Synthesis of some 1,2,4-Triazolyl-1,2,3-Triazole Derivatives: (1,3-Dipolar Cycloaddition Reaction)*

Sultan T. Abu-Orabi[a], Nuha A. Abu-Naaj[b], Sami Klaib[a], Lo´ay Al-Momani[a], Ibrahim Jibril[b]**

a Department of Chemistry, Tafila Technical University, P.O. Box 179, Tafila, Jordan.
b Department of Chemistry, Yarmouk University, Irbid, Jordan.

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Abstract

The reaction of 1-substituted benzyl-1*H*-1,2,3-triazole-4-carbohydrazides **2a-h** with equimolar amounts of isothiocynate produces 1-(1-substituted benzyl-1*H*-1,2,3-triazole-4-carbonyl)-*N*-phenylhydrazinecarbothioamide **3a-h**. Treatment of **3a-h** with sodium hydroxide afforded 5-(1-substituted benzyl-1*H*-1,2,3-triazol-4-yl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol **4a-h**. Nucleophlic addition of the corresponding sodium salts of **4a-h** to alkyl halide (methyl iodide or benzyl bromide) affords the 1-substituted benzyl-4-(5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole **5a-h** and **6a-h**.

Keywords: Triazoles; Cycloaddition; Hydrazinocarbonyl; Thiosemicarbazides; Nucleophlic addition.

Introduction

1,2,4-Triazoles and their derivatives constitute an important class of heterocyclic compounds that has significant biological activity. 1,2,4-Triazoles and their derivatives have been reported to posses various biological activities such as, anti-fungal, anti-microbial, anti-bacterial and anti-inflammatory properties. 1,2,4-Triazoles also have been tested as fungicides and herbicides.[1] The anti-tumor activity of 1,2,4-triazole and their derivatives have also been published recently.[2] Several compounds containing 1,2,4-triazole rings are nowadays known as drugs.[3-5] Moreover, 1,2,4-triazoles have been studied as ligands of transition-metal (II) cations. They are known to act as bridging ligands between cations such as Cu(II), Fe(II), Pt(II) and Ru(II) through their nitrogen atoms forming coordination compounds that are interesting for both magnetic and chemical aspects.[6] The organo-soluble polymer consisting of 1,2,4-triazole moieties in the main chain are potential candidates for the development of n-channel field-effect transistors that could be used for electron transporting materials in electronic devices.[7] Since the preparation of the first 1,2,4-triazole more than 100 years ago,[8] several routes were developed for the synthesis of 1,2,3- and 1,2,4-substituted triazoles. They can be prepared from the reaction of hydrazides with substituted isothiocyanates,[9] from the reaction of hydrazonyl chloride with nitriles,[10]

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** Corresponding author: S. T. Abu-Orabi, Telfax: 0096232250431, e-mail: *abuorabi@excite.com*

and from hetero-ring transformations of oxadiazoles and N-cyanocarbonimidodithioic esters from their reaction with amines and hydrazines respectively.[11] Moreover 1,2,4-triazoles have been prepared from the alkylation reaction of mercaptosubstituted 1,2,4-triazoles.[12] Substituted 1,2,4-triazoles have been also prepared from the reaction of 1,2,4-triazoles with substituted piperazines,[13] and from the reaction of 1,2,4-triazoles with cyclohexane carboxaldehyde and capronaldeheyde,[14] The oxidative cyclization of substituted alkylsemicarbazides and amino aryl 1,2,4-triazoles has been used to prepare substituted 1,2,4-triazoles.[15] Recently, Abu-Orabi and co-workers reported the synthesis of triazoles via 1,3-dipolar cycloaddition of azides derivatives with naphthoquinone and benzoquinone.[16] Despite the intensive research on substituted 1,2,4-triazoles, little is known about 1,2,4-triazoles attached to 1,2,3-triazole moiety. In addition to their various applications,[1-7] these observations promoted us to study the synthesis of a compound which posses a 1,2,3-triazole moiety linked to 1,2,4-triazole rings.

Materials and Methods

Ethyl propiolate, substituted benzyl halides, hydrazine hydrate, phenyl isothiocyanate were purchased from Aldrich, Fluka, Across and Janssen Chemica, and were used without any further purification. Melting points were performed on an electrothermal digital melting point apparatus and were uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer FT-IR SP 2000 spectrometer as potassium bromide (KBr) pellets. ^{1}H-NMR spectra were recorded on a WP 80 SY spectrometer. Chemical shifts are reported in δ unites (ppm) downfield from tetramethylsilane. Elemental analysis was performed by M-H-W Laboratories, Phoenix Arizona, USA.

General procedure for preparation of 1a-h. These compounds were prepared as reported in literature.[17a] Methyl propiolate of 0.889 g (10 mmol) was added to a solution of substituted benzyl azides (10 mmol) in 50 mL ethanol. The resulting mixture was heated under reflux conditions for 6 hrs. The solvent was removed under reduced pressure and the residue was crystallized from an ether/ petroleum ether (60- 80) mixture to give methyl 1-substituted benzyl 1*H*-1,2,3-triazoles-4-carboxylates **1a-h**.[17a]

General procedure for preparation of 2a-h. To an ethanolic solution of triazoles **1a-h** (20 mmol), an excess amount of hydrazine hydrate was added. The reactants mixture was heated under reflux conditions for 1 hr. The obtained solid was crystallised from ethanol yielding 1-substituted benzyl-1*H*-1,2,3-triazoles-4-carbohydrazide **2a-h**.[17b] Analytical and spectral data are summarized in table 1.

Table1: Analytical and spectral data for **2(e**-**h**)

Product	G	Molecular formula	Molecular mass g/mol)	Mp (ºC)	Yield (%)	IR(KBr, $\tilde{\upsilon}$, cm^{-1})	^{1}H-NMR(δ, ppm) DMSO-d_6/TMS
2e	4-F	$C_{10}H_{10}N_5FO$	235	186-7	82	3290, 1670, 1452	9.69 (br s. 1H, NH), 8.61 (s, 1H, H_{arom}), 7.32-7.10 (m, 4H, H_{arom}), 5.74 (s, 2H, CH_2, benzylic), 4.54 (br s, 2H, NH_2)
2f	4-Br	$C_{10}H_{10}N_5BrO$	295	193-5	93	3290, 1670, 1450	9.68 (br s. 1H, NH), 8.59 (s, 1H, H_{arom}), 7.51-7.32 (m, 4H, H_{arom}), 5.73 (s, 2H, CH_2, benzylic), 4.53 (br s, 2H, NH_2)
2g	2,4-Dichloro	$C_{10}H_9N_5Cl_2O$	285	196-7	95	3295, 1688, 1450	9.69 (br s. 1H, NH), 8.58 (s, 1H, H_{arom}), 7.31-7.11 (m, 3H, H_{arom}), 5.80 (s, 2H, CH_2, benzylic), 4.39 (br s, 2H, NH_2)
2h	2,6-Dichloro	$C_{10}H_9N_5Cl_2O$	285	182-3	89	3290, 1665, 1450	9.52 (br s. 1H, NH), 8.64 (s, 1H, H_{arom}), 7.57-7.31 (m, 3H, H_{arom}), 5.54 (s, 2H, CH_2, benzylic), 4.45 (br s, 2H, NH_2)

1-(4-Fluorobenzyl)-1*H*-1,2,3-triazole-4-carbohydrazide (**2e**)

1-(4-Bromobenzyl)-1*H*-1,2,3-triazole-4-carbohydrazide (**2f**)

1-(2,4-Dichlorobenzyl)-1*H*-1,2,3-triazole-4-carbohydrazide (**2g**)

1-(2,6-Dichlorobenzyl)-1*H*-1,2,3-triazole-4-carbohydrazide (**2h**)

General procedure for preparation of 3a-h. To a solution of hydrazinocarbonyl derivatives **2a-h** (25 mmol) in absolute ethanol (150 mL), phenyl isothiocyanate (30 mmol) was added. The reaction mixture was stirred at room temperature for about 20 hr, and then poured into cold water. The resulted precipitate was filtered and crystallized from ethanol to give 1-(1-substituted benzyl-1*H*-1,2,3-triazole-4-carbonyl)-*N*-phenylhydrazinecarbothioamides **3a-h.** Analytical and spectral data are summarized in table 2.

Table 2: Analytical and spectral data for **3(a-h)**

Product	G	Molecular formula	Molecular mass (g/mol)	Mp (ºC)	Yield (%)	IR(KBr, ῡ, cm^{-1})	^{1}H-NMR (δ, ppm) DMSO-d_6/TMS
3a	H	$C_{17}H_{16}N_6SO$	354	188-190	83	3388, 3105, 1685, 1550, 1448, 1206	10.60 (br s, 1H, NH), 9.71 (br s, 2H ,NH), 8.68 (s, 1H, H_{arom}), 7.22-7.51 (m, 10H, H_{arom}), 5.70 (s, 2H, CH_2, benzylic)
3b	4-CH_3	$C_{18}H_{18}N_6SO$	366	170-180	90	3390, 3160, 1680, 1555, 1440, 1200	10.68 (br s, 1H, NH), 9.79 (br s, 2H, NH), 8.70 (s, 1H, H_{arom}), 7.27-7.61 (m, 9H, H_{arom}), 5.73 (s, 2H, CH_2, benzylic), 2.20 (s, 3H, CH_3)
3c	4-OCH_3	$C_{18}H_{18}N_6SO_2$	382	186-7	76	3390, 3165, 1687, 1552, 1445, 1215	10.62 (br s, 1H, NH), 9.80 (br s, 2H, NH), 8.71 (s, 1H, H_{arom}), 7.30-7.62 (m, 9H, H_{arom}), 5.72 (s, 2H, CH_2,benzylic), 3.30 (s, 3H, OCH_3)
3d	4-Cl	$C_{17}H_{15}N_6SClO$	386	210-211	88	3320, 3116, 1700, 1545, 1497,1210	10.80 (br s, 1H, NH), 9.72 (br s, 2H, NH), 8.72 (s, 1H, H_{arom}), 7.33-7.56 (m, 9H, H_{arom}), 5.72 (s, 2H, CH_2, benzylic)
3e	4-F	$C_{17}H_{15}N_6SFO$	372	202-4	88	3390, 3170, 1690, 1550, 1446, 1210	10.54 (br s, 1H, NH), 9.88 (br s, 2H, NH), 8.70 (s, 1H, H_{arom}), 7.22-7.71 (m, 9H, H_{arom}), 5.73 (s, 2H, CH_2, benzylic)
3f	4-br	$C_{17}H_{15}N_6SBrO$	432	215-6	90	3390, 3126, 1695, 11454, 1492, 1220	10.72 (br s, 1H, NH), 9.88 (br s, 2H, NH), 8.73 (s, 1H, H_{arom}), 7.20-7.72 (m, 9H, H_{arom}), 5.72 (s, 2H, CH_2, benzylic)
3g	2,4-dichloro	$C_{17}H_{14}N_6SCl_2O$	420	208-9	80	3320, 3110, 1690, 1545, 1485, 1230	10.52 (br s, 1H, NH), 9.84 (br s, 2H, NH), 8.72 (s, 1H, H_{arom}), 7.21-7.71 (m, 8H, H_{arom}), 5.82 (s, 2H, CH_2, benzylic)
3h	2,6-dichloro	$C_{17}H_{14}N_6SCl_2O$	420	204-5	80	3320, 1700, 1450, 1490, 1205	10.63 (br s, 1H, NH), 9.69 (br s, 2H, NH), 8.73 (s, 1H, H_{arom}), 7.21-7.54 (m, 8H, H_{arom}), 5.67 (s, 2H, CH_2, benzylic)

1-(1-Benzyl-1*H*-1,2,3-triazole-4-carbonyl)-4-phenylthiosemicarbazide (**3a**)

1-(1-(4-Methylbenzyl)-1*H*-1,2,3-triazole-4-carbonyl)-4-phenylthiosemicarbazide (**3b**)

1-(1-(4-Methoxybenzyl)-1*H*-1,2,3-triazole-4-carbonyl)-4-phenylthiosemicarbazide (**3c**)

1-(1-(4-Chlorobenzyl)-1*H*-1,2,3-triazole-4-carbonyl)-4-phenylthiosemicarbazide (**3d**)

1-(1-(4-Fluorobenzyl)-1*H*-1,2,3-triazole-4-carbonyl)-4-phenylthiosemicarbazide (**3e**)

1-(1-(4-Bromobenzyl)-1*H*-1,2,3-triazole-4-carbonyl)-4-phenylthiosemicarbazide (**3f**)

1-(1-(2,4-Dichlorobenzyl)-1*H*-1,2,3-triazole-4-carbonyl)-4-phenylthiosemicarbazide (**3g**)
1-(1-(2,6-Dichlorobenzyl)-1*H*-1,2,3-triazole-4-carbonyl)-4-phenylthiosemicarbazide (**3h**)

General procedure for preparation of 4a-h. The appropriate thiosemicarbazides **3a-h** (20 mmol) were heated under reflux conditions in a solution of sodium hydroxide (10 %) for about 8 hrs. The reaction mixture was then cooled, diluted with water and filtered. The filtrate was acidified with cold dilute hydrochloric acid. The formed white precipitate was crystallized from methanol giving 5-(1-substituted benzyl-1*H*-1,2,3-triazol-4-yl)-4-phenyl**-**4*H*-1,2,4-triazole-3-thiols **4a-h.** Analytical and spectral data are summarized in table 3 and table 4.

Table 3: Analytical Data for **4(a-h)**

Product	G	Molecular Formula	Molecular mass (g/mol)	M.P (C^o)	Yield (%)	Elemental analysis Calculated (found)		
						C%	H%	N%
4a	H	$C_{17}H_{14}N_6S$	334	209-210	80	61.08 (61.20)	4.19 (4.36)	25.15 (24.92)
4b	4-CH_3	$C_{18}H_{16}N_6S$	348	202-3	80	62.07 (62.24)	4.60 (4.57)	24.15 (24.32)
4c	4-OCH_3	$C_{18}H_{16}N_6SO$	364	206-8	59	59.34 (59.25)	4.40 (4.35)	23.08 (23.50)
4d	4-Cl	$C_{17}H_{13}N_6Cl$	368	228-9	85	55.43 (55.23)	3.53 (3.71)	22.83 (22.82)
4e	4-F	$C_{17}H_{13}N_6SF$	352	222-3	85	57.95 (58.16)	3.69 (4.00)	23.86 (24.00)
4f	4-Br	$C_{17}H_{13}N_6SBr$	412	229-230	86	49.51 (49.25)	3.16 (3.39)	20.38 (20.42)
4g	2,4-dichloro	$C_{17}H_{12}N_6SCl_2$	402	226-7	83	50.75 (50.56)	2.99 (3.00)	20.90 (20.75)
4h	2,6-dichloro	$C_{17}H_{12}N_6SCl_2$	402	230-3	83	50.75 (50.59)	2.99 (3.18)	20.90 (20.75)

Table 4: Spectral Data for **4(a-h)**

Product	G	IR (KBr, $\tilde{u}$, cm^{-1})	Mass Spectra (m/z)	^{1}H-NMR (δ, ppm) DMSO-d_6	^{13} C-NMR (δ, ppm) DMSO-d_6
4a	H	3100, 2350, 1506, 1467, 1337, 1200	335, 344, 305, 157, 91 77, 65	14.13 (br s, 1H, SH), 8.24 (s, 1H, H_{arom}), 7.60-7.81 (m, 10H, H_{arom}), 5.79 (s, 2H, CH_2 benzylic)	168.5, 143.8, 134.4, 134.2, 134.1, 129.6, 129.2, 128.7, 128.3, 127.9, 57.1
4b	4-CH_3	3080, 2353, 1520, 1460, 1320, 1205	348, 157, 105, 77, 65	14.03 (br s, 1H, SH), 8.22 (s, 1H, H_{arom}), 7.13-7.82 (m, 9H, H_{arom}), 5.28 (s, 2H, CH_2 benzylic), 2.17 (s, 3H, CH_3)	-
4c	4-OCH_3	3100, 2345, 1425, 1460, 1337, 1200	366, 365, 364, 335, 159, 121, 77	14.22 (br s, 1H, SH), 8.13 (s, 1H, H_{arom}), 7.21-7.62 (m, 9H, H_{arom}), 5.62 (s, 2H, CH_2 benzylic), 3.53 (s, 3H,OCH_3)	168.6, 143.8, 143.2, 134.1, 131.5, 130.3, 129.6, 129.2, 128.7, 125.7, 57.0, 55.8
4d	4-Cl	3100, 2355, 1515, 1470, 1337, 1203	369, 368, 125, 77	14.11 (br s, 1H, SH), 8.12 (s, 1H, H_{arom}), 7.10-7.42 (m, 9H, H_{arom}), 5.53 (s, 2H, CH_2 benzylic)	168.6, 143.8, 138.5, 134.2, 134.1, 133.1, 129.9, 129.6, 129.2, 128.9, 128.7, 125.8, 57.3
4e	4-F	3080, 2350, 1506, 1467, 1337, 1200	353, 352, 323, 188, 109, 77	14.21 (br s, 1H,SH), 8.13 (s, 1H, H_{arom}), 7.21-7.61 (m, 9H, H_{arom}), 5.58 (s, 2H, CH_2 benzylic)	-

Product	G	IR (KBr, $\tilde{u}$, cm^{-1})	Mass Spectra (m/z)	^{1}H-NMR (δ, ppm) DMSO-d_6	^{13} C-NMR (δ, ppm) DMSO-d_6
4f	4-Br	3150, 2356, 1525, 1457, 1335. 1205	414, 412, 383, 383, 157, 77	14.14 (br s, 1H, SH), 8.30 (s, 1H, H_{arom}), 7.12-7.64 (m, 9H, H_{arom}), 5.61 (s, 2H, CH_2 benzylic)	-
4g	2,4-dichloro	3108, 2360, 1520, 1445, 1337, 1201	403, 402, 215, 154, 77	14.32 (br s, 1H, SH) 8.30 (s, 1H, H_{arom}) 7.40-7.91 (m, 8H, H_{arom}), 5.61 (s, 2H, CH_2 benzylic)	-
4h	2,6-dichloro	3108, 2354, 1506, 1440, 1353, 1200	403, 402, 373, 159, 77	14.30 (br s, 1H, SH), 8.17 (s, 1H, H_{arom}), 7.41-7.82 (m, 8H, H_{arom}), 5.53 (s, 2H, CH_2 benzylic)	-

5-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**4a**)

5-[1-(4-Methylbenzyl)-1*H*-1,2,3-triazol-4-yl]-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**4b**)

5-[1-(4-Methoxybenzyl)-1*H*-1,2,3-triazol-4-yl]-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**4c**)

5-[1-(4-Chlorobenzyl)-1*H*-1,2,3-triazol-4-yl]-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**4d**)

5-[1-(4-Fluorobenzyl)-1*H*-1,2,3-triazol-4-yl]-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**4e**)

5-[1-(4-Bromobenzyl)-1*H*-1,2,3-triazol-4-yl]-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**4f**)

5-[1-(2,4-Dichlorobenzyl)-1*H*-1,2,3-triazol-4-yl]-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**4g**)

5-[1-(2,6-Dichlorobenzyl)-1*H*-1,2,3-triazol-4-yl]-4-phenyl-4*H*-1,2,4-triazole-3-thiol (**4h**)

General procedure for preparation of 5a-h and 6a-h. To a freshly prepared sodium ethoxide solution (20 mmol) in absolute ethanol (40 mL), a solution of 1,2,4-triazoles **4a-h** (15 mmol) was added with stirring. A solution of the alkyl halide (methyl iodide or benzyl bromide) (15 mmol) in ethanol (25 mL) was added dropwise. The reaction mixture was stirred at room temperature for 1 hr, and then water (30 mL) was added. The resulting solid was collected by filtration, dried and crystallized from ethanol yielding 1-substituted benzyl-4-(5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole **5a-h** (R=CH_3) and **6a-h** (R=$CH_2C_6H_5$)**.** Analytical and spectral data for **5a-h** are summarized in tables 5 and 7, whereas analytical and spectral data for **6a-h** are summarized in tables 6 and 8.

Table 5: Analytical Data for **5(a-h)**

Product	G	Molecular Formula	Molecular mass (g/mol)	M.P (C°)	Yield (%)	Elemental analysis Calculated (found)		
						C%	H%	N%
5a	H	$C_{18}H_{16}N_6S$	342	189-190	95	62.7 (61.53)	4.60 (4.70)	24.14 (23.97)
5b	4-CH_3	$C_{19}H_{18}N_6S$	362	182-3	85	62.98 (60.91)	5.25 (5.29)	23.20 (22.46)
5c	4-OCH_3	$C_{19}H_{18}N_6SO$	378	183-5	90	62.98 (60.91)	4.76 (5.05)	22.22 (21.80)
5d	4-Cl	$C_{18}H_{15}N_6SCl$	382	207-8	93	56.54 (56.37)	3.39 (4.14)	21.99 (22.20)
5e	4-F	$C_{18}H_{15}N_6SF$	366	188-9	93	59.02 (58.98)	4.10 (4.25)	22.95 (23.05)
5f	4-Br	$C_{18}H_{15}N_6SBr$	426	221-2	95	50.70 (50.56)	3.52 (3.70)	19.71 (19.65)
5g	2,4-dichloro	$C_{18}H_{14}N_6SCl_2$	416	185-6	85	51.92 (52.09)	3.37 (3.60)	20.91 (20.01)
5h	2,6-dichloro	$C_{18}H_{14}N_6SCl_2$	416	190-1	79	51.92 (51.77)	3.37 (3.50)	20.91 (20.01)

Table 6: Analytical Data for **6(a-h)**

Product	G	Molecular Formula)	Molecular mass (g/mol)	M.P (C^o)	Yield (%)	Elemental analysis Calculated (found)		
						C%	H%	N%
6a	H	$C_{24}H_{20}N_6S$	424	180-1	80	67.99 (68.18)	4.27 (4.9o)	19.81 (20.02)
6b	4-CH_3	$C_{25}H_{22}N_6S$	438	184-5	65	68.94 (68.20)	4.79 (5.0)	19.18 (19.19)
6c	4-OCH_3	$C_{25}H_{22}N_6SO$	454	178-180	78	66.10 (66.31)	4.30 (4.50)	18.50 (18.71)
6d	4-Cl	$C_{24}H_{19}N_6SCl$	458	168-9	71	62.88 (----)	4.15 (----)	18.34 (----)
6e	4-F	$C_{24}H_{19}N_6SF$	442	171-2	80	65.16 (65.05)	4.85 (4.05)	19.00 (18.81)
6f	4-Br	$C_{24}H_{19}N_6SBr$	502	165-6	82	57.37 (57.95)	3.78 (4.00)	16.91 (16.91)
6g	2,4-dichloro	$C_{24}H_{18}N_6SCl_2$	492	167-8	70	58.54 (58.9)	3.66 (3.80)	17.07 (17.29)
6h	2,6-dichlor	$C_{24}H_{18}N_6SCl_2$	492	173-4	70	58.54 (57.71)	3.66 (4.08)	17.07 (16. 92)

Table 7: Spectral Data for **5(a-h)**

Product	G	IR (KBr, $\tilde{\upsilon}$, cm^{-1})	^{1}H-NMR (δ, ppm) DMSO-d_6/TMS
5a	H	1560, 1450, 1345	8.82 (s, 1H, H_{arom}), 7.22-7.54 (m, 9H, H_{arom}), 5.43 (s, 2H, CH_2), 2.33 (s, 3H, CH_3)
5b	4-CH_3	1550, 1445, 1320	8.26 (s, 1H, H_{arom}), 7.24-7.47 (m, 9H, H_{arom}), 4.4 (s, 2H, CH_2), 2.31 (s, 3H, CH_3), 2.11 (s, 3H, CH_3)
5c	4-OCH_3	1560, 1445, 1330	8.25 (s, 1H, H_{arom}), 7.23-7.51 (m, 9H, H_{arom}), 5.42 (s, 2H, CH_2), 3.42 (s, 3H, OCH_3), 2.44 (s, 3H, CH_3)
5d	4-Cl	1555, 1435, 1315	8.51 (s, 1H, H_{arom}), 7.19-7.45 (m, 9H, H_{arom}), 5.44 (s, 2H, CH_2), 2.30 (s, 3H, CH_3)
5e	4-F	1582, 1465, 1363	8.51 (s, 1H, H_{arom}), 7.21-7.51 (m, 9H, H_{arom}), 5.33 (s, 2H, CH_2), 2.34 (s, 3H, CH_3)
5f	4-Br	1550, 1334, 1450	8.58 (s, 1H, H_{arom}), 7.17-7.81 (m, 9H, H_{arom}), 5.31 (s, 2H, CH_2), 2.29 (s, 3H, CH_3)
5g	2,4-dichloro	1560, 1440, 1356	8.61 (s, 1H, H_{arom}), 7.15-7.80 (m, 9H, H_{arom}), 5.32 (s, 2H, CH_2), 2.33 (s, 3H, CH_3)
5h	2,6-dichloro	1550, 1334, 1450	8.61 (s, 1H, H_{arom}), 7.22-7.75 (m, 9H, H_{arom}), 5.34 (s, 2H, CH_2), 2.29 (s, 3H, CH_3)

Table 8: Spectral Data for **6(a-h)**

Product	G	IR (KBr, ũ, cm^{-1})	^{1}H-NMR (δ, ppm) DMSO-d_6/TMS
6a	H	1570, 1440, 1345	8.83 (s, 1H, H_{arom}), 7.21-7.82 (m, 15H, H_{arom}), 5.64 (s, 2H, CH_2), 4.43 (s, 2H, CH_2), 2.09 (s, 3H, CH_3)
6b	4-CH_3	1560, 1450, 1345	8.80 (s, 1H, H_{arom}), 7.22-7.81 (m, 15H, H_{arom}), 5.55 (s, 2H, CH_2), 4.38 (s, 2H, CH_2), 3.40 (s, 3H, OCH_3)
6c	4-OCH_3	1553, 1430, 1320	8.81 (s, 1H, H_{arom}), 7.20-7.81 (m, 15H, H_{arom}), 5.61 (s, 2H, CH_2), 4.44 (s, 2H, CH_2)
6d	4-Cl	1553, 1435, 1323	8.82 (s, 1H, H_{arom}), 7.22-7.84 (m, 15H, H_{arom}), 5.57 (s, 2H, CH_2), 4.39 (s, 2H,CH_2)
6e	4-F	1559, 1440, 1327	8.54 (s, 1H, H_{arom}), 7.17-7.56 (m, 15H, H_{arom}), 5.61 (s, 2H,CH_2), 4.44 (s, 2H,CH_2)
6f	4-Br	1570, 1473, 1350	8.80 (s, 1H, H_{arom}), 7.20-7.54 (m, 15H, H_{arom}), 5.62 (s, 2H,CH_2), 4.41 (s, 2H, CH_2)
6g	2,4-dichloro	1550, 1465, 1335	8.52 (s, 1H, H_{arom}), 7.21-7.88 (m, 15H, H_{arom}), 5.61 (s, 2H,CH_2), 4.40 (s, 2H,CH_2)
6h	2,6-dichlor	1550, 1450, 1334	8.58 (s, 1H, H_{arom}), 7.23-7.76 (m, 15H, H_{arom}), 5.61 (s, 2H, CH_2), 4.40 (s, 2H, CH_2)

1-Benzyl-4-(5-(methylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**5a**)

1-(4-Methylbenzyl)-4-(5-(methylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**5b**)

1-(4-Methoxybenzyl)-4-(5-(methylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**5c**)

1-(4-Chlorobenzyl)-4-(5-(methylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**5d**)

1-(4-Fluorobenzyl)-4-(5-(methylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**5e**)

1-(4-Bromobenzyl)-4-(5-(methylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**5f**)

1-(2,4-Dichlorobenzyl)-4-(5-(methylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**5g**)

1-(2,6-Dichlorobenzyl)-4-(5-(methylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**5h**)

1-Benzyl-4-(5-(benzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**6a**)

1-(4-Methylbenzyl)-4-(5-(benzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**6b**)

1-(4-Methoxybenzyl)-4-(5-(benzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**6c**)

1-(4-Chlorobenzyl)-4-(5-(benzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**6d**)

1-(4-Fluorobenzyl)-4-(5-(benzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**6e**)

1-(4-Bromobenzyl)-4-(5-(benzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**6f**)

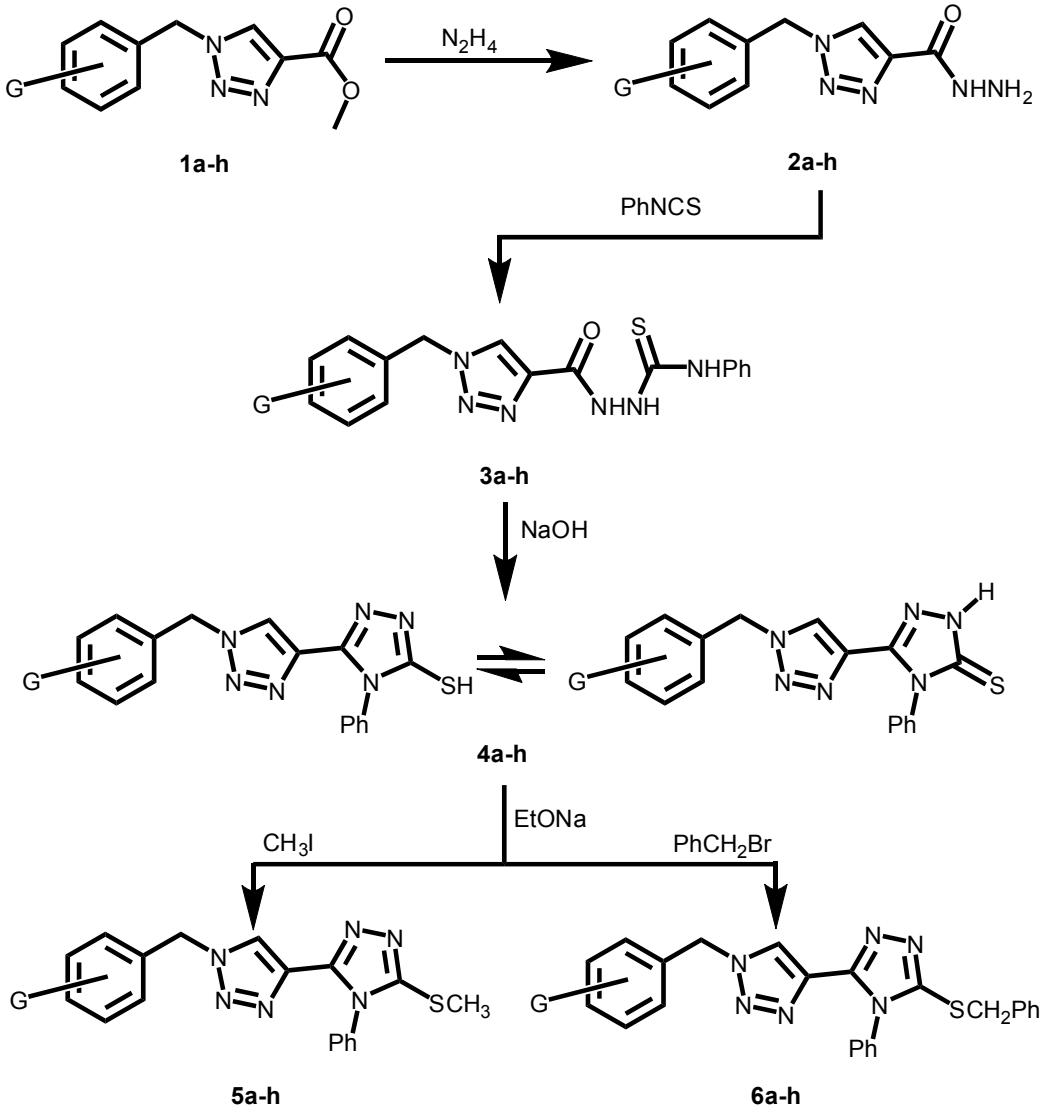
1-(2,4-Dichlorobenzyl)-4-(5-(benzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**6g**)

1-(2,6-Dichlorobenzyl)-4-(5-(benzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl)-1*H*-1,2,3-triazole (**6h**)

Results and Discussion

Thiosemicarbazides **3a-h** were prepared from the reaction of 1-substituted benzyl-4-hydrazinocarbonyl-1,2,3-triazoles **2a-h** with phenyl isothiocyanate in absolute ethanol at room temperature (Scheme 1). Compounds **3a-h** show absorption bands in the range 3115 - 3280 cm^{-1}assigned for N─H protons, bands in the range 1660-1670 and 1250-1200 cm^{-1}that could be assigned to carbonyl and thiocarbonyl groups respectively, N═N stretching frequencies appear in the range 1450-1440 cm^{-1}. The ^{1}H-NMR spectra shows that N─H protons resonates at 9.8-9.1 ppm and they undergo

hydrogen-deuterium exchange. The proton of 1,2,3-triazole ring appears in the aromatic region as singlet at 8.6-8.1 and benzylic protons appear as singlet at 5.8-5.6 ppm (Scheme 1). Cyclization of thiosemicarbazides **3a-h** is carried out in aqueous sodium hydroxide solution followed by acidification with hydrochloric acid yielded 1,2,4-triazoles **4a-h** (Scheme1).



a; G = H b; G = 4-CH_3 c; G = 4-OCH_3 d; G = 4-Cl

e; G = 4-F f; G = 4-Br g; G = 2,4-dichloro h; 2,6-dichloro

Scheme 1

Compounds **4a-h** show absorption bands in the range 3150 – 3200 cm^{-1} that are attributed to the S–H stretching frequency. Absorption bands in the range 1470-1510 and 1300-1330 cm^{-1} could be assigned to C=N and C–N stretching frequencies respectively, the IR spectra show also the disappearance of the bands of the carbonyl and thiocarbonyl groups, which are observed in the starting materials **3a-h.** The ^{1}H-NMR spectra of **4a-h** are in agreement with the proposed structures, the S–H protons

appear as a broad singlet at 14.3-14.1 ppm and undergo deuterium exchange. From the IR study, the S-H shows a stretching frequency about 2250-2350 cm^{-1}, as well as a medium to a strong band in the range of 1150-1205 cm^{-1}, this band indicates the presence of C═S bond. This observation gives evidence that SH proton undergoes tautomerization of the thiol to C═S and NH proton as shown for compounds **4a-h** in scheme 1. The proton of 1,2,3-triazole ring appears in the aromatic region as singlet at 8.3-8.1 ppm, where the phenyl group protons appear in the region between 7.9-7.1 ppm. the Ar─CH_3 and the ArO─CH_3 groups appear at 2.2-2.1 and 3.5 ppm respectively. Mass spectra of **4a-h** are in agreement with proposed structure. Besides the molecular ion peak $\mathbf{M}^+$, the compounds give peaks corresponding to the ions $[M-N_2H]^+$, $[Ph]^+$and $[ArCH_2]^+$.

Compounds **5a-h** and **6a-h** were prepared by the reaction of the corresponding 1,2,4-triazoles **4a-h** with the appropriate alkyl halide (methyl iodide or benzyl bromide) in ethanolic sodium ethoxide solution. The IR spectra of compounds **5a-h** and **6a-h** show that the absorption bands attributed to the S─H stretching frequency in the starting materials **4a-h** have disappeared. Absorption bands in the range 1515-1534 and 1320-1360 cm^{-1} are assigned to C═N and C─N stretching frequencies respectively. ^{1}H-NMR spectra of **5a-h** and **6a-h** show no signal in the low field region of the spectra (~14 ppm) which indicates the substitution of the S─H proton by the alkyl groups. The S-CH_2-Ph appears at 4.4 ppm.

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