecular structure of the title compound, showing displacement ellipsoids drawn at the 30% probability level.

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Table-1: Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{Å}^2 \times 10^3$) for title compound. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
Cl(1)	2410(1)	-993(2)	366(3)	93(1)
Cl(2)	5686(1)	-2112(2)	34(2)	76(1)
O(1)	2857(3)	2158(5)	1893(4)	64(1)
N(1)	3248(3)	109(5)	2925(5)	60(2)
N(2)	3076(3)	-559(5)	3977(5)	61(2)
N(3)	2367(3)	1375(5)	3656(5)	44(1)
C(1)	3515(4)	-988(6)	1023(7)	56(2)
C(2)	4083(4)	-1523(6)	365(7)	56(2)
C(3)	4969(4)	-1492(6)	904(6)	51(2)
C(4)	5290(4)	-969(8)	2067(7)	69(2)
C(5)	4713(5)	-441(8)	2747(6)	64(2)
C(6)	3832(4)	-438(6)	2231(6)	52(2)
C(7)	2829(4)	1320(6)	2702(6)	49(2)
C(8)	2554(4)	231(6)	4381(6)	53(2)
C(9)	2180(5)	-42(7)	5510(7)	74(2)
C(10)	1906(4)	2596(6)	3890(6)	52(2)
C(11)	933(4)	2514(6)	3367(6)	49(2)
C(12)	596(8)	2418(13)	2086(13)	56(4)
C(13)	-312(10)	2488(15)	1655(17)	79(5)
C(14)	-881(5)	2527(9)	2476(10)	84(2)
C(15)	-466(10)	2610(18)	3770(17)	80(5)
C(16)	416(9)	2601(18)	4233(17)	79(5)

Table-2: Selected bond lengths (Å) and angles ($^\circ$) for the title compound.

bond lengths	Å	Bond angles	$^\circ$
Cl(1)-C(1)	1.718(7)	C(7)-N(1)-N(2)	112.8(5)
Cl(2)-C(3)	1.737(6)	C(7)-N(1)-C(6)	126.0(5)
O(1)-C(7)	1.217(7)	N(2)-N(1)-C(6)	121.1(5)
N(1)-C(7)	1.370(8)	C(8)-N(2)-N(1)	104.0(5)
N(1)-N(2)	1.396(7)	C(8)-N(3)-C(7)	108.0(5)
N(1)-C(6)	1.421(8)	C(8)-N(3)-C(10)	129.7(5)
N(2)-C(8)	1.282(8)	C(7)-N(3)-C(10)	121.5(5)
N(3)-C(8)	1.377(8)	C(2)-C(1)-C(6)	120.1(6)
N(3)-C(7)	1.390(7)	C(2)-C(1)-Cl(1)	120.1(6)
N(3)-C(10)	1.468(7)	C(6)-C(1)-Cl(1)	119.8(5)
C(1)-C(2)	1.371(9)	C(1)-C(2)-C(3)	119.1(6)
C(1)-C(6)	1.397(9)	C(4)-C(3)-C(2)	121.9(6)
C(2)-C(3)	1.380(9)	C(4)-C(3)-Cl(2)	119.4(5)
C(3)-C(4)	1.346(10)	C(2)-C(3)-Cl(2)	118.7(5)
C(4)-C(5)	1.395(9)	C(3)-C(4)-C(5)	119.1(6)
C(5)-C(6)	1.367(9)	C(6)-C(5)-C(4)	120.4(6)
C(8)-C(9)	1.496(9)	C(5)-C(6)-C(1)	119.4(6)
C(10)-C(11)	1.505(9)	C(5)-C(6)-N(1)	120.0(6)
C(11)-C(12)	1.366(14)	C(1)-C(6)-N(1)	120.5(6)
C(11)-C(16)	1.375(16)	O(1)-C(7)-N(1)	129.5(5)
C(12)-C(13)	1.396(18)	O(1)-C(7)-N(3)	128.0(5)
C(13)-C(14)	1.396(19)	N(1)-C(7)-N(3)	102.5(5)
C(14)-C(15)	1.402(19)	N(2)-C(8)-N(3)	112.6(5)
C(15)-C(16)	1.36(2)	N(2)-C(8)-C(9)	124.5(6)
C(12')-C(13')	1.40(2)	N(3)-C(8)-C(9)	122.8(5)
C(15')-C(16')	1.35(2)	N(3)-C(10)-C(11)	112.9(5)

In general, the average bond lengths and bond angles of the ring systems (phenyl and triazole) are within the normal ranges [17-19]. However, it is observed that the C7-N1 bond [1.37 Å] is shorter than the normal C-N single bond (1.47 Å), which indicates a conjugation effect formed between C7-N1

bond with neighboring N2=C8 double bond. The bond length of C7=O1 (Table-1) is in agreement with other C=O counterparts existing in 1,2,4-triazole ring. From Table 3, the torsion angles of these rings are close to 0° or 180° respectively. The torsion angles of C6-N1-N2-C8, N2-N1-C7-O1 are close to 180° . The torsion angles of C7-N1-N2-C8, C1-C2-C3-C4 is close to 0° .

Table-3: Torsion angles [$^\circ$] for title compound.

Torsion angles	$^\circ$
C(7)-N(1)-N(2)-C(8)	0.4(7)
C(6)-N(1)-N(2)-C(8)	178.1(6)
C(6)-C(1)-C(2)-C(3)	-0.9(9)
Cl(1)-C(1)-C(2)-C(3)	179.2(5)
C(1)-C(2)-C(3)-C(4)	1.0(10)
C(1)-C(2)-C(3)-Cl(2)	-177.4(5)
C(2)-C(3)-C(4)-C(5)	-0.1(11)
Cl(2)-C(3)-C(4)-C(5)	178.3(6)
C(3)-C(4)-C(5)-C(6)	-0.9(11)
C(4)-C(5)-C(6)-C(1)	1.0(10)
C(4)-C(5)-C(6)-N(1)	-179.6(7)
C(2)-C(1)-C(6)-C(5)	0.0(9)
Cl(1)-C(1)-C(6)-C(5)	179.9(5)
C(2)-C(1)-C(6)-N(1)	-179.5(6)
Cl(1)-C(1)-C(6)-N(1)	0.4(8)
C(7)-N(1)-C(6)-C(5)	104.9(8)
N(2)-N(1)-C(6)-C(5)	-72.4(8)
C(7)-N(1)-C(6)-C(1)	-75.7(9)
N(2)-N(1)-C(6)-C(1)	107.0(7)
N(2)-N(1)-C(7)-O(1)	177.9(6)
C(6)-N(1)-C(7)-O(1)	0.4(11)
N(2)-N(1)-C(7)-N(3)	-1.0(7)
C(6)-N(1)-C(7)-N(3)	-178.5(6)
C(8)-N(3)-C(7)-O(1)	-177.7(6)
C(10)-N(3)-C(7)-O(1)	-7.1(10)
C(8)-N(3)-C(7)-N(1)	1.2(6)
C(10)-N(3)-C(7)-N(1)	171.8(5)
N(1)-N(2)-C(8)-N(3)	0.4(7)
N(1)-N(2)-C(8)-C(9)	-179.8(6)
C(7)-N(3)-C(8)-N(2)	-1.0(7)
C(10)-N(3)-C(8)-N(2)	-170.6(6)
C(7)-N(3)-C(8)-C(9)	179.1(6)
C(10)-N(3)-C(8)-C(9)	9.5(10)
C(8)-N(3)-C(10)-C(11)	-88.8(7)
C(7)-N(3)-C(10)-C(11)	102.8(6)
N(3)-C(10)-C(11)-C(12)	-64.8(9)
N(3)-C(10)-C(11)-C(16)	118.1(10)
C(16)-C(11)-C(12)-C(13)	3.5(18)

The triazole ring defined by N1, N2, C8, N3, C7 is rather planar. The least squares plane equation based on these atoms is $7.652x + -0.822y + 7.171z = 2.0855$ ($0.676x + 5.675y + 17.711z = 4.5981$; $-0.456x + 7.879y + 2.148z = 2.8182$), with a largest deviation of 0.0048 nm (0.0013 nm and 0.0031 nm). Meanwhile, the triazole ring is almost perpendicular to both phenyl rings, which is revealed by the corresponding dihedral angle of 97.4° and 40.1° .

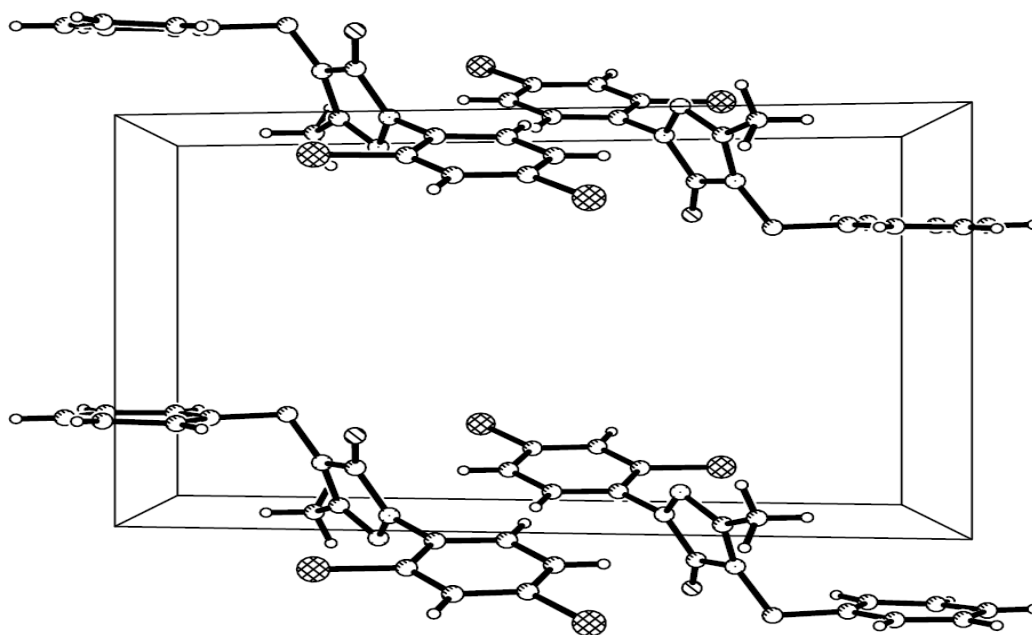


Fig. 2: The pack of title compound.

Table-4: Herbicidal Activity of Some Compounds (% Inhibition).

No.	Dosage (g of a.i./ha)	<i>Echinochloa crusgalli</i> (L.) Beauv.		<i>Digitaria adscendens</i>		<i>Brassica napus</i>		<i>Amaranthus retroflexus</i>	
		A	B	A	B	A	B	A	B
Carfentrazone ethyl	150.0	96.7	7.9	8.7	0	100	100	100	100
	300.0	100	18.5	8.7	18.8	100	100	100	100
	600.0	100	86.0	21.7	54.5	100	100	100	100
4	150.0	30.7	nd	8.7	nd	nd	nd	19.9	nd
	300.0	68.5	nd	34.8	nd	nd	nd	23.7	nd
	600.0	72.6	nd	41.3	nd	nd	nd	25.7	nd
	1500.0	93.7	58.5	100	17.6	28.8	46.3	100	37.1

A: Postmergence, B: Premergence, nd: not determined.

Herbicidal Activity

The postmergence and premergence herbicidal activities of the title compound were tested in a greenhouse at the concentration of 1500 g per a.i./ha. Carfentrazone-ethyl, a triazolinone-type commercial product, was used as the control. The primary bioassay shows that the title compound exhibits an excellent inhibiting activity towards *Echinochloa crusgalli* (L.) Beauv., *Digitaria adscendens*, *Brassica napus*, *Amaranthus retroflexus*. Under the postmergence, its inhibition rates to *Echinochloa crusgalli* (L.) Beauv., *Digitaria adscendens*, *Brassica napus*, *Amaranthus retroflexus* reach 93.7%, 100%, 28.8% and 100% respectively at a concentration of 1500 g/ha. But it didn't show appreciable herbicidal activities against *Echinochloa crusgalli* (L.) Beauv., *Digitaria adscendens*, *Brassica napus*, *Amaranthus retroflexus* under premergence. By comparison of the herbicidal activities listed in Tables-4, it is concluded that the title compound 4 is less effective than the commercial herbicide

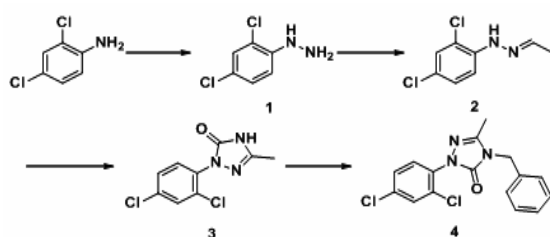
carfentrazone-ethyl at the dosage of 600, 300, 150 g of a.i./ha in postmergence treatment.

Experimental

Materials and Methods

2,4-dichloroaniline were purchased from Nanjing Tianzun Zezhong Chemical Co., Ltd with >95% purity confirmed by high-performance liquid chromatography (HPLC). Other reagents are of analytical grade. Melting points were determined using an X-4 apparatus and uncorrected. ¹H NMR spectra were measured on a Bruker AC-P500 instrument (300MHz) using TMS as an internal standard and CDCl₃ as the solvent. Elemental analyses were performed on a Vario EL elemental analyzer. Crystallographic data of the compound were collected on a Bruker SMART 1000 CCD diffractometer.

General procedure



Scheme 1: The synthetic route of title compound.

Synthesis of 3a-3c and 4

To solution of 2,4-dichloroaniline-hydrochloride (15 g, 92.5 mmol) in water (3 mL) and concentrated hydrochloric acid (100 mL) was added a solution of sodium nitrite (7.038 g, 102 mmol) in water (50 mL) dropwise during 15 min under ice-bath cooling. The reaction mixture was stirred for 1 h. Then a solution of tin(II) chloride (52 g, 231 mmol) in concentrated hydrochloric acid (50 mL) was added dropwise. After 1.5 h a bulky precipitate was collected by filtration and recrystallized from ethanol to give 2,4-dichlorophenylhydrazine hydrochloride. Next, the aqueous solution of this compound was neutralized by adding NaOH aqueous solution pH=9~10. The precipitation was formed during this course and collected by filtration. The product was further dried in vacuo. M.p.93~94°C (ref.94°C [20]). ¹H NMR (δ, CDCl₃): 7.07-7.24 (m, PhH, 3H), 5.70 (br, 1H, NH), 3.61 (br, 2H, NH₂).

To solution of 2,4-dichlorophenylhydrazine (2g, 0.019mol) in tert-butyl alcohol and water (V/V=9:1), 40 % acetaldehyde (17g, 160mmol) was added dropwise under ice-water bath cooling. After stirring for 5 min, sodium cyanate (9.2 g, 140.9 mmol) was added. Subsequently, acetic acid (9.3 g, 155.0 mmol) was added dropwise during 15 min. The resulting reaction mixture was stirred at 20°C for 3h. Next, a 10% aqueous solution of sodium hypochlorite (11.8g, 159.0 mmol) was added during 40 min. Then the reaction mixture was stirred for another 2h. After removing tert-butyl alcohol and water were on a rotary evaporator, a red residue was afforded which was further recrystallised from acetic ether and petroleum ether. The pure product was obtained as a white crystal. Mp.188-190 °C (ref.190-192°C [20]).¹H NMR (δ, CDCl₃):11.49 (br, 1H, NH), 7.35-7.55 (m, PhH, 3H), 2.28(s, 3H, CH₃).

To a mixture of 2-(2,4-Dichlorophenyl)-

5-methyl-2,4-dihydro-1,2,4-triazol-3-one (0.50 g, 2.0 mmol) and anhydrous potassium carbonate (0.35 g, 2.5 mmol) in dimethylformamide (DMF, 10 mL), benzyl chloride (0.46 g, 2.1 mmol) in DMF (2 ml) was added dropwise. The mixture was stirred at room temperature for 2 h. Then CH₂Cl₂ (30 mL) was added and the organic layer was separated, washed with water, and the solvent was then evaporated under the reduce pressure to afford compound 4 (yield 0.79 g, 90%, m.p. 157-158°C).

4-benzyl-1-(2,4-dichlorophenyl)-3-methyl-1H-1,2,4-triazol-5(4H)-one **4**: white crystal, yield, 87.1%; mp, 76-77°C; ¹H NMR (CDCl₃), δ 7.56 (m, PhH, 1H), 7.37 (m, PhH, 2H), 2.73 (s, CH₃, 3H), 2.56 (s, CH₃, 3H). Anal. Calcd for C₁₆H₁₃Cl₂N₃O (%): C, 57.50; H, 3.92; N, 12.57. Found: C, 57.58; H, 3.89; N, 12.62.

Crystal Structure Determination

The prism-shaped single crystal of the title compound was obtained by recrystallization from EtOH. The crystal with dimensions of 0.28mm × 0.24mm × 0.20mm was mounted on a Bruker SMART 1000 CCD area-detector diffractometer with a graphite-monochromated MoKα radiation (λ = 0.71073Å) by using a Phi scan modes at 294(2) K in the range of 1.3° ≤ θ ≤ 25.0°. A total of 7713 reflections were collected, of which 2851 were independent ($R_{int} = 0.118$) and 1354 were observed with $I > 2\sigma(I)$. The calculations were performed with SHELXS-97 program [21] and the empirical absorption corrections were applied to all intensity data. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were determined with theoretical calculations and refined isotropically. The final full-matrix least squares refinement gave $R = 0.0782$ and $wR = 0.2059$ ($w = 1/[s^2(F_o^2) + (0.0286P)^2]$), where $P = (F_o^2 + 2F_c^2)/3$, $S = 0.88$, $(\Delta/\sigma)_{max} = 0.0020$, $\Delta\rho_{max} = 0.49$ and $\Delta\rho_{min} = -0.31$ e Å⁻³. Atomic scattering factors and anomalous dispersion corrections were taken from International Table for X-Ray Crystallography [22]. A summary of the key crystallographic information were given in Table-5.

Table-5: Crystal data of the title compound.

Empirical Formula	C ₁₆ H ₁₃ Cl ₂ N ₃ O
Formula weight	332.18
T/K	294(2)
λ/nm	0.071073
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	$a = 15.710(10)$ Å $\alpha = 90^\circ$ $b = 9.969(6)$ Å $\beta = 103.271(11)^\circ$ $c = 10.800(7)$ Å $\gamma = 90^\circ$
V/nm ³	1646.3(18) Å ³
Z	4
Calculated density/(g·cm ⁻³)	1.340
Absorption coefficient/mm ⁻¹	0.398

Herbicidal Activities

Method of the Pot Culture (glasshouse tests)

Pre-emergence: Sandy clay (100 g) in a plastic box (11 × 7.5 × 6 cm) was wetted by water. Then the sprouting seeds (15 grains) of the weed were planted with fine earth (0.6 cm depth) covered in glasshouse. Spraying the solution of the compound evaluated in the suitable solvent was carried out at the rate of 1,500 g/ha.

Post-emergence: Spraying the same solution of the compound evaluated on the seedlings (one leaf and one core) of the weed was carried out at the same rate of pre-emergence.

For both methods, fifteen days later, the fresh weights were weighed and the percentage of the inhibition was calculated.

Supplementary Material

CCDC-832506 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk.

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