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Stereoselective synthesis of dihydrothiadiazinoazines and dihydrothiadiazinoazoles and their pyrolytic desulfurization ring contraction

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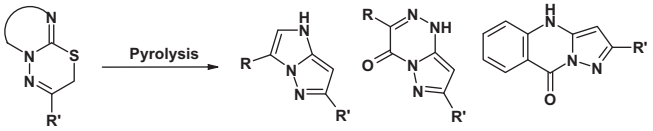
[1,2,4]Triazino[3,4-*b*][1,3,4]thiadiazin-4-ones
[1,3,4]Thiadiazino[2,3-*b*]quinazolin-10-ones
Pyrazolo[5,1-*b*][1,2,4]triazoles
Pyrazolo[5,1-*c*][1,2,4]triazin-4-ones
Pyrazolo[4,3-*b*]quinazolin-9-ones

ABSTRACT

Intramolecular base catalyzed C–C bond formation led to exclusive stereoselective syntheses of *trans*-6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines, *trans*-7,8-dihydro-6*H*-[1,2,4]triazino[3,4-*b*][1,3,4]thiadiazin-4-ones, and *trans*-3,4-dihydro-2*H*-[1,3,4]thiadiazino[2,3-*b*]quinazolin-10-one. *trans*-6,7-Dihydro-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines isomerize slowly in $CDCl_3$ and more rapidly in DMSO-d_6 into the corresponding cis-stereoisomers. The other *trans*-6,7-dihydro-[1,3,4]thiadiazines isomerize also in DMSO-d_6 into the corresponding cis-stereoisomers. Pyrolytic conversion of these heterocyclic condensed dihydrothiadiazines into their corresponding pyrazolo[5,1-*b*][1,2,4]triazoles, pyrazolo[5,1-*c*][1,2,4]triazin-4-ones and pyrazolo[4,3-*b*]quinazolin-9-ones via desulfurization ring contraction is described.

1. Introduction

Following our recent interest in the pyrolytic behavior of 1,2,4-triazine derivatives[1] we serendipitously discovered the pyrolytic desulfurization ring contraction of [1,2,4]triazino[3,4-*b*][1,3,4]thiadiazin-4-ones into their corresponding pyrazolo[5,1-*c*][1,2,4]triazin-4-ones.[2] This desulfurization ring contraction reaction has also been accomplished by the action of acetic anhydride and was extended to the synthesis of other pyrazoloazines and pyrazoloazoles, thus offering a generalized synthetic approach toward pyrazoloazines and pyrazoloazoles with bridgehead (ring junction) nitrogen atom via ring contraction of condensed thiadiazines (Scheme 1).[2] Much attention has been directed to the synthesis of pyrazoloazines and pyrazoloazoles with bridgehead (ring junction) nitrogen atom due to their diverse interesting applications included in numerous publications and several hundreds of patents. These important applications include biological activity, hair-dyes, photographic dyes, and applications in material sciences. The available literature methods for their synthesis have been reviewed in Comprehensive Heterocyclic Chemistry (CHCIII, CHCII).[3,4]



Scheme 1. Pyrolytic desulfurization ring contraction of thiadiazinoazines and thiadiazinoazoles.

The interesting synthesis of 6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines **4** via the base catalyzed C–C bond formation of the appropriate precursor acylmethylsulfanyl-*N*-arylideneamino-1,2,4-triazoles **3** (Scheme 2)[5,6] prompted us to investigate the same methodology to synthesize other condensed dihydrothiadiazine derivatives and to study their applications in the synthesis of pyrazoloazines and pyrazoloazoles via pyrolytic desulfurization ring contraction.

2. Results and discussion

In the present work additional examples of 6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*]1,3,4]thiadiazines **4** have been successfully obtained by careful optimization of the reaction conditions. Thus, refluxing the 4-arylideneamino-1,2,4-triazole-3(2*H*)-thiones **2** (obtained from **1** and ArCHO) with ethyl bromoacetate or ω-

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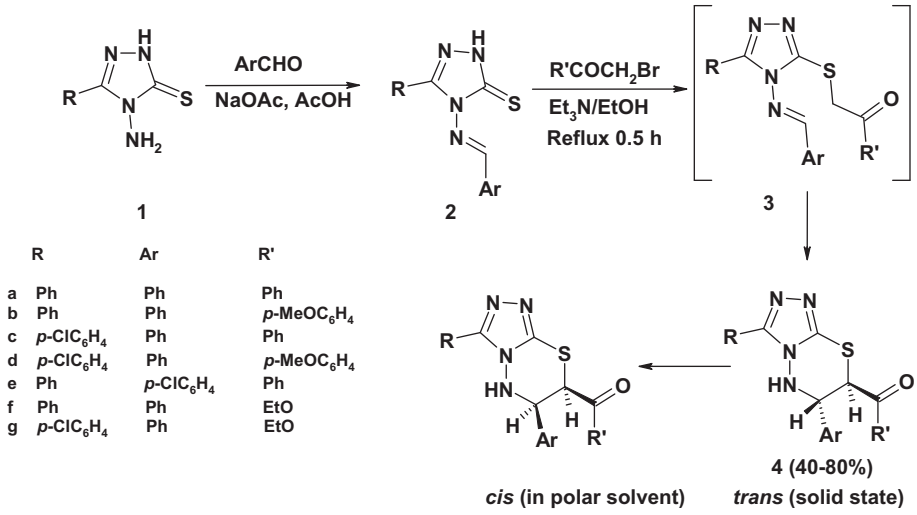


Scheme 2. Synthesis of 6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*]1,3,4]thiadiazines **4**.

bromoacetophenones in ethanol in the presence of triethylamine afforded the corresponding diastereomerically pure *trans*-6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines **4** via the base catalyzed C–C bond formation of the intermediate **3**. The stereochemistry of compounds **4** is indicated by X-ray crystallography (Fig. 1).[7] Surprisingly, ^{1}H NMR of compounds **4** in $CDCl_3$ showed broad non-resolved signals for N–(5)H, C-(6)H, C-(7)H, which change positions with time into a well resolved doublet for the N–(5)H, a doublet for C-(7)H and a triplet for C-(6)H with a ^3J=4–6 Hz (Fig. 2a and b shows the change with time of the ^{1}H NMR of **4a** in $CDCl_3$). This coupling constant is characteristic for the cis stereochemistry of compounds **4** as reported in literature.[5] This indicates that the *trans*-6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines isomerize in $CDCl_3$ into the corresponding *cis*-6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazines. This isomerization is more rapid in DMSO-d_6 (Fig. 2c) and on addition of D_2O the NH signal disappeared and the signal at δ 5.08 appeared as doublet. Similar phenomenon has been reported for [1,2,4]triazolo[3,4-*b*]thiadiazinium bromides where the crystalline trans derivatives equilibrate to 60:40 mixtures of trans and cis isomers in $CDCl_3$ solution.[5b]

Similar syntheses of the dihydrothiadiazino-1,2,4-triazine derivatives **8** had not yet been reported prior to this study. Therefore, the reaction of 4-arylideneamino-2,3-dihydro-3-thioxo-1,2-4-triazin-5(4*H*)-ones **6** (obtained from **5** and ArCHO) with ω-bromoacetophenone derivatives or ethyl bromoacetate has been studied under different conditions and the best condition was achieved by stirring for 2 h in acetonitrile at room temperature in the presence of anhydrous K_2CO_3 (Scheme 3). Under these conditions compounds **6a**–**d**, **6f**–**i**, **6k** gave the corresponding **8a**–**d**, **6f**–**i**, **6k**, respectively, however, **6e**,**j** gave the corresponding open intermediate **7e**,**j**, respectively. The latter have been cyclized to the corresponding **8e**,**j** upon refluxing for 30 min in ethanol in the presence of Et_3N. Other intermediates **7** (e.g., **7c**,**i**) could be prepared in high yield by stirring the reactants for 30 min at room temperature in ethanol in the presence of Et_3N. The 7,8-dihydro-6*H*-[1,2,4]triazino[3,4-*b*][1,3,4]thiadiazin-4-ones **8** have been produced in the pure trans stereochemistry in solid state as confirmed by X-ray crystallography[7] (Fig. 3) and also, as indicated by the ^{1}H NMR in $CDCl_3$, which showed a doublet for C-(7)H and a doublet for C-(8)H with a ^3J=8.8–9.2 Hz. In contrast to the 6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*]1,3,4]thiadiazines **4**, no trans, cis isomerization has been observed in this case in $CDCl_3$. However, in DMSO-d_6 such isomerization takes place immediately and only the cis isomers are detected as indicated by the coupling constant between C-(7)H and C-(8)H (^3J=5.2–5.6 Hz, Fig. 4), which become more clear upon D_2O addition.

An extension of this synthetic methodology to quinazolinothiadiazines was investigated. Thus, treatment of 3-benzylideneamino-1,2-dihydro-2-thioxoquinazolin-4-one **10** (obtained from **9** and PhCHO) with ω-bromoacetophenones in acetonitrile in the presence of Et_3N at room temperature for 2 h gave the corresponding 2-benzoylmethylsulfanyl-3-benzylideneaminoquinazolin-4(3*H*)-one **11**. Cyclization of the latter to 2-benzoyl-3-phenyl-3,4-dihydro-2*H*-[1,3,4]thiadiazino[2,3-*b*]quinazolin-10-one **12** has been achieved upon refluxing in ethanol in the presence of Et_3N for 30 min (Scheme 4). The latter has also been obtained stereoselectively in the trans form in the solid state similar to the 1,2,4-triazine derivatives as confirmed by X-ray crystallography[7] (Fig. 5). ^{1}H NMR of **12** showed a doublet for C-(2)H and a doublet for C-(3)H with a ^3J=8.9 Hz confirming their trans stereochemistry. Also, as in case of **8**, no trans, cis isomerization has been observed for **12** in $CDCl_3$ but readily occurs in DMSO-d_6 (Fig. 6).

Attempted conversion of compounds **4** into the corresponding pyrazolo derivatives **13** under various conditions only gave identifiable products with compounds **4f**,**g**, upon pyrolysis at 230 °C for 30 min, yielding the corresponding pyrazolotriazole derivatives **13a**,**c**. Compounds **13** have also been successfully obtained by alternative route. Thus, reacting the appropriate triazoles **1a**,**c**,**h** with

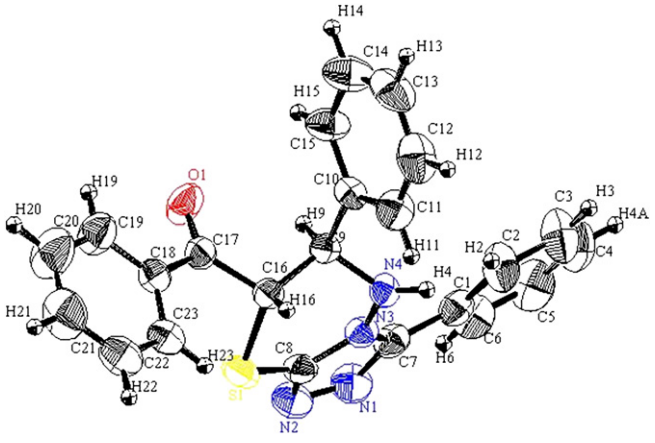


Fig. 1. ORTEP drawing of compound **4a**.[7]

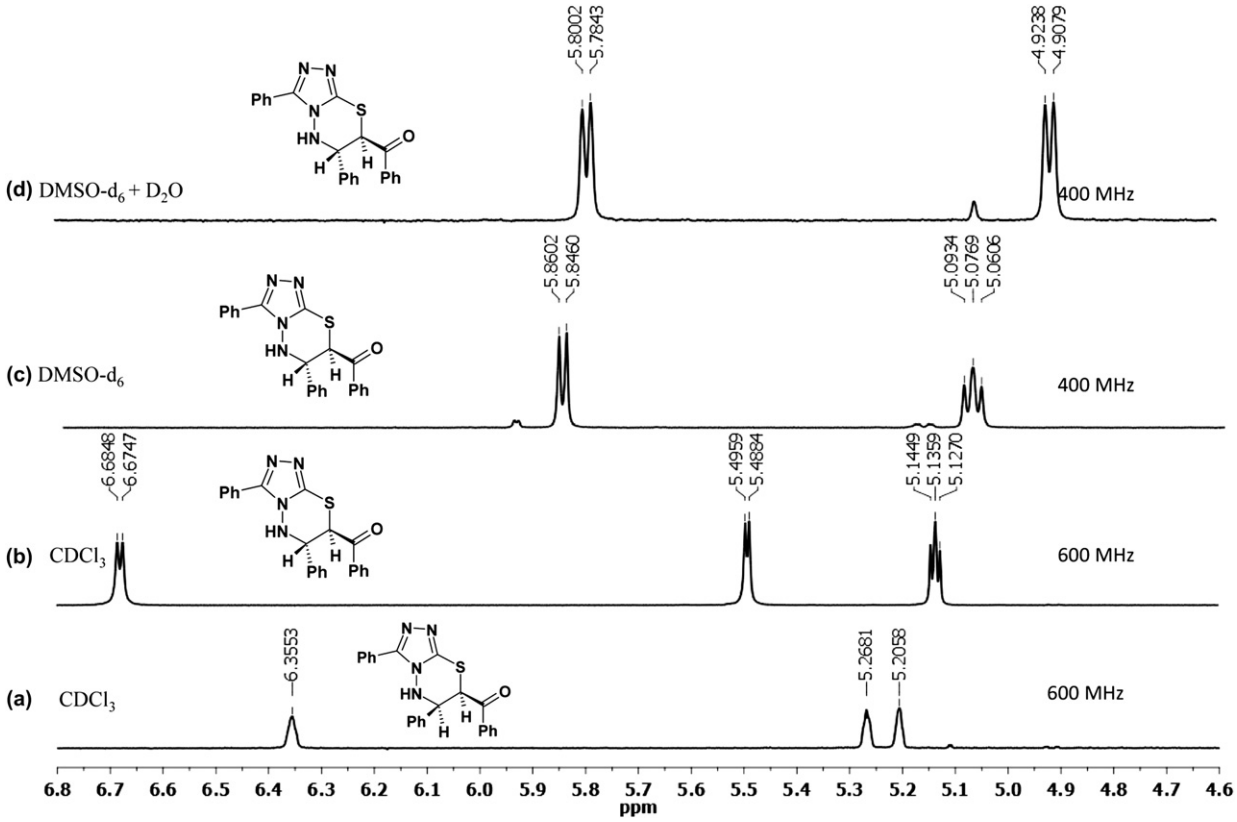
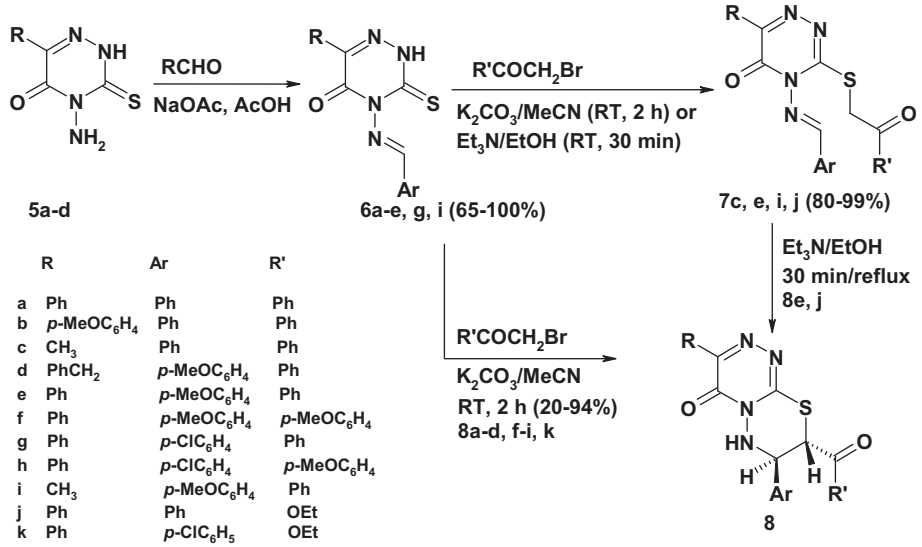


Fig. 2. ^{1}H NMR of **4a** in a: $CDCl_3$ immediately, b: $CDCl_3$ after 1 h, c: DMSO-d_6 and d: DMSO-d_6+D_2O.



	R	Ar	R'
a	Ph	Ph	Ph
b	*p*-$MeOC_6H_4$	Ph	Ph
c	CH_3	Ph	Ph
d	$PhCH_2$	*p*-$MeOC_6H_4$	Ph
e	Ph	*p*-$MeOC_6H_4$	Ph
f	Ph	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$
g	Ph	*p*-ClC_6H_4	Ph
h	Ph	*p*-ClC_6H_4	*p*-$MeOC_6H_4$
i	CH_3	*p*-$MeOC_6H_4$	Ph
j	Ph	Ph	OEt
k	Ph	*p*-ClC_6H_5	OEt

Scheme 3. Synthesis of 7,8-dihydro-6*H*-[1,2,4]triazino[3,4-*b*]thiadiazin-4-ones **8**.

ethyl α-bromoacetoacetate **14** in refluxing ethanol gave the corresponding pyrazolotriazoles **13a**,**c**,**h** (10–11%) and the triazolothiadiazines **15a**,**c**,**h** (40–48%). Pyrolysis of the latter at 230 °C for 45 min gave the corresponding pyrazolotriazoles **13a**–**c** in 10–44% yield. Similar condensation of compound **1a** with bromodibenzoylmethane **16** in refluxing ethanol gave directly the corresponding pyrazolotriazole **18** via the intermediate **17** (Scheme 5).

Pyrolysis of compounds **8a**–**j** at 230 °C for 45 min under 0.06 mbar afforded the corresponding pyrazolotriazines **19** together with the deacylated derivatives **20** (Scheme 6). Compounds **19** are thermally stable and were recovered completely unchanged when pyrolyzed under similar conditions. This indicates that compounds **19** are not the precursors of compounds **20**. Alternatively, compounds **19a** and **19j** have been readily obtained by heating the starting 4-amino-1,2,4-triazine derivatives **5a** with dibenzoylbromomethane and ethyl α-bromoacetoacetate, respectively, in ethanol following reported procedures.[8]

Moreover, compounds **20** were prepared by pyrolysis of the corresponding **24** at 230 °C as described previously.[2] The new derivatives **24** were synthesized from **5** as shown in Scheme 7 by

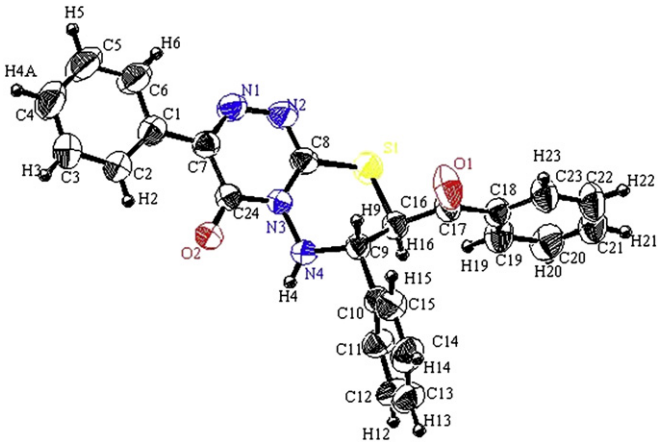


Fig. 3. ORTEP drawing of compound **8a**.[7]

give the corresponding condensed thiadiazines, which then undergo sulfur extrusion as explained in previous paper.[2] On the other hand, the formation of the deacylated derivatives **20**, **27** from the same substrates probably follows different ring contraction routes including thioester intermediates **28** followed by thermal elimination of thioic acid derivatives as shown in Scheme 9. Similar thioesters thermal eliminations have been reported.[9]

3. Conclusions

The present study describes an interesting stereoselective synthesis of dihydro-1,3,4-thiadiazinoazines and dihydro-1,3,4-thiadiazinoazoles by intramolecular base catalyzed C–C bond formation. Pyrolysis of these heterocyclic condensed dihydrothiadiazines offers synthetic routes toward pyrazoloazines and pyrazoloazoles with bridgehead (ring junction) nitrogen atom through desulfurization ring contraction. Many of these derivatives are expected to exhibit interesting diverse applications.

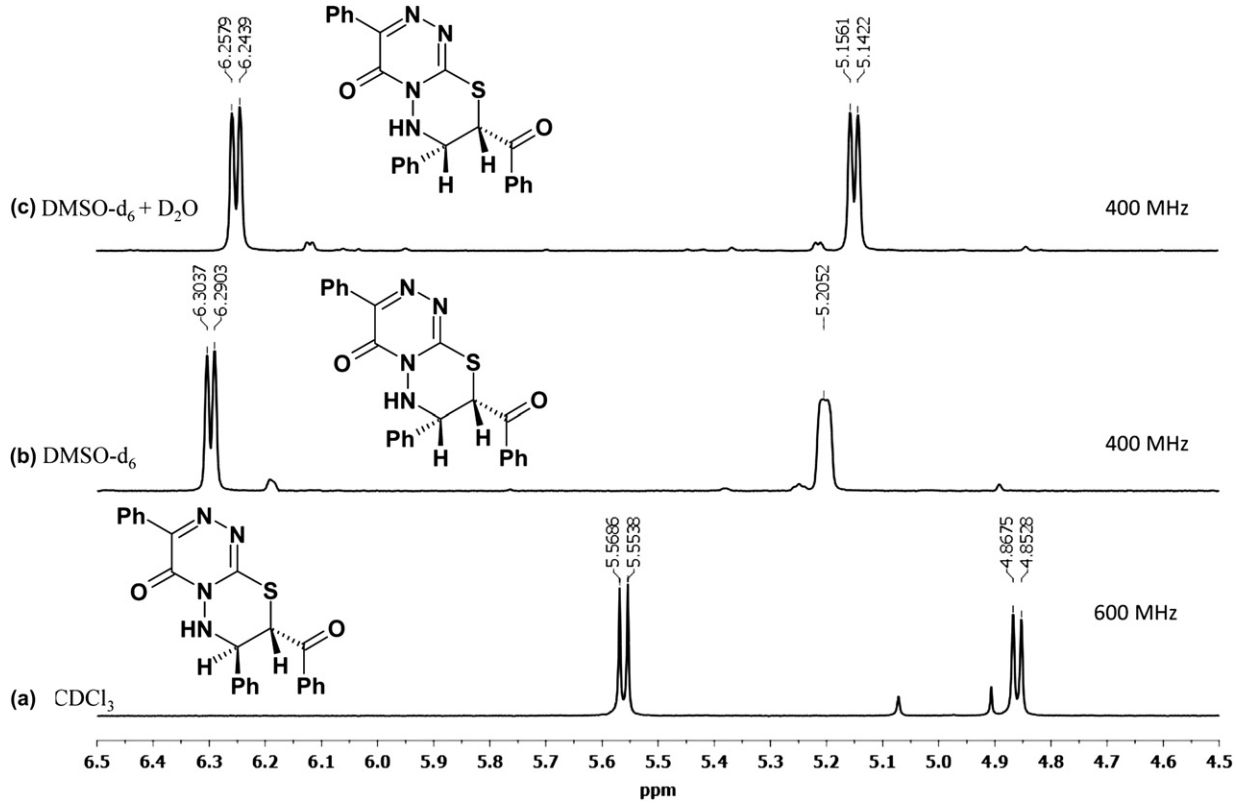


Fig. 4. ^{1}H NMR of compound **8a** in a: $CDCl_3$ and b: DMSO-d_6.

reacting with bromoacetophenone derivatives **22** to yield the corresponding 3-arolylmethylsulfanyltriazines **23**, which were then cyclized to **24** upon refluxing in ethanol in the presence of *p*-toluenesulfonic acid. Heating **20** with acetic anhydride gave the corresponding acetyl derivatives **25**.

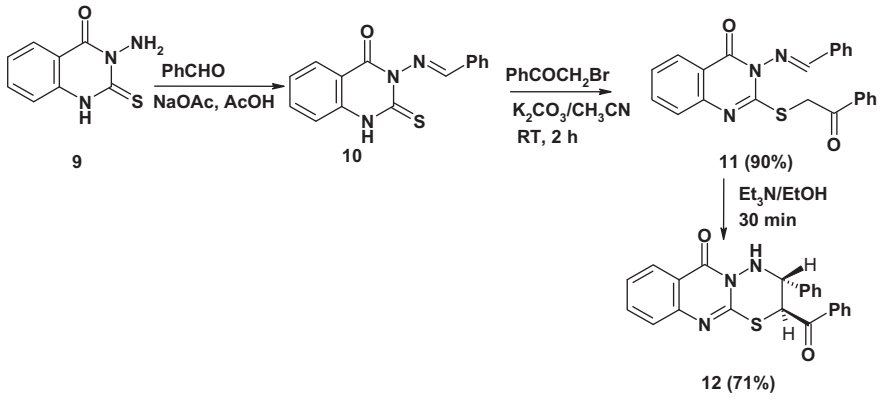
Similar pyrolysis of dihydrothiazoloquinazoline **12** at 230 °C under 0.06 mbar afforded the corresponding pyrazoloquinazoline derivatives **26a** and **27**. Condensation of **9** with each of dibenzoylbromomethane and ethyl α-bromoacetoacetate in refluxing ethanol gave the corresponding pyrazoloquinazolines **26a**,**b**, respectively (Scheme 8).

The formation of pyrazoloazines **13**, **19**, **26** in the pyrolysis products of **4**, **7**, **8**, and **12** can be explained as initial dehydrogenation to

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 and ^{13}C 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 GCMSDFS-Thermo 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**,[10] **14**,[11] and **16**[11] were prepared as reported.



Scheme 4. Synthesis of 2-benzoyl-3-phenyl-3,4-dihydro-2*H*-[1,3,4]thiadiazino[2,3-*b*]quinazolin-10-one **12**.

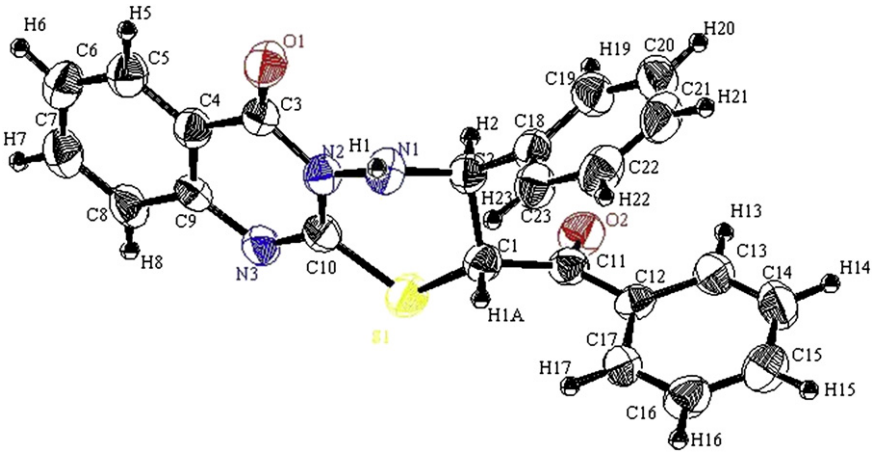


Fig. 5. ORTEP drawing of compound **12**.[7]

4.2. Synthesis of *trans*-6,7-dihydro-5*H*-[1,2,4]triazolo[3,4-*b*] thiadiazines 4a–g: General procedure

A mixture of each of compounds **2a**,**c**,**e** (1 mmol), triethylamine (1.5 mmol), and the appropriate α-haloketones or ethyl bromoacetate (1 mmol) in ethanol (10 mL) was heated under reflux for 0.5 h. The solvent was then removed in vacuo and the remaining residue was crystallized from ethanol to give the corresponding products **4a**–**g**.

4.2.1. trans-7-Benzoyl-3,6-diphenyl-6,7-dihydro-5H-[1,2,4]triazolo [3,4-b][1,3,4]thiadiazine ***4a***. Colorless crystals, yield 0.28 g (70%), mp 215 °C (lit.[6] mp 204–206 °C). MS: *m*/*z*=398 (M^+). IR: 3432, 3166, 3061, 3010, 2957, 1680, 1588, 1448, 1429, 1367, 1263, 1175, 1056, 942, 689. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (dd, 2H, *J* 7.9, 1.5), 7.97 (d, 2H, *J* 7.3), 7.66 (t, 1H, *J* 7.4), 7.51–7.48 (m, 4H), 7.42–7.39 (m, 3H), 7.34–7.30 (m, 3H), 6.68 (d, 1H, *J* 6.0), 5.49 (d, 1H, *J* 4.6), 5.14 (t, 1H, *J* 5.4). ^{13}C NMR (150 MHz, $CDCl_3$): δ 195.0, 152.6, 142.9, 135.9, 134.6, 134.4, 130.1, 129.2, 129.1, 128.9, 128.8, 128.5, 127.9, 127.4, 125.9, 59.3, 42.0. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.07–8.04 (m, 4H), 7.72 (t, 1H, *J* 7.2), 7.59 (t, 2H, *J* 8.0), 7.51–7.47 (m, 5H), 7.37 (d, 1H, *J* 7.6, NH, exchangeable), 7.33–7.26 (m, 3H), 5.85 (d, 1H, *J* 6.1), 5.08 (t, 1H, *J* 6.6). ^{13}C NMR (100 MHz, DMSO-d_6): δ 194.8, 152.0, 142.8, 137.0, 134.6, 134.5, 130.1, 129.3, 129.0, 128.8, 128.76, 128.4, 127.6, 127.5, 126.4, 58.9, 43.7. HRMS=398.1196 ($C_{23}H_{18}N_4OS$ requires 398.1196). Anal. Calcd for $C_{23}H_{18}N_4OS$: C 69.33; H 4.55; N 14.06; S 8.05. Found: C 69.38; H 4.76; N 14.06; S 8.34.

4.2.2. trans-3,6-Diphenyl-7-p-methoxybenzoyl-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***4b***. Colorless crystals, yield 0.27 g (62%), mp 233 °C. MS: *m*/*z*=428 (M^+). IR: 3426, 3153, 2974, 2929, 1665, 1595, 1470, 1426, 1372, 1315, 1267, 1170, 1120, 1030, 955, 928, 689. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (dd, 2H, *J* 8.0, 2.0), 7.96 (d, 2H, *J* 8.8), 7.49 (d, 2H, *J* 7.0), 7.42–7.37 (m, 3H), 7.35–7.28 (m, 3H), 6.93 (d, 2H, *J* 8.8), 6.85 (d, 1H, *J* 5.6), 5.52 (d, 1H, *J* 4.4), 5.09 (t, 1H, *J* 5.6), 3.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.7, 164.7, 152.7, 142.9, 136.0, 131.3, 130.0, 129.1, 128.7, 128.5, 127.9, 127.3, 127.2, 126.0, 114.4, 59.1, 55.7, 41.2. HRMS=428.1301 ($C_{24}H_{20}N_4O_2S$ requires 428.1196). Anal. Calcd for $C_{24}H_{20}N_4O_2S$: C 67.27; H 4.70; N 13.07; S 7.48. Found: C 66.98; H 5.00; N 12.98; S 7.70.

4.2.3. trans-7-Benzoyl-3-p-chlorophenyl-6-phenyl-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***4c***. Colorless crystals, yield 0.35 g (80%), mp 163 °C. MS: *m*/*z*=432 (M^+). LCMS: *m*/*z*=435 (M+3), 433 (M+1). IR: 3376, 3164, 3018, 2971, 2889, 2676, 1689, 1446, 1374, 1268, 1167, 1130, 1093, 948, 825, 691. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, 2H, *J* 7.2), 7.98 (d, 2H, *J* 7.2), 7.70 (t, 1H, *J* 7.2), 7.55 (t, 2H, *J* 8.0), 7.45 (d, 2H, *J* 7.2), 7.39 (d, 2H, *J* 7.2), 7.34–7.31 (m, 3H), 6.60 (d, 1H, *J* 5.2), 5.41 (d, 1H, *J* 4.0), 5.19 (t, 1H, *J* 4.8). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.0, 151.7, 143.2, 136.4, 135.6, 134.7, 134.3, 129.2, 129.1, 129.0, 128.9, 128.87, 128.8, 127.3, 124.2, 59.3, 41.7. HRMS=432.0806 ($C_{23}H_{17}{}^{35}ClN_4OS$ requires 432.0806). Anal. Calcd for $C_{23}H_{17}ClN_4OS$: C 63.81; H 3.96; N 12.94; S 7.41. Found: C 63.58; H 4.28; N 12.84; S 7.66.

4.2.4. trans-3-p-Chlorophenyl-7-p-methoxybenzoyl-6-phenyl-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***4d***. Colorless crystals, yield 0.13 g (51%), mp 233 °C. MS: *m*/*z*=462 (M^+), LCMS: *m*/*z*=465 (M+3), 463 (M+1). IR: 3427, 3146, 2986, 2927, 1666, 1596, 1456, 1431, 1270, 1170, 1025, 836. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, 2H, *J* 8.8), 7.96 (d, 2H, *J* 8.8), 7.46 (d, 2H, *J* 6.8), 7.37 (d, 2H, *J* 8.8),

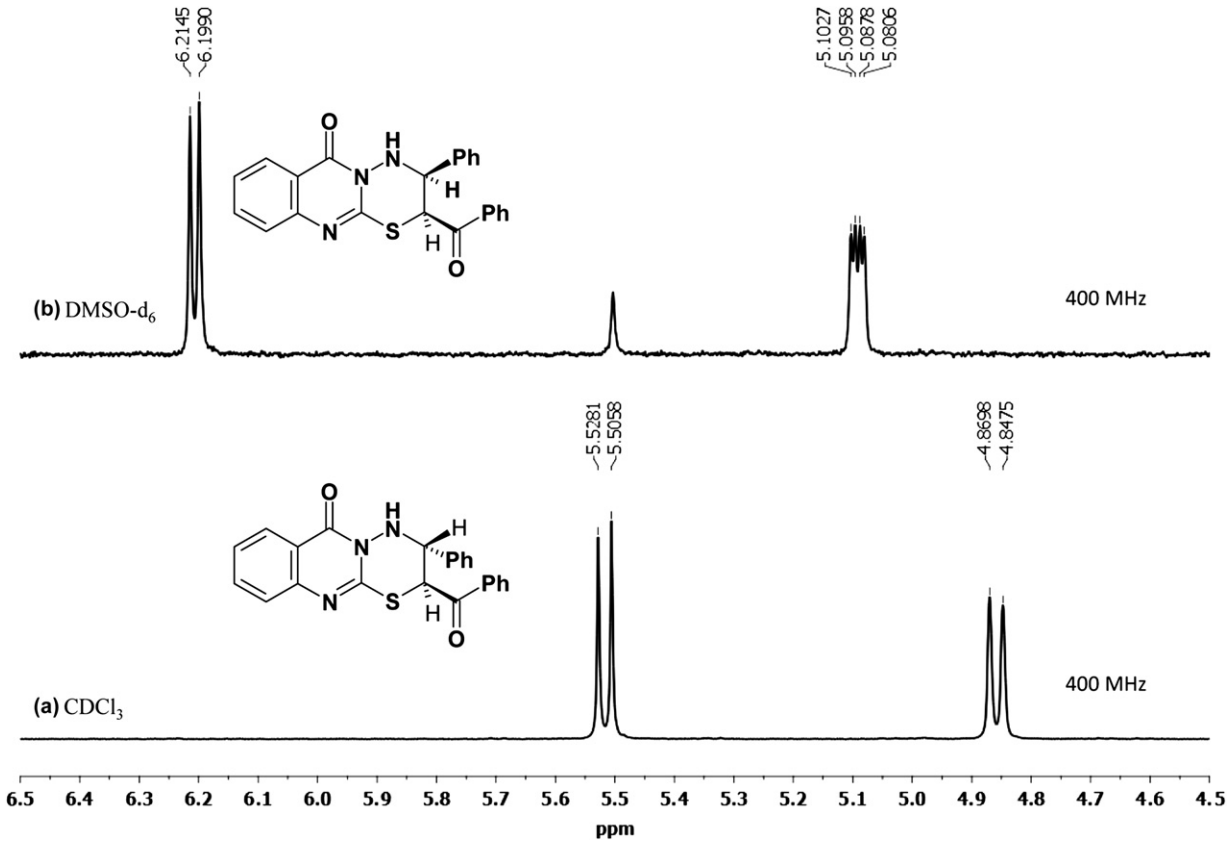


Fig. 6. ^{1}H NMR of **12** in a: $CDCl_3$ and b: DMSO-d_6.

7.33–7.31 (m, 3H), 6.96 (d, 2H, *J* 8.8), 6.76 (d, 1H, *J* 5.6), 5.46 (d, 1H, *J* 4.4), 5.11 (t, 1H, *J* 5.2), 3.91 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 193.6, 164.8, 151.8, 143.1, 136.0, 135.8, 131.3, 129.1, 129.0, 128.8 (two overlapped carbons), 127.3, 127.1, 124.6, 114.4, 59.0, 55.7, 41.1. HRMS=462.0912 ($C_{24}H_{19}{}^{35}ClN_4O_2S$ requires 462.0912).

4.2.5. trans-7-Benzoyl-6-p-chlorophenyl-3-phenyl-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***4e***. Colorless crystals, yield 0.2 g (46%), mp 229–230 °C. LCMS: *m*/*z*=435 (M+3), 433 (M+1). IR: 3161, 3058, 3003, 2974, 2950, 1684, 1594, 1493, 1449, 1423, 1355, 1281, 1265, 1092, 926, 689. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, 2H, *J* 7.2), 7.96 (d, 2H, *J* 7.6), 7.66 (t, 1H, *J* 7.4), 7.51–7.40 (m, 7H), 7.30 (d, 2H, *J* 7.6), 7.00 (br s, 1H), 5.58 (d, 1H, *J* 4.8), 5.06 (t, 1H, *J* 5.4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.0, 152.7, 142.1, 134.8, 134.7, 134.2, 134.1, 130.1, 129.3, 129.2, 128.8, 128.7, 128.6, 127.8, 125.9, 58.1, 41.1. HRMS=432.0806 ($C_{23}H_{17}{}^{35}ClN_4OS$ requires 432.0806). Anal. Calcd for $C_{23}H_{17}ClN_4OS$: C 63.81; H 3.96; N 12.94; S 7.41. Found: C 63.59; H 4.27; N 12.86; S 7.70.

4.2.6. trans-7-Ethoxycarbonyl-3,6-diphenyl-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***4f***. Colorless crystals, yield 0.19 g (51%), mp 217 °C. MS: *m*/*z*=366 (M^+). IR: 3447, 3146, 2982, 2956, 2931, 1738, 1457, 1430, 1258, 1165, 1130, 1004, 966, 771, 698. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07–8.05 (m, 2H), 7.44–7.42 (m, 3H), 7.37–7.36 (m, 2H), 7.32–7.30 (m, 3H), 6.42 (d, 1H, *J* 5.4), 4.96 (t, 1H, *J* 4.8), 4.43 (d, 1H, *J* 4.2), 4.30–4.23 (m, 2H), 1.30 (t, 3H, *J* 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 152.5, 141.9, 134.6, 129.9, 129.0, 128.7, 128.4, 127.6, 126.8, 126.1, 62.7, 58.3, 40.6, 13.8. HRMS=366.1145 ($C_{19}H_{18}N_4O_2S$ requires 366.1145). Anal. Calcd for $C_{19}H_{18}N_4O_2S$: C 62.28; H 4.95; N 15.29; S 8.75. Found: C 61.99; H 5.23; N 15.16; S 8.55.

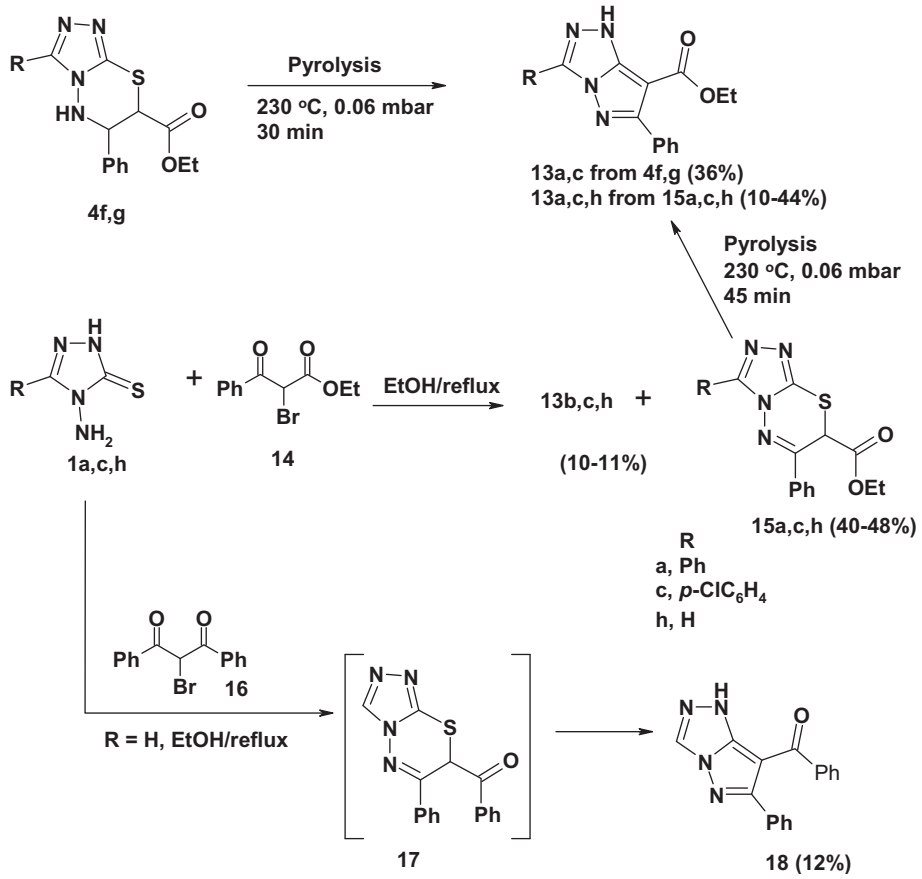
4.2.7. trans-7-Ethoxycarbonyl-3-p-chlorophenyl-6-phenyl-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***4g***. Colorless crystals, yield 0.22 g (55%), mp 170 °C. MS: *m*/*z*=402 (M+2, 32%), 400 (M^+, 100%). IR: 3201, 3139, 2972, 2937, 1735, 1648, 1464, 1440, 1374, 1295, 1271, 1256, 1173, 1090, 1013, 975, 694. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, 2H, *J* 8.8), 7.39 (d, 2H, *J* 7.6), 7.32–7.26 (m, 5H), 6.46 (d, 1H, *J* 4.9), 4.95 (t, 1H, *J* 4.1), 4.44 (d, 1H, *J* 3.7), 4.29–4.25 (m, 2H), 1.30 (t, 3H, *J* 6.4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 151.6, 142.4, 136.1, 134.6, 129.1, 128.9, 128.8 (2 overlapped CH's), 126.9, 124.6, 62.9, 58.4, 40.6, 13.9. HRMS=400.1235 ($C_{19}H_{17}{}^{35}ClN_4O_2S$ requires 400.1235). Anal. Calcd for $C_{19}H_{17}ClN_4O_2S$: C 56.93; H 4.27; N 13.98; S 8.00. Found: C 56.96; H 4.05; N 14.01; S 7.91.

4.3. General procedure for synthesis of compounds 6

A mixture of each of **5a**–**d** (10 mmol), sodium acetate (12 mmol), and the appropriate aldehyde (10 mmol) in acetic acid (20 mL) was refluxed for the specified time. The reaction mixture was cooled and the solid obtained was filtered and crystallized from ethanol.

4.3.1. 4-Benzylideneamino-3-mercapto-6-phenyl-1,2,4-triazin-5(4H)-one ***6a***. Reaction time: 1 h. Yellow crystals, yield 2.62 g (85%), mp 250 °C (lit.[10] mp 250 °C). MS: *m*/*z*=308 (M^+). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.51 (s, 1H), 8.52 (s, 1H, CH), 8.04 (dd, 2H, *J* 7.6, 1.2), 7.96 (dd, 2H, *J* 7.6, 1.6), 7.61 (t, 1H, *J* 7.6), 7.53 (d, 2H, *J* 7.6), 7.50–7.46 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 170.7, 149.2, 144.9, 133.5, 131.4, 131.1, 130.9, 129.6, 129.1, 128.5, 128.4.

4.3.2. 4-Benzylideneamino-3-mercapto-6-p-methoxyphenyl-1,2,4-triazin-5(4H)-one ***6b***. Reaction time: 4 h. Yellow crystals, yield 2.2 g (65%), mp 227–228 °C. MS: *m*/*z*=338 (M^+). IR: 3295, 3201, 3155, 3081, 3003, 2957, 1684, 1662, 1606, 1557, 1509, 1391, 1322, 1254, 1180, 1030, 835. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.43 (s, 1H), 8.51 (s, 1H, CH),



Scheme 5. Pyrolysis of dihydrotriazolo[3,4-*b*]thiadiazines **4** and **15**.

8.06 (d, 2H, *J* 8.8), 7.96 (dd, 2H, *J* 7.8, 1.2), 7.60 (tt, 1H, *J* 7.2, 1.2), 7.52 (t, 2H, *J* 7.4), 6.97 (d, 2H, *J* 8.8), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 170.4, 161.8, 149.3, 144.5, 133.4, 131.4, 130.0, 129.6, 129.0, 123.6, 113.9, 55.4. Anal. Calcd for $C_{17}H_{14}N_4O_2S$: C 60.34; H 4.17; N 16.56; S 9.48. Found: C 60.03; H 4.17; N 16.22; S 9.20.

4.3.3. 4-Benzylideneamino-3-mercapto-6-methyl-1,2,4-triazin-5(4H)-one ***6c***. Reaction time: 1 h. Colorless crystals, yield 1.9 g (77%), mp 210 °C (lit.[12] mp 213–214 °C). MS: *m*/*z*=246 (M^+). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.59 (s, 1H), 8.47 (s, 1H, CH), 7.93 (d, 2H, *J* 8.4), 7.59 (t, 1H, *J* 8.4), 7.51 (t, 2H, *J* 8.4), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$):δ 172.4, 171.4, 149.9, 147.4, 133.4, 131.3, 129.5, 129.0, 17.1.

4.3.4. 6-Benzyl-3-mercapto-4-p-methoxybenzylideneamino-1,2,4-triazin-5(4H)-one ***6d***. Reaction time: 3 h. Yellow crystals, yield 2.28 g (65%), mp 196 °C (lit.[13] mp 196 °C). MS: *m*/*z*=352 (M^+). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.81 (s, 1H), 8.52 (s, 1H, CH), 7.86 (d, 2H, *J* 8.8), 7.28–7.24 (m, 5H), 7.11 (d, 2H, *J* 8.8), 3.92 (s, 2H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.4, 170.7, 163.2, 149.6, 148.7, 136.3, 131.0, 129.2, 128.4, 126.6, 124.3, 114.7, 55.6, 35.9.

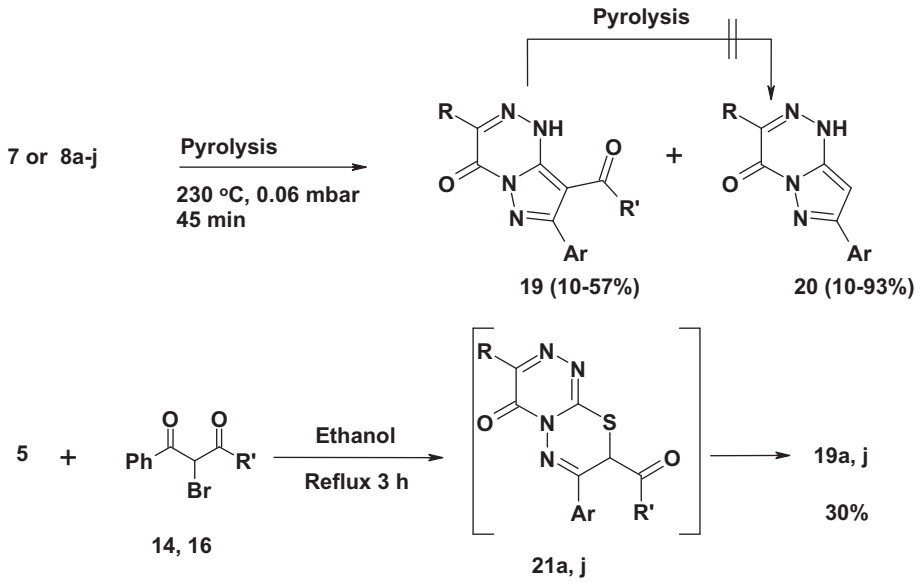
4.3.5. 3-Mercapto-4-p-methoxybenzylideneamino-6-phenyl-1,2,4-triazin-5(4H)-one ***6e***. Reaction time: 72 h. Yellow crystals, yield 2.54 g (75%), mp 245–246 °C. MS: *m*/*z*=338 (M^+). IR: 3174, 3118, 3036, 2970, 1699, 1596, 1569, 1509, 1444, 1406, 1316, 1268, 1167, 1024, 838, 760. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.09 (s, 1H), 8.60 (s, 1H, CH), 7.96–7.93 (m, 2H), 7.89 (d, 2H, *J* 8.8), 7.50–7.47 (m, 3H), 7.14 (d, 2H, *J* 8.8), 3.88 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.7, 170.6, 163.4, 149.6, 144.9, 132.3, 131.2, 130.3, 128.4 (2C), 124.5, 114.9, 55.8. Anal. Calcd for $C_{17}H_{14}N_4O_2S$: C 60.34; H 4.17; N 16.56; S 9.48. Found: C 60.43; H 4.13; N 16.30; S 9.42.

4.3.6. 4-p-Chlorobenzylideneamino-3-mercapto-6-phenyl-1,2,4-triazin-5(4H)-one ***6g***. Reaction time: 72 h. Colorless crystals, yield 2.1 g (60%), mp 240–241 °C. MS: *m*/*z*=344 (M+2, 11%), 342 (M^+, 31%). IR: 3158, 3097, 3022, 2963, 1695, 1562, 1497, 1405, 1307, 1267, 1184, 1090, 833, 771, 691. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.20 (s, 1H), 8.76 (s, 1H, CH), 7.97 (d, 2H, *J* 8.4), 7.95–7.93 (m, 2H), 7.68 (d, 2H, *J* 8.4), 7.50–7.46 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.3, 170.2, 149.2, 144.8, 138.0, 132.1, 130.7, 130.6, 130.1, 129.5, 128.3, 128.2. Anal. Calcd for $C_{16}H_{11}ClN_4OS$: C 56.06; H 3.23; N 16.34; S 9.35. Found: C 55.88; H 3.11; N 16.10; S 9.15.

4.3.7. 3-Mercapto-4-p-methoxybenzylideneamino-6-methyl-1,2,4-triazin-5(4H)-one ***6i***. Reaction time: 4 h. Colorless crystals, yield 2.34 g (85%), mp 196 °C (lit.[14] mp 196 °C). MS: *m*/*z*=276 (M^+). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.64 (s, 1H), 8.35 (s, 1H, CH), 7.88 (d, 2H, *J* 8.8), 6.99 (d, 2H, *J* 8.8), 3.89 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 171.5, 163.8, 150.1, 147.4, 131.5, 124.0, 114.5, 55.6, 17.1.

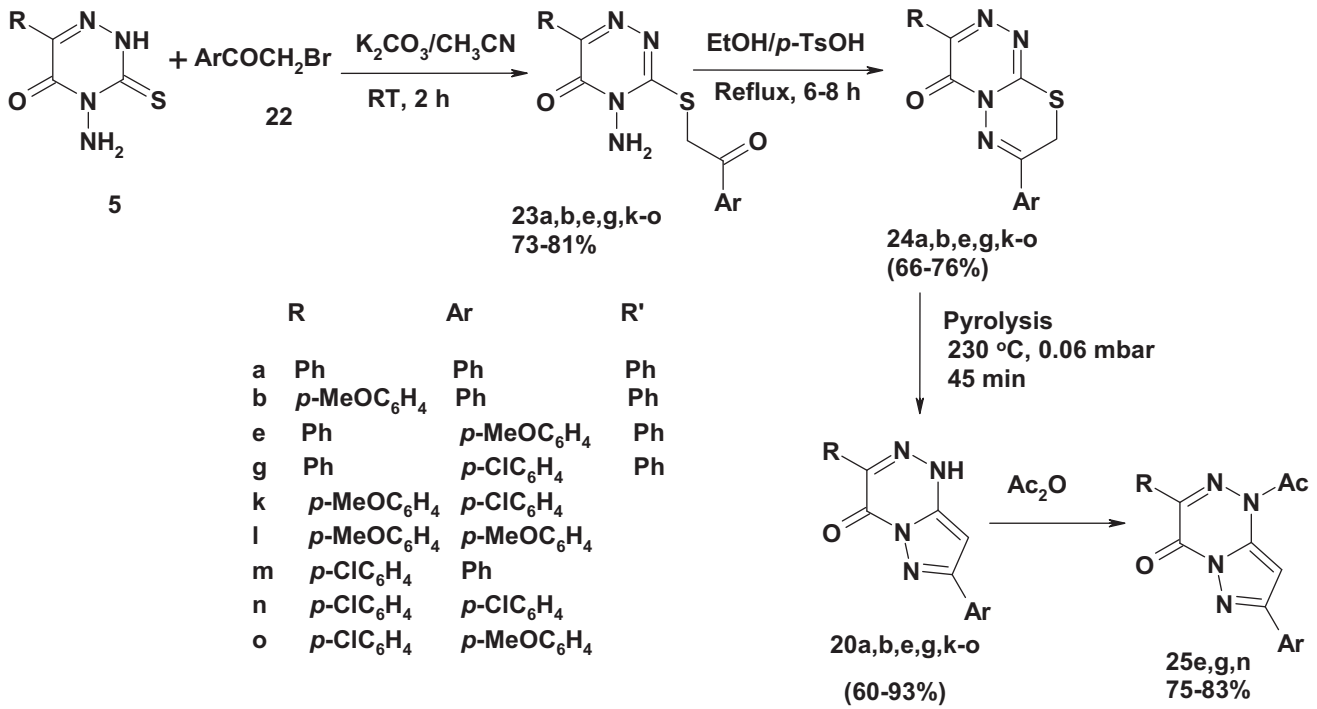
4.4. General procedure for synthesis of compounds 7c,i

To a mixture of each of **6c**,**i** (1 mmol) and triethylamine (0.14 mL, 1 mmol), in absolute ethanol (10 mL) was added the appropriate ω-bromoacetophenone (0.2 g, 1 mmol). The mixture was stirred at room temperature for 30 min. The solvent was then removed in vacou and the remaining mixture was then washed with water and the precipitate formed was collected and crystallized from ethanol/$CHCl_3$.



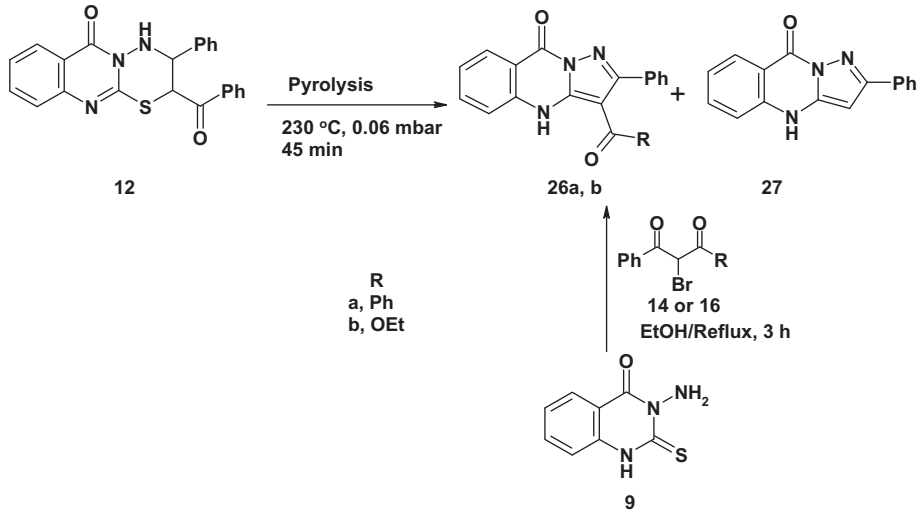
	R	Ar	R'
a	Ph	Ph	Ph
b	*p*-$MeOC_6H_4$	Ph	Ph
c	CH_3	Ph	Ph
e	Ph	*p*-$MeOC_6H_4$	Ph
f	Ph	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$
g	Ph	*p*-ClC_6H_4	Ph
h	Ph	*p*-ClC_6H_4	*p*-$MeOC_6H_4$
i	CH_3	*p*-$MeOC_6H_4$	Ph
j	Ph	Ph	OEt

Scheme 6. Pyrolysis of [1,2,4]triazino[3,4-*b*]thiadiazines **8a**–**j**.

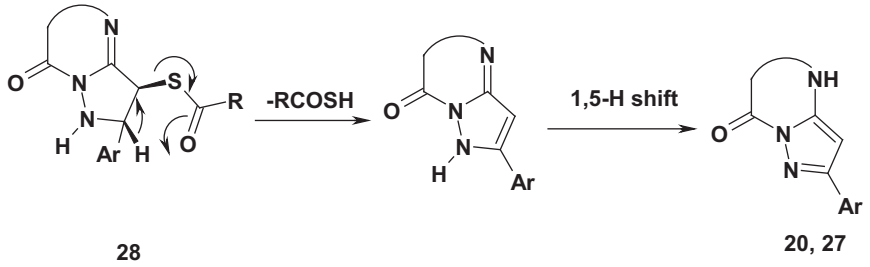


	R	Ar	R'
a	Ph	Ph	Ph
b	*p*-$MeOC_6H_4$	Ph	Ph
e	Ph	*p*-$MeOC_6H_4$	Ph
g	Ph	*p*-ClC_6H_4	Ph
k	*p*-$MeOC_6H_4$	*p*-ClC_6H_4	
l	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	
m	*p*-ClC_6H_4	Ph	
n	*p*-ClC_6H_4	*p*-ClC_6H_4	
o	*p*-ClC_6H_4	*p*-$MeOC_6H_4$	

Scheme 7. Synthesis and pyrolysis of [1,2,4]triazino[3,4-*b*]thiadiazines **24**.



Scheme 8. Pyrolysis of thiadiazino[3,2-*b*]quinazoline **12**.



Scheme 9. Possible mechanism for the formation of deacetylation products **20**, **27**.

4.4.1. 3-Benzoylmethylsulfanyl-4-benzylideneamino-6-methyl-1,2,4-triazin-5(4H)-one ***7c***. Colorless crystals, yield 0.29 g (80%), mp 178–180 °C. MS: *m*/*z*=364 (M^+). IR: 3061, 2918, 1682, 1471, 1292, 1200, 751, 731, 688. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.49 (s, 1H, CH), 8.08 (d, 2H, *J* 7.6), 7.90 (d, 2H, *J* 7.6), 7.62 (t, 1H, *J* 7.6), 7.59 (t, 1H, *J* 7.6), 7.51 (t, 4H, *J* 7.6), 4.79 (s, 2H, CH_2), 2.49 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.1, 165.1, 157.9, 156.6, 150.6, 135.8, 133.8, 133.3, 132.3, 129.4, 129.1, 128.8, 128.6, 39.9, 17.6. HRMS=364.0988 ($C_{19}H_{16}N_4O_2S$ requires 364.0988).

4.4.2. 3-Benzoylmethylsulfanyl-4-p-methoxybenzylideneamino-6-methyl-1,2,4-triazin-5(4H)-one ***7i***. Yellow crystals, yield 0.32 g (80%), mp 202–203 °C. MS: *m*/*z*=394 (M^+). IR: 3079, 3046, 2972, 2931, 2916, 2886, 1685, 1667, 1599, 1573, 1478, 1422, 1378, 1307, 1262, 1173, 1130, 954, 841, 817, 752, 692. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.48 (s, 1H, CH), 8.07 (d, 2H, *J* 8.8), 7.91 (d, 2H, *J* 7.6), 7.60 (t, 1H, *J* 7.6), 7.52 (t, 2H, *J* 7.6), 6.98 (d, 2H, *J* 8.8), 4.78 (s, 2H, CH_2), 3.91 (s, 3H, OCH_3), 2.50 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.6, 165.2, 164.1, 158.1, 156.5, 150.6, 133.2, 132.2, 130.9, 129.4, 129.1, 128.7, 114.0, 55.6, 39.8, 17.6. HRMS=394.1094 ($C_{20}H_{18}N_4O_3S$ requires 394.1094).

4.5. General procedure for synthesis of compounds 7e,j, 8a–d,f–i,k, 11

To a mixture of each of **6a**–**k**, 10 (1 mmol) and anhydrous potassium carbonate (2 mmol), in dry acetonitrile (10 mL) was added the appropriate α-haloketones (1 mmol). The mixture was stirred at room temperature for 2 h. The mixture was then diluted with water and the precipitate formed was collected and crystallized from ethanol/$CHCl_3$.

4.5.1. 3-Benzoylmethylsulfanyl-4-p-methoxybenzylideneamino-6-phenyl-1,2,4-triazin-5(4H)-one ***7e***. Yellow crystals, yield 0.45 g (99%), mp 211–212 °C. MS: *m*/*z*=456 (M^+). IR: 2957, 2911, 1678, 1596, 1564, 1492, 1446, 1423, 1324, 1304, 1262, 1201, 1167, 1020, 982, 839, 785, 688, 641, 530. ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.27 (s, 1H, CH), 8.20 (d, 2H, *J* 7.2), 8.11 (d, 2H, *J* 7.8), 7.90 (d, 2H, *J* 8.4), 7.65 (t, 1H, *J* 7.2), 7.53 (t, 2H, *J* 7.2), 7.48–7.47 (m, 3H), 7.03 (d, 2H, *J* 7.8), 4.92 (s, 2H, CH_2), 3.92 (s, 3H, OCH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ 193.0, 166.2, 164.0, 158.1, 153.5, 149.8, 135.6, 133.9, 132.8, 131.5, 130.5, 128.9, 128.8, 128.6, 128.2, 124.6, 114.6, 55.6, 40.2. HRMS=456.1250 ($C_{25}H_{20}N_4O_3S$ requires 456.1250).

4.5.2. 4-Benzylideneamino-3-ethoxycarbonylmethylsulfanyl-6-phenyl-1,2,4-triazin-5(4H)-one ***7j***. Yellow crystals from EtOH, yield 0.32 g (80%), mp 182–183 °C. MS: *m*/*z*=394 (M^+). IR: 3070, 2981, 2929, 1743, 1684, 1502, 1455, 1431, 1310, 1175, 1028, 689. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.49 (s, 1H, CH), 8.20–8.17 (m, 2H), 7.90 (dd, 2H, *J* 8.0, 1.6), 7.60 (t, 1H, *J* 7.6), 7.52 (d, 2H, *J* 8.0), 7.50–7.45 (m, 3H), 4.27 (q, 2H, *J* 7.2), 4.10 (s, 2H, CH_2), 1.32 (t, 3H, *J* 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 165.8, 157.6, 153.9, 149.9, 133.4, 132.6, 132.2, 130.6, 129.4, 129.1, 128.9, 128.3, 62.2, 33.9, 14.2. HRMS=394.1094 ($C_{20}H_{18}N_4O_3S$ requires 394.1094).

4.5.3. trans-8-Benzoyl-3,7-diphenyl-7,8-dihydro-6H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***8a***. Pale yellow crystals, yield 0.3 g (70%), mp 203–204 °C. MS: *m*/*z*=426 (M^+). IR: 3209, 3066, 1676, 1515, 1450, 1323, 1300, 1182, 1116, 976, 768, 691. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.31 (dd, 2H, *J* 7.2, 1.8), 7.85 (d, 2H, *J* 7.2), 7.64 (t, 1H, *J* 7.2), 7.56–7.47 (m, 8H), 7.43–7.39 (m, 3H), 5.56 (d, 1H, *J* 8.8), 4.86 (d, 1H, *J* 8.8). ^{13}C NMR (150 MHz, $CDCl_3$): δ 191.3, 151.4, 150.9, 148.0, 135.7,

134.7, 134.3, 132.7, 130.7, 129.9, 129.4, 129.2, 128.7, 128.6, 128.4, 127.9, 61.8, 52.2. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.21 (s, 1H, NH, exchangeable), 8.14–8.12 (m, 2H), 8.07 (d, 2H, *J* 7.2), 7.73 (t, 1H, *J* 7.2), 7.60 (t, 4H, *J* 8.0), 7.50–7.49 (m, 3H), 7.40 (t, 2H, *J* 7.2), 7.34 (t, 1H, *J* 7.2), 6.30 (d, 1H, *J* 5.4), 5.21 (br d, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 193.4, 152.1, 150.0, 148.0, 136.4, 134.8, 134.4, 133.2, 131.6, 130.5, 129.6, 129.2, 129.1, 128.6, 128.5, 127.7, 58.4, 51.6. HRMS=426.1144 ($C_{24}H_{18}N_4O_2S$ requires 426.1144).

4.5.4. trans-8-Benzoyl-3-p-methoxyphenyl-7-phenyl-7,8-dihydro-6H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***8b***. Colorless crystals, yield 0.14 g (31%), mp 239–240 °C. MS: *m*/*z*=456 (M^+). IR: 3208, 2916, 2846, 1671, 1598, 1509, 1454, 1325, 1300, 1261, 1222, 1178, 1109, 1022, 972, 849, 551. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, 2H, *J* 8.8), 7.84 (d, 2H, *J* 8.0), 7.62 (t, 1H, *J* 7.6), 7.54 (dd, 2H, *J* 8.0, 2.0), 7.49–7.47 (m, 3H), 7.42–7.37 (m, 3H), 6.98 (d, 2H, *J* 8.8), 5.52 (d, 1H, *J* 8.8), 4.83 (d, 1H, *J* 8.8), 3.87 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 161.7, 150.4, 150.3, 148.0, 135.8, 134.7, 134.3, 130.4, 129.8, 129.4, 129.2, 128.6, 127.9, 125.2, 113.8, 61.9, 55.4, 52.2. HRMS=456.1250 ($C_{25}H_{20}N_4O_3S$ requires 456.1250).

4.5.5. trans-8-Benzoyl-3-methyl-7-phenyl-7,8-dihydro-6H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***8c***. Pale yellow crystals, yield 0.19 g (51%), mp 154–155 °C. MS: *m*/*z*=364 (M^+). IR: 3251, 1669, 1594, 1529, 1463, 1378, 1303, 1214, 1172, 1111, 967, 807, 739, 692. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, 2H, *J* 8.8), 7.61 (t, 1H, *J* 7.2), 7.53–7.50 (m, 4H), 7.40–7.37 (m, 3H), 7.21 (s, 1H), 5.48 (d, 1H, *J* 8.8), 4.79 (d, 1H, *J* 8.8), 2.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 154.2, 151.2, 148.7, 135.8, 134.6, 134.3, 129.8, 129.4, 129.2, 128.6, 127.9, 61.7, 52.0, 17.7. HRMS=364.0989 ($C_{19}H_{16}N_4O_2S$ requires 364.0988).

4.5.6. trans-8-Benzoyl-3-benzyl-7-p-methoxyphenyl-7,8-dihydro-6H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***8d***. Colorless crystals, yield 0.26 g (58%), mp 156–157 °C. MS: *m*/*z*=470 (M^+). IR: 3241, 3060, 1675, 1608, 1514, 1455, 1309, 1252, 1219, 1176, 1116, 1028, 977, 835, 816, 721, 689. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, 2H, *J* 7.6), 7.58 (t, 1H, *J* 7.6), 7.46–7.36 (m, 6H), 7.29 (t, 2H, *J* 7.2), 7.24–7.22 (m, 1H), 7.13 (s, 1H), 6.83 (d, 2H, *J* 8.8), 5.44 (d, 1H, *J* 8.8), 4.67 (d, 1H, *J* 8.8), 4.16 (s, 2H), 3.74 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 160.4, 155.3, 151.7, 148.1, 136.1, 134.6, 134.3, 129.4, 129.2, 129.1, 128.6, 128.5, 127.2, 126.9, 114.6, 60.9, 55.3, 51.9, 37.7. HRMS=470.1407 ($C_{26}H_{22}N_4O_3S$ requires 470.1407).

4.5.7. trans-8-p-Methoxybenzoyl-7-p-methoxyphenyl-3-phenyl-7,8-dihydro-6H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***8f***. Colorless crystals, yield 0.46 g (94%), mp 242–243 °C. MS: *m*/*z*=486 (M^+). IR: 3237, 2933, 2837, 1668, 1598, 1513, 1322, 1259, 1173, 913, 744. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.32–8.30 (m, 2H), 7.84 (d, 2H, *J* 9.0), 7.50–7.44 (m, 6H), 6.95 (d, 2H, *J* 9.0), 6.91 (d, 2H, *J* 9.0), 5.48 (d, 1H, *J* 9.0), 4.78 (d, 1H, *J* 9.0), 3.89 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ 189.8, 164.8, 160.5, 151.7, 150.7, 147.9, 132.8, 131.1, 130.6, 129.2, 128.6, 128.4, 127.5, 127.4, 114.7, 114.4, 61.2, 55.7, 55.3, 51.8. HRMS=486.1356 ($C_{26}H_{22}N_4O_4S$ requires 486.1356).

4.5.8. trans-8-Benzoyl-7-p-chlorophenyl-3-phenyl-7,8-dihydro-6H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***8g***. Yellow crystals, yield 0.42 g (92%), mp 225–226 °C. MS: *m*/*z*=460 (M^+, 100%), 462 (M+2, 42%). IR: 3241, 1693, 1660, 1595, 1508, 1464, 1328, 1297, 1252, 1182, 1155, 1094, 1063, 932, 789, 767, 690, 662. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32–8.30 (m, 2H), 7.86 (d, 2H, *J* 7.6), 7.67 (t, 1H, *J* 7.6), 7.54–7.50 (m, 8H), 7.39 (d, 2H, *J* 7.2), 5.48 (d, 1H, *J* 9.0), 4.85 (d, 1H, *J* 9.0). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.1, 151.1, 151.0, 147.9, 136.0, 134.9, 134.2, 134.1, 132.6, 130.7, 129.7, 129.32, 129.3, 128.7, 128.6, 128.4, 61.0, 52.1. HRMS=460.0754 ($C_{24}H_{17}{}^{35}ClN_4O_2S$ requires 460.0755).

4.5.9. trans-7-p-Chlorophenyl-8-p-methoxybenzoyl-3-phenyl-7,8-dihydro-6H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***8h***. Colorless crystals, yield 0.4 g (82%), mp 255–256 °C. MS: *m*/*z*=490 (M^+, 100%), 492 (M+2, 41%). IR: 3232, 1663, 1598, 1571, 1513, 1463, 1418, 1319, 1296, 1261, 1223, 1171, 1111, 1013, 978, 827, 729. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.31–8.30 (m, 2H), 7.84 (d, 2H, *J* 7.2), 7.51–7.48 (m, 6H), 7.39 (d, 2H, *J* 8.4), 6.97 (d, 2H, *J* 9.0), 5.43 (d, 1H, *J* 9.0), 4.83 (d, 1H, *J* 9.0), 3.90 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 189.4, 165.0, 151.3, 150.8, 147.9, 135.9, 134.2, 132.6, 131.1, 130.7, 129.6, 129.3, 128.7, 128.4, 127.1, 114.5, 61.0, 55.7, 51.8. HRMS=490.0860 ($C_{25}H_{19}{}^{35}ClN_4O_3S$ requires 490.0860).

4.5.10. trans-8-Benzoyl-7-p-methoxyphenyl-3-methyl-7,8-dihydro-6H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***8i***. Pale yellow crystals, yield 0.21 g (54%), mp 201–202 °C. MS: *m*/*z*=394 (M^+). IR: 3247, 3062, 3004, 2959, 2838, 1674, 1608, 1514, 1466, 1377, 1306, 1254, 1213, 1180, 1113, 1031, 910, 837, 814, 731. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.83 (dd, 2H, *J* 8.4, 1.2), 7.63 (tt, 1H, *J* 7.2, 1.2), 7.49 (t, 2H, *J* 7.8), 7.44 (d, 2H, *J* 9.0), 7.16 (s, 1H, NH), 6.91 (d, 2H, *J* 9.0), 5.46 (d, 1H, *J* 9.0), 4.75 (d, 1H, *J* 9.0), 3.68 (s, 3H), 2.65 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 191.6, 160.5, 154.1, 151.2, 148.7, 134.6, 134.4, 129.2, 129.15, 128.6, 127.5, 114.7, 61.2, 55.3, 51.9, 17.7. HRMS=394.1094 ($C_{20}H_{18}N_4O_3S$ requires 394.1094).

4.5.11. trans-7-p-Chlorophenyl-4-oxo-3-phenyl-7,8-dihydro-6H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazine-8-carboxylic acid ethyl ester ***8k***. Colorless crystals from EtOH, yield 0.086 g (20%), mp 227 °C. MS: *m*/*z*=428 (M^+, 100%), 430 (M+2, 35%). IR: 3232, 2971, 1722, 1677, 1516, 1490, 1470, 1452, 1319, 1187, 1114, 1090, 1034, 864, 689. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28–8.25 (m, 2H), 7.48–7.43 (m, 8H), 4.59 (d, 1H, *J* 9.2), 4.53 (d, 1H, *J* 9.2), 4.23–4.10 (m, 2H), 1.22 (t, 3H, *J* 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 151.3, 150.8, 147.8, 136.2, 133.4, 132.6, 130.7, 129.7, 129.2, 128.6, 128.4, 62.9, 61.3, 51.3, 13.9. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.44 (d, 1H, *J* 2.4, exchangeable), 8.12–8.09 (m, 2H), 7.52–7.46 (m, 7H), 5.30 (d, 1H, *J* 5.2), 5.15 (dd, 1H, *J* 5.2, 2.4), 4.19 (q, 2H, *J* 7.2), 1.19 (t, 3H, *J* 7.2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.0, 151.6, 149.7, 147.7, 134.6, 133.4, 132.9, 130.1, 129.3, 128.8, 128.2, 128.1, 62.3, 57.1, 49.5, 13.9. HRMS=428.0704 ($C_{20}H_{17}{}^{35}ClN_4O_3S$ requires 428.0704). Anal. Calcd for $C_{20}H_{17}ClN_4O_3S$: C 56.01; H 4.00; N 13.06; S 7.48. Found: C 56.30; H 4.30; N 12.89; S 7.59.

4.5.12. 2-Benzoylmethylsulfanyl-3-benzylideneaminoquinazolin-4(3H)-one ***11***. Colorless crystals from EtOH, yield 0.36 g (90%), mp 181–182 °C. MS: *m*/*z*=399 (M^+). IR: 3060, 2921, 1677, 1605, 1580, 1551, 1469, 1452, 1318, 1291, 1273, 1204, 768, 755, 690. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 8.21 (dd, 1H, *J* 8.0, 1.2), 8.16–8.13 (m, 2H), 7.93 (dd, 2H, *J* 8.4, 1.6), 7.67–7.48 (m, 7H), 7.36 (dt, 1H, *J* 8.0, 1.2), 7.19 (dd, 1H, *J* 8.4, 0.8), 4.62 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.5, 162.5, 159.4, 156.9, 146.1, 136.8, 134.5, 133.5, 133.2, 132.3, 129.0, 128.9, 128.7, 128.5, 127.3, 126.0, 125.8, 120.3, 38.8. HRMS=399.1035 ($C_{23}H_{17}N_3O_2S$ requires 399.1035).

4.6. Cyclization of 7e,j and 11: general procedure

A mixture of each of compounds **7e**, **j**, **11** (1 mmol), triethylamine (1.5 mmol) in ethanol (5 mL) was heated under reflux for 0.5 h. The solvent was then removed in vacuo and the remaining residue was crystallized from ethanol to give the corresponding products **8e,j** and **12**, respectively.

4.6.1. trans-8-Benzoyl-7-p-methoxyphenyl-3-phenyl-7,8-dihydro-6H-[1,2,4]tiazino[3,4-b][1,3,4]thiadiazin-4-one ***8e***. Yellow crystals,

yield 0.23 g (50%), mp 196 °C. MS: m/z=456 (M^+). IR: 3232, 2966, 2931, 2910, 1687, 1661, 1514, 1465, 1446, 1326, 1299, 1259, 1191, 1035, 931, 692. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32–8.30 (m, 2H), 7.87 (d, 2H, J 7.2), 7.65 (t, 1H, J 7.2), 7.53–7.46 (m, 8H), 6.92 (d, 2H, J 8.8), 5.54 (d, 1H, J 8.8), 4.80 (d, 1H, J 8.8), 3.81 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 160.5, 151.4, 150.8, 147.9, 134.7, 134.4, 132.7, 130.6, 129.2, 129.1, 128.7, 128.6, 128.4, 127.3, 114.7, 61.2, 55.3, 52.1. HRMS=456.1250 ($C_{25}H_{20}N_4O_3S$ requires 456.1250).

4.6.2. trans-7-Phenyl-4-oxo-3-phenyl-7,8-dihydro-6H-[1,2,4]triazino [3,4-b][1,3,4]thiadiazine-8-carboxylic acid ethyl ester ***8j***. Colorless crystals, yield 0.19 g (50%), mp 132 °C. MS: m/z=394 (M^+). IR: 3229, 3063, 2976, 1730, 1680, 1468, 1451, 1321, 1305, 1180, 1115, 751, 697. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31–8.28 (m, 2H), 7.50–7.48 (m, 9H), 4.68 (d, 1H, J 9.2), 4.56 (d, 1H, J 9.2), 4.24–4.18 (m, 2H), 1.22 (t, 3H, J 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 151.5, 150.6, 147.8, 134.8, 132.6, 130.6, 130.1, 129.4, 128.6, 128.3, 127.8, 62.7, 62.0, 51.5, 13.8. HRMS=394.1094 ($C_{20}H_{18}N_4O_3S$ requires 394.1094).

4.6.3. trans-2-Benzoyl-3-phenyl-3,4-dihydro-2H-[1,3,4]thiadiazino [2,3-b]quinazolin-10-one ***12***. Colorless crystals, yield 0.28 g (71%), mp 210 °C. MS: m/z=399 (M^+). IR: 3426, 3240, 1660, 1530, 1482, 1453, 1314, 1302, 1201, 1176, 1105, 770, 692. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, 1H, J 8.0), 7.82 (d, 2H, J 7.2), 7.74 (dt, 1H, J 8.4, 1.6), 7.62–7.53 (m, 4H), 7.48–7.44 (m, 3H), 7.42–7.36 (m, 4H), 5.52 (d, 1H, J 8.9), 4.86 (d, 1H, J 8.9). ^{13}C NMR (150 MHz, $CDCl_3$): δ 192.2, 157.6, 149.0, 146.6, 136.9, 134.7, 134.4, 134.3, 129.5, 129.3, 129.0, 128.6, 127.8, 126.8, 126.7, 126.3, 118.9, 62.7, 53.1. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.07 (d, 1H, J 7.6), 8.03 (d, 2H, J 7.2), 7.79 (t, 1H, J 7.2), 7.72 (t, 1H, J 7.2), 7.65–7.56 (m, 6H), 7.48 (t, 1H, J 7.2), 7.39 (t, 2H, J 8.0), 7.33 (t, 1H, J 7.2), 6.20 (d, 1H, J 6.0), 4.09 (dd, 1H, J 6.0, 2.8). ^{13}C NMR (100 MHz, DMSO-d_6): δ 193.5, 156.9, 149.9, 145.9, 136.8, 134.5, 134.4, 134.3, 129.2, 128.8, 128.7, 128.6, 127.8, 126.2, 126.1, 126.07, 118.5, 59.5, 51.8. HRMS=399.1035 ($C_{23}H_{17}N_3O_2S$ requires 399.1035).

4.7. Procedures for synthesis of 13, 15, 18, 19, 20, 26, and 27: general procedure

(A) The substrate (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 purified using column chromatograph.

(B) A mixture of each of compound **1a**,**c**,**h**, **9**, **5a** (1 mmol) and each of compounds **14**, **16** (1 mmol) in EtOH (10 mL) was refluxed for 3 h. The solvent was removed in vacuo and the products were purified by column chromatography.

4.7.1. 3,6-Diphenyl-7-ethoxycarbonyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***13a***. Colorless crystals from EtOH, yield 0.03 g (10%, using general procedure A, from **15a**), 0.12 g (36%, using general procedure A, from **4f**), 0.03 g (10%, using general procedure **B**, from **1a** and **14**), R_f=0.6 (petroleum ether/EtOAc 2:1). MS: m/z=332 (M^+). IR: 2922, 2852, 1709, 1654, 1616, 1459, 1178, 1093, 908, 734, 697. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.41 (s, 1H), 8.51 (dd, 2H, J 8.0, 2.0), 7.98–7.95 (m, 2H), 7.58–7.45 (m, 6H), 4.33 (q, 2H, J 7.2), 1.35 (t, 3H, J 7.2). ^{13}C NMR (150 MHz, $CDCl_3$): δ 162.6, 161.2, 149.8, 140.7, 132.4, 130.8, 129.7, 129.3, 129.0, 127.9, 126.9, 125.1, 87.3, 60.2, 14.6. HRMS=332.1266 ($C_{19}H_{16}N_4O_2$ requires 332.1267).

4.7.2. 3-p-Chlorophenyl-7-Ethoxycarbonyl-6-phenyl-1H-pyrazolo [5,1-c][1,2,4]triazole ***13c***. Red crystals from EtOH, yield 0.16 g (44%, using general procedure A, from **15c**), 0.037 g (10%, using general procedure A, from **4g**), 0.04 g (11%, using general procedure **B**, from **1c** and **14**), mp 259 °C. LCMS: m/z=369 (M+3), 367 (M+1). IR: 3226, 3179, 1640, 1619, 1441, 1326, 1176, 1087, 1011, 693. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.64 (s, 1H), 8.48 (d, 2H, J 8.8), 7.98–7.96 (m, 2H), 7.55 (d, 2H, J 8.4), 7.50–7.49 (m, 3H), 4.36 (q, 2H, J 7.2), 1.36 (t, 3H, J 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 161.3, 149.7, 139.8, 136.9, 132.2, 129.7, 129.4, 129.3, 128.1, 127.9, 123.5, 87.5, 60.3, 14.5. HRMS=366.1266 ($C_{19}H_{15}{}^{35}ClN_4O_2$ requires 366.1267).

4.7.3. 7-Ethoxycarbonyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***13h***. Colorless oil from column chromatography, yield 0.06 g (25%, using general procedure A, from **15h**), 0.026 g (10%, using general procedure **B**, from **1h** and **14**), R_f=0.6 (petroleum ether/EtOAc 2:1). MS: m/z=257 (M^+). IR: 3018, 2926, 2854, 1710, 1616, 1462, 1216, 1189, 758. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.23 (s, 1H), 8.38 (s, 1H), 7.93–7.91 (m, 2H), 7.49–7.46 (m, 3H), 4.34 (q, 2H, J 7.2), 1.35 (t, 3H, J 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.5, 161.5, 148.6, 141.7, 132.1, 129.6, 129.4, 127.9, 87.4, 60.3, 14.5. HRMS=256.0954 ($C_{13}H_{12}N_4O_2$ requires 256.0954).

4.7.4. 3,6-Diphenyl-7-ethoxycarbonyl-7H-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazine ***15a***. Yellow crystals from EtOH, yield 0.16 g (45%, using general procedure B, from **1a** and **14**), mp 133–134 °C. R_f=0.3 (petroleum ether/EtOAc 1:1). MS: m/z=364 (M^+). IR: 3063, 2981, 2937, 1735, 1462, 1369, 1308, 1278, 1229, 1179, 1021, 758, 692. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.10–8.09 (m, 2H), 7.91 (dd, 2H, J 7.2, 1.2), 7.58 (tt, 1H, J 7.8, 1.2), 7.54 (d, 2H, J 7.8), 7.53–7.51 (m, 3H), 4.97 (s, 1H), 4.21–4.13 (m, 2H), 1.16 (t, 3H, J 7.2). ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.7, 152.6, 151.1, 138.5, 133.5, 132.2, 130.4, 129.3, 128.6, 128.5, 127.3, 125.9, 63.6, 38.3, 13.8. MS: 364. HRMS=364.0988 ($C_{19}H_{16}N_4O_2S$ requires 364.0988).

4.7.5. 3-p-Chlorophenyl-7-ethoxycarbonyl-6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazine ***15c***. Colorless crystals, yield 0.16 g (40%, using general procedure B, from **1c** and **14**), mp 215 °C. MS: m/z=398 (M^+, 100%), 400 (M+2, 42%). IR: 3064, 2982, 1735, 1453, 1275, 1230, 1178, 1092, 1014, 834, 754. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, 2H, J 8.2), 7.93 (d, 2H, J 7.6), 7.63 (t, 1H, J 7.6), 7.57 (t, 2H, J 7.6), 7.51 (d, 2H, J 8.2), 5.00 (s, 1H), 4.24–4.16 (m, 2H), 1.19 (t, 3H, J 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 151.5, 151.4, 138.7, 136.6, 133.3, 132.4, 129.6, 129.3, 128.9, 127.3, 124.2, 63.6, 38.1, 13.7. HRMS=398.1196 ($C_{19}H_{15}{}^{35}ClN_4O_2S$ requires 398.1196).

4.7.6. 7-Ethoxycarbonyl-6-phenyl-7H-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazine ***15h***. Colorless oil, yield 0.14 g (48%, using general procedure B, from **1h** and **14**), R_f=0.2 (petroleum ether/EtOAc 1:1). MS: m/z=288 (M^+). IR: 3132, 3063, 2986, 2934, 1736, 1480, 1450, 1365, 1296, 1268, 1218, 1179, 1021, 755, 690. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (s, 1H), 7.89 (dd, 2H, J 6.8, 1.6), 7.61–7.51 (m, 3H), 4.92 (s, 1H), 4.23–4.11 (m, 2H), 1.17 (t, 3H, J 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 151.2, 142.5, 137.3, 133.2, 132.4, 129.3, 127.2, 63.6, 39.4, 13.7. HRMS=288.0674 ($C_{13}H_{12}N_4O_2S$ requires 288.0675).

4.7.7. 7-Benzoyl-6-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazole ***18***. Colorless crystals from EtOH, yield 0.03 g (12%, using general procedure A, from **17**), mp 195 °C. R_f=0.2 (petroleum ether/EtOAc 2:1). MS: m/z=288.1 (M^+). IR: 3143, 3122, 3063, 2925, 2876, 2857, 1614, 1591, 1567, 1459, 1432, 1205, 979, 926, 739, 697. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.80 (s, 1H), 8.43 (s, 1H), 7.53 (dd, 2H, J 8.0, 1.2), 7.35–7.30 (m, 3H), 7.23 (tt, 1H, J 7.2, 1.6), 7.15 (2t overlapped, 4H, J 7.2, 7.6). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.4, 161.4, 149.3, 138.0, 132.3, 131.4, 129.4, 129.1, 128.8, 128.6, 127.7, 127.6, 97.9. HRMS=288.1006 ($C_{17}H_{12}N_4O$ requires 288.1005).

4.7.8. 8-Benzoyl-3,7-diphenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***19a***. Pale yellow crystals, yield 31% (using general procedure A, from **8a**), 30% (using general procedure B, from **5a** and **16**), mp 278–279 °C. R_f=0.7 (petroleum ether/EtOAc/DCM 2:1:1). MS: m/z=392 (M^+). IR: 2918, 2849, 1705, 1582, 1501, 1445, 1422, 1262, 1198, 1155, 1017, 930, 905, 769, 740, 691. ^{1}H NMR (400 MHz, $CDCl_3$):

δ 12.14 (s, 1H, NH), 8.21–8.18 (m, 2H), 7.53–7.52 (m, 3H), 7.44 (dd, 2H, *J* 8.4, 1.2), 7.37–7.32 (m, 3H), 7.25 (t, 1H, *J* 7.2), 7.16–7.11 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 157.1, 148.1, 146.9, 141.9, 137.4, 132.2, 131.8, 130.7, 130.4, 129.9, 129.5, 128.9, 128.8, 128.6, 128.0, 127.9, 102.5. HRMS=392.1267 ($C_{24}H_{16}N_4O_2$ requires 392.1267).

4.7.9. 8-Benzoyl-3-methyl-7-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***19c***. Colorless crystals, yield 17% (using general procedure A, from **8c**), mp 238 °C. R_f=0.4 (petroleum ether/EtOAc/DCM 2:1:1). MS: *m*/*z*=330 (M^+). IR: 3239, 3061, 3008, 1709, 1600, 1550, 1486, 1449, 1425, 1324, 1201, 1152, 927, 743, 697. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.75 (s, 1H, NH), 7.41 (dd, 2H, *J* 8.8, 1.6), 7.35–7.32 (m, 3H), 7.26 (t, 1H, *J* 7.2), 7.16–7.11 (m, 4H), 2.6 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.4, 157.1, 148.9, 147.6, 143.8, 137.4, 132.1, 130.7, 129.9, 129.4, 128.9, 128.0, 127.8, 102.1, 16.9. HRMS=330.1114 ($C_{19}H_{14}N_4O_2$ requires 330.1111).

4.7.10. 8-Benzoyl-7-p-methoxyphenyl-3-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***19e***. Yellow crystals, yield 51% (using general procedure A, from 8e), mp 251–252 °C. R_f=0.5 (petroleum ether/EtOAc/DCM 2:1:1). MS: *m*/*z*=422 (M^+). IR: 3199, 3058, 2930, 2834, 1710, 1679, 1605, 1515, 1442, 1251, 1175, 1025, 932, 694. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.49 (s, 1H, NH), 8.20–8.18 (m, 2H), 7.52–7.50 (m, 5H), 7.36 (t, 1H, *J* 7.2), 7.30 (d, 2H, *J* 6.8), 7.16 (t, 2H, *J* 7.6), 6.64 (d, 2H, *J* 8.8), 3.75 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.5, 160.6, 156.8, 148.1, 146.9, 141.7, 137.3, 132.3, 131.9, 131.4, 130.3, 129.2, 128.8, 128.5, 127.9, 123.0, 113.5, 102.3, 55.3. HRMS=422.1373 ($C_{25}H_{18}N_4O_3$ requires 422.1373).

4.7.11. 8-p-Methoxybenzoyl-7-p-methoxyphenyl-3-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***19f***. Yellow crystals, yield 57% (using general procedure A, from **8f**), mp 264–265 °C. R_f=0.4 (petroleum ether/EtOAc/DCM 2:1:1). MS: *m*/*z*=452 (M^+). IR: 3223, 1706, 1595, 1513, 1433, 1358, 1255, 1172, 1025, 779. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.13 (s, 1H, NH), 8.20–8.18 (m, 2H), 7.54–7.50 (m, 5H), 7.40 (d, 2H, *J* 8.8), 6.73 (d, 2H, *J* 8.8), 6.66 (d, 2H, *J* 8.8), 3.78 (s, 3H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.9, 163.1, 160.7, 156.6, 148.2, 146.8, 141.4, 132.0, 131.7, 131.5, 130.3, 129.9, 128.8, 128.5, 123.3, 113.6, 113.3, 102.3, 55.5, 55.3. HRMS=452.1479 ($C_{26}H_{20}N_4O_4$ requires 452.1479).

4.7.12. 8-Benzoyl-7-p-chlorophenyl-3-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***19g***. Yellow crystals, yield 34% (using general procedure A, from **8g**), mp 310–311 °C. R_f=0.7 (petroleum ether/EtOAc/DCM 2:1:1). MS: *m*/*z*=428 (M+2, 28%), 426 (M^+, 85%). IR: 3242, 1713, 1617, 1591, 1509, 1422, 1363, 1269, 1201, 933, 748, 693. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.08 (s, 1H, NH), 8.20–8.18 (m, 2H), 7.54–7.52 (m, 3H), 7.44 (d, 2H, *J* 7.2), 7.41 (t, 1H, *J* 7.6), 7.30 (d, 2H, *J* 8.4), 7.19 (t, 2H, *J* 8.0), 7.12 (d, 2H, *J* 8.4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.0, 155.7, 147.8, 146.7, 141.8, 137.1, 135.6, 132.3, 131.5, 131.0, 130.3, 129.1, 128.7, 128.6, 128.4, 128.1, 127.9, 102.2. HRMS=426.0878 ($C_{24}H_{15}{}^{35}ClN_4O_2$ requires 426.0878).

4.7.13. 7-p-Chlorophenyl-8-p-methoxybenzoyl-3-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***19h***. Yellow crystals, yield 30% (using general procedure A, from **8h**), mp 257 °C. R_f=0.5 (petroleum ether/EtOAc/DCM 2:1:1). MS: *m*/*z*=458 (M+2, 25%), 455 (M^+, 60%). IR: 2920, 2850, 1705, 1595, 1510, 1433, 1258, 1210, 1168, 907, 757, 733. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.28 (s, 1H, NH), 8.19–8.17 (m, 2H), 7.53–7.51 (m, 3H), 7.48 (d, 2H, *J* 8.8), 7.38 (d, 2H, *J* 8.4), 7.18 (d, 2H, *J* 8.4), 6.65 (d, 2H, *J* 8.8), 3.78 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.5, 163.3, 155.6, 148.1, 146.7, 141.4, 135.8, 131.8, 131.7, 131.2, 130.4, 129.6, 129.5, 128.8, 128.5, 128.4, 113.4, 102.4, 55.5. HRMS=456.0984 ($C_{25}H_{17}{}^{35}ClN_4O_3$ requires 456.0983).

4.7.14. 8-Benzoyl-7-p-methoxyphenyl-3-methyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***19i***. Colorless crystals, yield 10% (using general procedure A, from **8i**), mp 226–227 °C. R_f=0.2 (petroleum ether/EtOAc/DCM 2:1:1). MS: *m*/*z*=360 (M^+). IR: 3236, 3159, 3063, 3005, 1708, 1606, 1550, 1432, 1252, 1176, 1029, 928, 751. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.74 (s, 1H, NH), 7.42 (dd, 2H, *J* 8.4, 1.2), 7.35 (t, 1H, *J* 7.2), 7.27 (d, 2H, *J* 8.8), 7.15 (t, 2H, *J* 7.8), 6.64 (d, 2H, *J* 8.8), 3.75 (s, 3H), 2.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.5, 160.6, 156.8, 148.9, 147.6, 143.7, 137.5, 132.1, 131.4, 128.9, 127.9, 123.0, 113.5, 101.9, 55.3, 16.9. HRMS=360.1216 ($C_{20}H_{16}N_4O_3$ requires 360.1216).

4.7.15. 3,7-Diphenyl-8-ethoxycarbonyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***19j***. Colorless crystals from EtOH, yield 25% (using general procedure A, from **7j**), 30% (using general procedure B, from **5a**), mp 250–251 °C. MS: *m*/*z*=360 (M^+). IR: 3425, 3249, 2979, 2924, 1713, 1656, 1609, 1515, 1484, 1442, 1278, 1186, 1083, 769, 696. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.47 (s, 1H, NH), 8.16–8.13 (m, 2H), 7.89 (dd, 2H, *J* 7.2, 1.2), 7.51–7.47 (m, 6H), 4.40 (q, 2H, *J* 7.2), 1.34 (t, 3H, *J* 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 157.0, 148.1, 146.1, 140.7, 131.7, 130.5, 130.3, 130.1, 130.0, 128.8, 128.5, 127.8, 93.7, 61.3, 14.2. HRMS=360.1217 ($C_{20}H_{16}N_4O_3$ requires 360.1216).

4.7.16. 3,7-Diphenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20a***. Gray needles from DMF, yield 0.029 g (10%, using general procedure A, from **8a**), 0.058 g (20%, using general procedure A, from **7j**), 0.246 g (73%, using general procedure A, from **24a**), mp 398–400 °C. MS: *m*/*z*=288 (M^+, 100%), 259 (10%), 103 (40%). IR: 3031, 1549, 1421, 1378, 1347, 1165, 1069, 1023, 837, 745, 687. ^{1}H NMR (600 MHz, DMSO-d_6): δ 14.28 (br, 1H, NH), 8.09 (dd, 2H, *J* 8.4, 1.6), 8.04 (dd, 2H, *J* 8.4, 1.6), 7.53–7.45 (m, 6H), 6.85 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 155.2, 149.0, 144.0, 135.5, 133.4, 131.6, 129.6, 128.9, 128.7, 128.3, 128.1, 126.6, 84.4. Anal. calcd for $C_{17}H_{12}N_4O$: C 70.82; H 4.20; N 19.43. Found: C 70.80; H 4.16; N 19.40.

4.7.17. 3-p-Methoxyphenyl-7-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20b***. Gray plates from DMF, yield 0.17 g (53%, using general procedure A, from **24b**), mp 384–386 °C. MS: *m*/*z*=318 (M^+). IR: 3437, 3199, 3061, 2922, 1678, 1606, 1458, 1297, 1096, 928, 869, 696. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.16 (br, 1H, NH), 8.08 (d, 2H, *J* 7.8), 8.00 (d, 2H, *J* 8.8), 7.54–7.48 (m, 3H), 7.06 (d, 2H, *J* 8.8), 6.81 (s, 1H), 3.83 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.2, 155.6, 149.5, 144.5, 135.7, 132.1, 130.2, 130.1, 129.4, 127.1, 126.2, 114.0, 84.6, 55.7. Anal. calcd for $C_{18}H_{14}N_4O_2$: C 67.92; H 4.43; N 17.60. Found: C 67.88; H 4.41; N 17.48.

4.7.18. 3-Methyl-7-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20c***. Brown crystals from DMF, yield 0.05 g (22%, using general procedure A, from **8c**), 0.21 g (93%, using general procedure A, from **24c**), mp 350 °C (lit.[2] mp 350 °C).

4.7.19. 7-p-Methoxyphenyl-3-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20e***. Yellow plates from DMF, yield 0.086 g (27%, using general procedure A, from **8e**), yield 0.13 g (41%, using general procedure A, from **8f**), 0.248 g (78%, using general procedure A, from **24e**), mp 360–362 °C. MS: *m*/*z*=318 (M^+, 100%). IR: 3203, 3011, 2911, 1673, 1605, 1449, 1251, 1178, 1026, 950, 836, 783. ^{1}H NMR (600 MHz, DMSO-d_6): δ 14.21 (br, 1H, NH), 8.09–7.99 (m, 4H), 7.48–7.44 (m, 3H), 7.06 (d, 2H, *J* 8.4), 6.76 (s, 1H), 3.83 (s, 3H, OCH_3). ^{13}C NMR (150 MHz, $CDCl_3$): δ 160.4, 155.1, 148.9, 143.9, 135.4, 133.4, 128.7, 128.3, 128.1, 128.0, 124.1, 114.2, 83.8, 55.2. Anal. calcd for $C_{18}H_{14}N_4O_2$: C 67.92; H 4.43; N 17.60. Found: C 67.88; H 4.41; N 17.50.

4.7.20. 7-p-Chlorophenyl-3-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20g***. Greenish yellow plates from DMF, yield 0.032 g (10%, using general procedure A, from **8g**), yield 0.145 g (45%, using general procedure A, from **8h**), 0.24 g (75%, using general procedure A, from **24g**), mp 420–422 °C. MS: *m*/*z*=322 (M^+, 100%), 324 (M+2,

15%). IR: 3432, 3206, 3070, 1681, 1606, 1446, 1293, 1093, 950, 842, 787. ^{1}H NMR (600 MHz, DMSO-d_6): δ 14.21 (br, 1H, NH), 8.10 (d, 2H, *J* 7.8), 8.03 (d, 2H, *J* 8.0), 7.57 (d, 2H, *J* 8.0), 7.48 (t, 2H, *J* 7.8), 7.45 (t, 1H, *J* 7.6), 6.87 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 160.2, 153.9, 148.9, 143.7, 135.6, 134.2, 130.6, 128.9, 128.7, 128.3, 128.2, 128.1, 84.7. Anal. calcd for $C_{17}H_{11}ClN_4O$: C 63.26; H 3.44; N, 17.36. Found: C 63.20; H 3.44; N 17.30.

4.7.21. 3-Methyl-7-p-methoxyphenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20i***. Brown crystals from DMF, yield 0.07 g (27%, using general procedure A, from **8i**), 0.136 g (53%, using general procedure A, from **24e**), mp 326 °C (lit.[2] mp 326 °C).

4.7.22. 7-p-Chlorophenyl-3-p-methoxyphenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20k***. Gray plates from DMF, yield 0.24 g (68%, using general procedure A, from **24k**), mp 394–396 °C. MS: *m*/*z*=352 (M^+, 100%), 354 (M+2, 30%). IR: 3437, 3199, 3061, 2922, 1678, 1606, 1458, 1297, 1096, 928, 869, 696. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.18 (br, 1H, NH), 8.10 (d, 2H, *J* 8.6), 7.99 (d, 2H, *J* 8.6), 7.58 (d, 2H, *J* 8.6), 7.06 (d, 2H, *J* 8.6), 6.85 (s, 1H), 3.83 (s, 3H, OCH_3). ^{13}C NMR (150 MHz, DMSO-d_6): δ 162.3, 153.5, 148.8, 143.2, 135.6, 134.0, 130.6, 128.9, 128.6, 128.9, 128.3, 113.5, 84.7, 55.2. Anal. calcd for $C_{18}H_{13}ClN_4O_2$: C 61.28; H 3.71; N 15.88. Found: C 61.18; H 3.57; N 15.68.

4.7.23. 3,7-Di-p-methoxyphenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20l***. Gray plates from DMF, yield 0.21 g (60%, using general procedure A, from **24l**), mp 388–390 °C. MS: *m*/*z*=348 (M^+, 100%). IR: 3437, 3199, 3061, 2922, 1678, 1606, 1458, 1297, 1096, 928, 869, 696. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.15 (br, 1H, NH), 8.10 (d, 2H, *J* 8.4), 7.99 (d, 2H, *J* 8.4), 7.07 (d, 2H, *J* 8.4), 7.05 (d, 2H, *J* 8.4), 6.73 (s, 1H), 3.84 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3). ^{13}C NMR (150 MHz, DMSO-d_6): δ 162.1, 152.9, 148.6, 143.2, 135.6, 134.5, 130.1, 128.9, 128.5, 128.9, 114.1, 113.7, 84.4, 55.18, 55.23. Anal. calcd for $C_{19}H_{16}N_4O_3$: C 65.51; H 4.63; N 16.08. Found: C 65.50; H 3.45; N 16.10.

4.7.24. 3-p-Chlorophenyl-7-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20m***. Gray plates from DMF, yield 0.25 g (78%, using general procedure A, from **24m**), mp 394–396 °C. MS: *m*/*z*=322 (M^+, 100%), 324 (M+2, 30%). IR: 3437, 3199, 3061, 2922, 1678, 1606, 1458, 1297, 1096, 928, 869, 696. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.35 (br, 1H, NH), 8.09 (d, 2H, *J* 7.8), 8.06 (d, 2H, *J* 8.4), 7.57 (d, 2H, *J* 8.4), 7.52–7.46 (m, 3H), 6.87 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 156.3, 150.0, 145.1, 135.2, 134.5, 133.4, 132.6, 130.9, 130.7, 129.9, 129.2, 127.7, 85.7. Anal. calcd for $C_{17}H_{11}ClN_4O$: C 63.26; H 3.44; N 17.36. Found: C 63.18; H 3.41; N 17.38.

4.7.25. 3,7-Di-p-chlorophenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20n***. Gray plates from DMF, yield 0.25 g (70%, using general procedure A, from **24n**), mp above 420 °C. MS: *m*/*z*=356 (M^+, 100%), 358 (M+2, 55%), 360 (M+4, 10%). IR: 3437, 3199, 3061, 2922, 1678, 1606, 1458, 1297, 1096, 928, 869, 696. ^{1}H NMR (600 MHz, DMSO-d_6): δ 14.34 (br, 1H, NH), 8.09 (d, 2H, *J* 8.2), 8.07 (d, 2H, *J* 8.0), 7.57 (d, 2H, *J* 8.2), 7.50 (d, 2H, *J* 8.0), 6.86 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 156.3, 150.0, 145.1, 135.2, 134.5, 133.4, 132.6, 130.9, 130.7, 129.9, 129.0, 128.3, 85.7. Anal. calcd for $C_{17}H_{10}Cl_2N_4O$: C 57.16; H 2.82; N 15.68. Found: C 57.05; H 2.81; N 15.80.

4.7.26. 3-p-Chlorophenyl-7-p-methoxyphenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***20o***. Gray plates from DMF, yield 0.24 g (68%, using general procedure A, from **24o**), mp 394–396 °C. MS: *m*/*z*=352 (M^+, 100%), 354 (M+2, 10%). IR: 3427, 3200, 3014, 2936, 1680, 1610, 1456, 1255, 1080, 1032, 839, 786. ^{1}H NMR (400 MHz, DMSO-d_6): δ 14.29 (br, 1H, NH), 8.08 (d, 2H, *J* 8.8), 8.02 (d, 2H, *J* 8.8), 7.57 (d, 2H, *J* 8.8), 7.02 (d, 2H, *J* 8.8), 6.78 (s, 1H), 3.83 (s, 3H, OCH_3). ^{13}C NMR (150 MHz, DMSO-d_6): δ 156.3, 150.0, 145.8, 135.2, 134.5, 133.4, 132.6, 130.9, 130.7, 129.9, 129.2, 127.7, 85.7, 55.2. Anal. calcd for $C_{18}H_{13}ClN_4O_2$: C 61.28; H 3.71; N 15.88. Found: C 61.18; H 3.51; N 15.68.

4.8. Synthesis of compounds 23. General procedure

A mixture of the appropriate **5** (1 mmol), α-bromoacetophenone derivatives **22** (1 mmol), and anhydrous K_2CO_3 (2 mmol) in dry acetonitrile (10 mL) was stirred at room temperature for 2 h. The solvent was removed in vacuo and ice water (50 mL) was added to the reaction mixture, filtered, and washed several times with water. The product was collected and crystallized from the proper solvent.

4.8.1. 4-Amino-3-(2-oxo-2-phenylethylsulfanyl)-6-phenyl-4H-[1,2,4]triazin-5-one ***23a***. Colorless crystals from ethanol, yield 0.25 g (74%), mp 210–212 °C (lit.[15] mp 209–210). MS: *m*/*z*=338 (M^+, 15%). ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.10 (dd, 2H, *J* 7.8, 1.6), 8.06 (dd, 2H, *J* 7.8, 1.6), 7.71 (t, 1H, *J* 7.8), 7.59 (t, 2H, *J* 7.8), 7.49–7.44 (m, 3H), 6.18 (br, 2H, NH_2), 4.88 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6) δ 193.0, 161.4, 151.9, 151.0, 135.8, 133.6, 132.9, 130.0, 128.8, 128.3, 128.2, 128.0, 39.0.

4.8.2. 4-Amino-6-p-methoxyphenyl-3-(2-oxo-2-phenylethylsulfanyl)-4H-[1,2,4]triazin-5-one ***23b***. Yellow crystals from ethanol, yield 0.3 g (81%), mp 213–215 °C. MS: *m*/*z*=368 (M^+, 10%). IR: 3434, 276, 2919, 1698, 1661, 1604, 1494, 1439, 1310, 1294, 1253, 1179, 1073, 991, 841. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.12 (d, 2H, *J* 8.8), 8.12–8.07 (m, 2H), 7.71 (t, 1H, *J* 7.6), 7.59 (t, 2H, *J* 7.8), 7.02 (d, 2H, *J* 8.8), 6.17 (br, 2H, NH_2), 4.87 (s, 2H), 3.81 (s, 3H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6): δ 193.5, 161.3, 161.0, 152.5, 150.9, 136.3, 134.1, 130.3, 129.3, 128.8, 125.7, 114.1, 55.7, 39.3. Anal. calcd for $C_{18}H_{16}N_4O_3S$: C 58.68; H 4.38, N 15.21; S 8.70. Found: C 58.60; H 4.17; N 15.14; S 8.61.

4.8.3. 4-Amino-3-(2-p-methoxyphenyl-2-oxo-ethylsulfanyl)-6-phenyl-4H-[1,2,4]triazin-5-one ***23e***. White crystals from ethanol, yield 0.27 g (73%), mp 160–162 °C. MS: *m*/*z*=368 (M^+, 100%). IR: 3432, 3103, 2895, 1665, 1605, 1499, 1456, 1313, 1262, 1179, 1025, 825, 760. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.10 (dd, 2H, *J* 7.9, 1.6), 8.05 (d, 2H, *J* 8.8), 7.69 (t, 1H, *J* 7.8), 7.49 (t, 2H, *J* 7.8), 7.44 (d, 2H, *J* 8.8), 6.18 (br, 2H), 4.88 (s, 2H), 3.83 (s, 3H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6): δ 192.2, 160.8, 160.3, 151.9, 150.4, 138.4, 134.6, 130.3, 129.7, 128.9, 127.8, 113.7, 55.2, 39.2. Anal. calcd for $C_{18}H_{16}N_4O_3S$: C 58.68; H 4.38; N 15.21; S 8.70. Found: C 58.64; H 4.40; N 15.07; S 8.48.

4.8.4. 4-Amino-3-(2-p-chlorophenyl-2-oxo-ethylsulfanyl)-6-phenyl-4H-[1,2,4]triazin-5-ones ***23g***. Yellow crystals from ethanol, yield 0.28 g (75%), mp 196–198 °C. MS: *m*/*z*=374 (M+2, 5%), 372 (M^+, 15%). IR: 3443, 3280, 2916, 1697, 1666, 1589, 1499, 1360, 1291, 1206, 1094, 994, 794. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.11 (d, 2H, *J* 7.8), 8.05 (dd, 2H, *J* 7.8, 1.8), 7.67 (d, 2H, *J* 7.8), 7.50–7.45 (m, 3H), 6.19 (br, 2H, NH_2), 4.87 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.8, 161.8, 152.4, 151.6, 139.0, 135.2, 133.4, 130.7, 130.5, 129.4, 128.7, 128.6, 39.2. Anal. calcd for $C_{17}H_{13}ClN_4O_2S$: C 54.77; H 3.51; N 15.03; S 8.60. Found: C 54.64; H 3.50; N 15.07; S 8.46.

4.8.5. 4-Amino-3-(2-p-chlorophenyl-2-oxo-ethylsulfanyl)-6-p_methoxyphenyl-4H-[1,2,4]triazin-5-one ***23k***. Yellow crystals from ethanol, yield 0.31 g (77%), mp 210–212 °C. MS: *m*/*z*=402 (M^+, 20%), 404 (M+2, 10%). IR: 3421, 3093, 2841, 1674, 1601, 1490, 1305, 1261, 1183, 1089, 819. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.11 (d, 2H, *J* 8.0), 8.09 (d, 2H, *J* 8.0), 7.66 (d, 2H, *J* 8.0), 7.02 (d, 2H, *J* 8.0), 6.15 (br, 2H, NH_2), 4.84 (s, 2H), 3.81 (s, 3H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6): δ 192.3, 160.8, 160.4, 152.0, 150.4, 138.5, 134.6, 130.3, 129.8,

128.9, 125.2, 113.6, 55.2, 39.0. Anal. calcd for $C_{18}H_{15}ClN_4O_3S$: C 53.67; H 3.75; N 13.91; S 7.96. Found: C 53.48; H 3.64; N 13.88; S 7.93.

4.8.6. 4-Amino-6-p-methoxyphenyl-3-(2-p-methoxyphenyl-2-oxo-ethylsulfanyl)-4H-[1,2,4]triazin-5-one ***23l***. Yellow crystals from ethanol, yield 0.31 g (78%), mp 200–202 °C. MS: *m*/*z*=398 (M^+, 25%). IR: 3301, 3103, 2840, 1665, 1605, 1577, 1499, 1313, 1262, 1179, 1025, 832. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.11 (d, 2H, *J* 8.8), 8.06 (d, 2H, *J* 8.8), 7.10 (d, 2H, *J* 8.8), 7.03 (d, 2H, *J* 8.8), 6.16 (br, 2H, NH_2), 4.82 (s, 2H, CH_2), 3.87 (s, 3H, CH_3), 3.82 (s, 3H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6): δ 191.4, 163.5, 160.8, 160.5, 152.0, 150.3, 130.7, 129.8, 128.7, 125.3, 114.0, 113.6, 55.6, 55.2, 38.5. Anal. calcd for $C_{19}H_{18}N_4O_4S$: C 57.28; H 4.55; N 14.06; S 8.05. Found: C 57.20; H 4.54; N 13.98; S 8.00.

4.8.7. 4-Amino-6-p-chlorophenyl-3-(2-oxo-2-phenylethylsulfanyl)-4H-[1,2,4]triazin-5-one ***23m***. Yellow crystals from ethanol, yield 0.29 g (78%), mp 185–186 °C. MS: *m*/*z*=372 (M^+, 10%), 374 (M+2, 5%). IR: 3433, 3197, 2996, 1690, 1604, 1495, 1447, 1335, 1255, 1185, 1026, 839. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.32 (d, 2H, *J* 8.4), 8.29 (d, 2H, *J* 8.0), 7.91 (t, 1H, *J* 7.8), 7.79 (t, 2H, *J* 8.0), 7.74 (d, 2H, *J* 8.4), 6.39 (br, 2H, NH_2), 5.08 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 192.7, 162.2, 152.3, 150.5, 139.0, 135.9, 135.6, 132.8, 130.7, 130.2, 128.9, 128.4, 39.1. Anal. calcd for $C_{17}H_{13}ClN_4O_2S$: C 54.77; H 3.51; N 15.03; S 8.60. Found: C 54.64; H 3.40; N 15.07; S 8.48.

4.8.8. 4-Amino-6-p-chlorophenyl-3-(2-p-chlorophenyl-2-oxo-ethylsulfanyl)-4H-[1,2,4]-triazin-5-one ***23n***. Colorless crystals from ethanol, yield 0.3 g (74%), mp 233–235 °C. MS: *m*/*z*=407 (M^+, 85%), 409 (M+2, 15%), 411 (M+4, 5%). IR: 3434, 3300, 3070, 2850, 1676, 1600, 1497, 1439, 1291, 1213, 1179, 1065, 820, 760. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.11 (d, 2H *J* 7.8), 8.08 (d, 2H, *J* 8.0), 7.68 (d, 2H *J* 7.8), 7.54 (d, 2H *J* 8.0), 6.18 (br, 2H), 4.86 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 192.7, 162.2, 152.3, 150.5, 139.0, 135.4, 135.1, 132.2, 130.8, 130.4, 129.4, 128.7, 39.3. Anal. calcd for $C_{17}H_{12}Cl_2N_4O_2S$: C 50.13; H 2.97; N 13.76; S 7.87. Found: C 50.08; H 3.00; N 13.57; S 7.80.

4.8.9. 4-Amino-6-p-chlorophenyl-3-(2-p-methoxyphenyl-2oxo-ethylsulfanyl)-4H-[1,2,4]triazin-5-one ***23o***. Yellow crystals from ethanol, yield 0.31 g (77%), mp 230–232 °C. MS: *m*/*z*=402 (M^+, 15%), 404 (M+2, 5%). IR: 3434, 3300, 2908, 1676, 1600, 1497, 1422, 1318, 1291, 1179, 1045, 994, 838. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.12 (d, 2H, *J* 8.8), 8.07 (d, 2H, *J* 8.8), 7.55 (d, 2H, *J* 8.8), 7.10 (d, 2H, *J* 8.8), 6.19 (br, 2H, NH_2), 4.84 (s, 2H), 3.88 (s, 3H, CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 191.2, 163.9, 162.4, 152.4, 150.4, 135.4, 132.3, 131.2, 130.4, 129.1, 128.8, 114.5, 56.1, 39.1. Anal. calcd for $C_{18}H_{15}ClN_4O_3S$: C 53.67; H 3.75; N 13.91; S 7.96. Found: C 53.60; H 3.72; N 13.91; S 7.90.

4.9. General procedure for synthesis of compounds 24. General procedure

A mixture of compounds **23** (1 mmol) and *p*-toulenesulfonic acid (30 mg, 0.17 mmol) in ethanol (10 mL) was heated under reflux from 6 to 8 h. The solvent was removed under vacuo and ice water was added (20 mL), the precipitate was collected and crystallized from the proper solvent.

4.9.1. 3,7-Diphenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***24a***. Yellow crystals from ethanol, yield 0.21 g (66%), mp 228–230 °C. MS: *m*/*z*=320 (M^+, 100%). IR: 3055, 2905, 1701, 1594, 1492, 1451, 1331, 1276, 1054, 1008, 973, 752, 691. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.10 (d, 2H *J* 8.0), 8.07 (d, 2H, *J* 7.8), 7.65 (t, 1H, *J* 7.8), 7.61 (t, 2H, *J* 7.6), 7.53–7.45 (m, 3H), 4.41 (s, 2H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.7, 154.5, 152.3, 149.2, 133.6, 133.4, 133.0, 130.8, 129.6, 129.1, 128.7, 128.4, 22.3. Anal. calcd for $C_{17}H_{12}N_4OS$: C 63.73; H 3.78; N 17.49; S 10.01. Found: C 63.60; H 3.74; N 17.35; S 9.95.

4.9.2. 3-p-Methoxyphenyl-7-phenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***24b***. Yellow crystals from ethanol, yield 0.25 g (71%), mp 220–222 °C. MS: *m*/*z*=350 (M^+, 100%). IR: 3057, 2827, 1709, 1604, 1515, 1490, 1444, 1326, 1259, 1170, 1026, 836, 762. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.15 (d, 2H, *J* 8.8), 8.07 (d, 2H, *J* 7.8), 7.65–7.60 (m, 3H), 7.08 (d, 2H, *J* 8.8), 4.40 (s, 2H), 3.85 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.5, 159.7, 153.8, 151.3, 149.3, 133.5, 132.9, 130.7, 129.6, 128.3, 125.9, 114.2, 55.7, 22.4. Anal. calcd for $C_{18}H_{14}N_4O_2S$: C 61.70; H 4.03; N 15.99; S 9.15. Found: C 61.66; H 4.00; N 15.87; S 8.98.

4.9.3. 7-p-Methoxyphenyl-3-phenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***24e***. Yellow crystals from DMF, yield 0.25 g (71%), mp 213–215 °C. MS: *m*/*z*=350 (M^+, 100%). IR: 3074, 2843, 1678, 1607, 1485, 1445, 1345, 1298, 1265, 1178, 1012, 845, 793. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.10 (dd, 2H, *J* 7.6, 1.6), 8.06 (d, 2H, *J* 8.6), 7.54–7.51 (m, 3H), 7.17 (d, 2H, *J* 8.6), 4.37 (s, 2H), 3.88 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 159.2, 154.2, 152.5, 149.2, 133.6, 130.7, 130.4, 129.1, 128.6, 125.3, 115.1, 56.1, 22.0. Anal. calcd for $C_{18}H_{14}N_4O_2S$: C 61.70; H 4.03; N 15.99; S 9.15. Found: C 61.48; H 4.00; N 15.97; S 9.08.

4.9.4. 7-p-Chlorophenyl-3-phenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***24g***. Yellow crystals from DMF, yield 0.27 g (76%), mp 330–333 °C. MS: *m*/*z*=354 (M^+, 25%), 356 (M+2, 5%). IR: 3216, 3057, 2919, 1689, 1598, 1517, 1417, 1350, 1270, 1091, 1002, 784, 758. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, 2H, *J* 8.8), 8.07 (d, 2H, *J* 7.6), 7.67 (t, 1H, *J* 7.6), 7.63–7.59 (m, 4H), 4.41 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.0, 159.2, 153.3, 150.7, 148.7, 132.9, 132.3, 130.2, 129.0, 127.8, 128.3, 125.4, 21.9. Anal. calcd for $C_{17}H_{11}ClN_4OS$: C 57.55; H 3.12; N 15.79; S 9.04. Found: C 57.50; H 3.07; N 15.54; S 9.00.

4.9.5. 7-p-Chlorophenyl-3-p-methoxyphenyl-8H-[1,2,4]triazino[3,4-b][1,3,4] thiadiazin-4-one ***24k***. Yellow crystals from DMF, yield 0.25 g (73%), mp 298–300 °C. MS: *m*/*z*=384 (M^+, 100%), 386 (M+2, 40%). IR: 3070, 2925, 1688, 1603, 1488, 1440, 1300, 1276, 1252, 1165, 1090, 1006, 837, 815. ^{1}H NMR (600 MHz, DMSO-d_6): δ 8.14 (d, 2H, *J* 7.8), 8.07 (d, 2H, *J* 7.8), 7.68 (d, 2H, *J* 7.8), 7.06 (d, 2H *J* 7.8), 4.38 (s, 2H, CH_2), 3.83 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.1, 158.1, 153.4, 150.6, 148.7, 137.3, 131.8, 130.3, 129.7, 129.3, 125.4, 113.7, 55.3, 21.8. Anal. calcd for $C_{18}H_{13}ClN_4O_2S$: C 56.18; H 3.40; N 14.56; S 8.33. Found: C 55.99; H 3.40; N 14.54; S 8.32.

4.9.6. 3,7-Di-p-methoxyphenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***24l***. Yellow crystals from DMF, yield 0.29 g (76%), mp 235–236 °C. MS: *m*/*z*=380 (M^+, 100%). IR: 3046, 3024, 2935, 1704, 1608, 1588, 1487, 1442, 1311, 1262, 1180, 1029, 828. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.15 (d, 2H, *J* 8.8), 8.05 (d, 2H, *J* 8.8), 7.16 (d, 2H, *J* 8.8), 8.07 (d, 2H, *J* 8.8), 4.36 (s, 2H), 3.88 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.2, 161.5, 159.2, 153.5, 151.5, 149.3, 130.7, 130.4, 126.0, 125.4, 115.1, 114.1, 56.1, 55.8, 22.1. Anal. calcd for $C_{19}H_{16}N_4O_3S$: C 59.99; H 4.24; N 14.73; S 8.43. Found: C 59.95; H 4.28; N 14.77; S 8.42.

4.9.7. 3-p-Chlorophenyl-7-phenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***24m***. Yellow crystals from DMF, yield 0.25 g (70%), mp 270–273 °C. MS: *m*/*z*=354 (M^+, 100%), 356 (M+2, 5%). IR: 3062, 2919, 1705, 1592, 1488, 1445, 1323, 1298, 1091, 1009, 836, 758. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.16 (d, 2H, *J* 8.6), 8.07 (d, 2H, *J* 8.6), 7.60 (t, 1H, *J* 7.8), 7.57–7.53 (m, 4H), 4.41 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.8, 153.4, 152.7, 149.2, 135.6, 133.3, 133.0, 132.4,

130.8, 129.6, 128.8, 128.4, 22.3. Anal. calcd for $C_{17}H_{11}ClN_4OS$: C 57.55; H 3.12; N 15.79; S 9.04. Found: C 57.35; H 3.12; N 15.87; S 8.93.

4.9.8. 3,7-Di-p-chlorophenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***24n***. Yellow crystals from DMF/EtOH, yield 0.27 g (69%), mp 288–290 °C. MS: *m*/*z*=388 (M^+, 100%), 390 (M+2, 75%), 392 (M+4, 5%). IR: 3075, 3011, 1693, 1588, 1480, 1428, 1396, 1285, 1091, 1007, 839, 809. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.15 (d, 2H, *J* 7.6 Hz), 8.08 (d, 2H, *J* 7.6 Hz), 7.70 (d, 2H, *J* 7.8 Hz), 7.59 (d, 2H, *J* 7.6), 4.39 (s, 2H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 158.2, 152.9, 151.9, 148.6, 137.4, 135.2, 131.9, 131.7, 130.3, 129.7, 129.3, 128.3, 21.8. Anal. calcd for $C_{17}H_{10}Cl_2N_4OS$: C 52.46; H 2.59; N 14.39; S 8.24. Found: C 52.28; H 2.61; N 14.17; S 8.17.

4.9.9. 3-p-Chlorophenyl-7-p-methoxyphenyl-8H-[1,2,4]triazino[3,4-b][1,3,4]thiadiazin-4-one ***24o***. Yellow crystals from ethanol, yield 0.28 g (73%), mp 226–228 °C. MS: *m*/*z*=384 (M^+, 100%), 386 (M+2, 6%). IR: 3299, 3206, 2975, 1692, 1510, 1488, 1439, 1319, 1254, 1186, 1012, 838. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, 2H, *J* 8.8), 7.99 (d, 2H, *J* 7.6), 7.48 (d, 2H, *J* 7.8), 7.05 (d, 2H, *J* 8.8), 3.97 (s, 2H, CH_2), 3.93 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 163.5, 157.3, 153.5, 150.9, 149.1, 137.1, 131.2, 130.4, 129.9, 128.6, 124.7, 114.7, 55.7, 22.5. Anal. calcd for $C_{18}H_{13}ClN_4O_2S$: C 56.18; H 3.40; N 14.56, S 8.33. Found: C 56.15; H 3.40; N 14.50; S 8.32.

4.10. General procedure for synthesis of compounds 25

A mixture of compounds **24** (1 mmol) and acetic anhydride (10 mL) was heated under reflux for 2 h, and then ice water (20 mL) was added to the reaction mixture. The precipitate was collected and recrystallized from the stated solvent.

4.10.1. 1-Acetyl-7-p-methoxyphenyl-3-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***25e***. Gray needles from ethanol/acetone, yield 0.30 g (83%), mp 232–234 °C. MS: *m*/*z*=360 (M^+, 80%). IR: 3423, 2969, 1749, 1709, 1587, 1526, 1303, 1254, 1170, 928, 788. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.07 (d, 2H, *J* 7.8), 8.03 (d, 2H, *J* 8.4), 7.60–7.56 (m, 3H), 7.41 (s, 1H), 7.08 (d, 2H, *J* 8.4), 3.84 (s, 3H), 2.72 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 170.6, 160.7, 155.6, 147.7, 139.5, 139.0, 132.0, 130.2, 129.1, 128.3, 128.2, 123.4, 114.4, 92.1, 55.3, 22.0. Anal. calcd for $C_{20}H_{16}N_4O_3$: C 66.66; H 4.48; N 15.55. Found: C 66.50; H 4.41; N 15.50.

4.10.2. 1-Acetyl-7-p-chlorophenyl-3-phenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***25g***. Gray needles from ethanol/acetone, yield 0.29 g (80%), mp 243–245 °C. MS: *m*/*z*=364 (M^+, 80%), 366 (M+2, 5%). IR: 3156, 3060, 2923, 1717, 1630, 1559, 1433, 1302, 1264, 1171, 948, 815. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.14 (d, 2H, *J* 8.0), 8.08 (d, 2H, *J* 7.8), 7.61–7.54 (m, 5H), 7.52 (s, 1H), 2.73 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 170.7, 154.5, 147.9, 139.8, 139.2, 134.7, 131.9, 130.3, 129.9, 129.2 (2C), 128.5, 128.4, 92.7, 22.0. Anal. calcd for $C_{19}H_{13}ClN_4O_2$: C 62.56; H 3.59; N 15.36. Found: C 62.50; H 3.41; N 15.30.

4.10.3. 1-Acetyl-3,7-di-p-chlorophenyl-1H-pyrazolo[5,1-c][1,2,4]triazin-4-one ***25n***. Yellow needles from ethanol/acetone, yield 0.27 g (75%), mp 232–234 °C. MS: *m*/*z*=398 (M^+, 80%), 400 (M+2, 15%), 402 (M+4, 5%). IR: 3423, 2969, 1749, 1709, 1587, 1526, 1303, 1254, 1170, 928, 788. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.15–8.10 (m, 4H), 7.65 (d, 2H, *J* 8.4), 7.59 (d, 2H, *J* 8.4), 7.51 (s, 1H), 2.74 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 170.6, 154.6, 147.8, 139.7, 138.0, 135.2, 134.7, 130.9, 130.7, 129.8, 129.2, 128.4, 92.7, 55.3, 22.0. Anal. calcd for $C_{19}H_{12}Cl_2N_4O_2$: C 57.16; H 3.03; N 14.03. Found: C 57.10; H 3.01; N 14.00.

4.10.4. 3-Benzoyl-2-phenyl-4H-pyrazolo[5,1-b]quinazolin-9-one ***26a***. Yellow crystals from EtOH, yield 0.06 g (16%, using general procedure A, from **12**), yield 0.07 (20%, using general procedure B, from **9** and **16**), mp 233–234 °C. R_f=0.3 (petroleum ether/EtOAc 2:1). MS: *m*/*z*=365 (M^+). IR: 3434, 2984, 2924, 1734, 1684, 1551, 1470, 1310, 1177, 769, 691. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.83 (s, 1H), 8.54 (d, 1H, *J* 8.0), 7.81 (dt, 1H, *J* 8.4, 1.6), 7.49–7.43 (m, 3H), 7.38 (dd, 2H, *J* 8.4, 1.2), 7.33 (dd, 2H, *J* 7.2, 2.0), 7.30 (t, 1H, *J* 8.0, 1.2), 7.21 (dt, 1H, *J* 7.6, 1.2), 7.12–7.08 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.1, 156.7, 155.3, 147.2, 138.12, 138.06, 135.4, 131.7, 131.5, 129.8, 129.1, 129.0, 128.8, 127.8, 127.7, 124.2, 116.5, 115.1, 102.3. HRMS=365.1156 ($C_{23}H_{15}N_3O_2$ requires 365.1158).

4.10.5. 3-Ethoxycarbonyl-2-phenyl-4H-pyrazolo[5,1-b]quinazolin-9-one ***26b***. Colorless crystals, yield 21% (using general procedure B, from **9** and **14**), mp 230–231 °C. MS: *m*/*z*=333. IR: 3429, 3269, 1708, 1682, 1625, 1572, 1498, 1444, 1425, 1305, 1174, 1047, 762, 698. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.04 (s, 1H, NH), 8.51 (dd, 1H, *J* 8.0, 0.4), 7.86–7.84 (m, 2H), 7.79 (dt, 1H, *J* 8.4, 1.6), 7.47–7.38 (m, 5H), 4.33 (q, 2H, *J* 7.2), 1.29 (t, 3H, *J* 7.2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.1, 156.0, 155.1, 146.4, 137.8, 135.1, 131.2, 129.9, 129.3, 128.9, 127.4, 123.6, 115.9, 114.1, 93.0, 60.6, 13.9. HRMS=333.1106 ($C_{19}H_{15}N_3O_3$ requires 333.1107).

4.10.6. 2-Phenyl-4H-pyrazolo[5,1-b]quinazolin-9-one ***27***. Colorless crystals from EtOH, yield 0.08 g (31%, using general procedure A, from **12**), mp 293–295 °C (lit.[2] mp 293 °C).

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Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.06.034. These data include MOL files and InChIKeys of the most important compounds described in this article.

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