Tetrahedron 64 (2008) 10365–10374

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Pyrolytic desulfurization ring contraction of condensed thiadiazines as a general route towards pyrazoloazines and pyrazoloazoles with a bridgehead (ring junction) nitrogen atom

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ARTICLE INFO

Article history:
Received 22 June 2008
Received in revised form 7 August 2008
Accepted 21 August 2008
Available online 27 August 2008

Keywords:
Pyrolysis
Ionic liquid
1,2,4-Triazines
[1,2,4]Triazino[3,4-*b*][1,3,4]thiadiazin-4-ones
[1,3,4]Thiadiazino[2,3-*b*]quinazolines
[1,2,4]Triazolo[3,4-*b*][1,3,4]thiadiazines
Pyrazolo[5,1-*c*][1,2,4]triazin-4-ones
Pyrazolo[4,3-*b*]quinazolin-9-ones
Pyrazolo[5,1-*b*][1,2,4]triazoles

ABSTRACT

Pyrolytic conversion of [1,2,4]triazino[3,4-*b*][1,3,4]thiadiazin-4-ones, [1,3,4]thiadiazino[2,3-*b*]quinazolin-10-ones and [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines into their corresponding pyrazolo[5,1-*c*][1,2,4]triazin-4-ones, pyrazolo[4,3-*b*]quinazolin-9-ones and pyrazolo[5,1-*b*][1,2,4]triazoles via desulfurization ring contraction is described. The starting condensed 1,3,4-thiadiazines were prepared from the corresponding readily available 4-amino-3-thioxo-1,2,4-triazin-5(4*H*)-ones, 3-amino-2,3-dihydro-2-thioxoquinazolin-4(1*H*)-one and 4-amino-3(2*H*)-thioxo-1,2,4-triazoles upon reaction with the appropriate α-haloketones in two steps, or directly in one step in ethylpyridinium tetrafluoroborate (ionic liquid, IL).
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1. Introduction

Much attention has been directed to the synthesis of pyrazoloazines and pyrazoloazoles with a bridgehead (ring junction) nitrogen atoms due to their diverse interesting applications included in numerous publications and several hundreds of patents. These important applications including biological activity, hair dyes, photographic dyes and applications in material sciences, together with the available literature methods for their synthesis have been reviewed in Comprehensive Heterocyclic Chemistry (CHCIII, CHCII).[1,2]

During our recent interest[3] in the pyrolytic behaviour of 1,2,4-triazine derivatives, we serendipitously discovered the pyrolytic desulfurization ring contraction of [1,2,4]triazino[3,4-*b*][1,3,4]thiadiazin-4-ones **5**–**7** into their corresponding pyrazolo[5,1-*c*][1,2,4]triazin-4-ones **8**–**10**. This reaction took place upon heating compounds **5**–**7** at 230 °C. The present work describes the possibility of using this conversion as a generalized synthetic approach towards pyrazoloazines and pyrazoloazoles with a bridgehead (ring junction) nitrogen atoms via ring contraction of condensed thiadiazines.

2. Results and discussion

In the present work, we report our results on the pyrolytic behaviour of [1,2,4]triazino[3,4-*b*][1,3,4]thiadiazin-4-ones **5**–**7**. Thus, we found that heating each of compounds **5**–**7** at 230 °C for 45 min led to their clean conversion to the corresponding pyrazolo[5,1-*c*][1,2,4]triazin-4-ones **8**–**10** in excellent yields in most cases (Scheme 1).

The pyrolytic conversion of **5**–**7** to **8**–**10** was proposed to proceed as outlined in Scheme 2. The 1,3-H shift and 1,5-H shift may be viewed as simple imine to enamine and vinylogous imine to enamine tautomerisms, respectively. This reaction resembles the Eschenmoser coupling reaction, which represents a versatile and efficient method to prepare vinylogous amides and urethanes by alkylating secondary and tertiary thioamides with an appropriate electrophilic component followed by elimination of sulfur.[4]

Acetylation of each of **8b** and **10c** in acetic anhydride at reflux gave the corresponding 1-acetyl derivatives **11b** and **12c**, respectively. In addition, compound **11b** was obtained in 30% yield by

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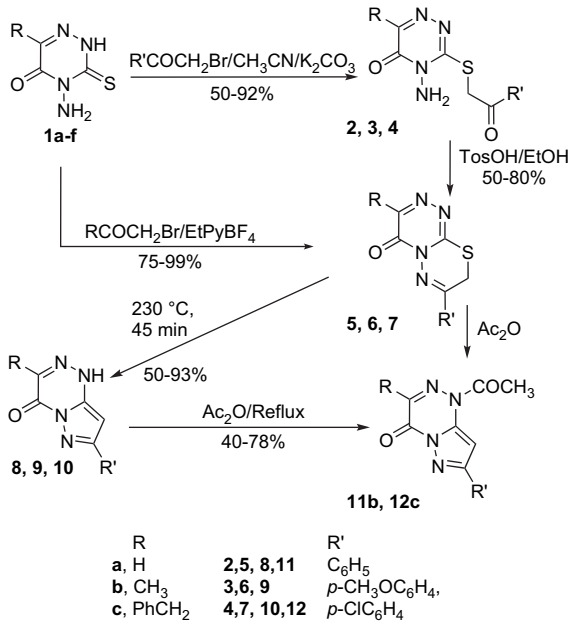
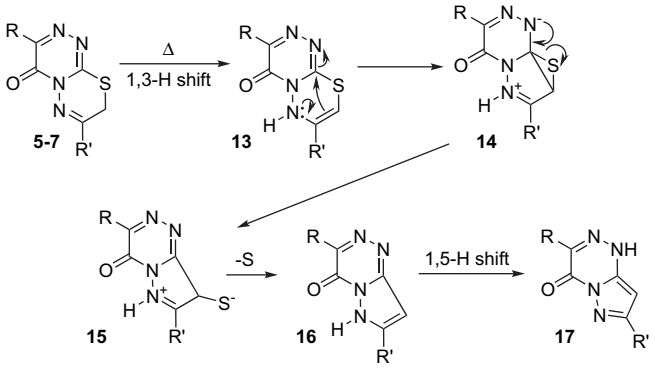
doi:10.1016/j.tet.2008.08.067



Scheme 1.

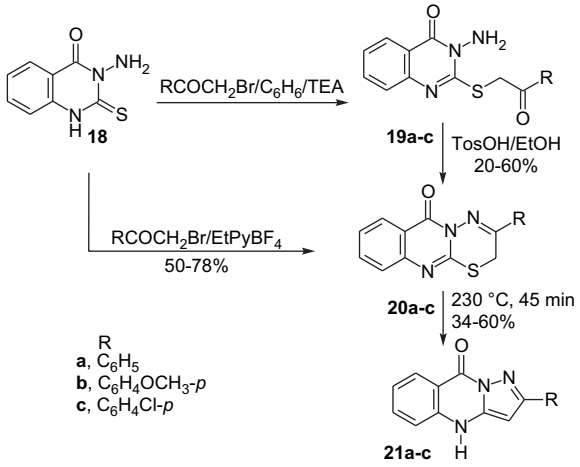


Scheme 2.

heating **5b** in acetic anhydride at reflux along with a mixture of other non-isolable products.

The starting compounds **5**–**7** were synthesized from the readily available 4-aminotriazines **1** upon alkylation with the appropriate α-haloketones in acetonitrile in the presence of K_2CO_3 to afford the corresponding 3-acylmethylsulfanyltriazines **2**–**4**. The latter were dehydrated into the corresponding [1,2,4]triazino[3,4-*b*][1,3,4]thiadiazin-4-ones **5**–**7** upon heating in ethanol in the presence of *p*-toluenesulfonic acid. The recently reported efficient synthesis of 2,4-disubstituted thiazoles using ionic liquid (IL) by the reaction of α-haloketones with thiourea derivatives[5] stimulated our interest to apply the same procedure to synthesize the thiadiazines **5**–**7**. Thus, we found that **5**–**7** could be formed directly by reacting **1** with the appropriate α-haloketones in ionic liquids. After several trials using imidazolium and pyridinium ionic liquids, ethylpyridinium tetrafluoroborate (ionic liquid, IL) was found to give the best results by stirring at 80 °C. The yield of **5**–**7** under these conditions ranges from 75 to 99% and the IL could be separated and reused efficiently.

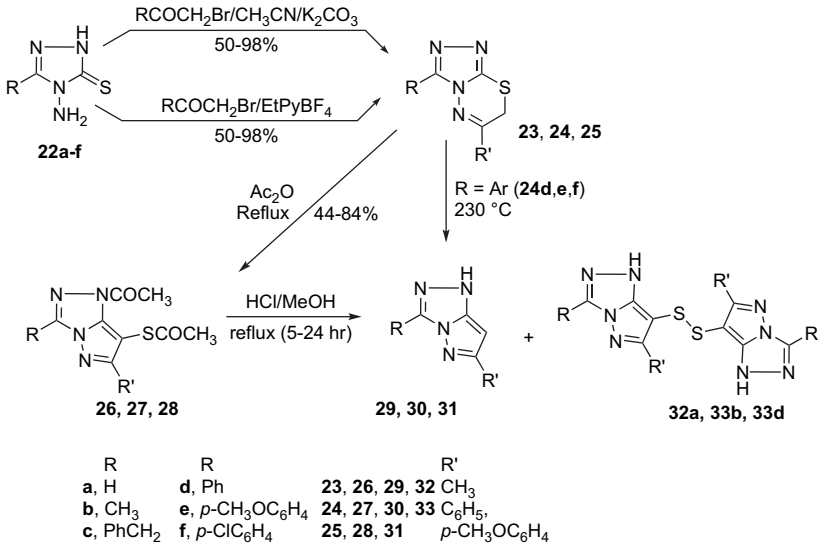
Extension of the pyrolytic synthesis of **8**–**10** (Scheme 1) to the synthesis of 4*H*-pyrazolo[5,1-*b*]quinazolin-9-ones **21a**–**c** was readily achieved in 34–60% yield as illustrated in Scheme 3 upon heating the precursors [1,3,4]thiadiazino[2,3-*b*]quinazolin-10-ones **20a**–**c** at 230 °C for 45 min. The latter were readily obtained from 3-amino-2,3-dihydro-2-thioxoquinazol-4(1*H*)-one **18** with the appropriate α-haloketones either in two steps or directly in ethylpyridinium tetrafluoroborate (ionic liquid, IL) in better yields.



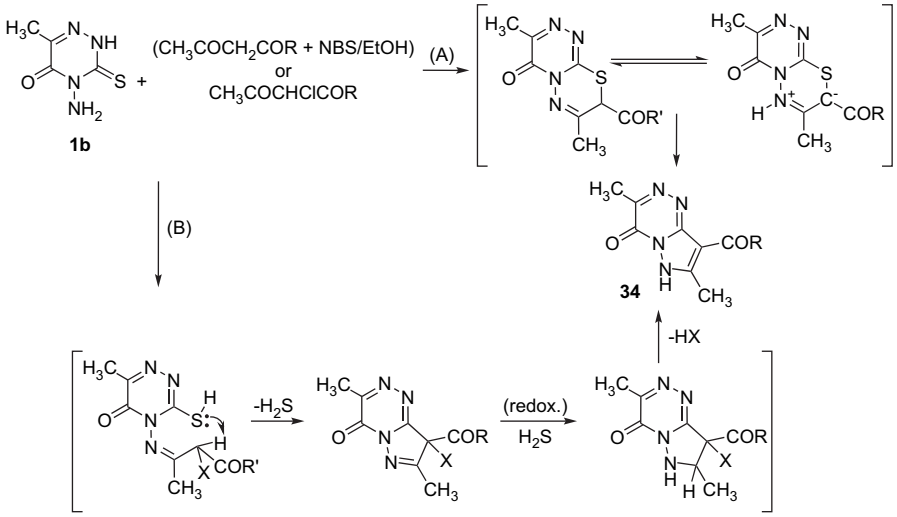
Scheme 3.

The present pyrolytic synthesis was also extended to explore the possibility of its applicability to the synthesis of 4*H*-pyrazolo[5,1-*c*][1,2,4]triazole derivatives **26**–**31**. Scheme 4 illustrates the results of our attempts to convert [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines **23**–**25** into the corresponding pyrazolo[5,1-*c*][1,2,4]triazoles. Thus, while heating the 3-aryl derivatives **24d**–**f** at 230 °C readily yielded the corresponding pyrazolotriazoles in 20–45% yield as a mixture with other products from which only **30e** could be obtained in a pure state; similarly pyrolysis of the 3-H, 3-CH_3 and 3-$PhCH_2$ derivatives gave a mixture containing starting materials together with some decomposition products in which none of the expected pyrazolotriazoles could be detected (by LCMS and NMR spectroscopy). On the other hand, clean conversion of [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines **23**–**25** into their corresponding 1-acetyl-7-acetylsulfanyl-1*H*-pyrazolo[5,1-*c*][1,2,4]triazoles **26**–**28** was readily achieved upon heating in acetic anhydride. Hydrolysis of the latter with methanolic HCl gave a mixture of the corresponding 1*H*-pyrazolo[5,1-*c*][1,2,4]triazoles **29**–**31** together with their disulfide derivatives. The latter was isolated in three cases (**32a**, **33b**,**d**) in good yield. Occasional formation of bis-(pyrazol-4-yl) disulfides was reported in the ring contraction of some uncondensed 1,3,4-thiadiazines.[6a] The decreased reactivity of the triazole ring in this conversion specially with the alkyl substituents might be attributed to the more electron rich five membered triazole ring, which disfavours the nucleophilic substitution reactions proposed for this pyrolytic conversion. On the other hand, when the reaction was conducted in acetic anhydride, initial acetylation of N-1 presumably takes place, thus activating the triazole ring towards this intramolecular ring contraction leading to the formation of the corresponding diacetyl derivatives **26**–**28**.

Sulfur extrusion leading to ring contractions of many derivatives of uncondensed 1,3,4-thiadiazines yielding pyrazole derivatives has been extensively studied under a variety of conditions using different reagents.[6] However, it does not seem that this reaction has been previously used for the synthesis of pyrazoloazines or pyrazoloazoles. There is only one paper describing the reaction of 2-halo-1,3-diones with 4-amino-1,2,4-triazine derivative **1b** to give the 7,8-disubstituted pyrazolotriazines **34**, however, the authors gave a mechanism (route B, Scheme 5), which does not involve the intermediacy of the possible thiadiazine derivatives.[7] However, we strongly believe that their product is formed via the initial formation of the corresponding thiadiazinotriazines (via route A). The



Scheme 4.



Scheme 5.

latter then undergoes rapid ring contraction facilitated by the activating carbonyl group, which increases dramatically the acidity of the α-CH group.

Assignments of the heterocyclic ring protons and carbons of compounds **8a**,**b** along with the numbering used in the NMR correlations are shown in Figure 1. Figures 2 and 3 show the same for the pyrazoloquinazoline **21a** and pyrazolotriazoles **30a**,**b**, **27a** and **33b**, respectively. These assignments were made based on H,H-COSY, HMQC (or HSQC) and HMBC experiments. Also, for the acetyl derivative **11b**, ^{15}N NMR signal assignments based on the ^{1}H–^{15}N HMBC experiment are shown in Figure 1. The important H–C long range correlations found in the HMBC experiments are indicated in each figure.

3. Conclusions

The present study offers interesting new general synthetic routes towards pyrazoloazines and pyrazoloazoles with

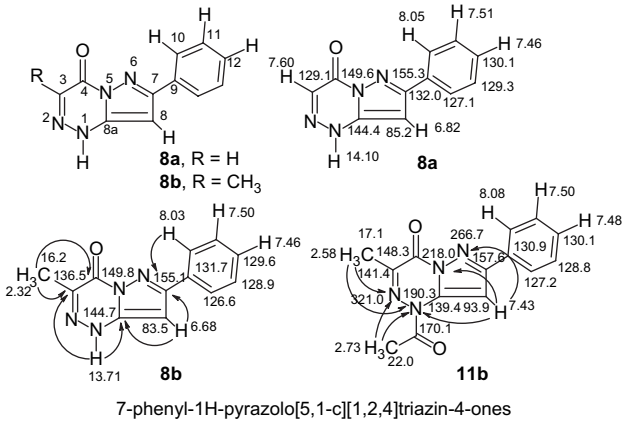


Figure 1. ^{1}H and ^{13}C NMR spectroscopic assignment of **8a**,**b** and also ^{15}N NMR assignment of **11b**.

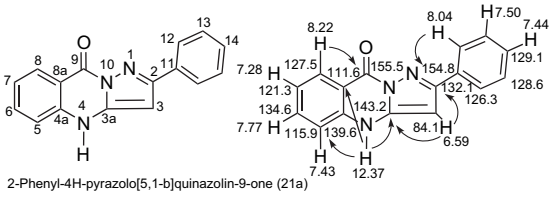


Figure 2. ^{1}H and ^{13}C NMR spectroscopic assignment of pyrazoloquinazoline **21a**.

a bridgehead (ring junction) nitrogen atom through desulfurization ring contraction of 1,3,4-thiadiazinoazines and thiadiazinoazoles. Many of these derivatives were shown to exhibit interesting diverse applications.

4. Experimental

4.1. General

All melting points are uncorrected. IR spectra were recorded in KBr disks on a Perkin Elmer System 2000 FT-IR spectrophotometer. ^{1}H, ^{13}C and ^{15}N NMR spectra were recorded on a Bruker DPX 400, 400 MHz, Avance^{II} 600, 600 MHz super-conducting NMR spectrometers. Mass spectra were measured on VG Auto-spec-Q (high resolution, high performance, tri-sector GC/MS/MS) and with LCMS using Agilent 1100 series LC/MSD with an API-ES/APCI ionization mode. Microanalyses were performed on LECO CH NS-932 Elemental Analyzer. The starting compounds **1**,[8] **18**[9] and **22**[10] were prepared as reported.

4.2. Preparation of starting compounds 2–4: general procedures

To a mixture of each of **1a–e** (10 mmol) and anhydrous potassium carbonate (2.8 g, 20 mmol), in dry acetonitrile (25 ml), was added the appropriate α-haloketones (10 mmol). The mixture was stirred at room temperature for 2–4 h. Water was then added to the mixture and the precipitate formed was collected and crystallized from the proper solvent.

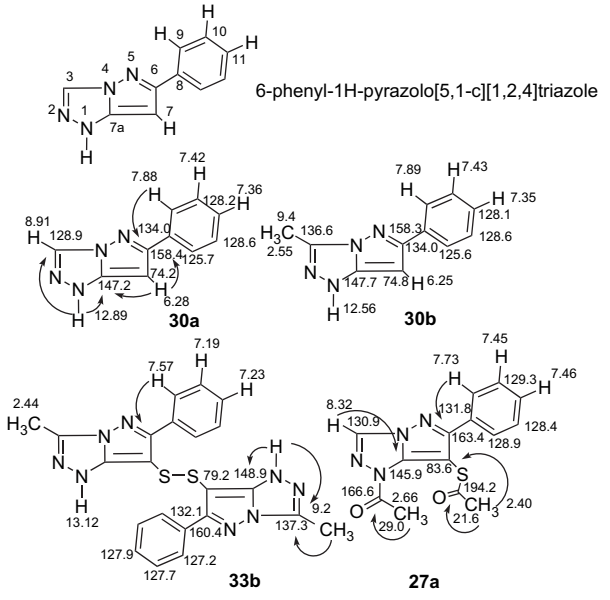


Figure 3. ^{1}H and ^{13}C NMR spectroscopy assignment of pyrazolotriazoles **30a**,**b**, **27a** and **33b**.

4.2.1. 4-Amino-3-(2-oxo-2-phenylethylsulfanyl)-1,2,4-triazin-5(4H)-one **2a**

Yellow crystals from EtOH/$CHCl_3$, yield 1.3 g (50%), mp 180 °C. MS: m/z=262 (M^+). IR: 3335, 3312, 3263, 3197, 3068, 2963, 2919, 2901, 1690, 1671, 1618, 1447, 1336, 1324, 1294, 1198, 1179, 1000, 757, 691. ^{1}H NMR (DMSO-d_6): δ 8.33 (s, 1H, H^6), 8.07 (d, 2H, J 7.6), 7.70 (t, 1H, J 7.6), 7.58 (t, 2H, J 7.6), 6.14 (s, 2H, NH_2), 4.83 (s, 2H, CH_2). ^{13}C NMR (DMSO-d_6): δ 193.3, 162.9, 152.1, 146.2, 136.0, 133.8, 129.0, 128.5, 39.0. Anal. Calcd for $C_{11}H_{10}N_4O_2S$ (262.3): C 50.37; H 3.84; N 21.36; S 12.22. Found: C 50.25; H 3.82; N 21.15; S 12.19.

4.2.2. 4-Amino-6-methyl-3-(2-oxo-2-phenylethylsulfanyl)-1,2,4-triazin-5(4H)-one **2b**

Colourless crystals from EtOH, yield 1.9 g (70%), mp 186–187 °C. MS: m/z=276 (M^+). IR: 3291, 3196, 2962, 2906, 1685, 1632, 1477, 1370, 1237, 1206, 1076, 995, 748, 684. ^{1}H NMR (DMSO-d_6): δ 8.06 (d, 2H, J 7.5), 7.70 (t, 1H, J 7.5), 7.58 (t, 2H, J 7.5), 6.06 (s, 2H, NH_2), 4.80 (s, 2H, CH_2), 2.35 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 193.1, 160.6, 153.9, 152.6, 135.9, 133.5, 128.7, 128.2, 38.4, 17.0. Anal. Calcd for $C_{12}H_{12}N_4O_2S$ (276.3): C 52.16; H 4.38; N 20.28; S 11.60. Found: C 52.00; H 4.40; N 20.17; S 11.66.

4.2.3. 4-Amino-6-benzyl-3-(2-oxo-2-phenylethylsulfanyl)-1,2,4-triazin-5(4H)-one **2c**

Colourless crystals from EtOH, yield 3.2 g (92%) of colourless crystals, mp 184–185 °C. MS: m/z=352 (M^+). IR: 3321, 3271, 3207, 3061, 2918, 1704, 1682, 1619, 1595, 1578, 1536, 1471, 1453, 1390, 1352, 1314, 1290, 1231, 1195, 1041, 1001, 968, 755, 690. ^{1}H NMR ($CDCl_3$): δ 8.08 (d, 2H, J 7.6), 7.65 (t, 1H, J 7.2), 7.53 (t, 2H, J 7.6), 7.40 (d, 2H, J 7.2), 7.31 (t, 2H, J 7.6), 7.24 (t, 1H J 7.2), 4.89 (s, 2H, NH_2), 4.81 (s, 2H, CH_2), 4.14 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 192.3, 159.7, 155.9, 151.9, 135.7, 135.2, 133.7, 129.1, 128.6, 128.3, 128.2, 126.7, 39.6, 37.1. Anal. Calcd for $C_{18}H_{16}N_4O_2S$ (352.4): C 61.35; H 4.58; N 15.90; S 9.10. Found: C 61.27; H 4.52; N 15.89; S 8.91.

4.2.4. 4-Amino-3-(2-p-methoxyphenyl-2-oxoethylsulfanyl)-1,2,4-triazin-5(4H)-one **3a**

Yellow crystals from EtOH, yield 1.75 g (60%), mp 182–183 °C. MS: m/z=292 (M^+). IR: 3310, 3259, 3193, 2915, 1684, 1664, 1626, 1598, 1570, 1508, 1450, 1420, 1349, 1308, 1295, 1251, 1188, 1168, 1025, 1007, 992, 845, 820. ^{1}H NMR (DMSO-d_6): δ 8.25 (s, 1H), 8.02 (d, 2H, J 8.8), 7.03 (d, 2H, J 8.8), 6.07 (s, 2H, NH_2), 4.74 (s, 2H, CH_2), 3.86 (s, 3H, OCH_3). ^{13}C NMR (DMSO-d_6): δ 190.9, 163.3, 162.6, 151.7, 145.6, 130.5, 128.4, 113.7, 55.3, 38.6. Anal. Calcd for $C_{12}H_{12}N_4O_3S$ (292.3): C 49.31; H 4.14; N 19.17; S 10.97. Found: C 49.08; H 4.23; N 18.96; S 10.97.

4.2.5. 4-Amino-3-(2-p-methoxyphenyl-2-oxoethylsulfanyl)-6-methyl-1,2,4-triazin-5(4H)-one **3b**

Colourless crystals from EtOH, yield 2.4 g (80%), mp 182–183 °C. MS: m/z=306 (M^+). IR: 3286, 3195, 2964, 2909, 1687, 1605, 1574, 1477, 1373, 1317, 1298, 1270, 1237, 1212, 1176, 1079, 1023, 993. ^{1}H NMR (DMSO-d_6): δ 8.03 (d, 2H, J 8.8), 7.08 (d, 2H, J 8.8), 6.04 (s, 2H, NH_2), 4.70 (s, 2H, CH_2), 3.86 (s, 3H, OCH_3), 2.26 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6) δ 191.5, 163.4, 160.6, 153.9, 152.6, 130.7, 128.8, 114.0, 55.6, 38.2, 17.0. Anal. Calcd for $C_{13}H_{14}N_4O_3S$ (306.4): C 50.97; H 4.61; N 18.29; S 10.47. Found: C 50.63; H 4.41; N 18.35; S 10.19.

4.2.6. 4-Amino-6-benzyl-3-(2-p-methoxyphenyl-2-oxoethylsulfanyl)-1,2,4-triazin-5(4H)-one **3c**

Colourless crystals from $CHCl_3$, yield 2.9 g (75%), mp 187 °C. MS: m/z=382 (M^+). IR: 3332, 3263, 3030, 2921, 1673, 1599, 1511, 1467, 1330, 1310, 1273, 1201, 1166, 996, 828, 755, 697. ^{1}H NMR (DMSO-d_6): δ 8.04 (d, 2H, J 8.8), 7.30–7.20 (m, 5H), 7.09 (d, 2H, J 8.8), 6.08 (s, 2H, NH_2), 4.73 (s, 2H, CH_2), 3.98 (s, 2H, CH_2), 3.87 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$): δ 191.0, 164.2, 160.1, 156.1, 152.2, 136.0, 130.9, 129.4, 128.6,

128.5, 127.0, 114.0, 55.6, 39.7, 37.4. Anal. Calcd for $C_{19}H_{18}N_4O_3S$ (382.4): C 59.67; H 4.74; N 14.65; S 8.38. Found: C 59.41; H 4.72; N 14.67; S 8.54.

4.2.7. 4-Amino-3-(2-p-chlorophenyl-2-oxoethylsulfanyl)-6-methyl-1,2,4-triazin-5(4H)-one **4b**

Colourless crystals from EtOH, yield 1.95 g (63%), mp 183–184 °C. MS: m/z=310 (M^+). IR: 3310, 3270, 3195, 3093, 2962, 2919, 1691, 1673, 1615, 1586, 1571, 1476, 1398, 1379, 1341, 1302, 1315, 1289, 1193, 1177, 1090, 996, 826, 815, 760. ^{1}H NMR (DMSO-d_6): δ 8.07 (d, 2H, J 8.4), 7.65 (d, 2H, J 8.4), 6.08 (s, 2H, NH_2), 4.74 (s, 2H, CH_2), 2.25 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 192.7, 160.9, 154.3, 152.9, 138.7, 135.0, 130.5, 129.2, 38.6, 17.3. Anal. Calcd for $C_{12}H_{11}ClN_4O_2S$ (310.8): C 46.38; H 3.57; N 18.03; S 10.32. Found: C 46.65; H 3.47; N 18.30; S 10.58.

4.2.8. 4-Amino-6-benzyl-3-(2-p-chlorophenyl-2-oxoethylsulfanyl)-1,2,4-triazin-5(4H)-one **4c**

Colourless crystals from EtOH, yield 2.7 g (70%), mp 182 °C. MS: m/z=386 (M^+). IR: 3290, 3246, 3181, 2919, 1687, 1673, 1618, 1589, 1467, 1193, 1174, 1093, 998, 816, 753, 694. ^{1}H NMR (DMSO-d_6): δ 8.08 (d, 2H, J 8.8), 7.65 (d, 2H, J 8.8), 7.28–7.25 (m, 5H), 6.10 (s, 2H, NH_2), 4.76 (s, 2H, CH_2), 3.97 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 191.5, 159.8, 156.3, 152.2, 140.5, 135.9, 133.9, 129.9, 129.4, 129.2, 128.6, 127.0, 39.5, 37.4. Anal. Calcd for $C_{18}H_{15}ClN_4O_2S$ (386.9): C 55.89; H 3.91; N 14.48; S 8.29. Found: C 56.04; H 3.96; N 14.56; S 8.50.

4.3. Preparation of starting compounds 5–7: general procedures

(A) To a solution of each of **2**–**4** (1 mmol) in absolute ethanol (25 ml) was added *p*-toluenesulfonic acid (40 mg). The solution was heated at reflux for 1 h. The solvent was then removed in vacuo and the remaining material was crystallized from ethanol.

(B) A mixture of each of **1a**–**c** (1 mmol) and the appropriate α-haloketones (1 mmol) in ethylpyridinium BF_4 (2 g) was stirred at 80 °C in an oil bath for 4 h. The reaction mixture was washed with water to remove the ionic liquid and the solid product obtained was crystallized from proper solvent. The water layer containing the ionic liquid was evaporated and dried in an oven at 80 °C and reused.

4.3.1. 7-Phenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one **5a**

Yellow crystals from EtOH/DMF, yield 0.12 g (50%, A), 0.2 g (80%, B), mp 210 °C. MS: m/z=244 (M^+). IR: 3060, 3001, 2930, 1703, 1609, 1443, 1415, 1316, 1270, 1218, 1204, 699. ^{1}H NMR ($CDCl_3$): δ 8.45 (s, 1H), 7.98 (d, 2H, J 7.5), 7.64 (t, 1H, J 7.5), 7.56 (t, 2H, J 7.5), 4.00 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 157.8, 152.3, 149.1, 148.9, 133.0, 132.6, 129.3, 127.8, 22.7. Anal. Calcd for $C_{11}H_8N_4OS$ (244.3): C 54.09; H 3.30; N 22.94; S 13.13. Found: C 53.90; H 3.54; N 22.67; S 13.20.

4.3.2. 3-Methyl-7-phenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one **5b**

Colourless crystals from EtOH, yield 0.15 g (60% A), 0.24 g (93%, B), mp 215 °C. LCMS: m/z=259 (M+1). IR: 3039, 2995, 2923, 1699, 1469, 1447, 1376, 1278, 1071, 771, 758, 691. ^{1}H NMR ($CDCl_3$): δ 7.97 (d, 2H, J 7.5), 7.61 (t, 1H, J 7.5), 7.54 (t, 2H, J 7.5), 3.97 (s, 2H, CH_2), 2.58 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 158.2, 158.0, 150.1, 149.8, 132.8, 132.7, 129.2, 127.7, 22.7, 18.1. Anal. Calcd for $C_{12}H_{10}N_4OS$ (258.3): C 55.80; H 3.90; N 21.69; S 12.41. Found: C 56.00; H 3.75; N 21.52; S 12.24.

4.3.3. 3-Benzyl-7-phenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one **5c**

Crystallized from EtOH to give 0.18 g (53%, A), 0.32 g (96%, B) of colourless crystals, mp 180 °C. MS: m/z=334 (M^+). IR: 2912, 1715, 1693, 1462, 1278, 759, 696. ^{1}H NMR ($CDCl_3$): δ 7.94 (d, 2H, J 7.5), 7.60 (t, 1H, J 7.5), 7.54–7.49 (m, 4H), 7.33 (t, 2H, J 7.2), 7.25 (t, 1H, J 7.2), 4.24 (s, 2H, CH_2), 3.92 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 159.4, 157.7, 150.5, 149.1, 135.8, 132.7, 132.6, 129.6, 129.1, 128.5, 127.7, 126.9, 37.8, 22.5. Anal. Calcd for $C_{18}H_{14}N_4OS$ (334.4): C 64.65; H 4.22; N 16.75; S 9.59. Found: C 64.62; H 4.27; N 16.54; S 9.90.

4.3.4. 7-p-Methoxyphenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one **6a**

Yellow crystals from EtOH, yield 0.17 g (62%, A), 0.23 g (84%, B), mp 196 °C. MS: m/z=274 (M^+). IR: 3068, 3012, 2921, 1698, 1611, 1584, 1560, 1517, 1451, 1425, 1310, 1265, 1213, 1183, 1027, 839. ^{1}H NMR (DMSO): δ 8.43 (s, 1H), 8.03 (d, 2H, J 8.8), 7.15 (d, 2H, J 8.8), 4.35 (s, 2H, CH_2), 3.87 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 163.2, 159.1, 153.8, 149.2, 149.1, 130.4, 125.2, 115.1, 56.1, 22.0. Anal. Calcd for $C_{12}H_{10}N_4O_2S$ (274.3): C 52.55; H 3.67; N 20.43; S 11.69. Found: C 52.28; H 3.69; N 20.14; S 11.54.

4.3.5. 7-p-Methoxyphenyl-3-methyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one **6b**

Crystallized from EtOH to give 0.15 g (52%, A), 0.22 g (75%, B) of colourless crystals, mp 216–217 °C. MS: m/z=288 (M^+). IR: 3047, 2994, 2942, 2836, 1704, 1594, 1517, 1468, 1306, 1269, 1178, 1033, 842. ^{1}H NMR (DMSO-d_6): δ 8.02 (d, 2H, J 8.4), 7.15 (d, 2H, J 8.4), 4.32 (s, 2H, CH_2), 3.87 (s, 3H, CH_3), 2.34 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 162.9, 158.9, 157.1, 151.3, 149.7, 130.0, 125.2, 114.8, 55.8, 21.8, 17.9. Anal. Calcd for $C_{13}H_{12}N_4O_2S$ (288.3): C 54.15; H 4.20; N 19.43; S 11.12. Found: C 54.18; H 3.98; N 19.17; S 11.00.

4.3.6. 3-Benzyl-7-p-methoxyphenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one **6c**

Colourless crystals from EtOH, yield 0.26 g (71%, A), 0.36 g (99%, B), mp 182–183 °C. MS: m/z=364 (M^+). IR: 3030, 2970, 2916, 2835, 1676, 1612, 1593, 1517, 1457, 1425, 1351, 1307, 1270, 1231, 1179, 1027, 832, 709, 697. ^{1}H NMR ($CDCl_3$): δ 7.93 (d, 2H, J 8.8), 7.50 (d, 2H, J 7.6), 7.32 (t, 2H, J 7.6), 7.24 (t, 1H, J 7.6), 7.01 (d, 2H, J 8.8), 4.24 (s, 2H, CH_2), 3.90 (s, 3H, OCH_3), 3.87 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 163.4, 159.2, 157.1, 150.8, 149.3, 136.1, 129.74, 129.69, 128.5, 126.9, 124.8, 114.6, 55.6, 37.9, 22.3. Anal. Calcd for $C_{19}H_{16}N_4O_2S$ (364.4): C 62.62; H 4.43; N 15.37; S 8.80. Found: C 62.40; H 4.41; N 15.38; S 8.46.

4.3.7. 7-p-Chlorophenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one **7a**

Brown crystals from EtOH/DMF, yield 0.17 g (62%, A), 0.25 g (90%, B), mp 232 °C. MS: m/z=278 (M^+). IR: 3419, 2920, 1708, 1586, 1443, 1418, 1275, 1232, 1090, 1011, 972, 850. ^{1}H NMR (DMSO-d_6): δ 8.46 (s, 1H), 8.06 (d, 2H, J 8.8), 7.69 (d, 2H, J 8.8), 4.38 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 158.0, 152.8, 149.0, 148.5, 137.3, 131.6, 129.1, 129.2, 21.7. Anal. Calcd for $C_{11}H_7ClN_4OS$ (278.7): C 47.40; H 2.53; N 20.10; S 11.50. Found: C 47.44; H 2.67; N 20.10; S 11.65.

4.3.8. 7-p-Chlorophenyl-3-methyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one **7b**

Colourless crystals from EtOH, yield 0.23 g (80%, A), 0.23 g (80%, B), mp 233–4 °C. MS: m/z=292 (M^+). IR: 3095, 3033, 3004, 2924, 1703, 1588, 1466, 1413, 1374, 1275, 1091, 1071, 1010, 847, 756. ^{1}H NMR ($CDCl_3$): δ 7.93 (d, 2H, J 8.4), 7.53 (d, 2H, J 8.4), 3.94 (s, 2H, CH_2), 2.58 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 158.2, 157.4, 150.7, 149.4, 137.4, 132.0, 129.7, 129.4, 22.0, 17.8. Anal. Calcd for $C_{12}H_9ClN_4OS$ (292.8): C 49.23; H 3.10; N 19.14; S 10.95. Found: C 49.10; H 3.09; N 19.09; S 10.98.

4.3.9. 3-Benzyl-7-p-chlorophenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one **7c**

Colourless crystals from EtOH/$CHCl_3$, yield 0.28 g (76%, A), 0.34 g (92%, B), mp 225–226 °C. MS: m/z=368 (M^+). IR: 3085, 3057, 3021,

2927, 1694, 1460, 1281, 1088, 846, 756, 701. ^{1}H NMR (DMSO-d_6): δ 8.04 (d, 2H, J 8.6), 7.67 (d, 2H, J 8.6), 7.35–7.29 (m, 4H), 7.23 (t, 1H, J 7.2), 4.35 (s, 2H, CH_2), 4.09 (s, 2H, CH_2). ^{13}C NMR (DMSO-d_6): δ 158.8, 158.5, 151.7, 149.1, 137.6, 136.9, 132.0, 129.9, 129.5, 129.46, 128.6, 126.9, 37.2, 22.0. Anal. Calcd for $C_{18}H_{13}ClN_4OS$ (368.9): C 58.62; H 3.55; N 15.19; S 8.69. Found: C 58.41; H 3.61; N 14.92; S 8.39.

4.4. Procedure for pyrolysis of 5–7, 20 and 24. Pyrolytic synthesis of 8–10, 21a–c and 30e: general procedures

Each of compounds **5–7**, **20** and **24e** (1 mmol) was introduced in the reaction tube, cooled in liquid nitrogen, sealed under vacuum (0.06 mbar) and placed in the pyrolyzer at 230 °C (static pyrolyzer) for 45 min. After cooling, the contents of the tube were dissolved and crystallized from the proper solvent to give the corresponding compounds **8–10**, **21ac** and **30e**.

*4.4.1. 7-Phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one **8a***

Brown crystals from EtOH/DMF, yield 0.13 g (61%), mp 324–325 °C. HRMS: m/z=212.0693 (calcd for $C_{11}H_8N_4O$: 212.0693). IR: 3235, 3166, 3138, 3059, 1696, 1611, 1536, 1458, 1444, 1374, 762, 692. ^{1}H NMR (DMSO-d_6): δ 14.10 (s, 1H, NH), 8.05 (d, 2H, J 8.4), 7.60 (s, 1H), 7.53–7.47 (m, 3H), 6.82 (s, 1H, CH[8]). ^{13}C NMR (DMSO-d_6): δ 155.3, 149.6, 144.4, 132.0, 130.1, 129.3, 129.1, 127.1, 85.2.

*4.4.2. 3-Methyl-7-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one **8b***

Brown crystals from DMF, yield 0.21 g (93%), mp 350 °C. LCMS: m/z=227 (M+1), HRMS: m/z=226.0849 (calcd for $C_{12}H_{10}N_4O$=226.0849). IR: 3208, 3067, 3001, 2925, 1673, 1606, 1461, 1442, 1271, 761, 692. ^{1}H NMR (DMSO-d_6): δ 13.71 (s, 1H, NH), 8.02 (d, 2H, J 7.2), 7.50 (t, 2H, J 7.2), 7.46 (t, 1H, J 7.2), 6.68 (s, 1H), 2.32 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 155.6, 150.2, 145.1, 136.9, 132.1, 130.0, 129.3, 127.0, 83.9, 16.7.

*4.4.3. 3-Benzyl-7-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one **8c***

Colourless crystals from DMF, yield 0.18 g (60%), chars at 300 °C. HRMS: m/z=302.1163 (calcd for $C_{18}H_{14}N_4O$: 302.1162). IR: 3239, 3145, 3083, 2929, 1681, 1614, 1541, 1459, 1447, 1204, 1164, 993, 763, 747, 689. ^{1}H NMR (DMSO-d_6): δ 13.90 (s, 1H, NH), 8.03 (d, 2H, J 7.2), 7.52–7.44 (m, 3H), 7.34–7.29 (m, 4H), 7.22 (t, 1H, J 6.8), 6.75 (s, 1H), 4.07 (s, 2H, CH_2). ^{13}C NMR (DEPT) (DMSO-d_6): δ 155.4 (C), 149.5 (C), 144.6 (C), 138.7 (C), 138.1 (C), 131.8 (C), 129.8 (CH), 129.14 (2CH), 129.12 (2CH), 128.5 (2CH), 126.8 (2CH), 126.6 (CH), 84.1 (CH), 35.6 (CH_2).

*4.4.4. 7-p-Methoxyphenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one **9a***

Brown crystals from DMF, yield 0.12 g (50%), chars at 274 °C. HRMS: m/z=242.0797 (calcd for $C_{12}H_{10}N_4O_2$: 242.0798). IR: 3179, 3146, 2936, 1681, 1607, 1578, 1527, 1452, 1437, 1289, 1256, 1178, 1030, 836, 767. ^{1}H NMR (DMSO-d_6): δ 14.09 (s, 1H, NH), 7.99 (d, 2H, J 8.8), 7.58 (s, 1H), 7.06 (d, 2H, J 8.8), 6.75 (s, 1H), 3.83 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 160.7, 155.0, 149.4, 144.1, 128.9, 128.4, 124.2, 114.5, 84.4, 55.5.

*4.4.5. 3-Methyl-7-p-methoxyphenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one **9b***

Brown crystals from DMF, yield 0.14 g (53%), mp 326 °C. HRMS: m/z=256.0954 (calcd for $C_{13}H_{12}N_4O_2$: 256.0954). IR: 3187, 2998, 2930, 2837, 1670, 1608, 1505, 1453, 1437, 1256, 1176, 1033, 838, 771. ^{1}H NMR (DMSO-d_6): δ 13.65 (s, 1H, NH), 7.97 (d, 2H, J 7.6), 7.04 (d, 2H, J 7.6), 6.61 (s, 1H), 3.82 (s, 3H, OCH_3), 2.31 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 160.6, 155.2, 149.9, 144.8, 136.6, 128.3, 124.4, 114.4, 83.1, 55.5, 16.5.

*4.4.6. 3-Benzyl-7-p-methoxyphenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one **9c***

Colourless crystals from DMF, yield 0.22 g (66%), mp 308 °C. HRMS: m/z=332.1267 (calcd for $C_{19}H_{16}N_4O_2$: 332.1267). IR: 3243, 3140, 3029, 2931, 2832, 1678, 1611, 1531, 1454, 1434, 1252, 1174, 1033, 992, 832, 773, 746, 698. ^{1}H NMR (DMSO-d_6): δ 13.83 (s, 1H, NH), 7.97 (d, 2H, J 8.8), 7.30 (m, 4H), 7.22 (m, 1H), 7.04 (d, 2H, J 8.8), 6.66 (s, 1H), 4.06 (s, 2H, CH_2), 3.82 (s, 3H, OCH_3). ^{13}C NMR (DMSO-d_6): δ 160.6, 155.4, 149.5, 144.6, 138.6, 138.2, 129.1, 128.6, 128.3, 126.6, 124.3, 114.5, 83.6, 55.5, 35.7.

*4.4.7. 7-p-Chlorophenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one **10a***

Brown crystals from DMF, yield 0.21 g (85%), mp >370 °C. HRMS: m/z=246.0302 (calcd for $C_{11}H_7ClN_4O$: 246.0308). IR: 3180, 3147, 1676, 1604, 1441, 1092, 1013, 835. ^{1}H NMR (DMSO-d_6): δ 14.20 (s, 1H, NH), 8.07 (d, 2H, J 7.6), 7.61 (s, 1H), 7.56 (d, 2H, J 7.6), 6.85 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 153.6, 149.1, 144.0, 134.2, 130.4, 128.9, 128.6, 128.3, 84.9.

*4.4.8. 7-p-Chlorophenyl-3-methyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one **10b***

Colourless crystals from acetone, yield 0.18 g (69%), mp >360 °C. HRMS: m/z=260.0458 (calcd for $C_{12}H_9ClN_4O$: 260.0459). IR: 3196, 3178, 3071, 2921, 1665, 1607, 1591, 1447, 1269, 1091, 1013, 834, 819, 774, 741. ^{1}H NMR (DMSO-d_6): δ 13.75 (s, 1H, NH), 8.07 (d, 2H, J 8.4), 7.57 (t, 2H, J 8.4), 6.74 (s, 1H), 2.32 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 154.4, 150.2, 145.2, 137.1, 134.6, 131.1, 129.4, 128.8, 84.1, 16.7.

*4.4.9. 3-Benzyl-7-p-chlorophenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one **10c***

Colourless crystals from DMF, yield 0.27 g (80%), mp 310 °C. HRMS: m/z=336.0772 (calcd for $C_{18}H_{13}ClN_4O$: 336.0772). IR: 3239, 3143, 3064, 2959, 1680, 1611, 1540, 1493, 1451, 1431, 1329, 1267, 1162, 1092, 1014, 992, 832, 773, 749, 698. ^{1}H NMR (DMSO-d_6): δ 13.92 (s, 1H, NH), 8.06 (d, 2H, J 8.4), 7.56 (d, 2H, J 8.4), 7.31 (m, 4H), 7.22 (t, 1H, J 6.8), 6.79 (s, 1H), 4.07 (s, 2H, CH_2). ^{13}C NMR (DMSO-d_6): δ 154.0, 149.2, 144.5, 138.5, 137.8, 134.2, 130.5, 128.9, 128.8, 128.31, 128.3, 126.3, 84.1, 35.4.

*4.4.10. 2-Phenyl-4H-pyrazolo[5,1-b]quinazolin-9-one **21a***

Colourless crystals from ethanol, yield 0.16 g (60%), mp 292–293 °C (lit.[12] mp 290 °C). LCMS: m/z=262 (M+1). IR: 3182, 3150, 3110, 3068, 3021, 1679, 1652, 1636, 1574, 1469, 1349, 1331, 748. ^{1}H NMR (DMSO-d_6): δ 12.37 (s, 1H, NH), 8.22 (d, 1H, J 7.8), 8.04 (d, 2H, J 7.8), 7.77 (t, 1H, J 7.8), 7.50 (t, 2H, J 7.8), 7.44 (t, 1H, J 7.2), 7.43 (d, 1H, J 7.8), 7.28 (t, 1H, J 7.8), 6.59 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 155.5, 154.8, 143.2, 139.6, 134.6, 132.1, 129.1, 128.6, 127.5, 126.3, 121.3, 115.9, 111.6, 84.1. HRMS: 261.0897 (calcd for $C_{16}H_{11}N_3O$=261.0897).

*4.4.11. 2-p-Methoxyphenyl-4H-pyrazolo[5,1-b]quinazolin-9-one **21b***

Colourless crystals from ethanol, yield 0.10 g (34%), mp >300 °C (lit.[12] mp 280 °C). HRMS: m/z=291.1002 (calcd for $C_{17}H_{13}N_3O_2$: 291.1002). ^{1}H NMR (DMSO-d_6): δ 12.34 (s, 1H, NH), 8.21 (d, 1H, J 8.0), 7.98 (d, 2H, J 8.4), 7.76 (t, 1H, J 8.0), 7.42 (t, 1H, J 8.0), 7.27 (d, 1H, J 8.0), 7.05 (d, 2H, J 8.4), 6.52 (s, 1H), 3.83 (s, 3H).

*4.4.12. 2-p-Chlorophenyl-4H-pyrazolo[5,1-b]quinazolin-9-one **21c***

Colourless crystals from ethanol, yield 0.15 g (50%), mp >350 °C (lit.[12] mp 280 °C). MS: m/z=295 (M^+), 297 (M+2). HRMS=295.0506 ($C_{16}H_{10}ClN_3O$ requires 295.0507). ^{1}H NMR (DMSO-d_6): δ 12.45 (s, 1H, NH), 8.22 (d, 1H, J 8.0), 8.08 (d, 2H, J 8.4), 7.78 (t, 1H, J 8.0), 7.57 (d, 2H, J 8.4), 7.43 (t, 1H, J 8.0), 7.29 (t, 1H, J 8.0), 6.64 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 155.6, 153.7, 143.2, 139.7, 134.8, 133.8, 129.3, 128.8, 128.5, 127.6, 121.5, 116.0, 111.6, 84.3.

4.4.13. 3-p-Methoxyphenyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***30e***

Colourless crystals from EtOH, yield 0.13 g (45%), mp 165–166 °C. MS: m/z=290 (M^+). IR: 3219, 3150, 3101, 3071, 3001, 2961, 2835, 1611, 1582, 1555, 1504, 1464, 1423, 1375, 1335, 1304, 1254, 1178, 1030, 833, 700. ^{1}H NMR ($CDCl_3$): δ 9.18 (s, 1H), 8.53 (d, 2H, J 8.8), 7.99 (d, 2H, J 7.6), 7.48 (t, 2H, J 7.6), 7.41 (t, 1H, J 7.6), 7.11 (d, 2H, J 8.8), 6.10 (s, 1H), 3.92 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 161.1, 160.2, 148.3, 139.9, 134.0, 128.7, 128.5, 128.3, 126.4, 118.4, 114.3, 75.3, 55.4. Anal. Calcd for $C_{17}H_{14}N_4O$ (290.3): C 70.33; H 4.86; N 19.30. Found: C 70.23; H 4.74; N 19.27.

4.5. Synthesis of 11b and 12c: general procedure

(A) A mixture of each of **8b** and **10c** (1 mmol) in acetic anhydride (3 ml) was heated under reflux for 2 h. The reaction mixture was poured over crushed ice and the precipitate formed was collected and crystallized from EtOH.

(B) A mixture of **5b** (0.26 g, 1 mmol) in acetic anhydride (3 ml) was heated under reflux for 2 h. The reaction mixture was poured over crushed ice and the precipitate formed was collected and crystallized from EtOH.

4.5.1. 1-Acetyl-3-methyl-7-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***11b***

Colourless crystals, yield 0.21 g (78%, A), 0.1 g (37%, B), mp 240 °C. MS: m/z=268 (M^+). IR: 3178, 3062, 2926, 1716, 1555, 1462, 1445, 1423, 1390, 1361, 1295, 1278, 1254, 1211, 1150, 953, 772, 746, 691. ^{1}H NMR ($CDCl_3$): δ 8.08 (dd, 2H, J 7.5, 1.6), 7.50 (m, 2H), 7.48 (m, 1H), 7.43 (s, 1H), 2.73 (s, 3H, CH_3), 2.58 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 170.1, 157.6, 148.3, 141.4, 139.4, 130.9, 130.1, 128.8, 127.2, 93.9, 22.0, 17.1. ^{15}N NMR ($CDCl_3$): δ 190.3, 218.0, 266.7, 321.0. Anal. Calcd for $C_{14}H_{12}N_4O_2$ (268.3): C 62.68; H 4.51; N 20.88. Found: C 62.63; H 4.55; N 20.63.

4.5.2. 1-Acetyl-3-benzyl-7-p-chlorophenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***12c***

Yellow crystals, yield 0.15 g (40%, A), mp 215 °C. MS: m/z=378 (M^+), 380 (M+2). IR: 3063, 3017, 2916, 2849, 1736, 1707, 1589, 1539, 1452, 1394, 1369, 1329, 1317, 1215, 1119, 978, 756, 696, 667. ^{1}H NMR ($CDCl_3$): δ 7.98 (d, 2H, J 8.4), 7.45 (d, 2H, J 8.4), 7.43 (d, 2H, J 7.2), 7.37 (s, 1H), 7.35 (t, 2H, J 7.2), 7.28 (t, 1H, J 7.2), 4.25 (s, 2H, CH_2), 2.64 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 170.1, 156.6, 147.9, 143.2, 139.4, 136.2, 135.5, 129.5, 129.4, 129.1, 128.7, 128.4, 127.3, 93.8, 36.4, 22.0. Anal. Calcd for $C_{20}H_{15}N_4O_2Cl$ (378.8): C 63.41; H 3.99; N 14.79. Found: C 63.23; H 3.72; N 14.57.

4.6. Synthesis of 7*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines 23–25: general procedure

(A) To a mixture of compounds **22a–f** (10 mmol) and anhydrous potassium carbonate (2.8 g, 20 mmol) in dry acetonitrile (25 ml) was added the appropriate α-haloketones (10 mmol). The mixture was stirred at room temperature for 24 h. The mixture was washed with water and the solid that remained was crystallized from the proper solvent.

(B) A mixture of each of **22a–f** (1 mmol) and the appropriate α-haloketones (1 mmol) in ethylpyridinium BF_4 (1 g) was stirred at 160 °C in an oil bath for 4 h. The mixture was then washed with water and the product was extracted with methylene chloride. The solvent was then removed in vacuo and the remaining material was crystallized from the proper solvent.

4.6.1. 6-Methyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***23a***

Yellow crystals from EtOAc/pet. ether, yield 1.1 g (71%, A), mp 97–98 °C. MS: m/z=154 (M^+). IR: 3093, 2956, 2902, 1629, 1489, 1480, 1449, 1426, 1415, 1378, 1283, 1277, 1220, 1191, 1181, 1162, 948, 942, 786, 643. ^{1}H NMR ($CDCl_3$): δ 8.46 (s, 1H), 3.55 (s, 2H, CH_2), 2.36 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 156.5, 142.0, 139.7, 26.6, 23.7. Anal. Calcd for $C_5H_6N_4S$ (154.2): C 38.95; H 3.92; N 36.34; S 20.79. Found: C 38.87; H 3.98; N 36.27; S 20.75.

4.6.2. 3,6-Dimethyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***23b***

Yellow crystals from EtOAc/pet. ether, yield 0.84 g (50%, A), mp 120–121 °C. MS: m/z=168 (M^+). IR: 2992, 2962, 2920, 2901, 1541, 1471, 1441, 1393, 1362, 1343, 1296, 1221, 1017, 808, 695. ^{1}H NMR ($CDCl_3$): δ 3.47 (s, 2H, CH_2), 2.51 (s, 3H, CH_3), 2.37 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 155.1, 150.8, 139.4, 25.9, 23.9, 10.3. Anal. Calcd for $C_6H_8N_4S$ (168.2): C 42.84; H 4.79; N 33.31; S 19.06. Found: C 42.83; H 4.92; N 33.26; S 19.04.

4.6.3. 6-Phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***24a***

Colourless crystals from EtOH, yield 1.6 g (75%, A), 0.15 g (69%, B), mp 122–123 °C. LCMS: m/z=217 (M+1). IR: 3116, 3055, 3023, 2916, 1481, 1449, 1414, 1385, 1359, 1285, 1182, 1165, 1150, 942, 774, 757, 688. ^{1}H NMR (DMSO-d_6): δ 9.18 (s, 1H), 7.99 (d, 2H, J 7.3), 7.61 (t, 1H, J 7.3), 7.60 (t, 2H, J 7.3), 4.47 (s, 2H, CH_2). ^{13}C NMR (DMSO-d_6): δ 155.7, 143.2, 140.4, 133.4, 132.0, 129.1, 127.4, 23.8. Anal. Calcd for $C_{10}H_8N_4S$ (216.3): C 55.54; H 3.73; N 25.91; S 14.83. Found: C 55.33; H 3.74; N 25.75; S 14.86.

4.6.4. 3-Methyl-6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***24b***

Yellow crystals from EtOH, yield 1.8 g (78%, A), 0.19 g (83%, B), mp 190 °C. MS: m/z=230 (M^+). IR: 3064, 3005, 2914, 1538, 1467, 1448, 1409, 1382, 1366, 1302, 760, 685. ^{1}H NMR ($CDCl_3$): δ 7.92 (dd, 2H, J 7.6, 1.2), 7.56 (m, 3H), 4.00 (s, 2H, CH_2), 2.61 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 153.1, 151.5, 140.0, 133.7, 132.0, 129.2, 127.2, 23.7, 10.4. Anal. Calcd for $C_{11}H_{10}N_4S$ (230.3): C 57.37; H 4.38; N 24.33; S 13.92. Found: C 57.47; H 4.42; N 24.26; S 13.71.

4.6.5. 3-Benzyl-6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***24c***

Colourless crystals from EtOH, yield 3.0 g (98%, A), 0.3 g (98%, B), mp 130–131 °C. MS: m/z=306 (M^+). IR: 3026, 2914, 1462, 1451, 1412, 1388, 721, 688. ^{1}H NMR ($CDCl_3$): δ 7.86 (d, 2H, J 7.6), 7.57 (m, 3H), 7.40 (d, 2H, J 7.5), 7.32 (t, 2H, J 7.5), 7.25 (t, 1H, J 7.5), 4.38 (s, 2H, CH_2), 3.97 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 153.4, 153.2, 140.4, 135.5, 133.6, 132.0, 129.2, 129.1, 128.7, 127.2, 127.1, 31.0, 23.5. Anal. Calcd for $C_{17}H_{14}N_4S$ (306.4): C 66.64; H 4.61; N 18.29; S 10.47. Found: C 66.47; H 4.72; N 18.26; S 10.38.

4.6.6. 3,6-Diphenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***24d***

Yellow crystals from EtOH, yield 1.6 g (53%, A), 0.15 g (50%, B), mp 217 °C. MS: m/z=292 (M^+). IR: 3059, 3030, 2999, 2934, 1460, 1441, 1371, 1304, 968, 770, 758, 739, 692. ^{1}H NMR ($CDCl_3$): δ 8.14 (m, 2H), 8.03 (d, 2H, J 7.2), 7.63–7.51 (m, 6H), 4.08 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 153.7, 152.8, 141.9, 133.6, 132.1, 130.3, 129.3, 128.6, 128.3, 127.3, 126.1, 23.3. Anal. Calcd for $C_{16}H_{12}N_4S$ (292.4): C 65.73; H 4.14; N 19.16; S 10.97. Found: C 65.63; H 4.12; N 19.14; S 10.81.

4.6.7. 3-p-Methoxyphenyl-6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***24e***

Colourless crystals from EtOH, yield 3.1 g (96%, A), 0.11 g (35%, B), mp 204–205 °C. MS: m/z=322 (M^+). IR: 3061, 3038, 2995, 2964, 2936, 2903, 2837, 1609, 1533, 1458, 1366, 1300, 1250, 1175, 1028, 966, 833, 692. ^{1}H NMR ($CDCl_3$): δ 8.10 (d, 2H, J 7.2), 7.93 (d, 2H, J 8.0), 7.63–7.53 (m, 3H), 7.04 (d, 2H, J 7.2), 4.03 (s, 2H), 3.90 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 161.2, 153.3, 152.6, 141.3, 132.7, 132.0, 129.8,

129.2, 127.3, 118.6, 114.1, 55.4, 23.3. Anal. Calcd for $C_{17}H_{14}N_4OS$ (322.4): C 63.34; H 4.38; N 17.38; S 9.95. Found: C 63.23; H 4.22; N 17.37; S 9.75.

4.6.8. 6-p-Chlorophenyl-3-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine **24f**

Colourless crystals from EtOH/$CHCl_3$, yield 3.0 g (93%, A), 0.28 g (86%, B), mp 266–267 °C. MS: m/z=326 (M^+), 328 (M+2). IR: 3067, 3040, 2934, 1460, 1448, 1394, 1364, 1300, 1092, 968, 827. ^{1}H NMR ($CDCl_3$): δ 8.11 (d, 2H, J 8.8), 7.93 (d, 2H, J 8.0), 7.65–7.59 (m, 3H), 7.51 (d, 2H, J 8.8), 4.05 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$): δ 153.9, 151.8, 142.1, 136.5, 133.5, 132.3, 129.5, 129.3, 129.0, 127.3, 124.6, 23.3. Anal. Calcd for $C_{16}H_{11}ClN_4S$ (326.8): C 58.80; H 3.39; N 17.14; S 9.81. Found: C 58.66; H 3.22; N 17.13; S 9.71.

4.6.9. 6-p-Methoxyphenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine **25a**

Colourless crystals from EtOAc/pet. ether, yield 2.2 g (91%, A), mp 157 °C. MS: m/z=246 (M^+). IR: 3113, 2988, 2920, 1608, 1565, 1515, 1480, 1445, 1424, 1290, 1245, 1189, 1031, 1017, 845, 821, 797. ^{1}H NMR ($CDCl_3$): δ 8.61 (s, 1H), 7.87 (d, 2H, J 8.4), 7.03 (d, 2H, J 8.4), 4.01 (s, 2H, CH_2), 3.92 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 162.8, 153.5, 142.6, 140.3, 129.0, 125.5, 114.5, 55.6, 24.1. Anal. Calcd for $C_{11}H_{10}N_4OS$ (246.3): C 53.64; H 4.09; N 22.75; S 13.02. Found: C 53.47; H 4.02; N 22.56; S 13.01.

4.6.10. 6-p-Methoxyphenyl-3-methyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine **25b**

Yellow crystals from EtOAc/pet. ether, yield 2.0 g (78%, A), mp 186–187 °C. MS: m/z=260 (M^+). IR: 3072, 2997, 2970, 2932, 1607, 1593, 1514, 1470, 1445, 1421, 1369, 1307, 1259, 1179, 1165, 1033, 849, 810. ^{1}H NMR (DMSO-d_6): δ 8.00 (d, 2H, J 8.0), 7.12 (d, 2H, J 8.0), 4.35 (s, 2H, CH_2), 3.86 (s, 3H, OCH_3), 2.48 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 162.1, 154.2, 150.2, 140.0, 129.3, 125.6, 114.4, 55.5, 22.6, 9.9. Anal. Calcd for $C_{12}H_{12}N_4OS$ (260.3): C 55.37; H 4.65; N 21.52; S 12.32. Found: C 55.23; H 4.42; N 21.46; S 12.20.

4.7. Acetic anhydride reaction: general procedure

A mixture of each of **23**–**25** (10 mmol) in acetic anhydride (3 ml) was heated under reflux for 1 h. The reaction mixture was poured over crushed ice and the precipitate formed was collected and crystallized from the proper solvent.

4.7.1. 1-Acetyl-7-acetylsulfanyl-6-methyl-1H-pyrazolo[5,1-c][1,2,4]triazole **26a**

Yellow crystals from EtOAc/pet. ether, yield 1.0 g (44%), mp 131–132 °C. LCMS: m/z=239 (M+1). IR: 3134, 3122, 3020, 2929, 1735, 1699, 1567, 1396, 1371, 1320, 1187, 1111, 954, 647, 618. ^{1}H NMR ($CDCl_3$): δ 8.20 (s, 1H), 2.63 (s, 3H), 2.45 (s, 3H), 2.34 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 194.4, 166.7, 163.0, 145.1, 130.7, 84.1, 29.1, 21.5, 13.4. Anal. Calcd for $C_9H_{10}N_4O_2S$ (238.3): C 45.37; H 4.23; N 23.51; S 13.46. Found: C 45.23; H 4.22; N 23.37; S 13.41.

4.7.2. 1-Acetyl-7-acetylsulfanyl-3,6-dimethyl-1H-pyrazolo[5,1-c][1,2,4]triazole **26b**

Colourless crystals from ethanol, yield 1.7 g (67%), mp 205 °C. MS: m/z=252 (M^+). IR: 2924, 2955, 1731, 1708, 1550, 1414, 1401, 1365, 1330, 1317, 1169, 1108, 975, 947, 657, 613. ^{1}H NMR ($CDCl_3$): δ 2.63 (s, 3H), 2.59 (s, 3H), 2.44 (s, 3H), 2.34 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 194.5, 166.6, 162.5, 145.3, 140.7, 84.6, 29.1, 21.5, 13.3, 9.6. Anal. Calcd for $C_{10}H_{12}N_4O_2S$ (252.3): C 47.61; H 4.79; N 22.21; S 12.71. Found: C 47.47; H 4.83; N 22.08; S 12.55.

4.7.3. 1-Acetyl-7-acetylsulfanyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole **27a**

Yellow crystals from ethanol, yield 2.1 g (71%), mp 125–126 °C. LCMS: m/z=301 (M+1). IR: 3146, 3132, 3059, 3024, 2927, 1738, 1695, 1563, 1395, 1370, 1331, 1318, 1191, 1112, 948, 849, 775, 698, 665, 622, 610. ^{1}H NMR ($CDCl_3$): δ 8.32 (s, 1H), 7.73 (m, 2H), 7.46 (m, 3H), 2.66 (s, 3H, CH_3), 2.40 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 194.2, 166.6, 163.4, 145.9, 131.8, 130.9, 129.3, 128.9, 128.4, 83.6, 29.0, 21.6. Anal. Calcd for $C_{14}H_{12}N_4O_2S$ (300.3): C 55.99; H 4.03; N 18.65; S 10.68. Found: C 55.98; H 4.07; N 18.76; S 10.45.

4.7.4. 1-Acetyl-7-acetylsulfanyl-3-methyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole **27b**

Yellow crystals from ethanol, yield 2.36 g (75%), mp 151–152 °C. MS: m/z=314 (M^+). IR: 3062, 3095, 2927, 1736, 1713, 1544, 1452, 1411, 1399, 1369, 1335, 1316, 1175, 1121, 1106, 973, 786, 672, 612. ^{1}H NMR (DMSO-d_6): δ 7.69 (m, 2H), 7.49 (m, 3H), 2.67 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 2.34 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 194.1, 166.4, 161.5, 145.5, 141.2, 131.6, 129.2, 128.5, 128.4, 82.8, 28.8, 21.5, 9.3. Anal. Calcd for $C_{15}H_{14}N_4O_2S$ (314.4): C 57.31; H 4.49; N 17.82; S 10.20. Found: C 57.28; H 4.52; N 17.80; S 10.21.

4.7.5. 1-Acetyl-3-benzyl-6-phenyl-7-acetylsulfanyl-1H-pyrazolo[5,1-c][1,2,4]triazole **27c**

Yellow crystals from EtOH, yield 3.3 g (84%), mp 132–133 °C. MS: m/z=390 (M^+). IR: 3060, 3028, 2936, 2916, 1730, 1713, 1587, 1543, 1443, 1414, 1394, 1367, 1319, 1157, 1121, 978, 777, 731, 700, 669, 615. ^{1}H NMR ($CDCl_3$): δ 7.73 (dd, 2H, J 7.8, 1.8), 7.53 (m, 2H), 7.46 (m, 3H), 7.39 (t, 2H, J 7.2), 7.33 (t, 1H, J 7.2), 4.39 (s, 2H, CH_2), 2.63 (s, 3H, CH_3), 2.40 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 194.4, 166.6, 163.0, 146.2, 143.0, 133.4, 132.0, 129.3, 129.1, 129.0, 128.9, 128.3, 127.6, 83.8, 30.4, 29.0, 21.6. Anal. Calcd for $C_{21}H_{18}N_4O_2S$ (390.5): C 64.60; H 4.65; N 14.35; S 8.21. Found: C 64.48; H 4.52; N 14.30; S 8.21.

4.7.6. 1-Acetyl-7-acetylsulfanyl-3,6-diphenyl-1H-pyrazolo[5,1-c][1,2,4]triazole **27d**

Colourless crystals from EtOH, yield 2.8 g (79%), mp 191–192 °C. MS: m/z=376 (M^+). IR: 3059, 2924, 1730, 1703, 1589, 1562, 1541, 1489, 1450, 1389, 1366, 1313, 1182, 1123, 1105, 964, 775, 696. ^{1}H NMR ($CDCl_3$): δ 8.59 (m, 2H), 7.81 (m, 2H), 7.60 (m, 3H), 7.48 (m, 3H), 2.77 (s, 3H, CH_3), 2.45 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 194.5, 166.9, 163.1, 147.0, 141.3, 132.0, 131.9, 129.2, 129.1, 129.0, 128.4, 127.8, 124.1, 83.4, 29.1, 21.8. Anal. Calcd for $C_{20}H_{16}N_4O_2S$ (376.4): C 63.81; H 4.28; N 14.88; S 8.52. Found: C 63.77; H 4.22; N 14.86; S 8.41.

4.7.7. 1-Acetyl-7-acetylsulfanyl-3-p-methoxyphenyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole **27e**

Colourless crystals from EtOH/$CDCl_3$, yield 2.4 g (60%), mp 183–184 °C. MS: m/z=406 (M^+). IR: 3057, 3036, 2974, 2934, 1736, 1692, 1612, 1545, 1504, 1441, 1406, 1389, 1369, 1337, 1306, 1258, 1186, 1126, 1024, 964, 835. ^{1}H NMR ($CDCl_3$): δ 8.55 (d, 2H, J 8.8), 7.81 (dd, 2H, J 8.0, 1.6), 7.48 (m, 3H), 7.10 (d, 2H, J 8.8), 3.94 (s, 3H), 2.74 (s, 3H), 2.42 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 194.6, 166.9 163.0, 162.4, 146.9, 141.3, 132.1, 129.6, 129.2, 129.1, 128.3, 116.4, 114.5, 83.4, 55.5, 29.1, 21.8. Anal. Calcd for $C_{21}H_{18}N_4O_3S$ (406.5): C 62.06; H 4.46; N 13.78; S 7.89. Found: C 62.03; H 4.22; N 13.65; S 7.82.

4.7.8. 1-Acetyl-7-acetylsulfanyl-3-p-chlorophenyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole **27f**

Colourless crystals from EtOH, yield 3.4 g (82%), mp 162–163 °C. MS: m/z=410 (M^+), 412 (M+2). IR: 3061, 1738, 1699, 1585, 1558, 1539, 1489, 1437, 1400, 1383, 1367, 1315, 1304, 1184, 1124, 1092, 962, 835, 700, 663, 621. ^{1}H NMR ($CDCl_3$): δ 8.55 (d, 2H, J 8.8), 7.80 (m, 2H), 7.58 (d, 2H, J 8.8), 7.50 (m, 3H), 2.74 (s, 3H), 2.43 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 194.2, 166.6, 163.1, 146.8, 140.2, 137.9, 131.7, 129.2, 129.1, 128.9, 128.8, 128.2, 122.4, 83.5, 28.9, 21.7. Anal. Calcd for

$C_{20}H_{15}ClN_4O_2S$ (410.9): C 58.46; H 3.68; N 13.64; S 7.80. Found: C 58.23; H 3.55; N 13.57; S 7.73.

4.7.9. 1-Acetyl-7-acetylsulfanyl-6-p-methoxyphenyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***28a***

Yellow crystals from ethanol, yield 2.3 g (70%), mp 145–146 °C. MS: m/z=330 (M^+). IR: 3131, 3111, 2966, 2939, 2921, 2842, 1741, 1715, 1700, 1612, 1561, 1524, 1430, 1398, 1368, 1336, 1315, 1253, 1180, 1110, 1035, 946, 855, 843, 636. ^{1}H NMR ($CDCl_3$): δ 8.31 (s, 1H), 7.68 (d, 2H, *J* 8.8), 6.99 (d, 2H, *J* 8.8), 3.88 (s, 3H, OCH_3), 2.66 (s, 3H, CH_3), 2.42 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 194.4, 166.7, 163.2, 160.5, 145.8, 131.0, 130.2, 124.2, 113.8, 83.2, 55.3, 29.0, 21.7. Anal. Calcd for $C_{15}H_{14}N_4O_3S$ (330.4): C 54.54; H 4.27; N 16.96; S 9.71. Found: C 54.55; H 4.24; N 16.95; S 9.56.

4.7.10. 1-Acetyl-7-acetylsulfanyl-6-p-methoxyphenyl-3-methyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***28b***

Yellow crystals from ethanol, yield 2.8 g (80%), mp 187–188 °C. MS: m/z=344 (M^+). IR: 3074, 3006, 2973, 2938, 1727, 1705, 1608, 1537, 1429, 1407, 1365, 1333, 1306, 1252, 1173, 1113, 1032, 1020, 973, 951, 839, 616. ^{1}H NMR ($CDCl_3$): δ 7.67 (d, 2H, *J* 8.8), 6.98 (d, 2H, *J* 8.8), 3.87 (s, 3H, OCH_3), 2.70 (s, 3H, CH_3), 2.62 (s, 3H, CH_3), 2.41 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$): δ 194.6, 166.6, 162.9, 160.3, 145.9, 140.9, 130.2, 124.4, 113.8, 83.5, 55.3, 29.0, 21.7, 9.7. Anal. Calcd for $C_{16}H_{16}N_4O_3S$ (344.4): C 55.80; H 4.68; N 16.27; S 9.31. Found: C 55.73; H 4.40; N 16.14; S 9.26.

4.8. Action of methanolic HCl on 26–28

A solution of each of compounds **26–28** (1 mmol) in methanol (20 ml) and HCl (2 ml, 10 M) was heated under reflux for 5–24 h (TLC and NMR monitored). The solvent was then removed in vacuo and the remaining materials were washed with sodium bicarbonate solution and the remaining materials were recrystallized from the proper solvent.

4.8.1. 3,6-Dimethyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***29b***

Yellow crystals from EtOH, yield 0.63 g (46%), mp 291 °C. IR: 3177, 3096, 3004, 2923, 2835, 1598, 1400, 1327, 1166, 858. ^{1}H NMR (DMSO-d_6): δ 12.60 (s, 1H, NH), 5.64 (s, 1H, H^7), 2.48 (s, 3H, CH_3), 2.28 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 156.3, 147.5, 136.4, 78.1, 14.5, 9.5. HRMS=136.0743 ($C_6H_8N_4$ requires 136.0743).

4.8.2. 6-Phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***30a***

Yellow crystals from EtOH, yield 0.17 g (90%), mp 187–188 °C. LCMS: m/z=185 (M+1). IR: 3159, 3125, 3086, 2917, 2891, 1602, 1577, 1458, 1440, 1387, 1341, 1282, 1191, 1035, 987, 709. ^{1}H NMR (DMSO-d_6): δ 12.89 (s, 1H, NH), 8.91 (s, 1H, H^3), 7.88 (dd, 2H, *J* 7.2, 1.2), 7.42 (t, 2H, *J* 7.2), 7.36 (dt, 1H, *J* 7.2, 1.2), 6.28 (s, 1H, H^7). ^{13}C NMR (DMSO-d_6): δ 158.4, 147.2, 134.0, 128.9, 128.6, 128.2, 125.7, 74.2. Anal. Calcd for $C_{10}H_8N_4$ (184.2): C 65.21; H 4.38; N 30.42. Found: C 65.21; H 4.32; N 30.44.

4.8.3. 3-Methyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***30b***

Pale yellow crystals from EtOH, yield 0.15 g (77%), mp 235–236 °C. MS: m/z=198 (M^+). IR: 3177, 3149, 3079, 2784, 1600, 1572, 1473, 1442, 1335, 1274, 1231, 1076, 963, 780, 722. ^{1}H NMR (DMSO-d_6): δ 12.56 (s, 1H, NH), 7.89 (d, 2H, *J* 7.7), 7.43 (d, 2H, *J* 7.7), 7.35 (t, 1H, *J* 7.7), 6.25 (s, 1H, H^7), 2.55 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6): δ 158.3, 147.7, 136.6, 134.0, 128.6, 128.1, 125.6, 74.8, 9.4. Anal. Calcd for $C_{11}H_{10}N_4$ (198.23): C 66.65; H 5.08; N 28.26. Found: C 66.46; H 4.99; N 28.11.

4.8.4. 3-Benzyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***30c***

Pale yellow crystals from EtOAc/pet. ether, yield 0.14 g (45%), mp 197–198 °C. MS: m/z=274 (M^+). IR: 3106, 3059, 3009, 2966, 2920, 2887, 2756, 2507, 2482, 1601, 1494, 1454, 1432, 1247, 1121, 950, 760, 721, 704, 684. ^{1}H NMR (DMSO-d_6): δ 12.79 (s, 1H, NH), 7.88 (d, 2H, *J* 7.9), 7.42 (m, 4H), 7.34 (m, 3H), 7.25 (t, 1H, *J* 7.3), 6.27 (s, 1H, H^7), 4.33 (s, 2H). ^{13}C NMR (DMSO-d_6): δ 158.3, 147.9, 138.9, 135.6, 133.9, 128.8, 128.5 (2C), 128.2, 126.8, 125.7, 74.9, 29.6. Anal. Calcd for $C_{17}H_{14}N_4\cdot HCl$ (310.8): C 65.70; H 4.86; N 18.03. Found: C 65.45; H 4.83; N 17.87.

4.8.5. 3-p-Methoxyphenyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***30e***

Colourless crystals from EtOH, yield 0.28 g (98%), mp 165–166 °C (identical with the compound prepared above from pyrolysis of **24e** (mp and NMR)).

4.8.6. 3-p-Chlorophenyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]-triazole ***30f***

Colourless crystals from EtOAc/pet. ether, yield 0.27 g (92%), mp 229–230 °C. MS: m/z=294 (M^+), 296 (M+2). IR: 3134, 3078, 2974, 2930, 2893, 1603, 1493, 1458, 1379, 1325, 1275, 1088, 1049, 881, 829, 727, 692. ^{1}H NMR (DMSO-d_6): δ 13.34 (s, 1H, NH), 8.50 (d, 2H, *J* 8.4), 7.99 (d, 2H, *J* 8.4), 7.73 (d, 2H, *J* 8.4), 7.48 (t, 2H, *J* 8.4), 7.40 (t, 1H, *J* 8.4), 6.64 (s, 1H). ^{13}C NMR ($CDCl_3$): δ 158.8, 148.6, 136.5, 134.4, 133.7, 129.2, 128.7, 128.4, 127.2, 125.9, 124.7, 75.2. Anal. Calcd for $C_{16}H_{11}ClN_4$ (294.8): C 65.20; H 3.76; N 19.01. Found: C 65.10; H 3.62; N 18.97.

4.8.7. 6-p-Methoxyphenyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***31a***

Yellow crystals from ethanol, yield 0.15 g (60%), mp 237–238 °C. MS: m/z=214 (M^+). IR: 3142, 2916, 2875, 2840, 2726, 2529, 1598, 1488, 1428, 1264, 1183, 1015, 986, 948, 841, 808, 768. ^{1}H NMR (DMSO-d_6): δ 12.87 (s, 1H, NH), 8.89 (s, 1H), 7.81 (d, 2H, *J* 8.8), 6.99 (d, 2H, *J* 8.8), 6.20 (s, 1H), 3.80 (s, 3H, OCH_3). ^{13}C NMR (DMSO-d_6): δ 159.3, 158.3, 147.2, 128.8, 127.0, 126.4, 114.0, 73.6, 55.1. Anal. Calcd for $C_{11}H_{10}N_4O\cdot HCl$ (250.7): C 52.70; H 4.42; N 22.35. Found: C 52.95; H 4.61; N 22.61.

4.8.8. 6-p-Methoxyphenyl-3-methyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***31b***

Yellow crystals from ethanol, yield 0.17 g (75%), mp 150–151 °C. MS: m/z=228 (M^+). IR: 3222, 3115, 2930, 2839, 1603, 1526, 1466, 1427, 1248, 1175, 1032, 837. ^{1}H NMR (DMSO-d_6): δ 12.50 (s, 1H, NH), 7.81 (d, 2H, *J* 8.8), 6.98 (d, 2H, *J* 8.8), 6.15 (s, 1H), 3.80 (s, 3H, OCH_3), 2.53 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 159.3, 158.2, 147.7, 136.5, 127.0, 126.5, 113.9, 74.2, 55.1, 9.4. Anal. Calcd for $C_{12}H_{12}N_4O$ (228.3): C 63.15; H 5.30; N 24.55. Found: C 63.10; H 5.22; N 24.33.

4.8.9. Bis(6-methyl-1H-pyrazolo[5,1-c][1,2,4]triazol-7-yl)-disulfide ***32a***

Yellow crystals from EtOH, yield 0.14 g (30%), mp above 360 °C. MS: m/z=306 (M^+). IR: 3129, 3071, 3030, 2969, 2868, 2731, 1599, 1447, 1411, 1387, 1371, 1328, 1217, 1002, 873, 834, 811, 710. ^{1}H NMR (DMSO-d_6): δ 13.41 (s, 2H, NH), 8.91 (s, 2H), 1.89 (s, 6H, $2CH_3$). ^{13}C NMR (DMSO-d_6): δ 160.9, 148.0, 129.7, 80.9, 11.9. Anal. Calcd for $C_{10}H_{10}N_8S_2$ (306.4): C 39.20, H 3.29, N 36.57; S 20.93. Found: C 39.12; H 3.10; N 36.42; S 20.80.

4.8.10. Bis(3-methyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazol-7-yl)disulfide ***33b***

Pale yellow crystals from ethanol, yield 038 g (83%), mp 209 °C. MS: m/z=458 (M^+). IR: 3187, 3116, 3064, 1594, 1567, 1452, 1425, 1393, 1371, 1237, 1173, 773, 694. ^{1}H NMR (DMSO-d_6): δ 13.12 (s, 2H, NH), 7.57 (d, 4H, *J* 7.5), 7.23 (t, 2H, *J* 7.5), 7.19 (t, 4H, *J* 7.5), 2.44 (s, 6H, $2CH_3$). ^{13}C NMR (DMSO-d_6): δ 160.4, 148.9, 137.3, 132.1, 127.9, 127.7, 127.2, 79.2, 9.2. Anal. Calcd for $C_{22}H_{18}N_8S_2$ (458.6): C 57.62; H 3.96; N 24.44; S 13.98. Found: C 57.48; H 3.77; N 24.20; S 13.78.

4.8.11. Bis(3,6-diphenyl-1H-pyrazolo[5,1-c][1,2,4]triazol-7-yl)disulfide ***33d***

Pale yellow crystals from ethanol, yield 0.29 g (50%), mp 238–239 °C. MS: *m*/*z*=582 (M^+). HRMS: *m*/*z*=582.1406 (calcd for $C_{32}H_{22}N_8S_2$: 582.1403). IR: 3219, 1593, 1452, 1425, 764, 683. ^{1}H NMR ($CDCl_3$): δ 10.89 (s, 2H, NH), 8.35 (m, 4H), 7.93 (d, 4H, *J* 7.2), 7.52 (m, 6H), 7.23 (t, 4H, *J* 7.2), 7.12 (t, 2H, *J* 7.2). ^{13}C NMR (DMSO-d_6): δ 162.0, 149.7, 140.21, 131.8, 130.6, 128.9, 128.8, 128.2, 126.6, 126.4, 81.0.

4.9. Preparation of starting compounds 18a–c: general procedures

(A) Following the reported method,[11] a mixture of **18** (1 mmol) and the appropriate α-haloketones (1 mmol) in benzene (30 ml) and triethylamine (0.5 ml) was stirred at room temperature for 6 h. The solvent was then removed in vacuo and the remaining solid was washed with water, dried and dissolved in absolute ethanol (10 ml) and *p*-toluenesulfonic acid (40 mg). The solution was then refluxed for 3 h. The solvent was then removed in vacuo and the remaining solid was crystallized from ethanol.

(B) A mixture of **18** (1 mmol) and the appropriate α-haloketones (1 mmol) in ethylpyridinium BF_4 (2 g) was stirred at 80 °C in an oil bath for 4 h. The reaction mixture was washed with water to remove the ionic liquid and the solid product obtained was collected and crystallized from EtOH. The water layer containing the ionic liquid was evaporated and dried in an oven at 80 °C and reused.

4.9.1. 3-Phenyl-2H-[1,3,4]thiadiazino[2,3-b]quinazolin-10-one ***20a***

Yellow crystals, yield 0.18 g (60%, A), 0.23 g (78%, B) mp 170 °C. MS: *m*/*z*=293 (M^+). IR: 3056, 3011, 2921, 1690, 1609, 1545, 1469, 1444, 1338, 1271, 1202, 1137, 768, 756, 689. ^{1}H NMR (DMSO-d_6): δ 8.18 (d, 1H, *J* 7.6), 8.05 (d, 2H, *J* 6.8), 7.85 (t, 1H, *J* 7.6), 7.60 (m, 4H), 7.52 (t, 1H, *J* 7.6), 4.40 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 158.7, 155.2, 149.0, 145.8, 135.0, 133.8, 131.9, 129.1, 127.9, 127.5, 126.7, 126.3, 120.9, 23.6. Anal. Calcd for $C_{16}H_{11}N_3OS$ (293.4): C 65.51; H 3.78; N 14.32; S 10.93. Found: C 65.40; H 3.80; N 14.46; S 10.79.

4.9.2. 3-p-Methoxyphenyl-2H-[1,3,4]thiadiazino[2,3-b]quinazolin-10-one ***20b***

Yellow crystals, yield 0.06 g (20%, A) 0.16 (50%, B), mp 204–205 °C. MS: *m*/*z*=323 (M^+). IR: 3067, 2998, 2912, 2837, 1688, 1607, 1595, 1577, 1542, 1514, 1470, 1421, 1336, 1262, 1235, 1206, 1179, 1143, 1025, 832, 762, 690. ^{1}H NMR (DMSO-d_6): δ 8.17 (d, 1H, *J* 8.0), 8.03 (d, 2H, *J* 8.8), 7.83 (t, 1H, *J* 8.0), 7.58 (d, 1H, *J* 8.0), 7.51 (t, 1H, *J* 8.0), 7.13 (d, 2H, *J* 8.8), 4.35 (s, 2H), 3.87 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 162.1, 157.6, 156.3, 150.4, 145.4, 134.9, 129.3, 126.9, 126.3, 125.9, 125.6, 120.4, 114.4, 55.5, 22.2. Anal. Calcd for $C_{17}H_{13}N_3O_2S$ (323.4): C 63.14; H 4.05; N 12.99; S 9.92. Found: C 63.12; H 4.00; N 12.85; S 9.82.

4.9.3. 3-p-Chlorophenyl-2H-[1,3,4]thiadiazino[2,3-b]quinazolin-10-one ***20c***

Yellow crystals from ethanol, yield 0.13 g (40%, A), 0.2 g (60%, B), mp 228 °C. MS: *m*/*z*=327 (M^+), 329 (M+2). IR: 3063, 2912, 1685, 1607, 1588, 1576, 1545, 1468, 1334, 1272, 1203, 1090, 763, 690. ^{1}H NMR (DMSO-d_6): δ 8.18 (d, 1H, *J* 7.6), 8.07 (d, 2H, *J* 8.4), 7.83 (t, 1H, *J* 7.6), 7.68 (d, 2H, *J* 8.4), 7.59 (d, 1H, *J* 7.6), 7.53 (t, 1H, *J* 7.6), 4.39 (s, 2H). ^{13}C NMR (DMSO-d_6): δ 157.5, 155.5, 150.0, 145.4, 136.5, 135.1, 132.5, 129.3, 129.1, 127.1, 126.5, 126.0, 120.5, 22.4. Anal. Calcd for $C_{16}H_{10}N_3OSCl$ (327.8): C 58.63; H 3.08; N 12.82; S 9.78. Found: C 58.40; H 3.00; N 12.66; S 9.69.

Acknowledgements

The support of the University of Kuwait received through research grant no. SC04/05 and the facilities of ANALAB and SAF (grants no. GS01/01, GS01/03, GS03/01) are gratefully acknowledged.

References and notes

1. (a) Marco-Contelles, J.; Pérez-Mayoral, E.; Ballesteros, P. Bicyclic 5–5 Systems with One Bridgehead (Ring Junction) Nitrogen Atom: Three Extra Heteroatoms 2:1. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Christopher A. Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier Academic: 2008; Vol. 11, pp 199–305; (b) Regan, A. C. Bicyclic 5–6 Systems with One Bridgehead (Ring Junction) Nitrogen Atom: Two Extra Heteroatoms 1:1. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Christopher A. Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier Academic: 2008; Vol. 11, pp 551–587; (c) Hajos, G.; Riedl, Z. Bicyclic 5–6 Systems with One Bridgehead (Ring Junction) Nitrogen Atom: Three Extra Heteroatoms 1:2. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Christopher A. Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier Academic: 2008; Vol. 11, pp 765–817.
2. (a) Schantl, J. G. Bicyclic 5–5 Systems with One Ring Junction Nitrogen Atom: Three Extra Heteroatoms 2:1. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, F. V., Eds.; Pergamon: London, 1996; Vol. 8, pp 123–190; (b) Sliskovic, D. R. Bicyclic 5–6 Systems with One Ring Junction Nitrogen Atom: Two Extra Heteroatoms 1:1. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, F. V., Eds.; Pergamon: London, 1996; Vol. 8, pp 345–365; (c) Hajós, G. Bicyclic 5–6 Systems with One Ring Junction Nitrogen Atom: Three Extra Heteroatoms 1:2. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, F. V., Eds.; Pergamon: London, 1996; Vol. 8, pp 445–464.
3. (a) Ibrahim, Y. A.; Al-Awadi, N. A.; Ibrahim, M. R. *Tetrahedron* **2004**, *60*, 9121; (b) Al-Awadi, H.; Ibrahim, M. R.; Al-Awadi, N. A.; Ibrahim, Y. A. *Tetrahedron* **2007**, *63*, 12948–12953.
4. (a) Roth, M.; Dubs, P.; Gotschi, E.; Eschenmoser, A. *Helv. Chim. Acta* **1971**, *54*, 710–734; (b) Shiosaki, K. The Eschenmoser Coupling Reaction. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 2, pp 865–892.
5. Poewar, T. M.; Ingale, S. A.; Srinivasan, K. V. *Tetrahedron* **2007**, *63*, 11066–11069.
6. (a) Smalley, R. K. 1,3,4-Oxadiazines and 1,3,4-Thiadiazines. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, F. V., Eds.; Pergamon: London, 1996; Vol. 6, pp 737–781; (b) Pfeiffer, W.-D. 1,3,4-Oxadiazines and 1,3,4-Thiadiazines. In *Comprehensive Heterocyclic Chemistry III*; Katritzky, A. R., Christopher A. Ramsden, C. A., Scriven, E. F. V., Taylor, R. J. K., Eds.; Elsevier Academic: 2008; Vol. 9, pp 401–455.
7. El-Barbary, A. A.; El-badawi, M. A.; Loksha, Y. M. *J. Heterocycl. Chem.* **2001**, *38*, 711–716.
8. Fawzi, M. M. Fr. Pat. 1,547,854, 1966; *Chem. Abstr.* **1969**, *71*, 91538; Dornow, A.; Menzel, H.; Marx, P. *Chem. Ber.* **1964**, *97*, 2173–2177.
9. Rusu, G. G.; Koval, D.; Gutsu, Ya E.; Barba, N. A. *Khim. Geterotsikl. Soedin.* **1995**, 1001–1002; *Chem. Abstr.* **1996**, *124*, 202154.
10. (a) Singh, H.; Shukla, K. N.; Dwivedi, R.; Yadav, L. D. S. *J. Agric. Food Chem.* **1990**, *38*, 1483–1486; (b) Bhalerao, U. T.; Muralikrishna, C.; Rani, B. R. *Tetrahedron* **1994**, *50*, 4019–4024; (c) Cartwright, D. D. J.; Clark, B. A. J.; McNab, H. *J. Chem. Soc., Perkin Trans. 1* **2001**, 424–428 and references cited therein.
11. Gakhar, H. K.; Gupta, S. C.; Kumar, N. *Indian J. Chem., Sect. B* **1981**, *20*, 14–16.
12. Ibrahim, S. S.; Abdel-Halim, A. M.; Gaber, Y.; El-Edfawy, S. *J. Chem. Res., Miniprint* **1997**, 1055–1063.