Articles

Studies on Synthesis and Biological Activities of Novel Triazole Compounds Containing *N,N*-Dialkyldithiocarbamate

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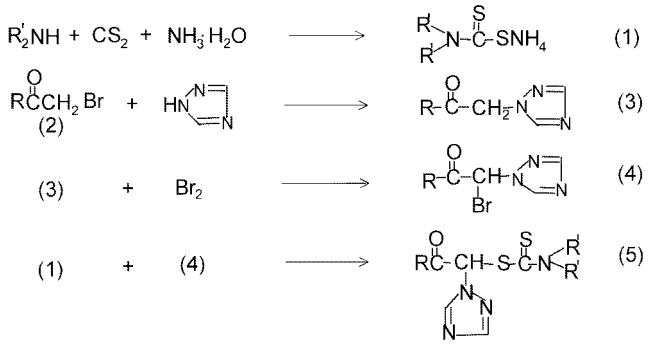
Nine titled compounds were synthesized and identified by IR, NMR, MS and elemental analysis. The results of the primary biological test show that all of these compounds have the activities of fungicide and plant growth regulator.

Key Words : *N,N*-Dialkyldithiocarbamate, Triazole, Biological

Introduction

As an important type of fungicides, triazole compounds are highly efficient, low poisonous and inward-absorbent.[1-3] At present, the studies on triazole derivatives are mainly concentrated on compounds with triazole as the only active group. The report of triazole compounds that contain both triazole group and other active group in a single molecule has rarely been found. Some of the triazole compounds containing organophosphorous group have been proved to have good bioactivities.[4] But triazole compounds containing *N,N*-dimethyldithiocarbamate have not been reported. *N,N*-dialkyldithiocarbamate has been known as broad-range fungicides and having different fungicidal mechanism with triazole compounds. In order to search for new triazole compounds with higher bioactivity, nine titled compounds were synthesized. The reactions are shown in Scheme 1:



Scheme 1

Experimental Section

Materials and instruments: IR spectra were taken by Schmadzu-IR-435 Spectrophotometer (KBr or liquid film). ^{1}H NMR was recorded with Bruker AC-P200Q nuclear magnetic resonance Spectrometer ($CDCl_3$ as solvent, TMS as internal standard). Mass spectra were taken by HP-5988A Spectrometer. Elemental analyses were performed using Yanaco-CHNCORDER MT-3 automatic elemental analyzer.

Preparation of intermediate (1): The intermediates (**1**) were prepared according to the literature report.[5] Carbon disulfide, ammonium and dimethylamine were added together at around 10 °C, then the mixture were dehydraled by refluxing with benzene. Three intermediates (**1**) were prepared in the same manner (CH_3: 79.2%, 86-87 °C; C_2H_5: 87.5%, 62-64 °C; *i*-C_3H_7: 90.3%, 46-48 °C).

Preparation of intermediate (2): The intermediates (**2**) were prepared according to the literature report.[6] Aryl (or alkyl) ethyl ketone reacted with bromine in anhydrous ether. Three intermediates (**2**) were prepared (*p*-ClC_6H_4: 87.0%, 66-67 °C; C_6H_5: 85.7%, 50-51 °C; Me_3C: 82.3%, n_D^{16} 1.4663).

Preparation of intermediate (3): Three intermediates (**3**) were prepared by the reactions of 1,2,4-triazole and intermediate (**2**) in the presence of triethylamine in acetone. (*p*-ClC_6H_4: 80.2%, 150-152 °C; C_6H_5: 81.0%, 117-119 °C; Me_3C: 74.5%, 62-64 °C).

Synthesis of S-[α-aryl-2-oxo-1-(1,2,4-triazol-1-yl)] ethyl-*N,N*-dialkyldithiocar-bamate: To a 100 mL flask 15 mmol intermediate (**3**), 25 mL acetic acid and 15 mmol sodium acetate were added. Then 15 mmol bromine was dropwise added with stirring at 15-25 °C. The reaction was maintained until the mixture was turned into colorless or light yellow for about 2-3 h. Then 50 mL water and 40 mL chloroform were added. 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 intermediate (**4**) was filtrated into a 100 mL flask. Cooled with ice-water and 30 mL acetone solution of intermediate (**1**) were added under stirring and the mixture was stirred at around 0 °C for 1 h. The solution was filtered, concentrated and purified by flash chromatography (silica gel, $V_{\text{ethyl ethanoate}} : V_{\text{cyclohexane}} = 5 : 1$) to afford target compounds (**5**).

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Table 1. The physical data and IR data of compounds **5a-5i**

Compound No.	R′	R	Yield %	m.p/°C	Elemental analysis (Calcd./%)			IR (ν/cm^{-1})	
					C	H	N	$\nu_{C=O}$	$\nu_{C=N}$
5a	CH_3	*p*-Cl-Ph	72.5	167-169	46.01(45.81)	3.70(3.84)	16.37(16.44)	1710	1511
5b	C_2H_5	*p*-Cl-Ph	70.4	110-112	48.69(48.84)	4.62(4.64)	15.27(15.19)	1690	1501
5c	*i*-C_3H_7	*p*-Cl-Ph	69.5	66-68	51.30(51.44)	5.28(5.33)	14.22(14.11)	1699	1500
5d	CH_3	Ph	71.2	125-127	50.77(50.69)	4.51(4.60)	18.31(18.28)	1683	1498
5e	C_2H_5	Ph	71.0	96-97	63.62(53.87)	5.38(5.42)	16.91(16.75)	1692	1501
5f	*i*-C_3H_7	Ph	68.3	52-53	56.17(56.32)	6.05(6.12)	15.63(15.45)	1675	1489
5g	CH_3	Me_3C	70.9	61-62	45.99(46.13)	6.32(6.33)	19.51(19.56)	1710	1490
5h	C_2H_5	Me_3C	67.5	n_D^{20} 1.5416	49.37(49.65)	7.02(7.05)	17.91(17.82)	1711	1498
5i	*i*-C_3H_7	Me_3C	62.1	n_D^{18} 1.5221	52.41(52.60)	7.53(7.65)	16.42(16.36)	1710	1493

Table 2. ^{1}H NMR (δ) and MS data of compounds **5a-5i**

Compound No.	R′	-SCH-	R	Tr[a]	MS (m/z)
5a	3.37 (s, 3H, CH_3) 3.62 (s, 3H, CH_3)	7.90 (s, 1H)	7.45-8.03 (AB, 4H, C_6H_4)	8.47-8.62 (AB, 2H)	340 (M^+), 229, 20, 139, 133, 120, 88
5b	1.25 (m, 6H, $2CH_3$) 3.62-4.05 (m, 4H, $2CH_2$)	7.88 (s, 1H)	7.45-8.03 (m, 4H, C_6H_4)	8.45-8.60 (AB, 2H)	
5c	1.42 (m, 12H, $4CH_3$) 4.51-4.72 (m, 2H, 2CH)	7.95 (s, 1H)	7.45-8.10 (m, 4H, C_6H_4)	8.48-8.67 (AB, 2H)	
5d	3.34 (s, 3H, CH_3) 3.58 (s, 3H, CH_3)	7.88 (s, 1H)	7.45-8.02 (m, 5H, C_6H_5)	8.44-8.61 (AB, 2H)	306 (M^+), 229, 20, 133, 120, 88, 77
5e	1.26 (m, 6H, $2CH_3$) 3.64-4.29 (m, 4H, $2CH_2$)	7.89 (s, 1H)	7.44-8.01 (m, 5H, C_6H_5)	8.47-8.60 (AB, 2H)	
5f	1.58 (m, 12H, $4CH_3$) 4.48-4.74 (m, 2H, 2CH)	7.96 (s, 1H)	7.45-8.02 (m, 5H, C_6H_5)	8.50-8.74 (AB, 2H)	
5g	3.38 (s, 3H, CH_3) 3.53 (s, 3H, CH_3)	7.91 (s, 1H)	1.22 (s, 9H, $3CH_3$)	7.96 (s, 1H) 8.50 (s, 1H)	286 (M^+), 229, 20, 120, 88, 57
5h	1.28 (m, 6H, $2CH_3$) 3.65-4.00 (m, 4H, $2CH_2$)	7.92 (s, 1H)	1.20 (s, 9H, $3CH_3$)	7.96 (s, 1H) 8.49 (s, 1H)	
5i	1.30 (m, 12H, $4CH_3$) 4.47-4.69 (m, 2H, 2CH)	7.94 (s, 1H)	1.20 (s, 9H, $3CH_3$)	8.01 (s, 1H) 8.56 (s, 1H)	

[a]Tr = 1,2,4-triazol-1-yl

Results and Discussion

Synthesis of intermediate (1) and target compounds (4): After a water solution of intermediate (**1**) being prepared according to literature,[5] the yellow crystal of intermediate (**1**) can be obtained by dehydration in benzene as reflux agent. When toluene was used as reflux agent instead of benzene, the color of the crystal became dark and the yield was reduced. The intermediate (**4**) was synthesized according to the literature.[7] We got two products. One is intermediate (**4**), another is the dibromo-substituted product confirmed by ^{1}H NMR spectrum and elemental analysis. The reaction between intermediate (**4**) and intermediate (**1**) can be performed directly in acetone.

Spectrum characterization of compounds 5a-5i: The experimental results with IR, ^{1}H NMR and MS data are shown in Tables 1 and Table 2. The measured values in the elemental analysis are in consistence with the corresponding calculated ones. All compounds (**5a-5i**) show very strong absorption bands in IR spectra at 1711 cm^{-1}-1675 cm^{-1} and 1489 cm^{-1}-1511 cm^{-1}, which are characteristic absorption bands for $\nu_{C=O}$ and $\nu_{C=N,}$ respectively.

The ^{1}H NMR data for compounds (**5a-5i**) are as predicted except for two protons on triazole ring. The chemical shifts for triazole ring protons are affected by R group. When R is *p*-ClC_6H_4 (or C_6H_5), the chemical shifts for the two protons are very close at δ = 8.44-8.74 and couple with each other into AB peak. When R is Me_3C, their chemical shifts are at δ = 8.00 and δ = 8.50, respectively.

Biological activity: Each of the target compounds has the fungicidal activity (Table 3). They exhibit better efficiency towards *P. asparagi* on the whole, such as **5g** and **5h**. The inhibiting rates reach 100% at 50 μg/mL. When R is *tert*-butyl group, the compounds have better comprehensive inhibiting rates than that R is aryl group. As far as R' is concerned, inhibiting activities of the compounds (R'=CH_3) are higher than the compounds (R'=CH_2CH_3). The activity order for R' is: CH_3 > CH_2CH_3 > *i*-C_3H_7. All the nine target

Table 3. The fungicidal and plant growth regulator activities of compounds **5**

Compound No.	Fungicidal activities (c = 0.005%, inhibition %)					Plant growth regulator activities (c = 0.0001%, %)		
	P. zeae	*A. solani*	*P. asparagi*	*P. piricola*	*C. Arachidicala*	wheat coleoptile elougation	Rooting of cumcumber cotyledon	Rape hypocotyl inhibition
5a	26.5	78.9	27.3	38.5	45.5	-17.6	+22.2	-5.3
5b	50.4	63.2	72.7	50.0	45.5	-12.0	+72.2	-30.1
5c	17.6	5.3	45.5	23.1	18.2	-10.2	+17.8	+0.9
5d	32.4	97.4	90.9	15.4	81.8	-10.2	+233.3	-30.1
5e	32.4	73.7	63.6	30.8	50.4	-16.7	+116.6	+5.3
5f	23.5	0	80.0	15.4	36.4	-9.3	+233.3	+4.4
5g	66.5	64.5	100.0	53.8	18.2	-14.8	+72.2	-0.9
5h	44.9	36.8	100.0	46.9	54.5	-16.7	+133.3	+3.5
5i	29.4	26.3	81.8	34.6	13.6	-18.52	+133.3	+0.9

compounds have plant growth regulating activity. They show inhibiting activity towards wheat coleoptile elougation. The inhibiting rates reach 9.26%-18.52%. The promoting activity towards Rooting cumcumber cotyledon, the promoting rates reach 17.78%-233.3%. Most of the compounds possess lower inhibiting activity towards *Rape hypocotyl*. The highest inhibiting rate is 30.1%.

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