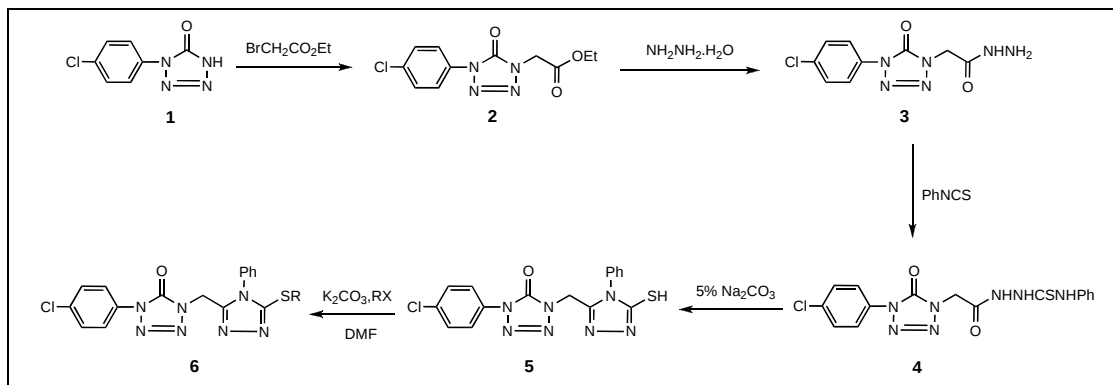


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Received June 26, 2006



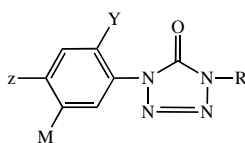
A novel series of 1-(4-chlorophenyl)-4-{[5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl]methyl}-1,4-dihydro-5*H*-tetrazol-5-ones **6a-y** were synthesized in good to excellent yields and their structures were identified by ^1H nmr, ^{13}C nmr, ms and elemental analysis. Determining the X-ray crystallography of compound **6j** indicated that there were strong intermolecular hydrogen bonds in the stacking interactions. The bioassay results showed that compound **6k** exhibited good insecticidal activities against *T. cinnabarinus* at the dosage of $250 \text{ mg}\cdot\text{L}^{-1}$. To our knowledge, this is the first report about the insecticidal activity of tetrazolinone derivatives.

J. Heterocyclic Chem., **44**, 937 (2007).

INTRODUCTION

Nitrogen-containing heterocyclic compounds have displayed a broad spectrum of biological activities. Within the synthesis of heterocyclic nitrogen-containing compounds, tetrazolinones attracted considerable attention due to their excellent herbicidal activity [1]. For example, 1-Aryl-4-substituted-1,4-dihydro-5*H*-tetrazol-5-ones (Scheme 1) were reported to be a new class of protoporphyrinogen oxidase inhibitor, whose weed spectrum and crop selectivity could be dramatically modified through manipulation of the substituent groups. The compound (Y, M = H; Z = Cl; R = $\text{CH}_2\text{CH}=\text{CH}_2$) showed 90% pre-emergence control of velvetleaf at 8000 g ai/ha. Such high application dosage motivated us to improve the herbicidal activity by modifying the R group.

Scheme 1



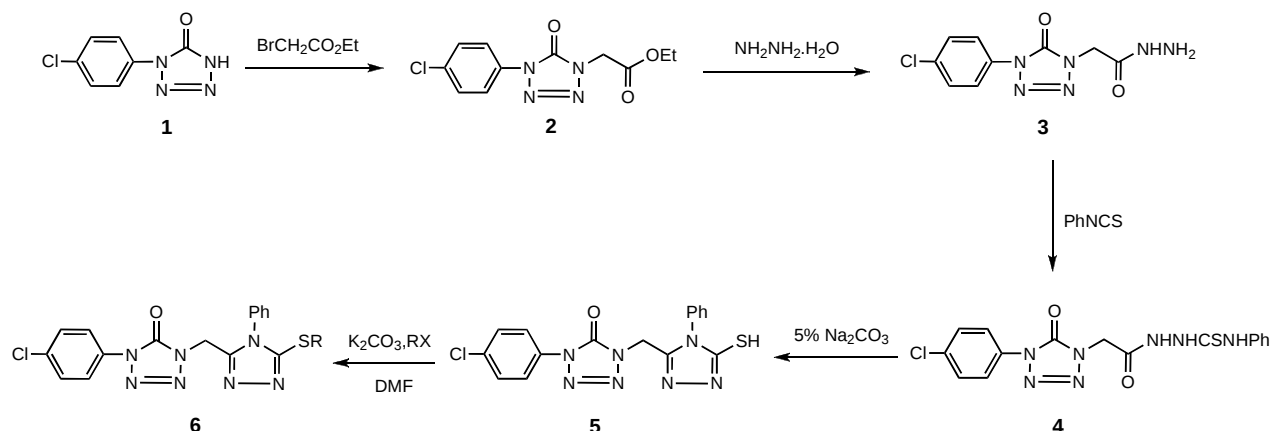
General structure of herbicidal tetrazolinones

Keep in mind that 1,2,4-triazole derivatives also exhibited various biological activities [2-8], and it is possible to improve the herbicidal activity of tetrazolinones if 1,2,4-triazole moiety is introduced into the tetrazolinone scaffold. Therefore, a series of the title compounds, 1-(4-chlorophenyl)-4-{[5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl]methyl}-1,4-dihydro-5*H*-tetrazol-5-ones **6** were designed and synthesized (Scheme 2).

RESULTS AND DISCUSSION

Synthesis. Using an experimental procedure as described in the literature [9], the starting material, 4-chlorophenylisocyanate reacted with sodium azide in *N,N*-dimethylformamide (DMF) to afford 1-(4-chlorophenyl)-1,4-dihydro-5*H*-tetrazol-5-one (**1**) (75%). Treatment of the tetrazolinone **1** with ethyl 2-bromoacetate in DMF gave compound (**2**) in good yields. Refluxing compound **2** with hydrazine hydrate in ethanol for 4 hours afforded 2-[4-(4-chlorophenyl)-5-oxo-4,5-dihydro-5*H*-tetrazol-1-yl]acetohydrazide (**3**). According to reference [10-11], the reaction of compound **3** with phenyl isothiocyanate in ethanol yielded novel 2-{2-[4-(4-chlorophenyl)-5-oxo-4,5-dihydro-5*H*-tetrazol-1-yl]acetyl}-*N*-phenylhydrazine carbothioamide (**4**). Refluxing the thiosemicarbazide **4** in 5% aqueous sodium carbonate solution gave 1-(4-

Scheme 1



chlorophenyl)-4-[(5-mercapto-4-phenyl-4*H*-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5*H*-tetrazol-5-one (**5**). Compound **5** reacted with alkyl halides or substituted benzyl halides to yield the title compounds **6**.

All compounds **6** gave satisfactory elemental analyses and spectroscopic data (^1H nmr, ^{13}C nmr and ms) consistent with their assigned structures. For example, in the ^1H nmr spectra, compounds **6** revealed a singlet at δ 5.21–5.26 ppm, which is attributed to the methylene between tetrazolinone and 1,2,4-triazole, a multiplet in the region δ 6.75–8.02 attributed to the aromatic protons; in the ^{13}C nmr spectra, C=O of tetrazol-5-one resonance was observed at δ 147.58–147.83 ppm, and two peaks in the region δ 149.1–154.5 ppm are attributed to 1,2,4-triazole. The ms spectra revealed that the molecular ion peaks and fragmentation peaks were in accordance with the synthesized structures of the title compound **6**, the molecular ion peak was observed for all the title compounds.

The single-crystal structure of **6j** was determined by X-ray crystallography as shown in Figure 1. The crystal packing revealed intermolecular hydrogen bond, which

played a fundamental role in the three-dimensional organization of the molecules in the solid state. An intermolecular hydrogen bond between the N atom and aromatic hydrogen is shown in Figure 2. The distance of C (12)... N (6) is 3.47 Å, and the angle of C (12)–H (12)–N (6) is 165.1°.

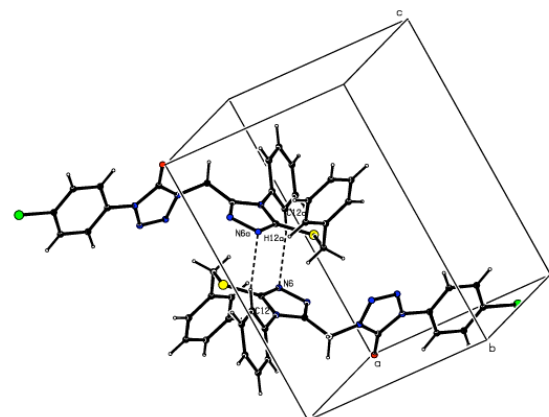


Figure 2. Chain of hydrogen-bonded molecules in crystal packing of compound **6j**.

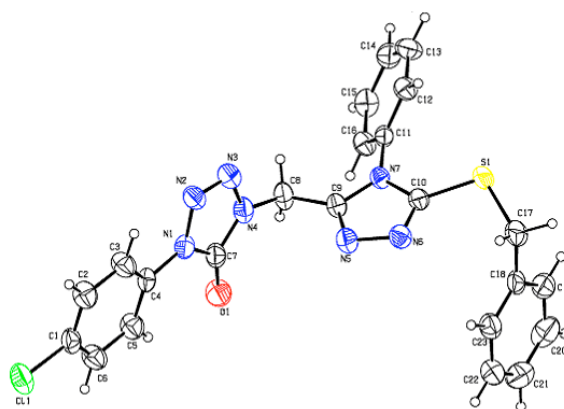


Figure 1. Crystal structure of compound **6j**.

Biological Activity. The biological activities of all compounds were investigated. None of them was proved to have significant herbicidal activities. However, it is very fortunate for us to find some compounds showing good insecticidal activity. For example, as it is shown in Table 1 that compound **6k** gave a mortality-level of 80.6% against *Tetranychus cinnabarnus* at the dosage of 250 mg.L⁻¹ *in vivo*. To our knowledge, this is the first report about the insecticidal activity of tetrazolinone derivatives. It should be mentioned that it is very difficult to control *T. cinnabarinus* in China. Therefore, the tetrazolinone scaffold might be identified as novel insecticidal lead structure for pesticide development.

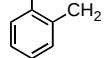
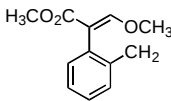
CONCLUSION

In conclusion, we developed a facile and mild method to synthesize a new series of 1-(4-chlorophenyl)-4-[(5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5*H*-tetrazol-5-ones **6** in good yields. As it comes out from their biological activity study, one of them compound **6k** showed good insecticidal activity at 250 mg.L⁻¹ against *Tetranychus cinnabarnus* *in vivo*. Further optimization and structure activity relationships of the title compounds are well under way.

chemical reagents were commercially available and were treated with standard methods before use. Solvents were dried in a routine way and redistilled.

Ethyl 2-[4-(4-chlorophenyl)-5-oxo-4,5-dihydro-5*H*-tetrazol-1-yl] acetate (2). A mixture of 1-(4-chlorophenyl)-1,4-dihydro-5*H*-tetrazol-5-one **1** (0.1 mol), ethyl 2-bromoacetate (0.11 mol) and anhydrous potassium carbonated (0.2 mol) in DMF (25 mL) was stirred for 6 hours at room temperature, according to thin layer chromatographic (TLC) analysis. And then ice water was added to the reaction mixture to form precipitate, which was collected by filtration, washed with water, dried and recrystallized from ethanol to obtain compound

Table 1
The results of insecticidal activities of compounds **6**

Com.	R	250 mg.L ⁻¹		500 mg.L ⁻¹	
		<i>T. cinnabarnus</i>	<i>A. medicagini</i>	<i>N. legen</i>	<i>M. separata</i>
6a	CH ₃	0.0	7.1	0.0	0.0
6b	C ₂ H ₅	0.0	10.0	3.3	0.0
6c	C ₃ C ₇	2.9	0.0	0.0	0.0
6d	CH ₂ =CHCH ₂	0.0	2.9	6.7	60.0
6e	C ₄ H ₉	1.4	4.3	3.3	0.0
6f	CH ₂ CO ₂ C ₂ H ₅	21.4	0.0	6.7	0.0
6g	CH(CH ₃)CO ₂ C ₂ H ₅	2.9	0.0	0.0	6.7
6h	C ₆ H ₁₃	0.0	1.4	3.3	0.0
6i	C ₈ H ₁₇	0.0	5.7	3.3	0.0
6j	C ₆ H ₅ CH ₂	1.4	0.0	6.7	20.0
6k	3-CH ₃ -C ₆ H ₄ CH ₂	80.6	1.4	3.3	37.5
6l	4-CH ₃ -C ₆ H ₄ CH ₂	2.9	1.4	0.0	0.0
6m	3-Br-C ₆ H ₄ CH ₂	2.9	1.4	3.3	0.0
6n	4-Br-C ₆ H ₄ CH ₂	0.0	2.9	0.0	64.7
6o	2-Cl-C ₆ H ₄ CH ₂	1.4	0.0	0.0	6.7
6p	3-Cl-C ₆ H ₄ CH ₂	8.6	0.0	0.0	15.0
6q	4-Cl-C ₆ H ₄ CH ₂	2.9	0.0	3.3	0.0
6r	3-F-C ₆ H ₄ CH ₂	0.0	0.0	3.3	0.0
6s	3,4-F ₂ -C ₆ H ₃ CH ₂	1.4	4.3	0.0	0.0
6t	2,4-F ₂ -C ₆ H ₃ CH ₂	5.7	5.7	20.0	40.0
6u	2,6-F ₂ -C ₆ H ₃ CH ₂	0.0	0.0	13.3	0.0
6v	2-Br-4-F-C ₆ H ₃ CH ₂	0.0	1.4	6.7	33.3
6w	2-NO ₂ -5-CH ₃ -C ₆ H ₃ CH ₂	0.0	2.9	0.0	0.0
6x		0.0	0.0	10.0	0.0
6y		1.4	4.3	0.0	0.0
Dichlorvos		-	-	100.0	100.0
Pyridabea		100.0	-	-	-

The application concentration of Dichlorvos and Pyridaben were 500 mg.L⁻¹ and 50 mg.L⁻¹, respectively.

EXPERIMENTAL

Melting points were uncorrected and determined with Electro thermal digital melting point apparatus, and ms spectra were determined using a Finnig an Trace MS organic mass spectrometer, and signals were given in *m/z*. ¹H nmr and ¹³C nmr were recorded in deuteriochloroform or dimethylsulfoxide on a Varian Mercury 400 spectrometer and resonances are given in ppm (δ) relative to TMS. Elementary analyses (EA) were performed on a Vario EL III elementary analysis instrument. All

2 as colorless needles; yield: 90%, mp 115-116°; ¹H nmr (deuteriochloroform): δ 1.32 (t, 3H, *J* = 7.2Hz, CH₃), 4.30 (q, 2H, *J* = 7.2Hz, CH₂), 4.81 (s, 2H, CH₂), 7.47 (dd, 4H, *J* = 8.4Hz, ArH); ms: *m/z* 282 (M⁺, 2), 155 (29), 153 (100), 125 (18). *Anal.* Calcd. for C₁₁H₁₁ClN₄O₃: C, 46.74; H, 3.92; N, 19.82. Found: C, 46.72; H, 3.95; N, 19.43.

2-[4-(4-Chlorophenyl)-5-oxo-4,5-dihydro-5*H*-tetrazol-1-yl] acetohydrazide (3). Hydrazine hydrate (0.5 mol) was added to a solution of ethyl 2-[2-(4-chlorophenyl)-5-oxo-4,5-dihydro-5*H*-tetrazol-1-yl]acetate (**2**) (0.1 mol) in ethanol (100 mL). The reaction mixture was heated under reflux for 4 hours,

concentrated in vacuum, cooled and diluted with water. The obtained precipitate was collected by filtration, washed with ice water, dried and recrystallized from ethanol. Yield: 88%; mp 235–237°; ¹H nmr (dimethylsulfoxide-*d*₆): δ 4.39 (s, 2H, NH₂), 4.69 (s, 2H, CH₂), 7.66 (dd, 4H, *J* = 8.8 Hz, ArH), 9.47 (s, 1H, NH); ms: *m/z* 268 (M⁺, 10), 181 (10), 155 (31), 153 (100), 127 (10), 125 (27), 115 (16). *Anal.* Calcd. for C₉H₉ClN₆O₂: C, 40.24; H, 3.38; N, 31.28. Found: C, 40.23; H, 3.27; N, 30.95.

2-{2-[4-(4-Chlorophenyl)-5-oxo-4,5-dihydro-5H-tetrazol-1-yl]acetyl}-N-phenylhydrazinecarbothioamide (4). A solution containing 2-[4-(4-chlorophenyl)-5-oxo-4,5-dihydro-5H-tetrazol-1-yl] acetohydrazide (3) (0.01 mol) and phenyl isothiocyanate (0.01 mol) in ethanol (20 mL) was heated under reflux for 4 hours and then cooled at room temperature. The obtained precipitate was collected by filtration, washed with water, dried, yield: 99%, mp 212–214°; this compound (4) was not recrystallized or identified, but was used directly in next step.

1-(4-Chlorophenyl)-4-(5-mercapto-4-phenyl-4H-1,2,4-triazol-3-yl)methyl-1,4-dihydro-5H-tetrazol-5-one (5). A stirring mixture of thiosemicarbazide (4) (1 mmol) and 5% aqueous sodium carbonate solution (10 mL) was refluxed for 5 hours. The reaction mixture was cooled, and then adjusted to pH 6 with 10% hydrochloric acid. The formed precipitate was collected by filtration, washed with water, dried and recrystallized from a mixture solution of DMF and water. Yield 95%; mp 248–250°; ¹H nmr (dimethylsulfoxide-*d*₆): δ 5.06 (s, 2H, CH₂), 7.20 (m, 9H, ArH), 14.26 (s, 1H, SH); ms: *m/z* 386 (M⁺, 22), 248 (15), 153 (20), 125 (48), 111(19), 90 (64), 63 (100). *Anal.* Calcd. for C₁₆H₁₂ClN₇OS: C, 49.81; H, 3.13; N, 25.41; S, 8.31. Found: C, 49.68; H, 2.95; N, 25.30; S, 8.12.

General Procedure for the preparation of 1-(4-chlorophenyl)-4-[(5-(alkylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6). To stirring solution of the mercaptotriazole (5) (1 mmol) in DMF (5 mL), the appropriate alkyl halide or substituted benzyl halide (1.1 mmol) and anhydrous potassium carbonate (2 mmol) were added gradually. The reaction mixture was stirred at room temperature for 6–8 hours, according to TLC. At the end of this duration, the reaction mixture was poured into ice water. The precipitate was collected by filtration, washed with water, dried and recrystallized from ethanol.

1-(4-Chlorophenyl)-4-[(5-methylthio-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6a). Colorless needles, yield 96%; mp 175–177°; ¹H nmr (deuteriochloroform): δ 2.72 (s, 3H, SCH₃), 5.25 (s, 2H, CH₂), 7.26–7.76 (m, 9H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 14.44, 39.27, 120.17, 126.73, 129.46, 130.15, 130.57, 131.89, 132.66, 133.40, 147.75, 149.00, 154.45; ms: *m/z* 400 (M⁺, 76), 153 (100), 125 (79). *Anal.* Calcd. for C₁₇H₁₄ClN₇OS: C, 51.06; H, 3.53; N, 24.52; S, 8.02. Found: C, 51.12; H, 3.31; N, 24.29; S, 8.22.

1-(4-Chlorophenyl)-4-[(5-ethylthio-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6b). Colorless needles, yield 98%; mp 152–153°; ¹H nmr (deuteriochloroform): δ 1.41 (t, 3H, *J* = 7.2 Hz, CH₃), 3.25 (q, 2H, *J* = 7.2 Hz, SCH₂), 5.24 (s, 2H, CH₂), 7.25–7.77 (m, 9H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 14.61, 26.75, 39.32, 120.14, 126.80, 129.43, 130.06, 130.47, 132.01, 132.66, 133.31, 147.74, 148.84, 153.89; ms: *m/z* 413.4 (M⁺, 65), 385.3 (40.17), 279 (100), 309 (37), 260 (61), 233 (28), 231 (36), 218 (29), 153 (26), 125 (19). *Anal.* Calcd. for C₁₈H₁₆ClN₇OS: C, 52.24; H, 3.90; N, 23.69; S, 7.75. Found: C, 52.15; H, 3.60; N, 23.50; S, 7.90.

1-(4-Chlorophenyl)-4-[(4-phenyl-5-propylthio-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6c). Colorless needles, yield 96%; mp 100–102°; ¹H nmr (deuteriochloroform): δ 1.00 (t, 3H, *J* = 7.2 Hz, CH₃), 1.75–1.80 (m, 2H, CH₂), 3.23 (t, 2H, *J* = 7.2 Hz, SCH₂), 5.24 (s, 2H, CH₂), 7.25–7.77 (m, 9H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 13.16, 22.60, 34.28, 39.33, 120.17, 126.81, 129.46, 130.09, 130.49, 132.05, 132.68, 133.39, 147.77, 148.80, 153.89; ms: *m/z* 428 (M⁺, 13), 388 (32), 385 (100), 380 (52), 231 (50), 203 (20), 153 (19), 125 (11). *Anal.* Calcd. for C₁₉H₁₈ClN₇OS: C, 53.33; H, 4.24; N, 22.91; S, 7.49. Found: C, 53.02; H, 4.00; N, 22.65; S, 7.78.

1-[(5-Allylthio-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6d). Colorless needles, yield 95%; mp 138–140°; ¹H nmr (deuteriochloroform): δ 3.86 (d, 2H, *J* = 7.2 Hz, SCH₂), 5.26 (s, 2H, CH₂), 5.13–5.30 (m, 2H, CH₂), 5.90–5.97 (m, 1H, CH), 7.24–7.79 (m, 9H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 35.28, 39.36, 119.22, 120.20, 126.87, 129.50, 130.12, 130.57, 131.98, 132.20, 132.70, 133.45, 147.81, 149.01, 153.03; ms: *m/z* 425.5 (M⁺, 100), 427.5 (M⁺+2, 85), 410 (74), 272 (18), 257 (24), 153 (29), 125 (22). *Anal.* Calcd. for C₁₉H₁₆ClN₇OS: C, 53.58; H, 3.79; N, 23.02; S, 7.53. Found: C, 53.39; H, 3.49; N, 22.80; S, 7.63.

1-[(5-Butylthio-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6e). Colorless needles, yield 64%; mp 104–106°; ¹H nmr (deuteriochloroform): δ 0.91 (t, 3H, *J* = 7.2 Hz, CH₃), 1.38–1.74 (m, 4H, CH₂), 3.25 (t, 2H, *J* = 7.2 Hz, SCH₂), 5.24 (s, 2H, CH₂), 7.25–7.77 (m, 9H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 13.47, 21.71, 31.08, 32.00, 39.28, 120.14, 126.76, 129.47, 130.11, 130.52, 131.94, 132.61, 133.37, 147.73, 148.79, 153.99; ms: *m/z* 443 (M⁺+1, 47), 395 (88), 386 (19), 241 (11), 153 (100), 125 (58), 90 (46). *Anal.* Calcd. for C₂₀H₂₀ClN₇OS: C, 54.35; H, 4.56; N, 22.19; S, 7.26. Found: C, 54.07; H, 4.27; N, 21.96; S, 7.48.

1-(4-Chlorophenyl)-4-[(5-(α-acetate ethyl)thio-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6f). Colorless needles, yield 79°; mp 110–112°; ¹H nmr (deuteriochloroform): δ 1.27 (t, 3H, *J* = 7.2 Hz, CH₃), 4.08 (s, 2H, SCH₂), 4.20 (q, 2H, *J* = 7.2 Hz, CH₂), 5.24 (s, 2H, CH₂), 7.26–7.78 (m, 9H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 14.02, 34.42, 39.25, 62.09, 120.19, 126.80, 129.49, 130.22, 130.71, 131.72, 132.69, 133.44, 147.79, 149.22, 152.34, 167.94; ms: *m/z* 472 (M⁺, 62), 426 (22), 398 (22), 153 (100), 124.9 (59), 111 (15), 90 (37). *Anal.* Calcd. for C₂₀H₁₈ClN₇O₃S: C, 50.90; H, 3.84; N, 20.78; S, 6.79. Found: C, 50.96; H, 3.54; N, 20.60; S, 6.88.

1-(4-Chlorophenyl)-4-[(5-(2-ethoxy-1-methyl-2-oxoethyl)thio-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6g). Colorless needles, yield 95°; mp 108–110°; ¹H nmr (deuteriochloroform): δ 1.24 (t, 3H, *J* = 7.2 Hz, CH₂CH₃), 1.62 (d, 3H, CHCH₃), 4.16 (q, 1H, *J* = 7.2 Hz, CH), 4.50 (q, 2H, *J* = 7.2 Hz, SCH₂), 5.24 (s, 2H, CH₂), 7.26–7.78 (m, 9H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 13.95, 18.17, 39.32, 44.62, 61.83, 120.17, 126.85, 129.47, 130.12, 130.61, 131.82, 132.68, 133.41, 147.77, 149.13, 151.82, 171.20; ms: *m/z* 486 (M⁺, 60), 441 (41), 413 (70), 386 (58), 153 (100), 125 (61), 118 (20), 90 (38). *Anal.* Calcd. for C₂₁H₂₀ClN₇OS: C, 51.90; H, 4.15; N, 20.18; S, 6.60. Found: C, 52.06; H, 3.87; N, 20.08; S, 6.68.

1-(4-Chlorophenyl)-4-[(5-hexylthio-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6h). Colorless needles, yield 67%; mp 119–121°; ¹H nmr (deuteriochloroform): δ 0.86 (t, 3H, *J* = 7.2 Hz, CH₃), 1.25–1.75 (m, 8H, CH₂), 3.23 (t,

2H, $J = 7.2$ Hz, SCH₂), 5.23 (s, 2H, CH₂), 7.24-7.77 (m, 9H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 13.95, 22.43, 28.28, 29.14, 31.16, 32.15, 39.37, 120.22, 126.85, 129.51, 130.13, 130.52, 132.11, 132.74, 133.46, 147.83, 148.81, 154.02; ms: m/z 470 (M⁺, 23), 423 (98), 386 (43), 153 (100), 125 (58), 111 (18), 90 (37). *Anal.* Calcd. for C₂₂H₂₄ClN₇OS: C, 56.22; H, 5.15; N, 20.86; S, 6.82. Found: C, 56.18; H, 4.81; N, 20.86; S, 6.82.

1-(4-Chlorophenyl)-4-[(5-octylthio-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6i). Colorless needles, yield 94%; mp 108-110°; ¹H nmr (deuteriochloroform): δ 0.87 (t, 3H, $J = 7.2$ Hz, CH₃), 0.88-1.77 (m, 12H, 6 $\times$ CH₂), 3.25 (t, 2H, $J = 7.2$ Hz, SCH₂), 5.24 (s, 2H, CH₂), 7.25-7.77 (m, 9H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 14.01, 22.54, 28.59, 28.93, 29.03, 29.15, 31.68, 32.44, 39.35, 120.18, 126.83, 129.48, 130.10, 130.50, 132.07, 132.71, 133.42, 147.79, 148.79, 153.96; ms: m/z 498 (M⁺, 99.6), 451 (100), 386 (78), 311 (22), 231 (88), 153 (58), 125 (32). *Anal.* Calcd. for C₂₄H₂₈ClN₇OS: C, 57.88; H, 5.67; N, 19.69; S, 6.44. Found: C, 57.74; H, 5.37; N, 19.64; S, 6.86.

1-[(5-Benzylthio-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6j). Colorless needles, yield 93°; mp 142-144°; ¹H nmr (deuteriochloroform): δ 4.44 (s, 2H, SCH₂), 5.22 (s, 2H, CH₂), 7.05-7.77 (m, 14H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 37.11, 39.17, 120.01, 126.63, 127.60, 128.49, 128.96, 129.35, 129.89, 130.36, 131.66, 132.50, 133.21, 135.97, 147.58, 148.96, 153.00; Ms: m/z 475 (M⁺, 100), 477 (M⁺+2, 24), 385 (51), 366 (20), 124 (22), 89 (81), 61 (27). *Anal.* Calcd. for C₂₃H₁₈ClN₇OS: C, 58.04; H, 3.81; N, 20.60; S, 6.74. Found: C, 58.15; H, 3.51; N, 20.80; S, 6.67.

1-(4-Chlorophenyl)-4-[(5-(3-methyl-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6k). Colorless needles, yield 93%; mp 166-168°; ¹H nmr (deuteriochloroform): δ 2.28 (s, 3H, CH₃), 4.45 (s, 2H, SCH₂), 5.22 (s, 2H, CH₂), 7.01-7.77 (m, 13H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 18.95, 35.77, 39.34, 120.17, 126.21, 126.79, 128.14, 129.49, 129.95, 130.08, 130.41, 130.50, 131.92, 132.69, 133.42, 133.69, 137.01, 147.75, 149.01, 153.22; ms: m/z 489 (M⁺, 100), 491 (M⁺+1, 33), 492 (M⁺+2, 36), 474 (25), 456 (46), 385 (15), 105 (30). *Anal.* Calcd. for C₂₄H₂₀ClN₇OS: C, 58.83; H, 4.11; N, 20.01; S, 6.54. Found: C, 59.05; H, 3.92; N, 19.91; S, 6.60.

1-(4-Chlorophenyl)-4-[(5-(4-methyl-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-1,4-dihydro-5H-tetrazol-5-one (6l). Colorless needles, yield 91%; mp 136-138°; ¹H nmr (deuteriochloroform): δ 2.31 (s, 3H, CH₃), 4.40 (s, 2H, CH₂), 5.22 (s, 2H, CH₂), 7.07-7.77 (m, 13H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 21.05, 37.04, 39.33, 120.15, 126.78, 128.97, 129.27, 129.47, 129.97, 130.42, 131.90, 132.69, 133.01, 133.40, 137.51, 147.74, 148.95, 153.29; ms: m/z 489 (M⁺, 100), 491 (M⁺+1, 30), 492 (M⁺+2, 36), 385 (34), 105 (34). *Anal.* Calcd. for C₂₄H₂₀ClN₇OS: C, 58.83; H, 4.11; N, 20.01; S, 6.54. Found: C, 58.67; H, 3.81; N, 19.97; S, 6.75.

1-[(5-(3-Bromo-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6m). Colorless needles, yield 75%; mp 160-162°; ¹H nmr (deuteriochloroform): δ 4.39 (s, 2H, SCH₂), 5.23 (s, 2H, CH₂), 7.09-7.77 (m, 13H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 36.29, 39.20, 113.28, 120.09, 122.38, 126.66, 127.75, 129.43, 130.06, 130.55, 130.76, 131.61, 131.91, 132.56, 133.33, 138.49, 147.66, 149.14, 152.63; ms: m/z 555 (M⁺, 100), 557

(M⁺+2, 31), 474 (36), 385 (39), 170.9 (18). *Anal.* Calcd. for C₂₃H₁₇BrClN₇OS: C, 49.79; H, 3.09; N, 17.67; S, 5.78. Found: C, 49.48; H, 2.77; N, 17.51; S, 5.82.

1-[(5-(4-Bromo-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6n). Colorless needles, yield 94%; mp 142-144°; ¹H nmr (deuteriochloroform): δ 4.38 (s, 2H, SCH₂), 5.22 (s, 2H, CH₂), 7.07-7.78 (m, 13H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 36.44, 39.36, 120.18, 121.71, 126.77, 129.51, 130.10, 130.58, 130.81, 131.71, 131.82, 132.72, 133.41, 135.52, 147.78, 149.17, 152.74; ms: m/z 555 (M⁺-1, 100), 558 (M⁺+2, 31), 446 (37), 444 (28), 385 (49), 285 (15), 170 (46), 152 (23). *Anal.* Calcd. For C₂₃H₁₇BrClN₇OS: C, 49.79; H, 3.09; N, 17.67; S, 5.78. Found: C, 49.95; H, 2.82; N, 17.54; S, 5.88.

1-[(5-(2-Chloro-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6o). Colorless needles, yield 94%; mp 135-136°; ¹H nmr (deuteriochloroform): δ 4.56 (s, 2H, SCH₂), 5.21 (s, 2H, CH₂), 7.07-7.77 (m, 13H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 34.86, 39.30, 120.12, 126.71, 126.92, 129.19, 129.43, 129.50, 129.99, 130.44, 131.41, 131.77, 132.65, 133.35, 134.20, 134.23, 147.72, 149.13, 152.99; ms: m/z 510 (M⁺, 2), 477 (51), 475 (100), 321 (64). *Anal.* Calcd. for C₂₃H₁₇Cl₂N₇OS: C, 54.12; H, 3.36; N, 19.23; S, 6.28. Found: C, 54.12; H, 3.09; N, 19.30; S, 6.39.

1-[(5-(3-Chloro-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6p). Colorless needles, yield 99%; mp 139-140°; ¹H nmr (deuteriochloroform): δ 4.40 (s, 2H, SCH₂), 5.22 (s, 2H, CH₂), 7.09-7.77 (m, 13H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 36.46, 39.30, 120.17, 126.74, 127.29, 127.91, 129.09, 129.48, 129.82, 130.08, 130.58, 131.76, 132.68, 133.43, 134.31, 138.30, 147.76, 149.15, 152.71; ms: m/z 510 (M⁺, 55), 400 (16), 279 (100), 251 (21), 241 (20), 124.7 (22). *Anal.* Calcd. for C₂₃H₁₇Cl₂N₇OS: C, 54.12; H, 3.36; N, 19.23; S, 6.28. Found: C, 54.00; H, 3.21; N, 18.94; S, 6.18.

1-[(5-(4-Chloro-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6q). Colorless needles, yield 99%; mp 157-159°; ¹H nmr (deuteriochloroform): δ 4.39 (s, 2H, SCH₂), 5.22 (s, 2H, CH₂), 7.08-7.78 (m, 13H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 36.21, 39.24, 120.08, 126.64, 128.67, 129.44, 130.03, 130.43, 130.53, 131.64, 132.56, 133.33, 133.48, 134.83, 147.67, 149.12, 152.76; ms: m/z 510 (M⁺, 94), 400 (46), 279 (100), 355 (20), 312 (26), 247 (25), 241 (100), 153 (27), 125 (95). *Anal.* Calcd. for C₂₃H₁₇Cl₂N₇OS: C, 54.12; H, 3.36; N, 19.23; S, 6.28. Found: C, 54.40; H, 3.09; N, 18.96; S, 6.40.

1-[(5-(3-Fluoro-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6r). Colorless needles, yield 89%; mp 158-160°; ¹H nmr (deuteriochloroform): δ 4.42 (s, 2H, SCH₂), 5.23 (s, 2H, CH₂), 6.95-7.77 (m, 13H, ArH); ¹³C nmr (100 MHz, deuteriochloroform): δ 36.46, 39.29, 114.59, 114.80, 115.86, 116.07, 120.16, 124.76, 126.73, 129.46, 130.06, 130.55, 131.78, 132.67, 133.04, 138.65, 138.72, 147.75, 149.14, 152.77, 161.47, 163.84; ms: m/z 493 (M⁺, 100), 495 (M⁺+1, 25), 496 (M⁺+2, 32), 384 (14), 108 (84). *Anal.* Calcd. for C₂₃H₁₇ClFN₇OS: C, 55.93; H, 3.47; N, 19.85; S, 6.49. Found: C, 55.95; H, 3.22; N, 19.99; S, 6.23.

1-[(5-(3,4-Difluoro-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl)methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6s). Colorless needles, yield 67%; mp 165-167°; ¹H nmr (deuteriochloroform): δ 4.39 (s, 2H, SCH₂), 5.23 (s, 2H, CH₂),

7.05-7.78 (m, 12H, ArH); ^{13}C nmr (100 MHz, deuteriochloroform): δ 35.61, 39.20, 117.10, 117.27, 117.96, 118.13, 120.07, 125.24, 126.62, 129.42, 130.09, 130.62, 131.57, 132.54, 133.33, 147.68, 148.60, 148.74, 149.19, 151.08, 151.21, 152.57; ms: m/z 511 (M^+ , 100), 513 ($\text{M}^+ + 1$, 14), 514 ($\text{M}^+ + 2$, 42), 385 (48), 242 (25), 127 (63). *Anal.* Calcd. for $\text{C}_{23}\text{H}_{16}\text{ClF}_2\text{N}_7\text{OS}$: C, 53.96; H, 3.15; N, 19.15; S, 6.26. Found: C, 53.91; H, 2.85; N, 18.90; S, 6.37.

1-[[5-(2,4-Difluoro-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl]methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6t). Colorless needles, yield 62%; mp 122-124 $^\circ$; ^1H nmr (deuteriochloroform): δ 4.44 (s, 2H, SCH_2), 5.23 (s, 2H, CH_2), 6.75-7.78 (m, 12H, ArH); ^{13}C nmr (100 MHz, deuteriochloroform): δ 29.58, 39.34, 103.91, 104.16, 111.22, 111.43, 119.85, 120.18, 126.72, 129.51, 130.13, 130.61, 131.77, 132.21, 132.70, 133.47, 147.80, 149.22, 152.86; ms: m/z 511 (M^+ , 47), 514 ($\text{M}^+ + 2$, 13), 385 (5), 242 (8), 126 (100). *Anal.* Calcd. for $\text{C}_{23}\text{H}_{16}\text{ClF}_2\text{N}_7\text{OS}$: C, 53.96; H, 3.15; N, 19.15; S, 6.26. Found: C, 53.86; H, 2.94; N, 19.11; S, 6.46.

1-[[5-(2,6-Difluoro-benzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl]methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6u). Colorless needles, yield 69%; mp 136-138 $^\circ$; ^1H nmr (deuteriochloroform): δ 4.47 (s, 2H, SCH_2), 5.26 (s, 2H, CH_2), 6.84-7.77 (m, 12H, ArH); ^{13}C nmr (100 MHz, deuteriochloroform): δ 24.48, 39.38, 111.27, 111.51, 112.06, 120.22, 126.79, 129.51, 129.76, 130.10, 130.57, 131.92, 132.71, 133.47, 147.81, 149.31, 152.47, 160.08, 162.50; ms: m/z 511 (M^+ , 100), 514 ($\text{M}^+ + 2$, 41), 385 (32), 242 (23), 127 (63). *Anal.* Calcd. for $\text{C}_{23}\text{H}_{16}\text{ClF}_2\text{N}_7\text{OS}$: C, 53.96; H, 3.15; N, 19.15; S, 6.26. Found: C, 54.07; H, 2.90; N, 19.33; S, 6.10.

1-[[5-(4-Bromo-2-fluorobenzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl]methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6v). Colorless needles, yield 64%; mp 136-137 $^\circ$; ^1H nmr (deuteriochloroform): δ 4.41 (s, 2H, SCH_2), 5.23 (s, 2H, CH_2), 7.12-7.78 (m, 13H, ArH); ^{13}C nmr (100 MHz, deuteriochloroform): δ 29.68, 39.33, 118.95, 119.19, 120.17, 122.00, 122.10, 123.09, 123.24, 126.70, 127.49, 129.50, 130.13, 130.62, 131.72, 132.47, 132.69, 133.46, 147.79, 149.28, 152.66, 159.32, 161.84; ms: m/z 573 (M^+ , 10), 574 ($\text{M}^+ + 1$, 56), 575 ($\text{M}^+ + 2$, 15), 493 (2), 385 (100), 241 (4), 188.9 (26). *Anal.* Calcd. for $\text{C}_{23}\text{H}_{14}\text{BrClFN}_7\text{OS}$: C, 48.22; H, 2.82; N, 17.12; S, 5.60. Found: C, 48.16; H, 2.52; N, 16.95; S, 5.74.

1-[[5-(5-Methyl-2-nitrobenzylthio)-4-phenyl-4H-1,2,4-triazol-3-yl]methyl]-4-(4-chlorophenyl)-1,4-dihydro-5H-tetrazol-5-one (6w). Yellow needles, yield 99%; mp 167-169 $^\circ$; ^1H nmr (deuteriochloroform): δ 2.42 (s, 3H, CH_3), 4.79 (s, 2H, SCH_2), 5.21 (s, 2H, CH_2), 7.11-8.02 (m, 12H, ArH); ^{13}C nmr (100 MHz, deuteriochloroform): δ 21.37, 34.23, 39.30, 120.14, 125.54, 126.64, 129.46, 130.15, 130.61, 131.58, 132.65, 131.31, 133.41, 133.54, 145.14, 145.43, 147.76, 149.21, 153.42; ms: m/z 535 (M^+ , 17), 489 (100), 385 (15), 335 (68), 231 (14), 150 (3), 125 (10). *Anal.* Calcd. for $\text{C}_{24}\text{H}_{19}\text{ClN}_8\text{O}_3\text{S}$: C, 53.88; H, 3.58; N, 20.93; S, 5.99. Found: C, 53.93; H, 3.42; N, 20.79; S, 6.02.

Methyl(2E)-(2-((5-((4-(4-chlorophenyl)-5-oxo-4,5-dihydro-5H-tetrazol-1-yl)methyl)-4-phenyl-4H-1,2,4-triazol-3-ylthio)methyl)phenyl)-2-(methoxyimino) acetate (6x). Yellow needles, yield 85%; mp 180-182 $^\circ$; ^1H nmr (deuteriochloroform): δ 3.79 (s, 3H, CO_2CH_3), 3.97 (s, 3H, OCH_3), 4.32 (s, 2H, SCH_2), 5.21 (s, 2H, CH_2), 7.10-7.77 (m, 13H, ArH); ^{13}C nmr (100 MHz, deuteriochloroform): δ 34.92, 39.24, 52.86, 63.64, 120.12, 126.75, 127.58, 128.32, 129.40, 129.56, 129.89, 130.19, 130.29, 131.79, 132.63, 133.31,

134.57, 147.71, 148.86, 149.06, 152.92, 162.99; ms: m/z 591 (M^+ , 31), 560 (88), 532 (67), 501 (42), 475 (69), 386 (31), 349 (29), 205 (58), 153 (80), 125 (44), 116 (100). *Anal.* Calcd. for $\text{C}_{27}\text{H}_{23}\text{ClN}_8\text{O}_4\text{S}$: C, 54.87; H, 3.92; N, 18.96; S, 5.43. Found: C, 54.83; H, 3.75; N, 18.77; S, 5.50.

Methyl(2E)-(2-((5-((4-(4-chlorophenyl)-5-oxo-4,5-dihydro-5H-tetrazol-1-yl)methyl)-4-phenyl-4H-1,2,4-triazol-3-ylthio)methyl)phenyl)-3-methoxyacrylate (6y). Colorless needles, yield 73%; mp 186-188 $^\circ$; ^1H nmr (deuteriochloroform): δ 3.59 (s, 3H, CO_2CH_3), 3.74 (s, 3H, OCH_3), 4.38 (s, 2H, SCH_2), 5.22 (s, 2H, CH_2), 7.08-7.77 (m, 13H, ArH); ^{13}C nmr (100 MHz, deuteriochloroform): δ 35.24, 39.25, 51.48, 61.64, 109.46, 120.13, 126.75, 127.66, 128.16, 129.41, 129.86, 130.01, 130.25, 131.11, 131.82, 132.57, 132.82, 133.29, 135.07, 147.67, 149.07, 153.69, 160.28, 167.59; ms: m/z 590 (M^+ , 7), 513 (17), 385 (14), 204 (32), 145 (100), 125 (13), 115 (19). *Anal.* Calcd. for $\text{C}_{28}\text{H}_{24}\text{ClN}_8\text{O}_4\text{S}$: C, 56.99; H, 4.10; N, 16.62; S, 5.43. Found: C, 57.00; H, 4.14; N, 16.36; S, 5.81.

Insecticidal Tests. The insecticidal activities against *Aphis medicagini*, *Nilaparvata lugen*, *Mythima separata* and *T. cinnabarinus* of the title compounds were investigated using the commercial products, Dichlorvos and Pyridabea. The insects were reared in a room maintained at 25 (± 1) $^\circ$, 60 (± 5)% relative humidity, and 14 h light photoperiod. Stock solutions of each test compound were prepared in DMF at a concentration of 1.0 g litre $^{-1}$, and then diluted to the required test concentrations with water containing TW-80. Groups of 10 insects of each species were transferred to glass Petri dishes and sprayed with test solutions using a Potter sprayer. After air-drying, they were kept in a room for normal cultivation. The mortality was determined by the number and size of live larvae in the treated bottles relative to that in the untreated controls in 72 h. In the case of *Nilaparvata lugen*, rice seedlings (second semester) were dipped in the test solution for 5 s, air-dried and then placed in a large test tube. Each test tube contained 20 seedlings. Twenty insects (fifth instar) were introduced into the tube, and the mouth of the tube was covered with white cheesecloth. The tube was kept at room temperature, and the number of live and dead insects counted after 72 h. In a control experiment, carried out under the same conditions, 1 mL of DMF was applied on each insect. All experiments and the respective controls were carried out in three replicates and percentage mortality was estimated with Abbott's formula [12]. The results of insecticidal activities were listed in Table 1.

X-Ray Analysis of Compound 6j. The single crystal **6j** was obtained by evaporating the solvent. A crystal with dimensions of 0.30 mm x 0.20 mm x 0.06 mm was mounted on a Bruker SMART 1000 diffractometer at 292(2) K with a graphite monochromated $\text{MoK}\alpha$ radiation ($\lambda = 0.71073$ Å). The Crystal data for **6j**: $\text{C}_{23}\text{H}_{18}\text{ClN}_7\text{OS}$; Triclinic, space group P-1, $a = 8.6328(18)$, $b = 10.083(2)$, $c = 13.148(3)$ Å, $\beta = 87.077(4)^\circ$, $V = 1105.0(4)$ Å 3 , $Z = 2$, $D_c = 1.431$ mg/m 3 . A total of 5535 reflections were measured in the range of $1.56^\circ \leq \theta \leq 25.00^\circ$, of which 3832 ($R_{\text{int}} = 0.0193$) were independent and 2782 were observed with $I > 2\sigma(I)$. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares procedure with Bruker SHELXTL-97 package [13].

Acknowledgement. We should thank Dr Jie Chen for the tests of biological assay. We also should thank the financial support from the National Key Project for Basic Research (2003CB114400, 2002CCA00500), National NSFC (No. 20572030, 20432010, and 20528201), Program for New Century

Excellent Talents in University of China and Program for Excellent Research Group of Hubei Province (No. 2004ABC002).

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