Graphical abstract

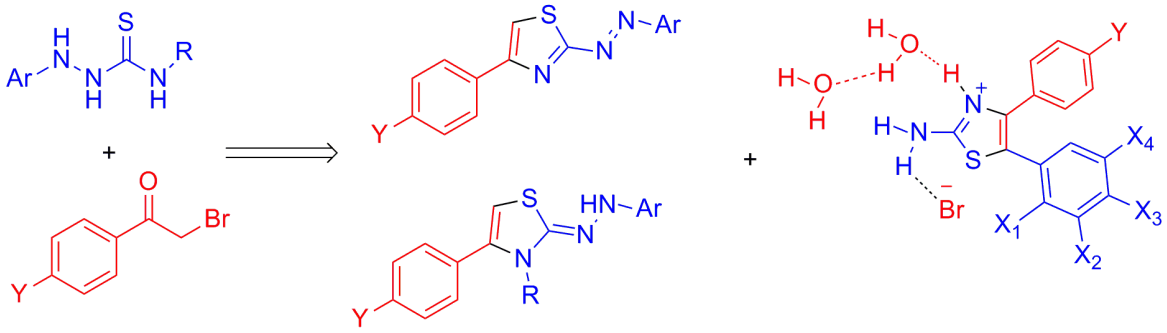
Synthesis and crystallographic evaluation of diazenyl- and hydrazothiazoles. [5.5] Sigmatropic rearrangement and formation of thiazolium bromide dihydrate derivatives

Alaa A. Hassan,[1*] Nasr K. Mohamed,[1] Ashraf A. Aly,[1] Hendawy N. Tawfeek,[1] Stefan Bräse,[2] Martin Nieger[3]

[1] Chemistry Department, Faculty of Science, Minia University, 61519-El-Minia, Egypt.

[2] Institute of Organic Chemistry, Karlsruhe Institute of Technology, Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany.

[3] Laboratory of Inorganic Chemistry, Department of Chemistry, University of Helsinki, P.O.Box55 (A. I. Virtasenaukio I), 00014, Helsinki, Finland.



Synthesis and crystallographic evaluation of diazenyl- and hydrazothiazoles. [5.5] Sigmatropic rearrangement and formation of thiazolium bromide dihydrate derivatives

Alaa A. Hassan,[1*] Nasr K. Mohamed,[1] Ashraf A. Aly,[1] Hendawy N. Tawfeek,[1] Stefan Bräse,[2] Martin Nieger[3]

[1] Chemistry Department, Faculty of Science, Minia University, 61519-El-Minia, Egypt.

[2] Institute of Organic Chemistry, Karlsruhe Institute of Technology, Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany.

[3] Laboratory of Inorganic Chemistry, Department of Chemistry, University of Helsinki, P.O.Box55 (A. I. Virtasenaukio I), 00014, Helsinki, Finland.

✉ Corresponding Authors: Tel./fax: +20 862363011. alaahassan2001@mu.edu.eg

Abstract:

In this investigation the synthesis of diazenylthiazoles (**3a-e**) by the reaction of arylthiosemicarbazides with *ω*-bromoacetophenones *via* Eschenmoser-coupling reaction in acetonitrile and equimolar amounts of triethylamine and triphenylphosphine. Upon heating 1,4-disubstituted thiosemicarbazides with *ω*-bromoacetophenones in absolute ethanol, hydrazothiazoles (**16a-i**) were precipitated. On the other hand, the reaction of arylthiosemicarbazides with *ω*-bromoacetophenones in refluxing ethanol yielded 2-amino-5-[4-aminophenyl]-4-phenylthiazolium bromide dihydrate derivatives (**19a-g**) via [5.5] sigmatropic shift The studied products were further characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectrometry. X-ray single crystal of **3a** and **16h** showed that, the molecules crystallized in the triclinic crystal system, space group $P2_1/c$. Whereas the X-ray single crystal of **19b** showed the molecule crystalized in orthorhombic, space group $P2_12_12_1$. In the crystal of **19b**, the lattice water and bromide ion associated through hydrogen bonded with thiazole-NH_2.

Keywords: Diazenylthiazoles; Hydrazothiazoles; Thiazoliumbromidedihydrates; Thiosmicarbazides; X-Ray analyses.

1. Introduction

The azo-dyes of heterocyclic compounds are useful structural components, due to their applications in textiles, papers, leather additives, foodstuffs, cosmetic industries and as organic solar cells and chemosensors [1-6]. Thiazole-azo dyes were synthesized during the reaction of thiourea with *p*-methoxyphenyl-ω-bromoacetophenone followed by coupling with *N*,*N*-diethylaniline [7], whereas 1,3-thiazolyl diazenyl-3-naphthalene derivatives have been synthesized by diazotization of 4-[4-ethylphenyl]thiazole-2-amine and coupling to *N*-[4-chloro-2-methylphenyl]-3-hydroxynaphthalen-2-carboxamede [8]. Various derivatives of diazenyl-1,3-thiazoles were synthesized and their biological activities were evaluated [9,10].

Recently, we reported that the reaction of hydrazinecarbothioamides with tetracyanoethylene (TCNE) gave azothiazoles [11]. Azo-benzothiazole chromophores possess large molecular hyperpolarizeability and showed that they are a good choice for nonlinear optics (NLO) materials [12,13].

2-(3-(1*H*-Indol-3-yl)-5-(*p*-tolyl-4,5-dihydro-1*H*-pyrazol-1-yl)-5-(aryldiazenyl)-4-thiazoles were synthesized from 3-(1*H*-indolyl)-5-(*p*-tolyl)-4,5-dihydropyrazole-1-carbothioamide and keto-hydrazonyl halides. The latter compounds have been evaluated for their antitumor activity against the MCF-7 human breast carcinoma cell line [14], also, indolylmethylidenehydrazinyl-4-aryl-5-(aryldiazenyl)-thiazoles also have been synthesized [15].

2,4,5-Trisubstituted-1,3-thiazole derivatives including a hydrazide-hydrazone moiety have been synthesized and evaluated towards antitumor activity against some human cancer [16].

The reaction of *ω*-bromoacetophenones with ethylidene hydrazinecarbothioamides gave substituted ethylidene hydrazinylthiazoles which exhibited anti-bacterial activity [17]. (*E*)-2-(2-(2-Nitrobenzylidene)thiazoles and (*E*)-3,4-diaryl-2-(cycloalkylidene-hyrazono)-thiazoles were formed during the reaction of *ω*-bromoacetophenones with 2-(1-alkyl-methylidene)hydrazinecarbothioamides and cycloalkylidene-*N*-phenylhydrazine-carbothioamides [18].

4-Methyl-(1-benzyllidenehydrazinyl)-2-carbothioamide reacted with ethylbromopyruvate to give ethyl-2-(4-methyl-(2-benzylidenehydrazinyl)thiazole-4-carboxylates [19].

Gomha et al. reported that, 1,4-bis(1-(5-aryldiazenyl)thiazol-2-yl)-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-5-yl)benzene was formed during the reaction of 5,5`-(4,4-phenlene)-bis-(3-thiophen-2-yl)-4,5-dihydro-pyrazole-1-carbothioamide with hydrazonyl halides [20].

Heterocyclization of 2-(1-alkylethylidene)hydrazinecarbothioamides afforded the formation of monohydrated pyridinium bromide-1,3-thiazolidenehydrazinylidene ethyl, 1,3-thiazolylidenehydrazinium bromide and thiazolylidenehydrazines [21].

Hydrazine derivatives are known to undergo rearrangements with N-H bond fission [22]. It has been reported, that the addition of benzophenonephenylhydrazone to polyphosphoric acid (PPA) under heating, *o*-phenylenediamine and benzophenone was observed [22].

A [5.5]sigmatropic shift of bis-thiazolylhydrazines in acidic catalyzed rearranged to *p*-aminophenylthiazoles in addition to, bis(2-aminothiazoles) [23].

2. Experimental

2.1. Instrumentation

Gallenkamp melting point apparatus was used to determine the melting points. IR spectra were recorded with Alpha, Bruker FT-IR instruments using potassium bromide pellets. NMR spectra were recorded for ^{1}H NMR at 400 MHz and ^{13}C NMR at 100 MHz on a Bruker AM 400 spectrometry with TMS as internal standard (δ = 0), and data are reported as follows: Chemical shift, multiplicity (s = singlet, d = doublet, m = multiplet, br = broad). For ^{13}C NMR, TMS (δ = 0) was used as internal standard and spectra were obtained with complete proton decoupling. Finnigan MAT instrument was used to record the mass spectra (70 eV, EI-mode). Elemental analyses for C, H, N, and S were carried out using an Elmyer 306. Preparative layer chromatography (plc) was carried out on glass plates covered with a 1.0 mm thick layer of slurry-applied silica gel (Merck Pf_{254}).

2.2. Chemicals

2.2.1. *Starting materials*

Monosubstituted and disubstituted thiosemicarbazides were prepared according to literature methods (**1a** [23], **1b** [24], **1c** [11], **1d** [25], **15a-d** [26]). ω-Bromoacetophenone **2a,b** were prepared according to literature [27,28].

2.2.2. Synthesis of substituted diazenylthiazoles 3a-e.

Equimolar amounts of thiosemicarbazides **1a-d** (1**a**, 0.167; 1**b**, 0.201; 1**c**, 0.245 and 1**d**, 0.257g) and ω-bromoacetophenone **2a/b** (**2a**, 0.198; **2b**, 0.277 g) were stirred in 20 ml dry CH_3CN for 16 h at room temperature. The dried salt was redissolved in CH_3CN, followed

by adding other equivalents of triethylamine and triphenylphosphine. The mixture was refluxed for 10-16 h, H_2O (30 ml) was added and the resulting mixture was extracted with CH_2Cl_2. The organic extracts were dried over anhydrous $CaCl_2$, filtered and concentrated. The residue was subjected to chromatographic plates (plc) using toluene/ethyl acetate (10:1) to give an orange main zone which was extracted with acetone to give compounds **3a-e** (Scheme 1).

2.2.2.1. *(E)-4-Phenyl-2-(phenyldiazenyl)thiazole* (**3a**)

Orange crystals (acetonitrile); yield 217 mg (82%); Mp. 158-159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.58 (m, 6H, Ar-H), 7.62 (s, 1H, thiazole-H), 8.03-8.88 (m, 4H, Ar-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 115.88 (thiazole-CH), 123.25, 125.62, 126.83, 128.75, 129.53, 130.81 (Ar-CH), 133.91, 134.23, (Ar-C), 155.85 (thiazole-C4), 168.46 (thiazole-C2) ppm; IR (KBr): ν = 3105 (Ar-CH), 1600 (C=N), 1585 (Ar-C=C), 1560, 1444 cm^{-1} (N=N); MS (70 eV): m/z (%) = 265 (M^+, 58), 189 (12), 160 (28), 105 (17), 77 (100); Anal. Calcd for $C_{15}H_{11}N_3S$ (265.33): C 67.90, H 4.18, N 15.84, S 12.08; Found: C 67.78, H 4.11, N 16.02, S 11.97.

2.2.2.2. *(E)-2-((3-Chlorophenyl)diazenyl))-4-phenylthiazole*

(**3b**) Pale orange crystals (acetonitrile); yield 248 mg (83%); Mp. 148-149°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.45 (m, 5H, Ar-H), 7.55 (s, 1H, thiazole-H), 7.85-7.88 (m, 1H, Ar-H), 7.92-8.00 (m, 3H, Ar-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 116.69 (thiazole-CH), 123.98, 124.00, 127.20, 129.68, 129.86, 131.27, 133.48 (Ar-CH), 134.60, 136.43, 142.12 (Ar-C), 157.48 (thiazole-C4), 169.84 (thiazole-C2) ppm; IR (KBr): ν = 3080 (Ar-CH), 1608 (C=N), 1592 (Ar-C=C), 1562, 1442 cm^{-1} (N=N); MS (70 eV): m/z (%) = 301/299 (M^+, 38), 223 (13), 189 (67), 160 (100), 141 (17), 113 (12); Anal. Calcd for

$C_{15}H_{10}ClN_3S$ (299.78): C, 60.10, H 3.36, Cl 11.83, N 14.02, S 10.70; Found: C 59.97, H 3.45, Cl 11.77, N 13.91, S 10.82.

2.2.2.3. *(E)-4-Phenyl-2-(tosyldiazenyl)thiazole* (**3c**)

Orange crystals (acetonitrile); yield 274 mg (80%); Mp. 175-176°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.50 (s, 3H, CH_3); 6.90-7.00 (m, 2H, Ar-H), 7.15-7.41 (m, 5H, Ar-H), 7.52 (s, 1H, thiazole-H), 7.62-7.79 (m, 2H, Ar-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.37 (CH_3), 116.75 (thiazole-CH), 123.77, 127.61, 128.54, 129.70, 130.12 (Ar-CH), 135.48, 141.01, 142.86 (Ar-C), 156.67 (thiazole-C4), 168.55 (thiazole-C2) ppm; IR (KBr): ν = 3085 (Ar-CH), 1605 (C=N), 1594 (Ar-C=C), 1568, 1450 cm^{-1} (N=N); MS (70 eV): m/z (%) = 343 (M^+, 100), 265 (46), 189 (58), 184 (30), 160 (23), 155 (43), 91 (17), 77 (51); Anal. Calcd for $C_{16}H_{13}N_3O_2S_2$ (343.42): C 55.96, H 3.82, N 12.24, S 18.67; Found: C 56.12, H 3.91, N 12.15, S 18.58.

2.2.2.4. *(E)-2-((2,4-Dinitrophenyl)diazenyl))-4-phenylthiazole* (**3d**)

Orange crystals (acetonitrile); yield 287 mg (81%); Mp. 193-195 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.35-7.43 (m, 6H, Ar-H), 7.55 (s, 1H, thiazole-H), 7.94-8.03 (m, 1H, Ar-H), 8.30-8.40 (m, 1H, Ar-H) ppm, ^{13}CNMR (100 MHz, DMSO-d_6): δ 115.59 (thiazole-CH), 121.73, 126.10, 128.48, 128.81, 129.16, 129.63 (Ar-CH), 133.49, 134.55, 140.12, 142.16 (Ar-C), 157.11 (thiazole-C4), 169.69 (thiazole-C2) ppm; IR (KBr): ν = 3078 (Ar-CH), 1612 (C=N), 1602 (Ar-C=C), 1558, 1448 cm^{-1} (N=N); MS (70 eV): m/z (%) = 355 (M^+, 100), 279 (38), 197 (53), 189 (71), 183 (80), 167 (28), 160 (56), 123 (22); Anal. Calcd for $C_{15}H_9N_5O_4S$ (355.33): C 50.70, H 2.55, N 19.71, S 9.02; Found: C 50.61, H 2.49, N 19.83, S 8.89.

2.2.2.5. *(E)-4-(4-Bromophenyl)-2-((2,4-dinitrophenyl)diazenyl)thiazole* (**3e**)

Orange crystals (acetonitrile); yield 373 mg (86%); Mp. 182-183°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.24-7.55 (m, 4H, Ar-H), 7.58 (s, 1H, thiazole-H), 7.81-7.86 (m, 1H, Ar-H), 7.92-8.00 (m, 1H, Ar-H), 8.31-8.39 (m, 1H, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 114.34 (thiazole-CH), 121.32, 125.98, 128.03, 130.12, 131.87 (Ar-CH), 132.71, 134.16, 138.73, 139.14, 141.82 (Ar-C), 156.35 (thiazole-C4), 167.91 (thiazole-C2) ppm; IR (KBr) ν: 3063 (Ar-CH), 1608 (C=N), 1596 (Ar-C=C), 1570, 1442 cm^{-1} (N=N); MS (70 eV): m/z (%) = 437/435 (M^+, 63), 279 (14), 267 (100), 238 (81), 197 (53), 167 (27), 155 (62), 123 (22); Anal. Calcd for $C_{15}H_8BrN_5O_4S$ (434.22): C 41.49, H 1.86, Br 18.40, N 16.13, S 7.38; Found: C 41.61, H 1.72, Br 18.29, N 16.25, S 7.47.

2.2.3. Synthesis of substituted hydrazono-2,3-dihydrothiazoles 16a-i

A mixture of ω-bromoacetophenone **2a/b** (1.0 mmol, **2a**, 0.198; **2b**, 0.277 g) and 1,4-disubstituted thiosemicarbazides **15a-e** (1.0 mmol, **15a**, 0.333; **15b**, 0.339; **15c**, 0.285; **15 d**, 0.297 and **15e**, 0.335 g) in 30 ml absolute ethanol was heated under reflux with stirring for 4-6 h, the reaction was followed up by TLC analysis. The precipitate was allowed to stand, filtered, washed with 5 ml ethanol, dried and recrystallized from the mentioned solvent to give hydrazothiazoles **16a-i** (Scheme 4).

2.2.3.1. *(Z)-2-(2-(2,4-Dinitrophenyl)hydrazono)-3,4-diphenyl-2,3-dihydrothiazole* (**16a**)

Brown crystals (methanol); yield 390 mg (90%); Mp. 241-243°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.82 (s, 1H, thiazole-H), 7.12-7.50 (m, 10H, Ar-H), 7.96-8.08 (m, 1H, Ar-H), 8.24-8.26 (m, 1H, Ar-H), 8.83-8.85 (m, 1H, Ar-H), 10.54 (br, s, 1H, NH, exchange with

D_2O) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 116.15 (thiazole-CH), 124.17, 125.24, 126.82, 128.34, 129.07, 130.00, 130.90, 131.87, 132.50, (Ar-CH), 132.84, 135.66, 136.59, 140.85, 141.18 (Ar-C), 145.00 (thiazole-C4), 165.83 (thiazole-C2) ppm; IR (KBr): ν = 3254 (hydrazo-NH), 3015 (Ar-CH), 1621 (C=N), 1578 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 433 (M^+, 100), 357 (28), 251 (14), 167 (13), 137 (73), 123 (32); Anal. Calcd for $C_{21}H_{15}N_5O_4S$ (433.44): C 58.19, H 3.49, N 16.16, S 7.40; Found: C 58.22, H 3.56, N 16.02, S 7.29.

2.2.3.2. *(Z)-3-Cyclohexyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-phenyl-2,3-dihydrothiazole* (**16b**)

Brown crystals (methanol); yield 386 mg (88%); Mp. 230-232°C; ^1H NMR (400 MHz, DMSO-d_6): δ 1.06-1.09 (m, 4H, cyclohexyl-CH_2), 1.76-1.78 (m, 6H, cyclohexyl-CH_2), 3.72-3.74 (m, 1H, cyclohexyl-CH), 6.91 (s, 1H, thiazole-H), 7.48-7.52 (m, 6H, Ar-H), 8.28-8.38 (m, 1H, Ar-H), 8.87-8.89 (m, 1H, Ar-H), 10.53 (br, s, 1H, NH, exchange with D_2O) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 24.68, 25.56, 27.78 (cyclohexyl-CH_2), 58.88 (cyclohexyl-CH), 115.45 (thiazole-CH), 123.48, 128.80, 128.94, 129.59, 130.16, 131.15 (Ar-CH), 135.62, 137.18, 139.00, 141.53 (Ar-C), 144.90 (thiazole-C4), 164.40 (thiazole-C2) ppm; IR (KBr): ν = 3263 (hydrazo-NH), 3007 (Ar-CH), 2927-2865 (Ali-CH), 1613 (C=N), 1585 cm^{-1} (Ar-C=C) ppm; MS (70 eV): m/z (%) = 439 (M^+, 16), 363 (34), 357 (32), 257 (55), 168 (8), 156 (100), 137 (73), 123 (47); Anal. Calcd for $C_{21}H_{21}N_5O_4S$ (439.49): C 57.39, H 4.82, N 15.94, S 7.30; Found: C 57.27, H 4.91, N 16.08, S 7.44.

2.2.3.3. *(Z)-2-(2-(2,4-Dinitrophenyl)hydrazono)-3-ethyl-4-phenyl-2,3-dihydrothiazole* (**16c**)

Brown crystals (methanol); yield 335 mg (87%); Mp. 222-224°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.28 (t, 3H, CH_3, J = 7.66), 3.52 (q, 2H, CH_2, J = 7.66), 7.10 (s, 1H, thiazole-H), 7.45-7.75 (m, 6H, Ar-H), 8.22-8.30 (m, 1H, Ar-H), 8.92-8.94 (m, 1H, Ar-H), 10.32 (br, s, 1H, NH, exchange with D_2O) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.28 (CH_3), 38.78 (CH_2), 115.20 (thiazole-CH), 123.23, 126.71, 128.78, 129.81, 130.40, 131.20 (Ar-CH), 131.88, 134.96, 139.11, 141.32 (Ar-C), 145.61 (thiazole-C4), 164.86 (thiazole-C2) ppm; IR (KBr): ν = 3195 (hydrazo-NH), 3018 (Ar-CH), 2925-2860 (Ali-CH), 1611 (C=N), 1581 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 385 (M^+, 100), 307 (32), 285 (15), 204 (12), 183 (38), 167 (13), 137 (73), 123 (29); Anal. Calcd for $C_{17}H_{15}N_5O_4S$ (385.40): C 52.98, H 3.92, N 18.17, S 8.32; Found: C 53.11, H 4.09, N 18.06, S 8.21.

2.2.3.4. *(Z)-4-(4-Bromophenyl)-2-(2-(2,4-dinitrophenyl)hydrazono)-3-phenyl-2,3-dihydrothiazole* (**16d**)

Brown crystals (methanol); yield 430 mg (84%); Mp. 252-254°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 6.86 (s, 1H, thiazole-H), 7.09-7.50 (m, 9H, Ar-H), 7.90-8.00 (m, 1H, Ar-H), 8.20-8.27 (m, 1H, Ar-H), 8.78-8.84 (m, 1H, Ar-H), 10.53 (br, s, 1H, NH, exchange with D_2O) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 115.60 (thiazole-CH), 122.20; 123.31, 128.38, 128.56, 129.17, 129.41, 129.86, 130.12 (Ar-CH), 130.33, 131.33, 135.96, 136.79, 139.22, 140.89 (Ar-C), 146.29 (thiazole-C4), 166.04 (thiazole-C2) ppm; IR (KBr): ν = 3254 (hydrazo-NH), 3015 (Ar-CH), 1621 (C=N), 1578 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 513/511 (M^+, 100), 357 (38), 329 (70), 267 (64), 181 (44), 167 (33), 135 (76), 123 (25); Anal. Calcd for $C_{21}H_{14}BrN_5O_4S$ (512.34): C 49.23, H 2.75, Br 15.60, N 13.67, S 6.26; Found: C 49.10, H 2.67, Br 15.73, N 13.59, S 6.39.

2.2.3.5. *(Z)-3-Allyl-4-(4-bromophenyl)-2-(2-(2,4-dinitrophenyl)hydrazono)-2,3-*

dihydrothiazole (**16e**)

Brown crystals (methanol); yield 409 mg (86%); Mp. 229-231°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.30-4.45 (m, 2H, allyl-CH_2N), 4.90-5.00 (m, 2H, allyl-CH_2=), 5.76-5.86 (m, allyl-CH=), 6.85 (s, 1H, thiazole-H), 7.41-7.45 (m, 2H, Ar-H), 7.69-7.73 (m, 2H, Ar-H), 7.76-7.79 (m, 1H, Ar-H), 8.25-8.29 (m, 1H, Ar-H), 8.82-8.92 (m, 1H, Ar-H), 10.58 (br, s, 1H, NH, exchange with D_2O) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 47.68 (allyl-CH_2N), 115.73 (thiazole-CH), 117.18 (allyl-CH_2=), 124.80, 128.65, 129.87, 130.47, 133.57 (Ar-CH), 134.28 (allyl-CH=), 135.96, 136.88, 138.11, 141.51, 142.92 (Ar-C), 145.15 (thiazole-C4), 165.36 (thiazole-C2) ppm; IR (KBr): ν = 3193 (hydrazo-NH), 3014 (Ar-CH), 1626 (C=N), 1602 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 477/475 (M^+, 100), 435 (29), 321 (61), 293 (15), 183 (12), 167 (64), 136 (71), 123 (54); Anal. Calcd for $C_{18}H_{14}BrN_5O_4S$ (476.30): C 45.39, H 2.96, Br 16.78, N 14.70, S 6.73; Found: C 45.51, H 3.06, Br 16.69, N 14.81, S 6.61.

2.2.3.6. *(Z)-3-Allyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-phenyl-2,3-dihydro-thiazole* (**16f**)

Brown crystals (methanol); yield 353 mg (89%); Mp. 235-237°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.30-4.34 (m, 2H, allyl-CH_2N), 5.11-5.20 (m, 2H, allyl-CH_2=), 5.75-5.88 (m, allyl-CH=), 7.12 (s, 1H, thiazole-H), 7.22-7.32 (m, 3H, Ar-H), 7.43-7.48 (m, 2H, Ar-H), 7.50-7.61 (m, 1H, Ar-H), 8.10-8.13 (m, 1H, Ar-H), 9.00-9.02 (m, 1H, Ar-H), 10.31 (br, s, 1H, NH, exchange with D_2O) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 46.95 (allyl-CH_2N), 116.76 (thiazole-C5), 118.38 (allyl-CH_2=), 124.42, 129.48, 130.65, 132.85, 132.94, 133.04 (Ar-CH), 134.53 (allyl-CH=), 134.72, 137.25, 138.12, 143.16 (Ar-C), 145.82 (thiazole-C4), 164.98 (thiazole-C2) ppm; IR (KBr): ν = 3223 (hydrazo-NH), 3018 (Ar-CH), 3018

(Ar-CH), 2975, 2852 (Ali-CH), 1619 (C=N), 1584 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 397 (M^+, 100), 321 (58), 215 (23), 183 (23), 136 (84), 123 (65); Anal. Calcd for $C_{18}H_{15}N_5O_4S$ (397.41): C 54.40, H 3.80, N 17.62, S 8.07; Found: C 54.29, H 3.87, N 17.78, S 7.91.

2.2.3.7. *(Z)-4-(4-Bromophenyl)-2-(2-(2,4-dinitrophenyl)hydrazono)-3-ethyl-2,3-dihydrothiazole* (**16g**)

Brown crystals (methanol); yield 413 mg (89%); Mp. 227-228°C; ^1H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, 3H, CH_3, *J* = 7.77), 3.84 (q, 2H, CH_2, *J* = 7.77), 7.06 (s, 1H, thiazole-H), 7.25-7.32 (m, 2H, Ar-H), 7.42-7.65 (m, 2H, Ar-H), 7.85-7.92 (m, 1H, Ar-H), 8.35-8.42 (m, 1H, Ar-H), 8.80-8.94 (m, 1H, Ar-H), 10.30 (br, s, 1H, NH, exchange with D_2O) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.37 (CH_3), 39.56 (CH_2), 116.60 (thiazole-C5), 123.77, 125.54, 128.40, 129.60, 130.87 (Ar-CH), 131.25, 134.62, 136.51, 139.34, 141.32 (Ar-C), 145.90 (thiazole-C4), 164.48 (thiazole-C2) ppm; IR (KBr): ν = 3195 (hydrazo-NH), 3018 (Ar-CH), 2925-2860 (Ali-CH), 1611 (C=N), 1581 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 465/463 (M^+, 100), 308 (45), 283 (56), 204 (41), 183 (22), 176 (32), 167 (14), 156 (51), 136 (67), 123 (22); Anal. Calcd for $C_{17}H_{14}BrN_5O_4S$ (464.29): C 43.98, H 3.04, Br 17.21, N 15.08, S 6.91; Found: C 43.85, H 2.97, Br 17.09, N 14.96, S 6.87.

2.2.3.8. *(Z)-N'-(3-Benzyl-4-phenylthiazol-2(3H)-ylidene)-4-methylbenzenesulfono-hydrazide* (**16h**)

Violet crystals (methanol); yield 357 mg (82%); Mp. 212-214 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 2.30 (s, 3H, CH_3), 4.82 (s, 2H, CH_2Ph), 6.75 (s, 1H, thiazole-H), 6.92-7.42 (m, 15H, Ar-H and NH, exchange with D_2O) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.60 (CH_3), 46.25 (CH_2Ph), 115.76 (thiazole-C5), 125.87, 126.52, 127.62, 128.32, 128.60,

128.74, 129.05, 129.23 (Ar-CH), 132.71, 133.66, 135.20, 139.00 (Ar-C), 146.86 (thiazole-C4), 163.45 (thiazole-C2) ppm; IR (KBr): ν = 3150 (hydrazo-NH), 3038 (Ar-CH), 2973 (Ali-CH), 1614 (C=N), 1553 and 1491 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 435 (M^+, 100), 358 (52), 264 (36), 188 (25), 170 (87), 155 (54), 91 (73), 77 (60); Anal. Calcd for $C_{23}H_{21}N_3O_2S_2$ (435.56): C 63.42, H 4.86, N 9.65, S 14.72; Found: C 63.34, H 4.76, N 9.55, S 14.57.

2.2.3.9. *(Z)-3-Benzyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-phenyl-2,3-dihydrothiazole* (**16i**)

Brown crystals (methanol); yield 402 mg (90%); Mp. 226-228 °C; ^1H NMR (400 MHz, DMSO-d_6): δ 5.08 (s, 1H, CH_2Ph), 6.98 (s, 1H, thiazole-H), 7.05-7.50 (m, 11H, Ar-H), 8.04-8.13 (m, 1H, Ar-H), 8.79-8.82 (m, 1H, Ar-H), 10.60 (br, s, 1H, NH, exchange with D_2O) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 46.50 (CH_2Ph), 115.51 (thiazole-C5), 123.36, 126.52, 126.62, 127.27, 128.53, 128.87, 129.55, 129.96, 130.83 (Ar-CH), 131.80, 135.35, 136.47, 138.64, 142.10 (Ar-C), 145.30 (thiazole-C4), 162.50 (thiazole-C2) ppm; IR (KBr) ν = 3117 (hydrazo-NH), 3058, 3027 (Ar-CH), 2944 (Ali-CH), 1616 (C=N), 1587 and 1491 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 447 (M^+, 100), 371 (51), 265 (33), 189 (73), 183 (40), 167 (83), 123 (32); Anal. Calcd for $C_{22}H_{17}N_5O_4S$ (447.47): C 59.05, H 3.83, N 15.65, S 7.17; Found: C 58.98, H 3.76, N 15.48, S 7.03.

2.2.4. Synthesis of substituted thiazolium bromide dihydrate 19a-g.

ω-Bromoacetophenone **2a/b** (1.0 mmol, **2a**, 0.198; **2b**, 0.277 g) and substituted thiosemicarbazides **1a-d** (l.0 mmol, **1a**, 0.167; 1 **b**, 0.201; 1 **c**, 0.257 and 1**d**, 0.245 g) in 30 ml absolute ethanol were stirred under reflux for 8-12 h. The reaction was follow up by TLC analysis. A precipitate from the salt **19a-g** was formed (Scheme 6), filtered, washed

with a little of ethanol, dried and recrystallized from the mentioned solvent.

2.2.4.1. *2-Amino-5-(4-aminophenyl)-4-phenylthiazol-3-ium bromide dihydrate* (**19a**)

Colorless crystals (ethanol); yield 426 mg (88%); Mp. 215-217°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.43-6.52 (br, s, 2H, NH_2), 6.68-6.74 (br, s, 2H, thiazole-NH_2), 7.05-7.10 (m, 2H, Ar-H), 7.18-7.32 (m, 4H, Ar-H), 7.47-7.52 (m, 3H, Ar-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 115.09, 122.37, 128.12, 128.79, 130.61 (Ar-CH), 123.24, 127.24 (Ar-C), 135.37 (thiazole-C4), 144.33 (Ar-C-NH_2), 149.84 (thiazole-C5), 168.51 (thiazole-C2) ppm; IR (KBr): ν = 3325-3343 (NH_2`s), 1607 (C=N), 1592 cm^{-1} (Ar-C=C) ppm; MS (70 eV): m/z (%) = 387/385 (M^+, 15), 365 (M^+ - HBr, 23), 267 (M^+ - (HBr + H_2O), 100), 190 (16), 176 (33), 92 (19), 81 (38); Anal. Calcd for $C_{15}H_{18}BrN_3O_2S$ (384.29): C 46.88, H 4.72, Br 20.79, N 10.93, S 8.34; Found: C 46.97, H 4.83, Br 20.66, N 11.09, S 8.19.

2.2.4.2. *2-Amino-5-(4-amino-2-chlorophenyl)-4-phenylthiazol-3-ium bromide dehydrate* (**19b**)

Colorless crystals (ethanol); yield 334 mg (80%); Mp. 210-212 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.53-6.58 (br, s, 2H, NH_2), 6.72-6.76 (br, s, 2H, thiazole-NH_2), 7.05-7.10 (m, 2H, Ar-H), 7.23-7.49 (m, 6H, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 113.49, 116.02, 125.60, 127.73, 128.61, 129.08 (Ar-CH), 129.41, 131.43, 133.65 (Ar-C), 134.26 (thiazole-C4), 143.89 (Ar-C-NH_2), 150.35 (thiazole-C5), 168.08 (thiazole-C2) ppm; IR (KBr): ν = 3298-3275 (NH_2`s), 1610 (C=N), 1588 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 423/419 (M^+, 8), 337 (M^+ - HBr, 25), 302 (M^+ - (HBr + H_2O), 100), 225 (10), 127(9), 81 (31); Anal. Calcd for $C_{15}H_{17}BrClN_3O_2S$ (418.74): C 43.02, H 4.09, Br 19.08, Cl 8.47, N 10.03, S 7.66; Found: C 42.89, H 4.16, Br 18.96, Cl 8.58, N 9.91, S 7.59.

2.2.4.3. *2-Amino-5-(2-methyl-5-sulfamoylphenyl)-4-phenylthiazol-3-ium bromide dihydrate* (**19c)**

Colorless crystals (ethanol); yield 379 mg (82%); Mp. 232-234°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.23 (s, 3H, CH_3), 6.72-6.80 (br, s, 2H, thiazole-NH_2), 7.09-7.15 (m, 2H, Ar-H), 7.22-7.30 (m, 4H, Ar-H), 7.42-7.50 (br, s, 2H, SO_2NH_2),[29,30] 7.65-7.75 (m, 2H, Ar-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.27 (CH_3); 123.36, 125.50, 127.47, 128.61, 129.55, 129.94 (Ar-CH), 133.13, 133.37 (Ar-C), 134.08 (thiazole-C4), 136.44 (Ar-C-SO_2NH_2), 144.82 (Ar-C-CH_3); 150.62 (thiazole-C5), 169.20 (thiazole-C2) ppm; IR (KBr, cm^{-1}): ν = 3332-3312 (NH_2`s), 1625 (C=N), 1585 (Ar-C=C); MS (70 eV): m/z (%) = 465/463 (M^+, 7), 346 (M^+ - (HBr + H_2O), 100), 175 (24), 171 (21), 157 (26), 91 (42), 81 (17); Anal. Calcd for $C_{16}H_{20}BrN_3O_4S_2$ (462.38): C 41.56, H 4.36, Br 17.28, N 9.09, S 13.87; Found: C 41.38, H 4.45, Br 17.19, N 8.88, S 14.04.

2.2.4.4. *2-Amino-5-(2-amino-3,5-dinitrophenyl)-4-phenylthiazol-3-ium bromide dihydrate* (**19d**)

Brown crystals (ethanol); yield 403 mg (85%); Mp. 245-247°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.68-6.76 (br, s, 2H, thiazole-NH_2), 7.10-7.15 (br, s, 2H, NH_2), 7.40-7.65 (m, 3H, Ar-H), 8.10-8.18 (m, 2H, Ar-H), 8.60-8.70 (d, 1H, Ar-H), 8.96-9.10 (d, 1H, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 120.43, 121.27, 126.04, 128.76, 129.06 (Ar-CH); 123.37, 127.84 (Ar-C), 135.74 (thiazole-C4), 145.79 (Ar-C-NH_2), 146.68, 148.63 (Ar-C-NO_2), 150.62 (thiazole-C5), 169.59 (thiazole-C2) ppm; IR (KBr): ν = 3332-3312 (NH_2`s), 1625 (C=N), 1585 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 477/475 (M^+, 12), 396 (M^+ - HBr, 26), 358 (M^+ - (HBr + H_2O), 100), 183 (24), 176 (22), 138 (69), 81 (17); Anal. Calcd for $C_{15}H_{16}BrN_5O_6S$ (474.29): C 37.99, H 3.40, Br 16.85, N 14.77, S 6.76; Found: C

38.12, H 3.49, Br 16.73, N 14.64, S 6.94.

2.2.4.5. *2-Amino-5-(4-aminophenyl)-4-(4-bromophenyl)-thiazol-3-ium bromide dihydrate* (**19e**)

Colorless crystals (ethanol); yield 426 mg (88%); Mp. 228-230°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.44-6.56 (br, s, 2H, NH_2), 6.66-6.74 (br, s, 2H, thiazole-NH_2), 7.12-7.17 (m, 2H, Ar-H), 7.20-7.30 (m, 4H, Ar-H), 7.38-7.46 (m, 2H, Ar-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 116.32, 123.44, 128.35, 132.22 (Ar-CH), 123.13, 124.57, 133.78 (Ar-C), 136.33 (thiazole-C4), 143.83 (Ar-C-NH_2), 149.73 (thiazole-C5), 168.30 (thiazole-C2) ppm; IR (KBr): ν = 3310-3243 (NH_2`s), 1623 (C=N), 1586 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 467/463 (M^+, 18), 381 (M^+ - HBr, 23), 346 (M^+ - (HBr + H_2O), 100), 225 (20), 191 (46), 92 (57), 81 (31); Anal. Calcd for $C_{15}H_{17}Br_2N_3O_2S$ (463.19): C 38.90, H 3.70, Br 34.50, N 9.07, S 6.92; Found: C 39.04, H 3.61, Br 34.66, N 8.89, S 7.09.

2.2.4.6. *2-Amino-4-(4-bromophenyl)-5-(2-methyl-5-sulfamoylphenyl) thiazol-3-ium bromide dihydrate* (**19f**)

Colorless crystals (ethanol); yield 433 mg (80%); Mp. 241-243°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.27 (s, 3H, CH_3), 6.60-6.72 (br, s, 2H, thiazole-NH_2), 7.00-7.15 (m, 2H, Ar-H), 7.32-7.38 (m, 3H, Ar-H), 7.45-7.52 (br, s, 2H, SO_2-NH_2),[30,31] 7.72-7.78 (m, 2H, Ar-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.72 (CH_3), 127.35, 128.52, 129.90, 130.09, 131.72 (Ar-CH), 124.63, 128.26, 135.50 (Ar-C), 134.82 (thiazole-C4), 136.28 (Ar-C-SO_2NH_2), 145.30 (Ar-C-CH_3), 150.43 (thiazole-C5), 170.18 (thiazole-C2) ppm; IR (KBr): ν = 3332-3312 (NH_2`s), 1625 (C=N), 1585 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 545/541 (M^+, 39), 460 (M^+ - HBr, 20), 426 (M^+ - (HBr + H_2O), 100), 255 (34), 171 (68), 157 (36), 91 (92); Anal. Calcd for $C_{16}H_{19}Br_2N_3O_4S_2$ (541.28): C 35.50, H 3.54, Br 29.52,

N 7.76, S 11.85; Found: C 35.39, H 3.62, Br 29.43, N 7.64, S 11.69.

2.2.4.7. *2-Amino-5-(2-amino-3,5-dinitrophenyl)-4-(4-bromophenyl)thiazol-3-ium bromide dihydrate* (**19g**)

Brown crystals (ethanol); yield 459 mg (83%); Mp. 256-258°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.78-6.83 (br, s, 2H, thiazole-NH_2), 7.00-7.08 (br, s, 2H, NH_2), 7.28-7.40 (m, 4H, Ar-H), 8.23-8.65 (d, 1H, Ar-H), 8.82-8.98 (d, 1H, Ar-H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 122.70, 129.47, 130.47, 131.59 (Ar-CH), 123.21, 125.81 (Ar-C), 135.75 (thiazole-C4), 145.60 (Ar-C-NH_2), 147.67, 148.70 (Ar-C-NO_2), 150.00 (thiazole-C5), 168.00 (thiazole-C2); IR (KBr): ν = 3332-3312 (NH2`s), 1625 (C=N), 1585 cm^{-1} (Ar-C=C); MS (70 eV): m/z (%) = 557/553 (M^+, 32), 472 (M^+ - HBr, 34), 436 (M^+ - (HBr + H_2O), 100), 183 (51), 176 (22), 168 (26); Anal. Calcd for $C_{15}H_{15}Br_2N_5O_6S$ (553.18): C 32.57, H 2.73, Br 28.89, N 12.66, S 5.80; Found: C 32.71, H 2.64, Br 29.03, N 12.76, S 5.69.

2.3. Single crystal X-ray structure determination of 3a, 16h and 19b

The single crystal X-ray diffraction studies for **3a**, **16h** and **19b** were carried out on a Bruker D8 Venture diffractometer with Photon 100 detector at 123 K using CuKα radiation (λ = 1.54178 Å) for **3a** and **19b** or MoKα radiation (λ = 0.71073 Å) for **16h**. Direct methods (SHELXS-97)[31] were used for structure solution and refinement was carried out using SHELXS-2013/2014[32] (full-matrix least squares on F^2). Hydrogen atoms were localized by difference Fourier synthesis map and refined using a riding model [H(N, O) free]. Semi-empirical absorption corrections were applied. For **16h** and **19b** extinction correction was applied. The absolute structure of **19b** is determined by refinement of Parsons Flack parameter.[33]

2.3.1. **Compound 3a**: $C_{15}H_{11}N_3S$, Mr = 265.33 g mol^{-1}, orange blocks, crystal size = 0.22 x 0.10 x 0.05 mm, monoclinic space group $P2_1/c$ (no. 14), a = 21.7180(5) Å, b = 5.1347(1) Å, c = 11.3211(3) Å, β = 92.280 (1)°, V = 1261.48(5) $Å^3$, Z = 4, D_{calcd} = 1.397 Mg m^{-3}, F(000) = 552, μ = 2.170 mm^{-1}, T =123 K, 14789 measured reflections ($2\theta_{max}$ = 144.0°), 2473 independent reflections [R_{int} = 0.027], 172 parameters, R_1[for 2305 with I>2σ(I)] = 0.028, wR_2 (for all data) = 0.073, S = 1.04, largest diff. peak and hole = 0.327 e $Å^{-3}$ /-0.184 e $Å^{-3}$.

2.3.2. **Compound 16h:** $C_{23}H_{21}N_3O_2S_2$, Mr = 435.55 g mol^{-1}, violet blocks, crystal size = 0.45 x 0.35 x 0.20 mm, monoclinic space group $P2_1/c$ (no. 14), a = 9.3897(5) Å, b = 11.0215(5) Å, c = 20.0638(9) Å, β = 101.146 (2)°, V = 2037.21(17) $Å^3$, Z = 4, D_{calcd} = 1.420 Mg m^{-3}, F(000) = 912, μ = 0.288 mm^{-1}, T = 123 K, 59879 measured reflections ($2\theta_{max}$ = 55.0°), 4684 independent reflections [R_{int} = 0.033], 276 parameters, 1 restraint, R_1 [for 4231 with I>2σ(I)] = 0.032, wR_2 [for all data] = 0.079, S = 1.07, largest diff. peak and hole = 0.499 e $Å^{-3}$ /-0.431 e $Å^{-3}$.

2.3.3. **Compound 19b**: $C_{15}H_{13}ClN_3S{\cdot}Br{\cdot}2(H_2O)$, Mr = 418.74 g mol^{-1}, colorless blocks, crystal size = 0.25 x 0.20 x 0.10 mm, orthorhombic space group $P2_12_12_1$ (no. 19), a = 7.2127(2) Å, b = 10.7593(3) Å, c = 21.8730(5) Å, V = 1697.42(8) $Å^3$, Z = 4, D_{calcd} = 1.639 Mg m^{-3}, F(000) = 848, μ = 6.008 mm^{-1}, T = 123 K, 17133 measured reflections ($2\theta_{max}$ = 144.2°), 3324 independent reflections [R_{int} = 0.027], 236 parameters, R_1[for 3291with I>2σ(I)], wR_2[for all data] = 0.045, S = 1.08, largest diff. peak and hole = 0.382 e $Å^{-3}$ /-0.252 e $Å^{-3}$.

3. Results and Discussion

In our present studies arylthiosemicarbazides **1a-d** and *ω*-bromoacetophenones **2a,b** were selected as reagents under Eschenmoser-contraction method [34,35] (Scheme 1 and 2) to receive a new C-C bond and synthesize aminophenylpyrazoles **14** (Scheme 3) instead, 4-aryl (2-alkyldiazenylthiazole) **3a-e** were observed (Scheme 1).

(Scheme 1)

The mechanism for the formation of **3a-e** is illustrated in scheme 2. Upon adding different amounts of triphenylphosphine as a thiophile and triethylamine as the base, the reaction does not produce a significant change in the products **3a-e**, and the yields were roughly the same. Also, it was found that Et_3N plays an important role on the reaction efficiency and products **3a-e**, even in the absence of thiophile Ph_3P (Scheme 2 and Scheme 3).

(Scheme 2)

(Scheme 3)

The present study will discuss the behavior of *ω*-bromoacetophenones **2a,b** towards 1,4-disubstituted thiosemicarbazides **15a-e** and will be compared to the behavior of the same compounds towards **1a-d**. Hydrazinothiazoles **16a-i** was formed during the reaction of **2a,b** with **15a-e** (Scheme 4).

(Scheme 4)

The mechanism for the formation of the compounds **16a-i** is shown in scheme 5.

(Scheme 5)

In the present study, condensation of *ω*-bromoacetophenones **2a,b** with substituted thiosemicarbazides **1a-d** afforded 2-amino-5-(4-aminophenyl)-4-phenyl-thiazol-3-ium bromide dihydrate **19a-g** *via* [5.5] sigmatropic rearrangement (Scheme 6).

(Scheme 6)

The mechanism for the formation of **19a-g** is described in Scheme 7, whereas, the mechanism for the formation of **19c,f** is described in Scheme 8.

(Scheme 7)

(Scheme 8)

All the synthesized compounds have been characterized by means of both analytical and spectroscopic methods, as follows.

3.1. Infrared spectroscopy of 3a-e, 16a-I and 19a-g.

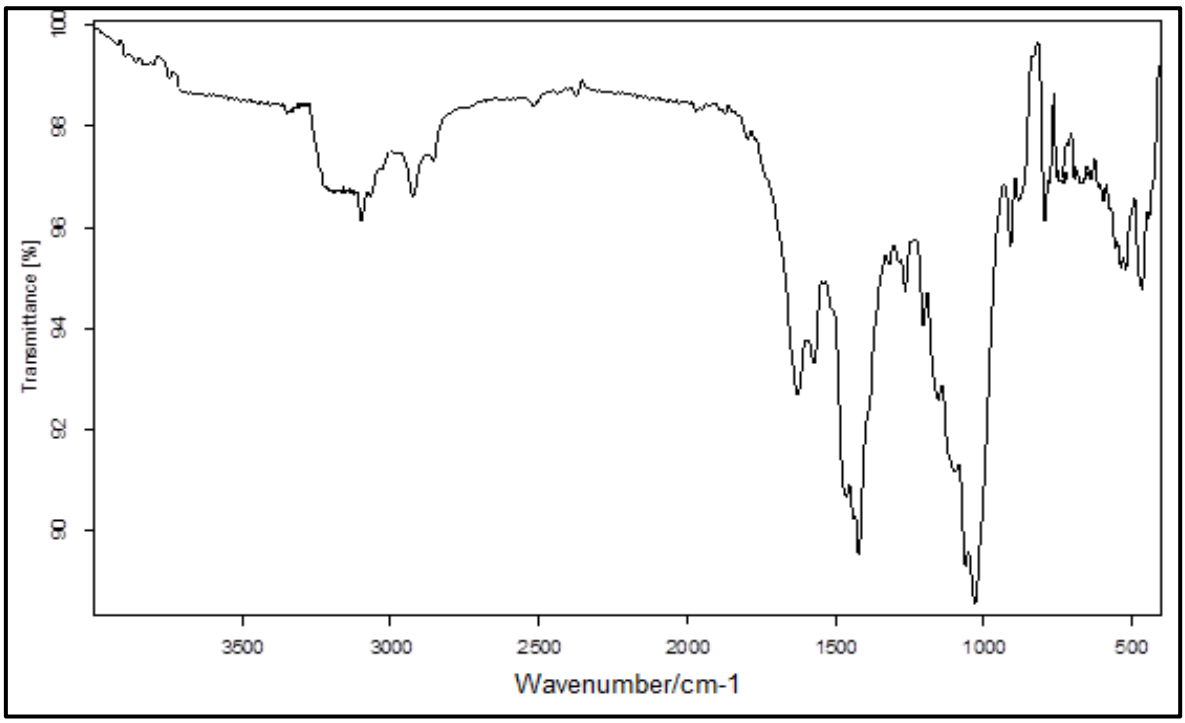


Figure 1

All compounds **3a-e** exhibit orange colors: The IR spectrum of **3a** (Fig. 1 as an example of diazenylthiazoles) showed characteristic bands of aromatic groups were observed at 1585 cm^{-1} corresponding to Ar-C=C stretching vibration of benzene and thiazole rings. The

C=N stretching band at 1600 cm^{-1}. The IR spectrum of **3a** confirm the presence of azo group (N=N) at 1560 and 1444 cm^{-1}.

In the hydrazothiazoles **16a-i** the IR peaks showed at 3263-3193 cm^{-1} broad bands of hydrazo-NH group, C=N at 1626-1611 cm^{-1}.

The IR spectrum of **19b** showed bands at 3298-3275 cm^{-1} due to NH_2 groups and bands at 1610 (C=N), 1588 cm^{-1} (Ar-C=C).

3.2. ^{1}H and ^{13}C NMR spectra of 3a-e, 16a-i and 19a-g.

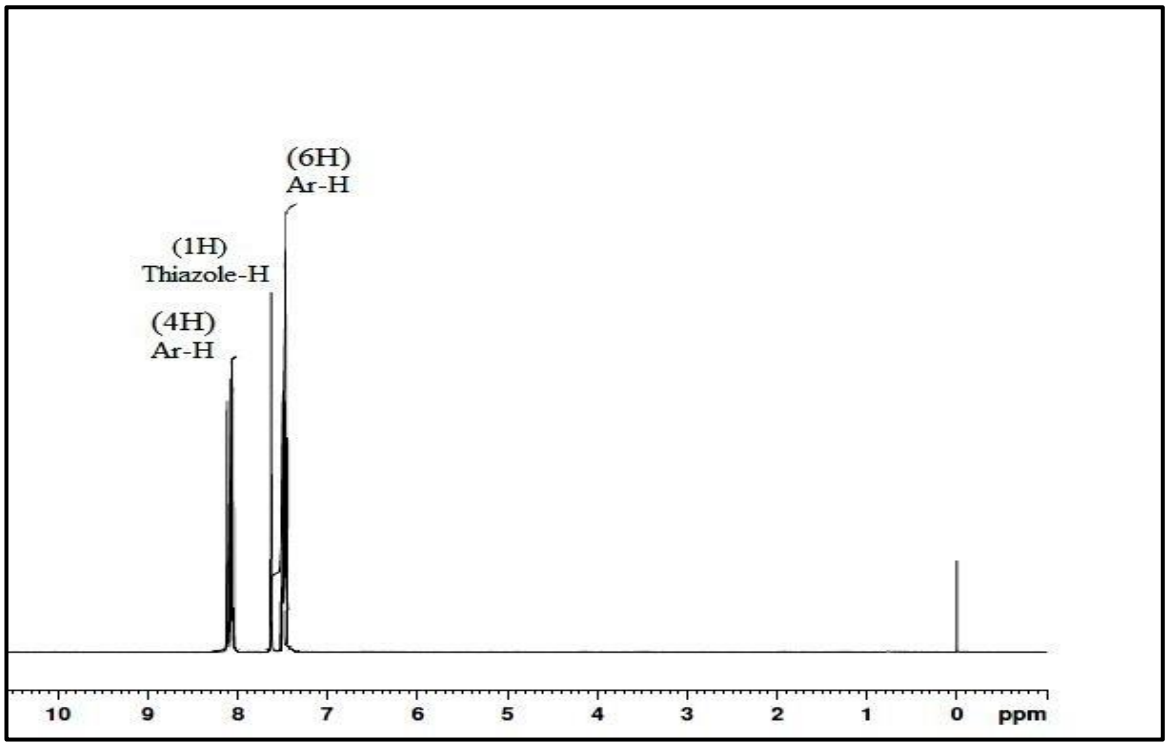


Figure 2

The NMR spectra ($^{1}H$and ^{13}C) of compound **3a** were recorded using $CDCl_3$ as solvent and TMS as an internal standard (Figure 2) which showed three multiplets corresponding to ten protons at δ = 7.40-7.58 and 8.03-8.88 ppm due to aryl protons.

The ^{13}C NMR of **3a** (Figure 3) contained three signals at δ = 168.46 (thiazole-C2), 155.85

(thiazole-C4) and 115.88 ppm (thiazole-CH), with the absence of C=S group. The downfield shift of thiazole-C2,4 is due to the high conjugation of thiazole ring with respect to azo- and aryl groups. From the spectral data, it can be concluded that *[1]NH, [3]NH,[4]NH* and thioxo group are the nucleophilic sites to form the products **3**a-e.

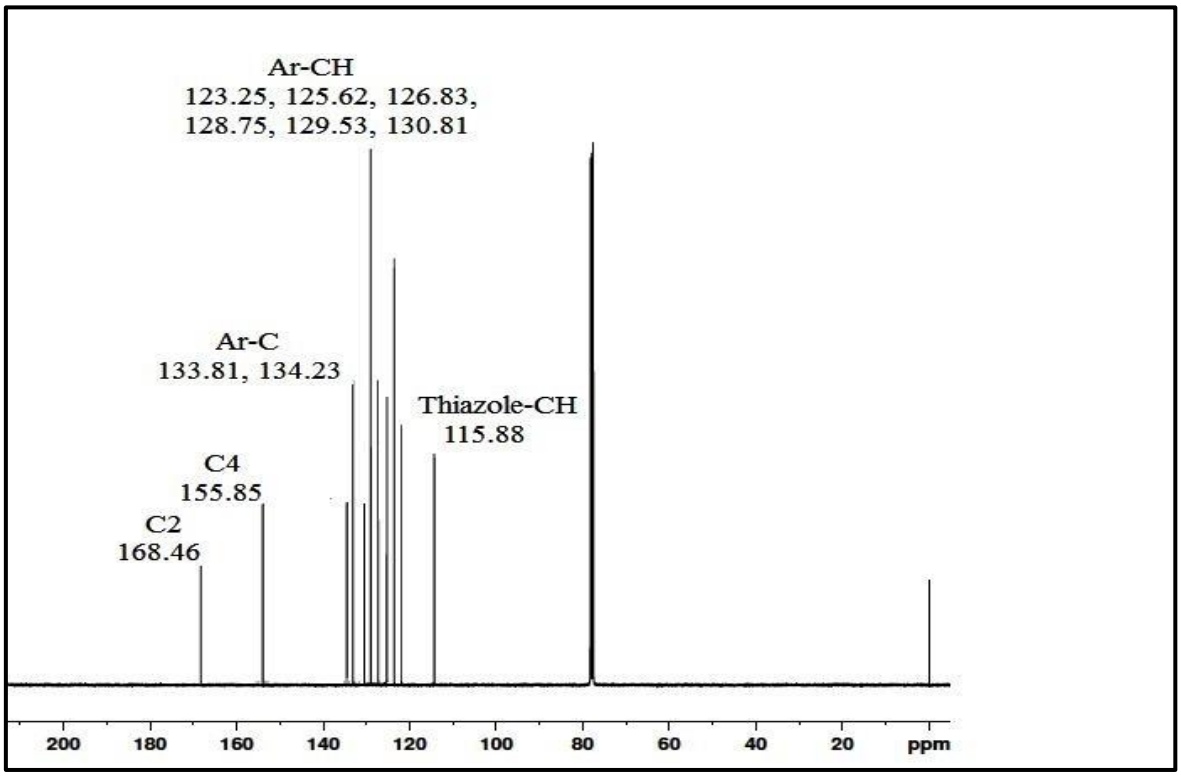


Figure 3

The ^{1}H NMR spectrum of **16b** showed one broad signal at δ = 10.53 ppm due to hydrazo-NH which was confirmed further by H_2O exchange experiment. Also, the aromatic protons observed in the expected region 7.48-7.52, 8.28-8.38 and 8.87-8.89 ppm. One singlet at δ = 6.91 because of thiazole-CH. Signals at 1.06-1.09, 1.76-1.78 and 3.72-3.74 due to cyclohexyl-CH_2 and CH.

In the ^{13}C NMR spectra of **16b** signals at δ = 164.40, 144.90 and 115.45 ppm were assigned to thiazole-C2, thiazole-C4 and thiazole-CH, respectively.

On the other hand, in the ^{1}H NMR spectrum of **19b**, two broad signals at 6.53-6.58 and 6.72-6.76 ppm are due to NH_2 attached to phenyl ring and the other for NH_2 attached to thiazole ring. Eight protons were observed at δ = 7.05-7.10 and 7.23-7.49 ppm because of aromatic protons.

The ^{13}C NMR spectra of **19b** showed downfield shifted signals at 168.08 (thiazole-C2) and 150.35 (thiazole-C5). Signals at 129.41, 131.43 and 133.65 (Ar-C), 143.89 (Ar-*C*-NH_2), 134.26 (thiazole-C4), in addition to the signals of Ar- CH.

3.3. Mass spectrometry of 3a-e, 16a-I and 19a-g.

Elemental analyses and mass spectra of compounds **3a-e** clearly showed that the azothiazoles **3a-e** were formed during the addition equimolar amounts of thiosemicarbazides **1a-d** and acetophenones **2a,b** *via* elimination (HBr + H_2O).

Form the mass spectrometry of **16b**, the molecular ion peak at *m/z* = 439 (16%) with abstraction HBr and H_2O from the reactants.

The molecular ion peak of **19b** as an example of thiazolium bromide dihydrates at *m/z* = 423/419 (M^+, 9%) with molecular formula $C_{15}H_{17}BrClN_3O_2S$ and fragmentation patterns at 337 (M^+ - HBr, 25), 302 (M^+ - (HBr + H_2O), 100).

3.4. X-ray structure determination of 3a, 16h and 19b.

Suitable single crystals for X-ray analysis of compound **3a** were obtained by crystallization from acetonitrile. X-ray crystallography (Fig. 6, Tables S1-S6 in the supporting information) provided unambiguous proof that (*E*)-4-phenyl-2-(phenyldiazenyl)thiazole **3a** was formed exclusively during the reaction of **1a** with **2a**. The

X-ray analysis of **3a** confirms a *transiod* geometry with respect to the N7-N8 double bond. Sum of angles around C2, C4 and C5 are 360° revealing the planarity of the thiazole ring (Figure 4).

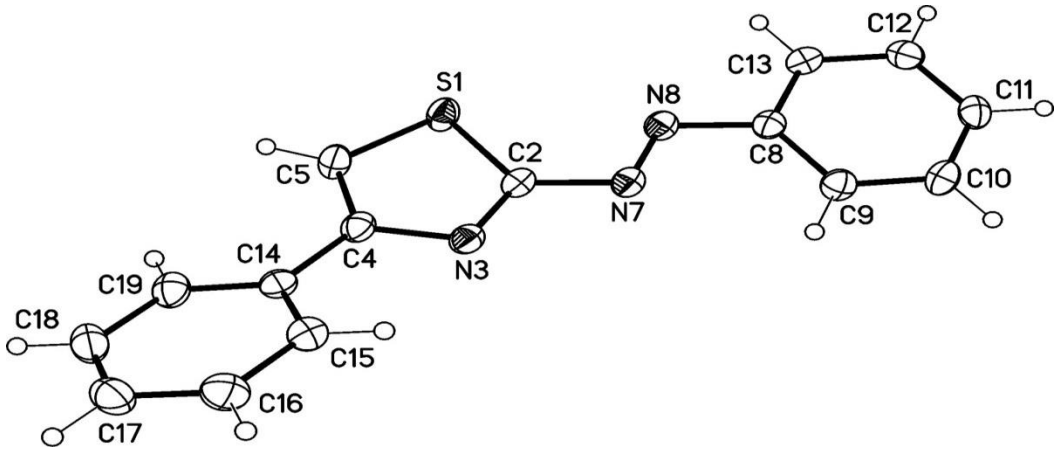


Figure 4

For the hydrazonothiazoles **16a-i**, the overall structure including the *Z*-configuration was also confirmed by X-ray crystallography of one derivative **16h** (Figure 5, Tables S7-S13).

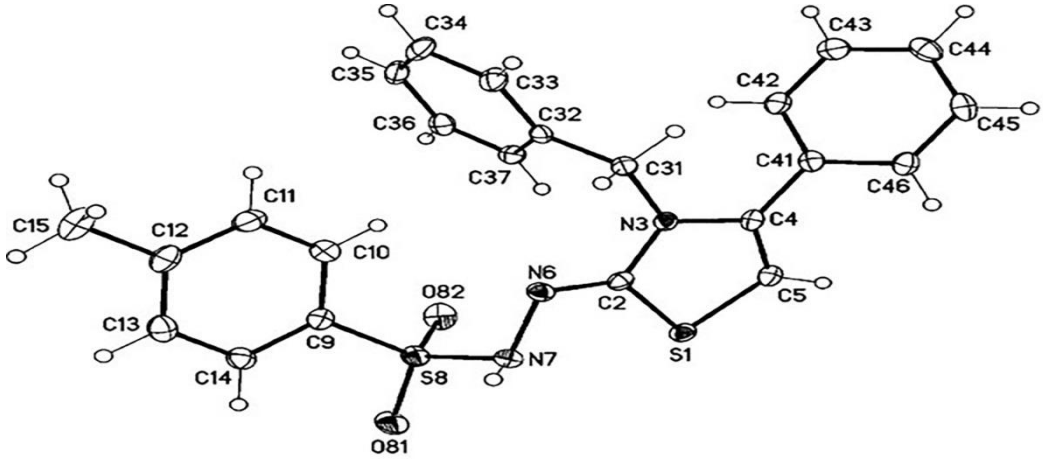


Figure 5

The molecular structure of 5-(4-amino-2-chlorophenyl)-4-phenylthiazol-2(3*H*)-iminium bromide dihydrate **19b** was established by single crystal X-ray analysis (Figure 6, Tables S14-S20).

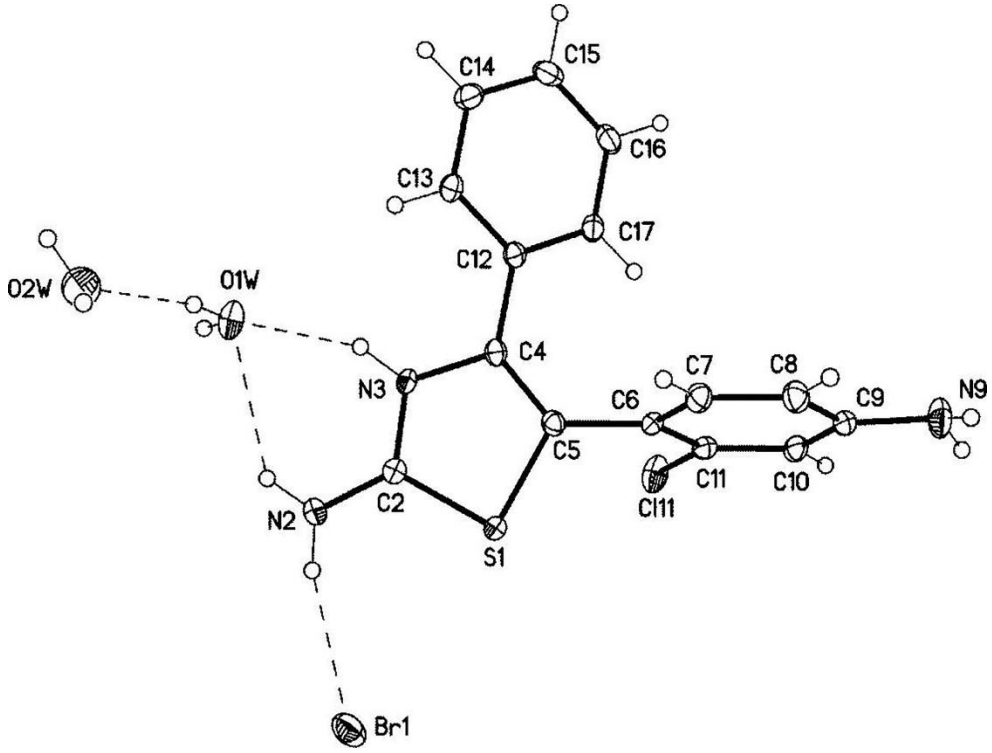


Figure 6

The dihedral angle between S1/N3-C2-C5 thiazole and C6-C11 in phenyl rings is 75.0°. In the crystal, the lattice water and bromide ion associated through hydrogen bonded with thiazole-NH_2.

4. Conclusions

Novel diazenylthiazoles, hydrazothiazoles and substituted thiazolium bromide dihydrates have been synthesized from the nucleophilic addition followed by condensation between mono or disubstituted thiosemicarbazides and *ω*-bromoacetophenones.

Appendix A. Supplementary data

Crystallographic data (excluding structure factors) for the structure reported in this work have been deposited with Cambridge Crystallographic Data Center as supplementary

publication no CCDC 1583184 (**3a**), 1589939 (**16h**) and 1583185 (**19b**) contain the supplementary crystallographic data for this paper [36]. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif

Acknowledgement

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[36] Crystallographic data (excluding structure factors) for the structure reported in this work have been deposited with Cambridge Crystallographic Data center as supplementary publication no CCDC 1583184 (**3a**), 1589939 (**16h**) and 1583185 (**19b**). Copies of the data can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44(1223) 336 033: e-mail: deposit@ccdc.cam.ac.

Figure captions:

Figure 1: FT-IR Spectrum of compound **3a**.

Figure 2: ^{1}H NMR of (*E*)-4-Phenyl-2-(phenyldiazenyl)thiazole (**3a**) obtained in $CDCl_3$.

Figure 3: ^{13}C NMR of (*E*)-4-Phenyl-2-(phenyldiazenyl)thiazole (**3a**) obtained in $CDCl_3$.

Figure 4: The X-ray structure of compound **3a** in crystal (displacement parameters are drawn at 50% probability level).

Figure 5: The overall structure including the *Z*-configuration was also confirmed by X-ray crystallography of one derivative **16h** displacement parameters are drawn at 50% probability level).

Figure 6: The hydrogen bonds formed *via* the bromide ion as well as H_2O molecules in compound **19b** (displacement parameters are drawn at 50% probability level).

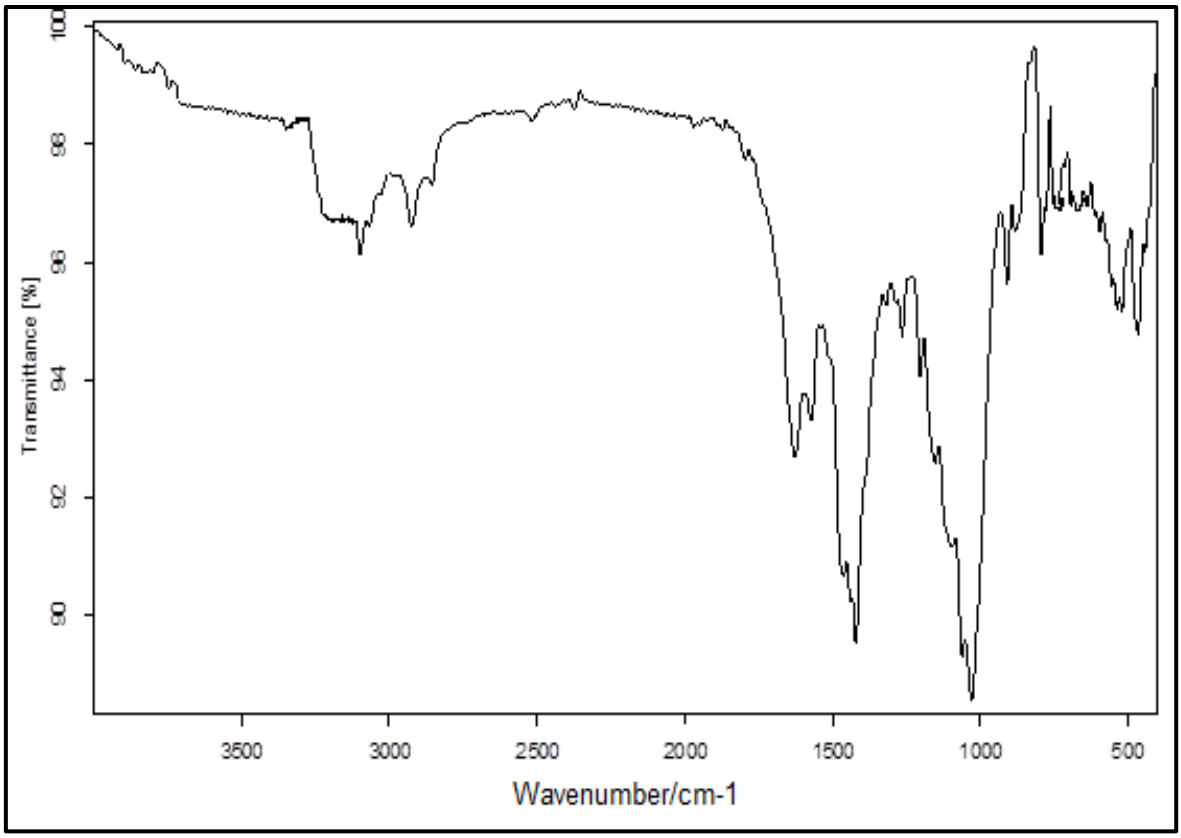


Figure 1

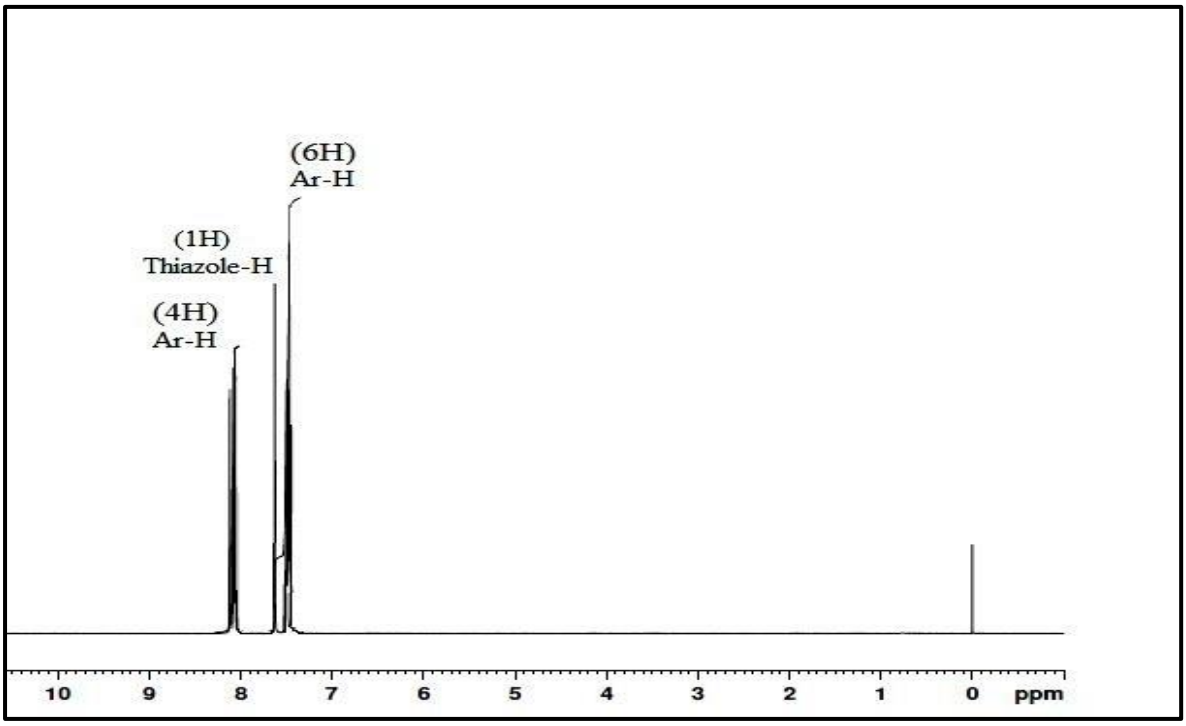


Figure 2

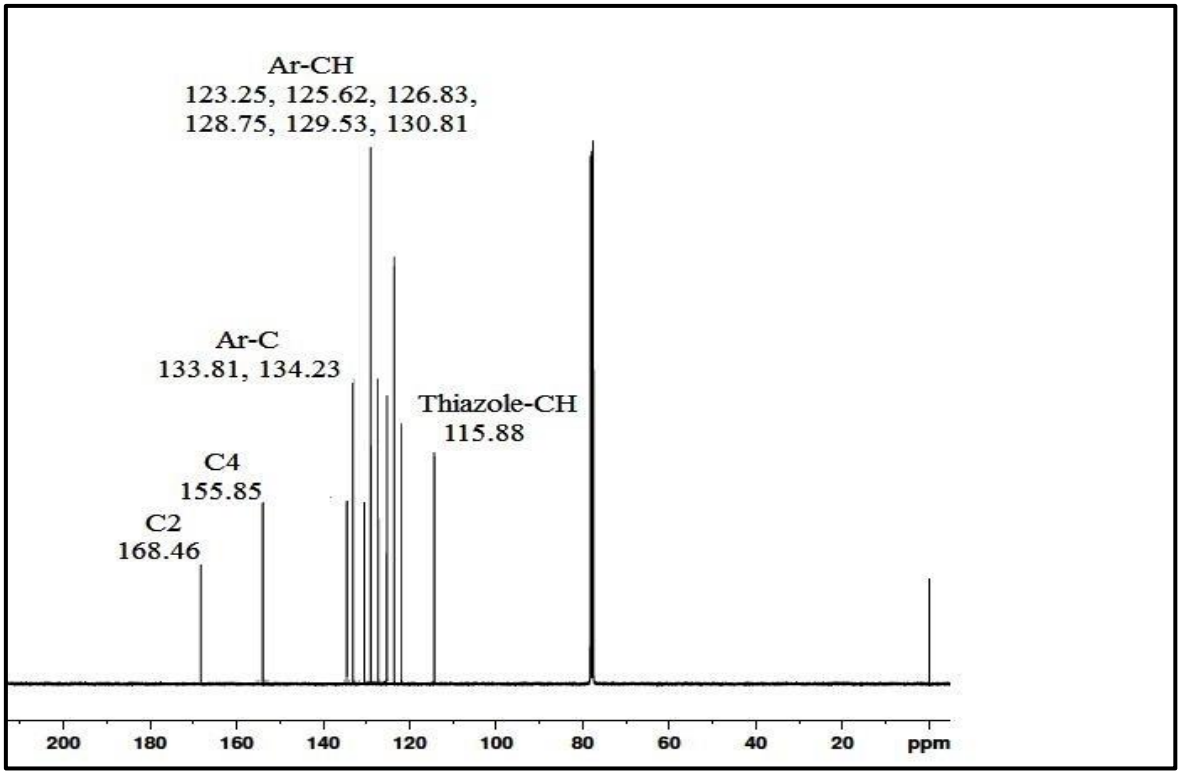


Figure 3

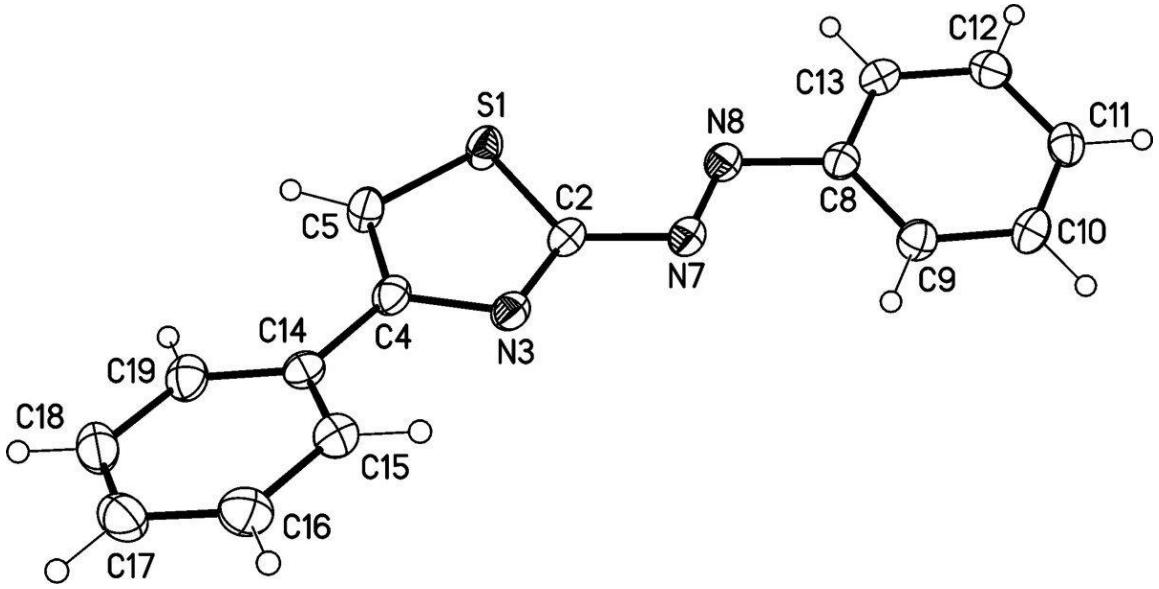


Figure 4

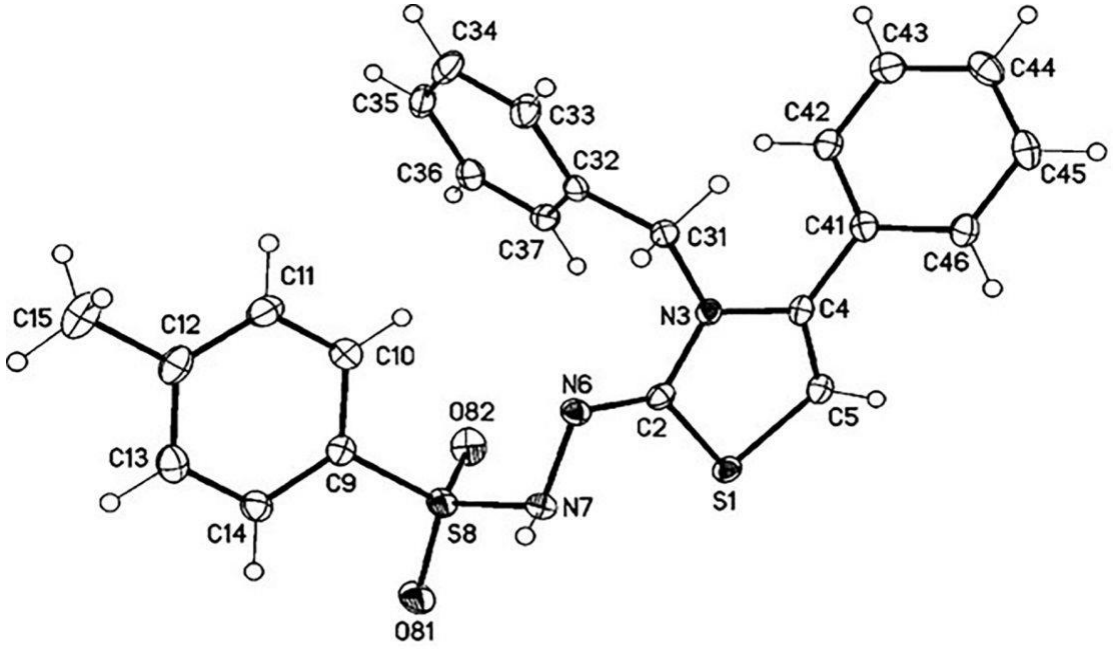


Figure 5

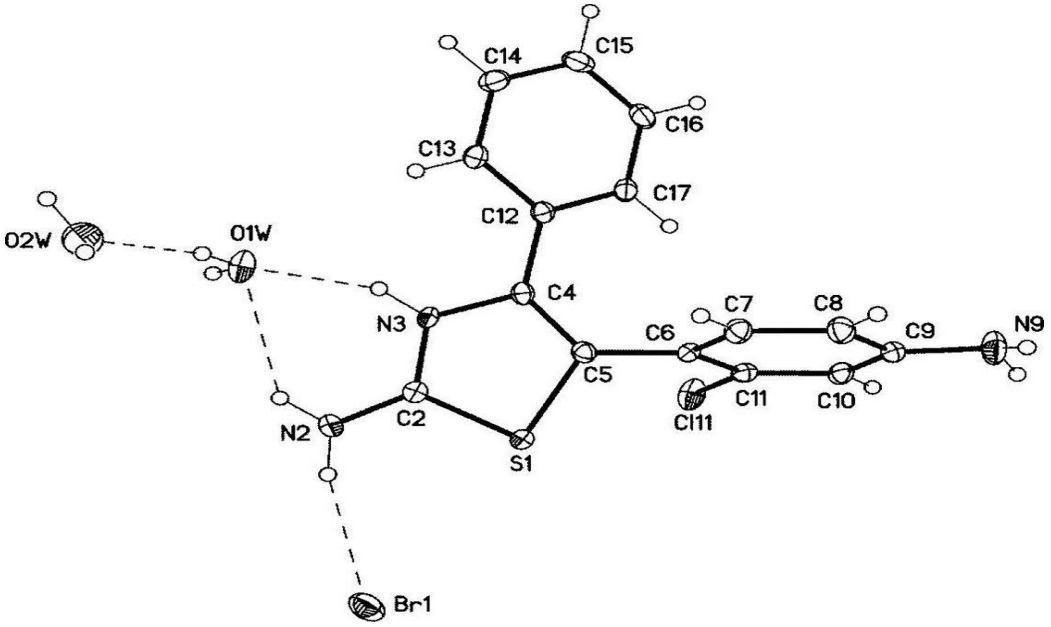
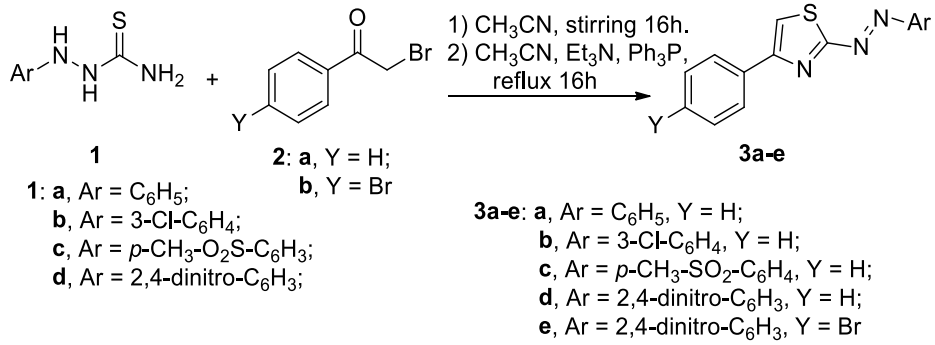
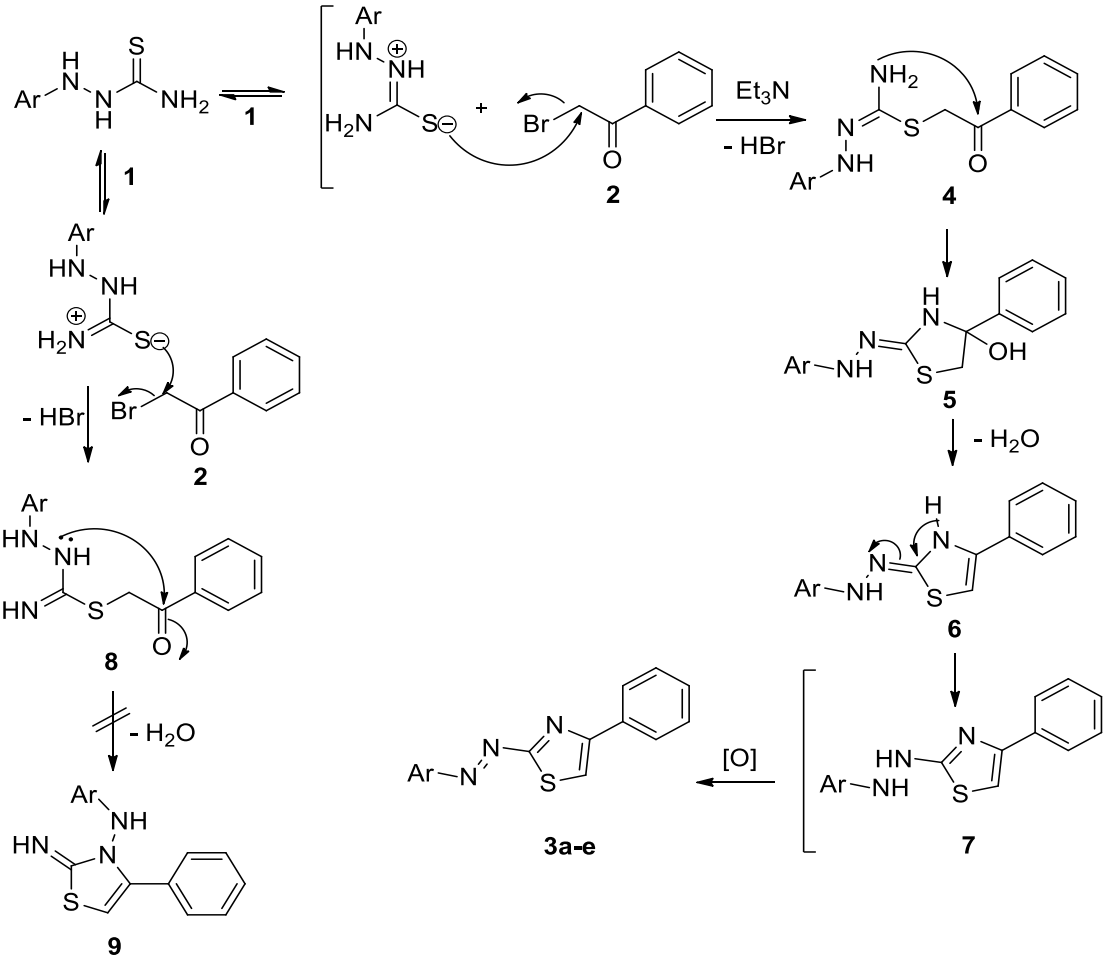


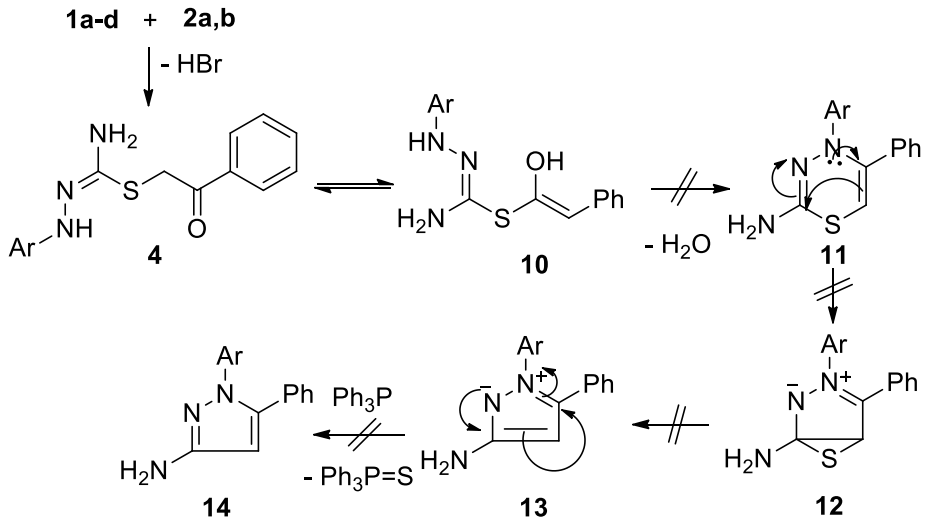
Figure 6



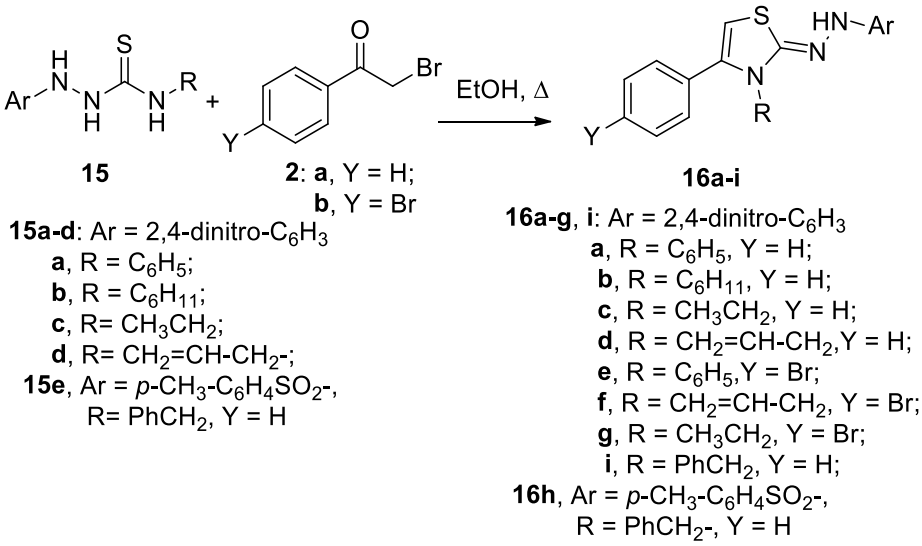
Scheme 1. Synthesis of 4-aryl-2-aryldiazenylthiazoles **3a-e**.



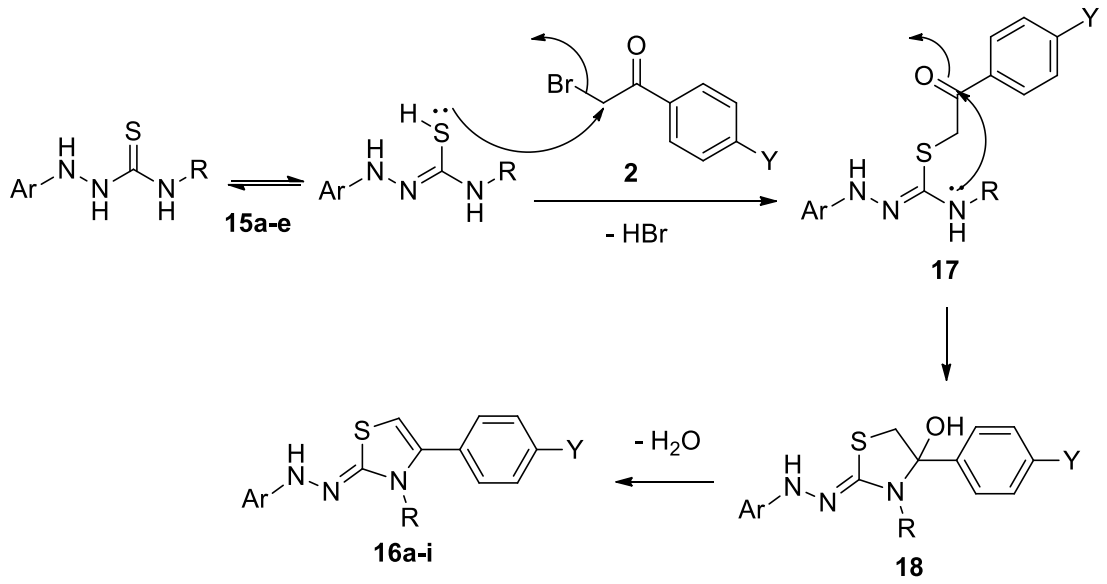
Scheme 2. The rationale for the formation of azo-thiazole derivatives **3a-e**.



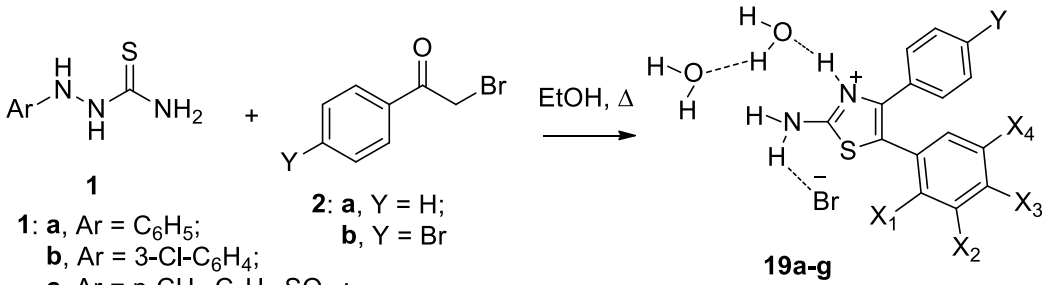
Scheme 3: The unreactivity of **1a-d** and **2a,b** towards Eschenmoser-contraction and formation of pyrazoles **14**.



Scheme 4: Synthesis of hydrazinothiazoles **16a-i**.



Scheme 5: Mechanism of the formation of hydrazinothiazoles **16a-i**.



1

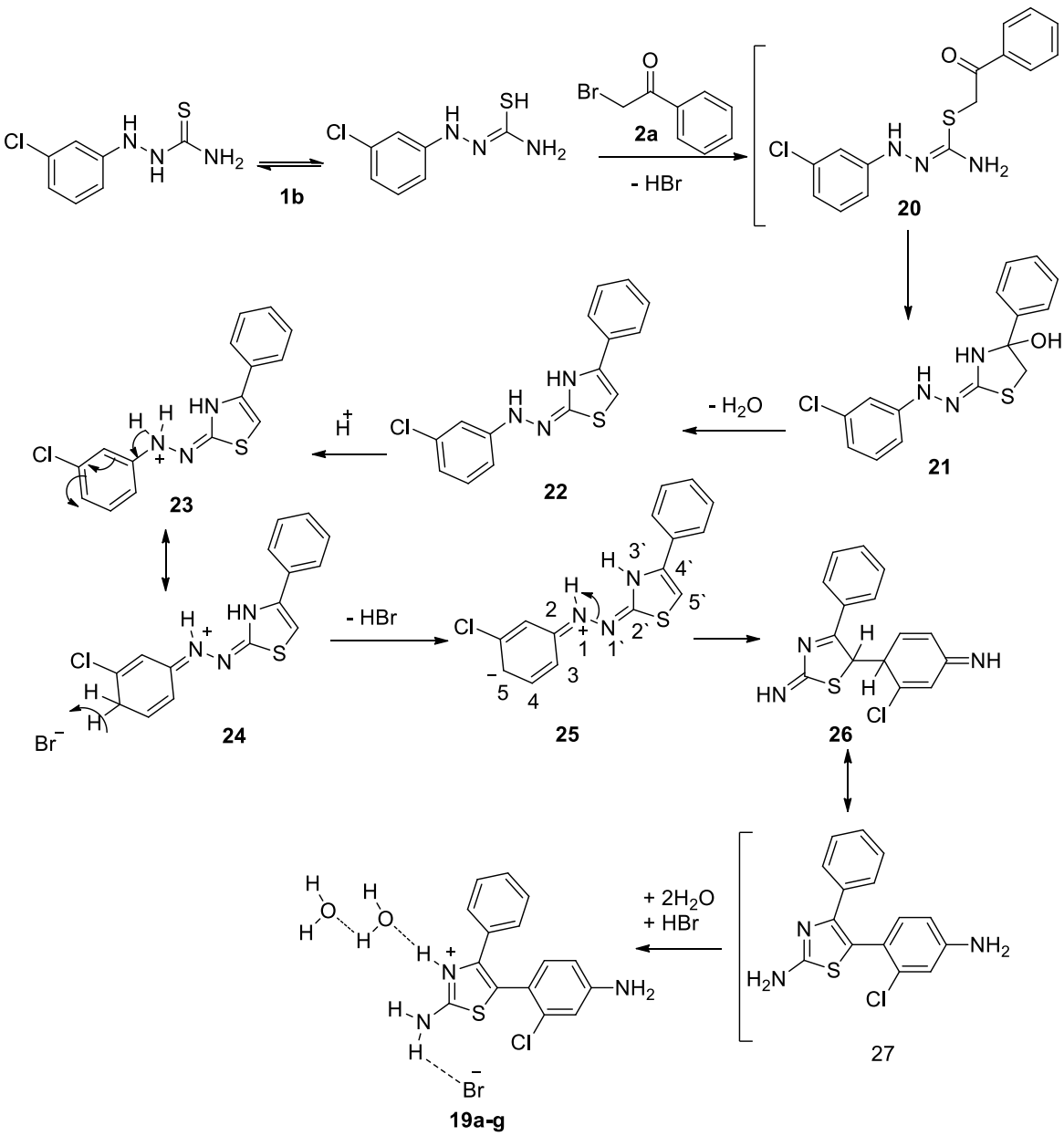
1: **a**, Ar = C_6H_5;
b, Ar = 3-Cl-C_6H_4;
c, Ar = p-CH_3-C_6H_4-SO_2-;
d, Ar = 2,4-dinitro-C_6H_3;

2: **a**, Y = H;
b, Y = Br

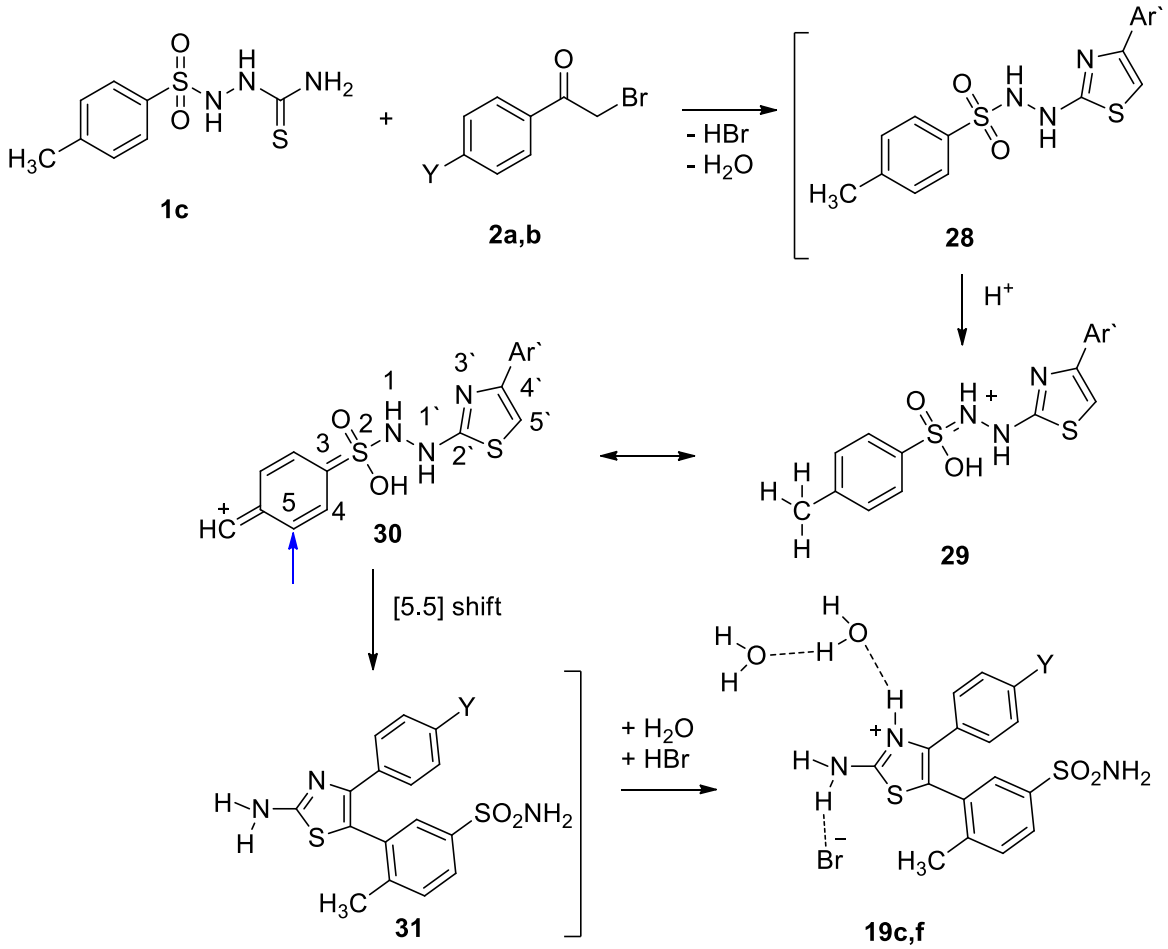
19a-g

19: **a**, Y = H, $X_1 = X_2 = X_4$ = H, $X_3 = NH_2$;
b, Y = H, X_1 = Cl, X_2 = H, $X_3 = NH_2$, X_4 = H;
c, Y = H, $X_1 = CH_3$, $X_2 = X_3$ = H, $X_4 = SO_2NH_2$;
d, Y = H, $X_1 = NH_2$, $X_2 = X_4 = NO_2$, X_3 = H;
e, Y = Br, $X_1 = X_2 = X_4$ = H, $X_3 = NH_2$;
f, Y = Br, $X_1 = CH_3$, $X_2 = X_3$ = H, $X_4 = SO_2NH_2$;
g, Y = Br, $X_1 = NH_2$, $X_2 = X_4 = NO_2$, X_3 = H;

Scheme 6: Synthesis of 2-amino-5-(4-aminophenyl)- 4-phenylthisazol-3-ium bromides dihydrates **19a-g**.



Scheme 7: Mechanism for the formation of compounds **19a-g**.



Scheme 8: Mechanistic considerations for the formation of compounds **19c,f.**

Highlights:

- Eschenmoser-coupling reaction and synthesis of diazenylthiazoles.
- Synthesis of hydrazothiazoles.
- Synthesis of thiazolium bromide dihydrate derivatives *via* [5.5] sigmatropic shift.
- Crystallographic behavior of the title compounds.
- Lattice water and bromide ion associated through hydrogen bonded with thiazole-NH_2 in thiazolium bromide.