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Synthesis and insecticidal activity of 1,2,4-triazolo-thiazolidin-4-one derivatives

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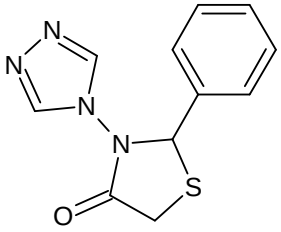
ABSTRACT

Fourteen novel compounds were synthesized and their insecticidal activities were tested. The compounds of ***2b, 2d, 2e, 3b, 3d*** *and* ***3e*** *showed insecticidal activity against Heliothis armigera. All the title compounds were characterized on the basis of IR, [1]HNMR and Mass spectra.*

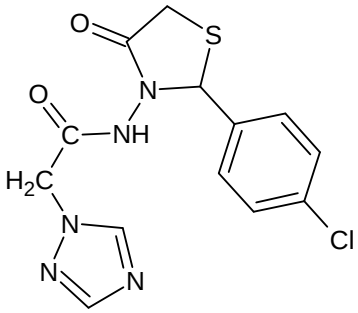
Keywords: Synthesis, insecticidal activity, 1,2,4-triazole, thiazolidine.

INTRODUCTION

The azole moiety is an important and frequent insecticidal, agrochemical structure feature of many biologically active compounds such as cytochrome P450 enzyme inhibitors[1] and peptide analog inhibitors[2]. Recently, much attention has been focused on 4H-1,2,4-triazole derivatives for their broad-spectrum activities, such as fungicidal, herbicidal, anticonvulsants and plant growth regulatory activities[3-5]. Further, the disubstituted 1,2,4-triazole derivatives were also reported to show antifungal, insecticidal, herbicidal and anti-inflammatory properties which were similar to 4H-1,2,4-triazole derivatives[6-8]. promoted by the above observations that the combination of two or more heterocyclic systems enhances the biological profile many-fold than its parent nuclei, we consider to synthesis some compounds bearing 4H-1,2,4-triazole in a molecular framework. Thiazolidinones and their derivatives have been reported having fungicidal, insecticidal and pharmacological activities[9-11]. Some of them showed similar activity[12-13], such as SN-1 and SS-2. (Scheme 1).Taking these structural features into consideration, it was thought worthwhile to synthesis the novel compounds that combining the 1,2,4-triazole with thiazolidinone by nitrogen heteroatom.



SN-1

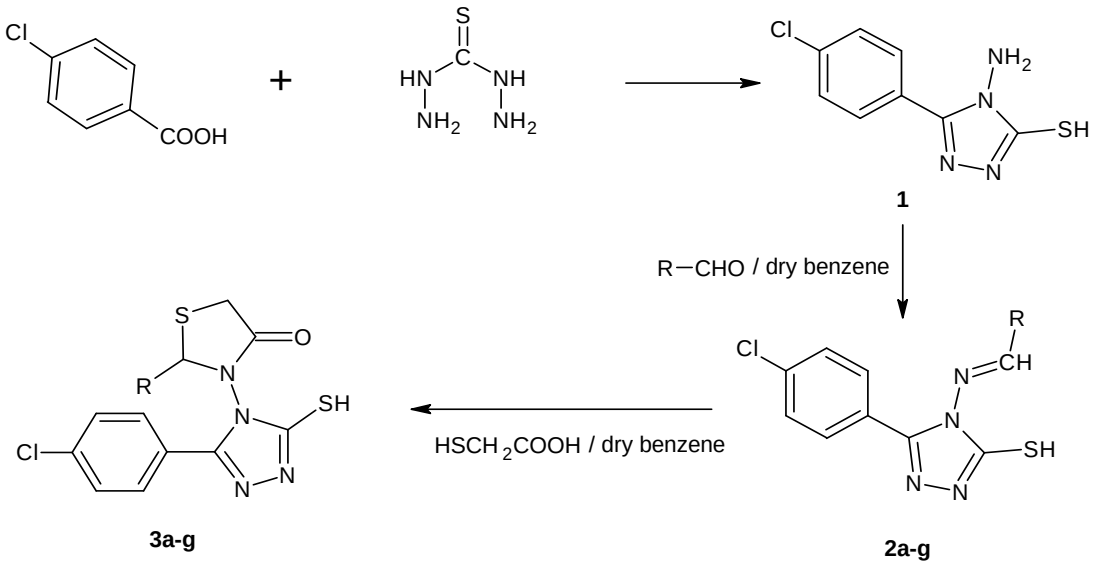


SS-2

Scheme 1

MATERIALS AND METHODS

The Synthetic route of the title compounds was seen in **Scheme 2.**



3a-g **2a-g**

Where R = a) C_6H_5, b) $C_6H_4Cl(p)$, c) $C_6H_4OH(p)$, d) $C_6H_4Br(p)$, e)$C_6H_4OCH_3(p)$, f) $C_6H_4N(CH_3)_2$, g) C_4H_4O.

General Procedures. Infrared spectra were taken on a Shimadzu FT-IR-8400S spectrometer using KBr disks; ^{1}H NMR spectra on a Advance 300 MHz spectrometer with DMSO-d_6 or $CDCl_3$ as solvent and TMS as internal standard, ^{13}C NMR (40 MHz, DMSO-d_6) and Mass spectra on a Shimadzu QP 2010 PLUS GC-MS system. Melting points were measured by open capillaries and were uncorrected. The elemental analyses of the compounds were recorded on Carlo Erba 1108 elemental analyzer. All reactions were followed by TLC.

Materials. Unless otherwise stated, these were commercial samples. All organic solvents were of analytical quality and used as purchased. Solvent mixtures are defined by volume ratio (v/v).

Scheme 2
The intermediate **1,** were synthesized according to the literature[14] and got the accept yield.

General preparation of the compounds 2a-g: Compound **1** (0.01 mol), substituted aromatic aldehydes (0.01 mol) and anhydrous zinc chloride (100 mg) were solved in benzene (30 mL). The mixture was refluxed for 15 hrs. The reactive process was monitored by TLC until the starting material nearly disappeared. The solvent was filtered and evaporated under the reduced pressure; the residue was purified by column chromatography (n-hexane/ethyl acetate 2:1) to afford the compounds 2a-g then crystallized from suitable solvent.

General preparation of the compounds 3a-g: Compound **2a-g** (0.01 mol), mercaptoacetic acid (0.01 mol) and anhydrous zinc chloride (100 mg) were solved in DMF (30 mL). The mixture was refluxed for 8 hrs. The reactive process was monitored by TLC until the starting material nearly disappeared. The solvent was filtered and evaporated under the reduced pressure; the residue was purified by column chromatography (n-hexane/ethyl acetate 2:1) to afford the compounds 3a-g then crystallized from suitable solvent.

5-(4-chlorophenyl)-4-{[(1*E*)-phenylmethylene]amino}-4*H*-1,2,4-triazole-3-thiol (2a).
mp 216-8^{o}C yield 72 % IR (KBr cm^{-1}): 1690 (CN) 1590 (CC) 800 (CCl) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.2-8.2 (m, 9H, Ar-H) 9.3 (s, 1H, SH) 10.1 (s, 1H, N=CH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 128.90, 131.10, 133.82, 143.00, 148.11, 167.51. MS: m/z 314 (m^+, 10). Calculated for $C_{15}H_{11}N_4SCl$ (%); C, 57.23; H, 3.52; N, 17.80; found (%); C, 57.20; H, 3.52; N, 17.75.

5-(4-chlorophenyl)-4-{[(1*E*)-(4-chlorophenyl)methylene]amino}-4*H*-1,2,4-triazole-3-thiol (2b).
mp 212-4^{o}C yield 62 % IR (KBr cm^{-1}): 1695 (CN) 1592 (CC) 804 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.2-8.0 (m, 8H, Ar-H) 9.2 (s, 1H, SH) 10.0 (s, 1H, N=CH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 129.01, 131.92, 134.31, 136.64, 143.61, 148.22, 168.21. MS: m/z 349 (m^+, 10). Calculated for $C_{15}H_{10}N_4SCl_2$ (%); C, 51.59; H, 2.89; N, 16.04; found (%); C, 51.51; H, 2.85; N, 16.01.

4-[(*E*)-{[3-(4-chlorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl]imino}methyl]phenol (2c).
mp 214-6^{o}C yield 65 % IR (KBr cm^{-1}): 3750 (OH) 1695 (CN) 1592 (CC) 804 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.1-8.0 (m, 8H, Ar-H) 9.1 (s, 1H, SH) 10.0 (s, 1H, N=CH) 11.2 (s, 1H, OH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 116.12, 126.41, 129.43, 134.31, 143.06, 143.00, 148.11, 160.82, 167.51. MS: m/z 330 (m^+, 9). Calculated for $C_{15}H_{11}N_4OSCl$ (%); C, 54.46; H, 3.35; N, 16.94; found (%); C, 54.41; H, 3.34; N, 16.91.

4-{[(1*E*)-(4-bromophenyl)methylene]amino}-5-(4-chlorophenyl)-4*H*-1,2,4-triazole-3-thiol (2d).
mp 204-6^{o}C yield 64 % IR (KBr cm^{-1}): 1690 (CN) 1585 (CC) 799 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.0-8.0 (m, 8H, Ar-H) 9.1 (s, 1H, SH) 10.0 (s, 1H, N=CH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 125.46, 128.92, 134.31, 143.06, 148.16, 167.56. MS: m/z 393 (m^+, 15). Calculated for $C_{15}H_{10}N_4SClBr$ (%); C, 45.76; H, 2.56; N, 14.23; found (%); C, 45.71; H, 2.54; N, 14.21.

5-(4-chlorophenyl)-4-{[(1*E*)-(4-methoxyphenyl)methylene]amino}-4*H*-1,2,4-triazole-3-thiol (2e).
mp 220-2^{o}C yield 62 % IR (KBr cm^{-1}): 1680 (CN) 1585 (CC) 801 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.9 (s, 3H, OCH_3) 7.2-8.2 (m, 8H, Ar-H) 9.0 (s, 1H, SH) 10.2 (s, 1H, N=CH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 55.92, 114.44, 126.12, 128.81, 134.31, 143.07, 148.00, 163.06,

167.55. MS: m/z 344 (m^+, 12). Calculated for $C_{16}H_{13}N_4OSCl$ (%); C, 55.73; H, 3.80; N, 16.25; found (%); C, 55.70; H, 3.79; N, 16.23.

5-(4-chlorophenyl)-4-({(1*E*)-[4-(dimethylamino)phenyl]methylene}amino)-4*H*-1,2,4-triazole-3-thiol (2f).
mp 210-2^{o}C yield 70 % IR (KBr cm^{-1}): 1686 (CN) 1585 (CC) 800 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.5 (s, 6H, $(CH_3)_2$) 7.1-8.2 (m, 8H, Ar-H) 9.2 (s, 1H, SH) 10.0 (s, 1H, N=CH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 40.31, 114.44, 123.31, 128.96, 134.34, 143.01, 148.05, 148.08, 151.93, 167.56. MS: m/z 357 (m^+, 10). Calculated for $C_{17}H_{16}N_5SCl$ (%); C, 57.06; H, 4.51; N, 19.57; found (%); C, 57.02; H, 4.50; N, 19.51.

5-(4-chlorophenyl)-4-{[(1*E*)-2-furylmethylene]amino}-4*H*-1,2,4-triazole-3-thiol (2g).
mp 255-2^{o}C yield 68 % IR (KBr cm^{-1}): 1680 (CN) 1585 (CC) 805 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.0-8.1 (m, 7H, Ar-H) 9.1 (s, 1H, SH) 10.0 (s, 1H, N=CH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 109.51, 128.88, 134.71, 134.76, 143.91, 148.06, 149.11, 167.56. MS: m/z 304 (m^+, 10). Calculated for $C_{13}H_9N_4OSCl$ (%); C, 51.23; H, 2.98; N, 18.38; found (%); C, 51.21; H, 2.95; N, 18.32.

3-[3-(4-chlorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl]-2-phenyl-1,3-thiazolidin-4-one (3a).
mp 255-7^{o}C yield 82 % IR (KBr cm^{-1}): 1720 (CO) 1680 (CN) 1585 (CC) 805 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.2 (s, 1H, CH-Ar) 3.7 (s, 2H, CH_2) 7.0-8.0 (m, 9H, Ar-H) 9.3 (s, 1H, SH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 35.76, 55.12, 128.72, 134.31, 139.21, 148.06, 167.51, 171.06. MS: m/z 388 (m^+, 10).Calculated for $C_{17}H_{13}N_4OS_2Cl$ (%); C, 52.50; H, 3.37; N, 14.41; found (%); C, 52.45; H, 3.32; N, 14.35.

2-(4-chlorophenyl)-3-[3-(4-chlorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl]-1,3-thiazolidin-4-one (3b).
mp 261-3^{o}C yield 52 % IR (KBr cm^{-1}): 1725 (CO) 1695 (CN) 1593 (CC) 806 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.1 (s, 1H, CH-Ar) 3.6 (s, 2H, CH_2) 7.2-8.1 (m, 8H, Ar-H) 9.2 (s, 1H, SH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 35.78, 55.18, 127.82, 133.33, 137.32, 148.08, 167.51, 172.00. MS: m/z 423 (m^+, 10). Calculated for $C_{17}H_{12}N_4OS_2Cl_2$ (%); C, 48.23; H, 2.86; N, 13.23; found (%); C, 48.21; H, 2.85; N, 13.21.

3-[3-(4-chlorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl]-2-(4-hydroxyphenyl)-1,3-thiazolidin-4-one (3c).
mp 275-6^{o}C yield 75 % IR (KBr cm^{-1}): 3750 (OH) 1730 (CO) 1693 (CN) 1596 (CC) 801 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.3 (s, 1H, CH-Ar) 3.9 (s, 2H, CH_2) 7.1-8.2 (m, 8H, Ar-H) 9.1 (s, 1H, SH) 11.0 (s, 1H, OH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 35.72, 56.12, 115.81, 128.91, 134.33, 148.01, 156.91, 167.51, 171.01. MS: m/z 404 (m^+, 14). Calculated for $C_{17}H_{13}N_4O_2S_2Cl$ (%); C, 50.43; H, 3.24; N, 13.84; found (%); C, 50.41; H, 3.33; N, 13.81.

2-(4-bromophenyl)-3-[3-(4-chlorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl]-1,3-thiazolidin-4-one (3d).
mp 244-6^{o}C yield 72 % IR (KBr cm^{-1}): 1725 (CO) 1691 (CN) 1588 (CC) 796 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.3 (s, 1H, CH-Ar) 3.7 (s, 2H, CH_2) 7.1-8.0 (m, 8H, Ar-H) 9.0 (s, 1H, SH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 35.77, 55.56, 121.55, 128.91, 134.33, 138.21, 148.01, 167.51,

171.03. MS: m/z 467 (m^+, 20). Calculated for $C_{17}H_{12}N_4OS_2ClBr$ (%); C, 43.65; H, 2.59; N, 11.98; found (%); C, 43.61; H, 2.54; N, 11.91.

3-[3-(4-chlorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl]-2-(4-methoxyphenyl)-1,3-thiazolidin-4-one (3e).

mp 280-2^{o}C yield 72 % IR (KBr cm^{-1}): 1720 (CO) 1683 (CN) 1583 (CC) 803 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.2 (s, 1H, CH-Ar) 3.6 (s, 2H, CH_2) 3.9 (s, 3H, OCH_3) 7.0-8.0 (m, 8H, Ar-H) 9.1 (s, 1H, SH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 34.99, 55.11, 55.90, 114.21, 128.96, 134.31, 148.06, 155.96, 167.56, 171.12. MS: m/z 418 (m^+, 20). Calculated for $C_{18}H_{15}N_4O_2S_2Cl$ (%); C, 51.61; H, 3.61; N, 13.37; found (%); C, 51.60; H, 3.60; N, 13.33.

3-[3-(4-chlorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl]-2-[4-(dimethylamino) phenyl]-1,3-thiazoli -din-4-one (3f).

mp 262-4^{o}C yield 65 % IR (KBr cm^{-1}): 1710 (CO) 1687 (CN) 1580 (CC) 806 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.6 (s, 6H, $(CH_3)_2$) 3.2 (s, 1H, CH-Ar) 3.7 (s, 2H, CH_2) 7.1-8.0 (m, 8H, Ar-H) 9.1 (s, 1H, SH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 35.66, 40.31, 55.12, 114.23, 128.71, 134.41, 148.06, 167.56, 171.06. MS: m/z 431 (m^+, 15). Calculated for $C_{19}H_{18}N_5OS_2Cl$ (%); C, 52.83; H, 4.20; N, 16.21; found (%); C, 52.82; H, 4.17; N, 16.20.

3-[3-(4-chlorophenyl)-5-mercapto-4*H*-1,2,4-triazol-4-yl]-2-(2-furyl)-1,3-thiazolidin-4-one (3g).

mp 305-2^{o}C yield 62% IR (KBr cm^{-1}): 1720 (CO) 1686 (CN) 1586 (CC) 806 (CCl). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.3 (s, 1H, CH-Ar) 3.6 (s, 2H, CH_2) 7.0-8.0 (m, 7H, Ar-H) 9.2 (s, 1H, SH). ^{13}C NMR (40 MHz, DMSO-d_6): δ 33.33, 54.82, 106.71, 110.62, 128.91, 134.31, 142.11, 148.01, 151.61, 167.51, 171.00. MS: m/z 378 (m^+, 18). Calculated for $C_{15}H_{11}N_4O_2S_2Cl$ (%); C, 47.55; H, 2.93; N, 14.79; found (%); C, 47.50; H, 2.91; N, 14.73.

RESULTS AND DISCUSSION

All the title compounds bioactivity was screened by the method contact poison and stomach poison. A stock solution of the title compounds (1000ppm) in DMSO was used for preparing various concentrations for bioactivity screening. The compounds **2b, 2d, 2e, 3b, 3d** and **3e** showed 60-80% mortality against *Heliothis armigera* at the concentration of 500ppm. The insecticidal activity decreases clearly when the concentration was decreased. The results are tabulated in **Table 1** and **2.**

Table 1. Bioefficacy testing of compounds by contact poison method

Sl.No	Test sample	Dose concentration (ppm)	Mortality Rate (Per 10 Larvae) 24hrs	48hrs	72hrs	Larval mortality (%) 24hrs	48hrs	72hrs
1	2a	500	01	02	02	10	20	20
2	2b	500	08	07	07	80	70	70
3	2c	500	02	04	03	20	40	30
4	2d	500	07	08	07	70	80	70
5	2e	500	08	08	07	80	80	70
6	2f	500	03	04	03	30	40	30
7	2g	500	02	03	04	20	30	40
8	3a	500	01	02	02	10	20	20
9	3b	500	07	08	07	70	80	70
10	3c	500	02	03	02	20	30	20
11	3d	500	07	08	07	70	80	70
12	3e	500	08	07	07	80	70	70
13	3f	500	02	03	03	20	30	20
14	3g	500	03	02	02	30	20	20
15	Endosulfan (Std).	500	08	08	09	80	80	90
16	UTC	500	00	01	02	00	10	20

Table 2. Bioefficacy testing of compounds by stomach poison method

Sl.No	Test sample	Dose concentration (ppm)	Mortality Rate (Per 10 Larvae) 24hrs	48hrs	72hrs	Larval mortality (%) 24hrs	48hrs	72hrs
1	2a	500	01	02	03	10	20	30
2	2b	500	07	08	07	70	80	70
3	2c	500	02	02	03	20	20	30
4	2d	500	08	07	07	80	70	70
5	2e	500	08	07	07	80	70	70
6	2f	500	03	02	03	30	20	30
7	2g	500	02	03	04	20	30	40
8	3a	500	01	03	02	10	30	20
9	3b	500	08	08	07	80	80	70
10	3c	500	03	03	02	30	30	20
11	3d	500	07	08	08	70	80	80
12	3e	500	08	07	08	80	70	80
13	3f	500	02	02	03	20	20	30
14	3g	500	03	02	03	30	20	30
15	Endosulfan (Std).	500	08	08	09	80	80	90
16	UTC	500	00	01	02	00	10	20

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