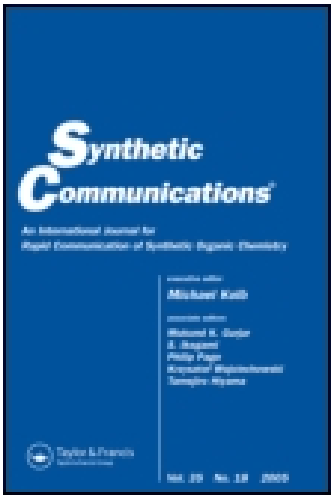

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Solid-Phase Synthesis of 4,5-Disubstituted-1,2,4-triazole-3-thione Derivatives Based on the Resin-Bound Acylhydrazines

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SOLID-PHASE SYNTHESIS OF 4,5-DISUBSTITUTED-1,2,4-TRIAZOLE-3-THIONE DERIVATIVES BASED ON THE RESIN-BOUND ACYLHYDRAZINES

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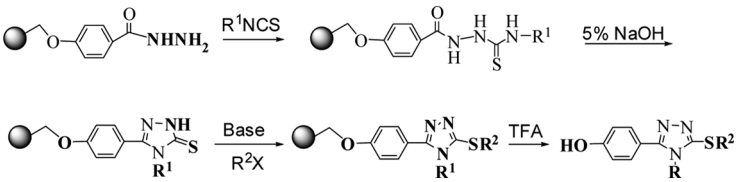
GRAPHICAL ABSTRACT



Abstract *Highly efficient solid-phase synthesis of 4,5-disubstituted-1,2,4-triazole-3-thiones under mild conditions has been developed. 4,5-Disubstituted-1,2,4-triazole-3-thione derivatives were synthesized from resin-bound acylhydrazines in several steps, providing 76–89% overall yields and excellent purity.*

Keywords Resin-bound acylhydrazine; solid-phase synthesis; 1,2,4-triazole-3-thiones

INTRODUCTION

Many natural and synthetic compounds bearing five-membered heterocyclic rings in their structure have an extensive spectra of pharmacological activities. Among these heterocycles, new derivatives of 1,2,4-triazole-3-thiones have potential anticonvulsant,[1] antimicrobial,[2] and anti-inflammatory activities.[3] It is also well established that various derivatives of 1,2,4-triazole can be used for treating non-Hodgkin's lymphoma.[4]

As a result of these useful applications, chemists have been encouraged to design new synthetic methodologies for the preparation of this medicinally important heterocyclic building block. In the literature, several methods for the synthesis of 1,2,4-triazole-3-thiones derivatives were described. 1,2,4-triazole-3-thiones have been prepared from the reaction of thiosemicarbazide with acyl halides and a

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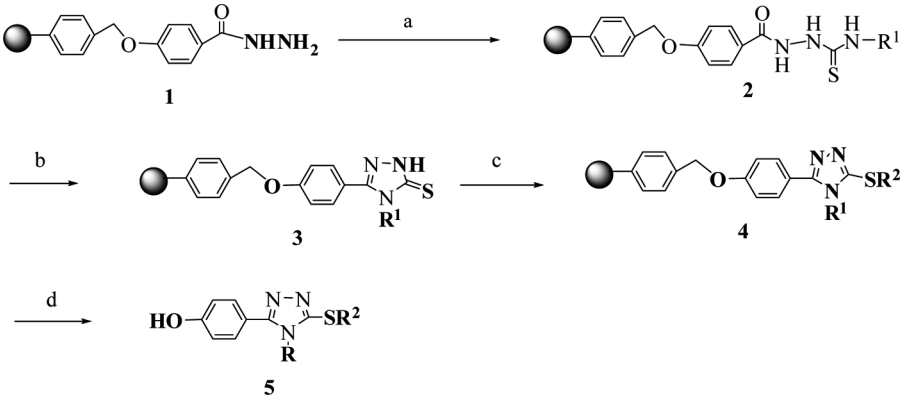
subsequent cyclization of the intermediate acylthiosemicarbazides in basic media.[5,6] They also have been prepared from the reaction of acid hydrazides and isothiocyanates.[3b,7–9] Formation of these compounds from the reaction of acid hydrazides with carbon disulfide and hydrazine hydrate was also reported in the literature.[10] The reaction of aroyl isothiocyanates with hydrazine derivatives has also led to the formation of these types of compounds.[11,12] Thionation of 1,2,4-triazole-3-ones is another synthetic route to these compounds.[13]

Many of the solution-phase methodologies described possess important drawbacks such as long reaction times, poor yields, and exhaustive purification protocols. In the process of drug development and/or lead structure optimization, it is most welcome to use a method that allows easy access to diverse compounds. Synthetic routes on solid support offer the opportunity for development of novel methodologies for construction of libraries of small heterocyclic compounds.[14] A few examples of solid-phase synthesis of 3-thio-1,2,4-triazoles have been reported,[15] including polymer-bound base 2-*tert*-butylimino-2-diethylamino-1,3-dimethyl-perhydro-1,3,2-diazaphosphorine on polystyrene (P-BEMP)–mediated synthesis and a Rink amide resin–supported route. In this context, we have foreseen that the use of new solid-phase strategies to obtain 1,2,4-triazole-3-thiones could overcome some of the deficiencies observed in previous synthetic protocols. We present a novel solid-phase procedure that can be conducted in parallel form.

Substituted 1,2,4-triazole-3-thiones have been successfully prepared by traditional synthesis via acylhydrazine. To the best of our knowledge, solid-phase synthesis of 1,2,4-triazole-3-thione derivatives has not been reported until now. In continuation of our particular interest in solid-phase synthesis of heterocycles from resin-bound acylhydride,[16] herein we describe a new method for solid-phase synthesis of 1,2,4-triazole-3-thione derivatives from resin-bound acylhydrazines.

Scheme 1 shows the synthetic route of 1,2,4-triazole-3-thione derivatives. We have prepared resin-bound acylhydrazine **1** from the Merrifield resin according to our previously reported method.[15] The acylhydrazine resin **1** was reacted with excess aryl/alkyl isothiocyanates in EtOH to give the corresponding resin-bound thiosemicarbazides **2**. After alkaline ring closures of the corresponding



Scheme 1. Reagents and conditions: (a) R^1NCS, EtOH, reflux, 6 h; (b) 5% NaOH, reflux, 8 h; (c) (i) NaOH in EtOH, reflux, 2 h; (ii) R^2X, reflux, 4 h; (d) $TFA/CH_2Cl_2(1/6)$, rt.

Table 1. Solid-phase synthesis of 1,2,4-triazole-3-thione derivatives

Entry	Product	R^1	R^2	Yield[a] (%)	Purity[b] (%)
1	**5a**	Ph	H	89	92
2	**5b**	$C_6H_5CH_2$	H	76	88
3	**5c**	4-CH_3-C_6H_4	H	88	90
4	**5d**	4-CH_3O-C_6H_4	H	86	95
5	**5e**	Ph	n-C_4H_9	81	86
6	**5f**	Ph	CH_3	84	90
7	**5g**	Ph	4-NO_2-$C_6H_4CH_2$	86	92
8	**5h**	Ph	Allyl	82	89
9	**5i**	Ph	$C_6H_5CH_2$	84	90

[a]Yield of crude product based on the loading of acylhydrazine resin **1**.
[b]Determined by HPLC analysis (area %).

aroylthiosemicarbazides resin **2**, the resin **3** was obtained. Further reaction with NaOH and electrophilic reagents (R^2X) gave the corresponding resin **4**. The desired 1,2,4-triazole-3-thiones derivatives **5** were released at trifluoroacetic acid/dichloromethane (TFA/DCM) cleavage for 4 h in good yield and purity and were characterized by spectroscopic methods. The results are summarized in Table 1.

The successful formation of resin 2 was supported by a comparative FT-IR (Fourier transform–infrared) study and a sample of resin **2** (KBr pellets). The N-H stretch at 3429, 3318 cm^{-1} shifted to 3298 and 3247 cm^{-1}, and a strong C=O stretch appeared at 1676 cm^{-1} for aroylsemicarbazide resin **2**, which is different from the C=O signal of acylhydrazine resin at 1630 cm^{-1}. When resin **2** was converted into resin **3,** a strong carbonyl peak at 1676 cm^{-1} disappeared, and the signal of N-H shifted to 3470 cm^{-1}. The resin **3** was treated with the base (NaOH) and then reacted with a variety of electrophilic reagents, such as alkyl halides, allyl bromide, and benzyl halides. When the resin **4** was cleaved by TFA/DCM, product **5** was obtained in good yields and high purity.

Using this methodology, we have synthesized a representative set of 1,2,4-triazole-3-thione derivatives 5 (Table 1) in 76–89% overall yield, indicating a good yield for each step of the reaction.

In summary, we have studied and developed a new strategy for the preparation of 4,5-disubstituted-1,2,4-triazole-3-thiones on solid support. The use of resin-bound acylhydrazines in the reaction benefits the solid-phase synthetic route because it not only provides a short synthetic route to the desired products but also its chemical versatility adds to the diversity of the library. The 1,2,4-triazole-3-thione derivatives were synthesized in several steps, providing 76–89% overall yields and excellent purity. This synthetic methodology is ideally suitable for the high-throughput synthesis of drug libraries for potential drug discovery because all the reactions were carried out under mild conditions. Further work is in progress on the solid-phase synthesis of heterocyclic compounds via the resin-bound acylhydrazines.

EXPERIMENTAL

Starting materials were obtained from commercial suppliers and used without further purification. Solvents were distilled before use: CH_2Cl_2 was distilled from

CaH_2. Merrifield resin (100–200 mesh, cross-linked with 1% divinylbenzene, loading°C1.95 mmol/g Cl) was purchased from a commercial source (Nankai University).

Acylhydrazine resin **1** was prepared from the Merrifield resin according to our previously reported method.[15] ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker Avance (400-MHz) spectrometer, using $CDCl_3$ as the solvent and tetramethylsilane (TMS) as internal standard. MS spectra (EI, 70 eV) were recorded on a HP5989B mass spectrometer. IR spectra were recorded on a Bruck Vector 22 spectrophotometer. Elemental analyses were performed on a Flash EA1112 instrument. High-performance liquid chromatography (HPLC) was performed on an Agilent 1100 (column, Eclipse XDB-C18 5 μm, 4.6 × 150 mm; mobile phase, MeOH/H_2O, 80/20 (v/v); flow rate, 1.0 mL/min; detector, UV 254 nm). The samples were further purified by thin-layer chromatography (TLC) for ^{13}C NMR and microanalyses.

General Procedure for Synthesis of 1,2,4-Triazole-3-thiones

Phenyl isothiocyanate (0.324 g, 2.4 mmol) was added to the mixture of the acylhydrazine resin **1** (0.5 g, loading°C1.59 mmol/g, based on N microanalysis) in absolute EtOH (5 mL). Then the mixture was stirred and refluxed for 6 h. The resin was filtered and washed with EtOH (5 mL × 3) and CH_2Cl_2 (5 mL × 3) to remove contaminated species and then dried to afford resin **2**.

Resin **2** was added to 2 mL of 5% NaOH solution. The mixture was heated to reflux for 8 h. Then it was filtered, and the resin was washed with 10% HCl (5 mL × 3), H_2O (10 mL × 3), EtOH (5 mL × 3), and CH_2Cl_2 (5 mL × 3) and dried to affored resin **3**.

To the solution of NaOH (2 mmol, 80 mg) in 5 mL EtOH, resin **3a** was added. The mixture was heated under reflux for 2 h, n-BuBr (2 mmol, 0.272 g) and was added, and the reaction mixture was filtered after reflux for another 4 h. The resin was washed with H_2O (10 mL × 3), EtOH (5 mL × 3), and CH_2Cl_2 (5 mL × 3) and dried to afford the resin **4**.

The resin **4e** was well swollen in 3 mL CH_2Cl_2, and then 0.5 mL TFA was added. The mixture was stirred at room temperature for 4 h and then filtered. The resin was washed completely with EtOH (5 mL × 3) and acetone (5 mL × 3). The filtrate was combined to afford the crude product **5** by evaporation.

Compounds **5a–5d** were obtained directly from resin **3**, which was cleaved by TFA/CH_2Cl_2 using a similar procedure.

All compounds gave satisfactory ^{1}H NMR, IR, and MS spectra.

Selected Data

2,4-Dihydro-5-(4-hydroxyphenyl)-4-phenyl-3*H*-1,2,4-triazole-3-thione (5a). Mp 252–256 °C; ^{1}H NMR 6.65 (m, 2H), 7.07–7.45 (m, 7H), 9.95 (s, 1H) 13.95 (s, 1H); ^{13}C NMR 115.60, 116.59, 126.95, 129.02, 129.56, 130.06, 135.06, 151.02, 159.45, 168.55; MS (EI, 70 eV): *m/z* (%) 269 (100), 216 (16), 149 (9.8); IR 3421, 3243, 3145, 2940, 1610, 1594, 1513, 1498, 1399, 1330, 1315, 1281, 1246, 1176, 843,

757, 694 cm^{-1}. Calcd. for $C_{14}H_{11}N_3OS$: C, 62.43; H, 4.12; N, 15.60; O, 5.94; S, 11.91. Found: C, 62.67; H, 4.38; N, 15.88.

2,4-Dihydro-5-(4-hydroxyphenyl)-4-benzyl-3*H*-1,2,4-Triazole-3 (2*H*)-thione (5b). Mp 303 °C; ^{1}H NMR 5.32 (s, 2H), 6.82 (d, 2H, $J = 8.2$ Hz), 7.04 (d, 2H, $J = 7.0$ Hz), 7.25 (m, 3H), 7.34 (d, 2H, $J = 8.2$ Hz), 10.11 (s, 1H), 13.98 (s, 1H); ^{13}C NMR 47.07, 116.02, 116.88, 126.95, 127.86, 128.93, 130.36, 136.31, 152.06, 159.88, 168.19; MS (EI, 70 eV): m/z (%) 283 (6.2), 254 (13), 121 (100); IR 3366, 3133, 2958, 1611, 1515, 1439, 1401, 1275, 1208, 1176, 1140, 843, 728 cm^{-1}. Calcd. for $C_{15}H_{13}N_3OS$: C, 63.58; H, 4.62; N, 14.83; O, 5.65; S, 11.32. Found: C, 63.89; H, 4.68; N, 14.97.

2,4-Dihydro-5-(4-hydroxyphenyl)-4-(4-methylphenyl)-3*H*-1,2,4-triazole-3 (2*H*)-thione (5c). Mp 234–236 °C. ^{1}H NMR 2.34 (s, 3H), 6.66 (m, 2H), 7.10–7.26 (m, 4H), 7.71 (m, 2H), 9.94 (s, 1H), 13.92 (s, 1H); ^{13}C NMR 21.11, 115.79, 116.72, 126.74, 130.26, 132.00, 132.39, 139.49, 151.40, 159.44, 168.56; MS (EI, 70 eV): m/z (%) 283 (M^+, 100), 282 (74), 269 (23); IR 3269, 3113, 1611, 1561, 1511, 1478, 1403, 1326, 1274, 1238, 1174, 1069, 972, 846, 818 cm^{-1}. Calcd. for $C_{15}H_{13}N_3OS$: C, 63.58; H, 4.62; N, 14.83; O, 5.65; S, 11.32. Found: C, 63.71; H, 4.44; N, 14.69.

2,4-Dihydro-5-(4-hydroxyphenyl)-4-(4-methoxyphenyl)-3*H*-1,2,4-triazole-3 (2*H*)-thione (5d). Mp 256–258 °C; ^{1}H NMR 3.79 (s, 3H), 6.68 (d, 2H, $J = 8.4$ Hz), 7.01 (d, 2H, $J = 8.4$ Hz), 7.11 (d, 2H, $J = 8.0$ Hz), 7.23 (d, 2H, $J = 8.0$ Hz), 9.97 (s, 1H), 13.93 (s, 1H); ^{13}C NMR 59.90, 118.93, 119.83, 120.95, 131.80, 134.29, 134.42, 155.41, 163.65, 166.82, 172.98; IR 3321, 3147, 2943, 1612, 1593, 1514, 1496, 1398, 1329, 1315, 1281, 1246, 1176, 843, 757, 694 cm^{-1}. MS (EI, 70 eV): m/z (%) ° 299 (M^+, 13), 180 (100), 121 (40). Calcd for $C_{15}H_{13}N_3O_2S$: C, 60.18; H, 4.38; N, 14.04; O, 10.69; S, 10.71. Found: C, 60.47; H, 4.49; N, 13.88.

4-[5-(Butylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl] phenol (5e). Mp 254–256 °C. ^{1}H NMR 0.80 (t, 3H, $J = 7.2$ Hz), 1.27 (m, 2H), 1.58 (m, 2H), 3.05 (t, 2H, $J = 6.8$ Hz), 6.63 (d, 2H, $J = 8.0$ Hz), 7.12 (d, 2H, $J = 8.0$ Hz), 7.31 (m, 2H), 7.49 (m, 3H), 9.88 (s, 1H); ^{13}C NMR 17.90, 26.62, 35.63, 36.37, 119.85, 122.19, 123.94, 132.30, 134.01, 134.41, 138.73, 151.05, 159.06, 163.71; MS (EI, 70 eV): m/z (%) 325 (M^+, 17.43), 278 (100), 268 (97), 121 (37), 77 (48), 91 (27); IR 3427, 2925, 2683, 1609, 1477, 1438, 1385, 1319, 1286, 1256 cm^{-1}. Calcd. for $C_{18}H_{19}N_3OS$: C, 66.43; H, 5.88; N, 12.91; O, 4.92; S, 9.85. Found: C, 66.72; H, 5.67; N, 13.17.

4-[5-(Methylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl] phenol (5f). Mp 242–244 °C; ^{1}H NMR 2.58 (s, 3H), 6.68 (d, 2H, $J = 7.8$ Hz), 7.16 (d, 2H, $J = 7.8$ Hz), 7.37 (m, 2H), 7.54 (m, 3H), 9.91 (s, 1H); ^{13}C NMR 18.95, 119.82, 121.64, 132.16, 133.99, 134.46, 138.52, 156.60, 159.04, 163.20; MS (EI, 70 eV): m/z (%) 283 (M^+, 100), 267 (9.5), 250 (28), 174 (27), 121 (24), 91 (82), 77 (44); IR 3423, 2923, 2684, 1609, 1477, 1438, 1384, 1319, 1283, 1256, 1208, 1138, 836, 804, 771, 698 cm^{-1}. Calcd. for $C_{15}H_{13}N_3OS$: C, 63.58; H, 4.62; N, 14.83; O, 5.65; S, 11.32. Found: C, 63.42; H, 4.81; N, 15.04.

4-[5-(4-Nitrobenzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl] phenol (5g). Mp 272–274 °C. ^{1}H NMR 4.52 (s, 2H), 6.69 (d, 2H, $J = 8.4$ Hz), 7.15 (d, 2H, $J = 8.8$ Hz),

7.30 (d, 2H, $J = 8.0$ Hz), 7.537 (m, 3H), 7.66 (d, 2H, $J = 8.8$ Hz), 8.18 (d, 2H, $J = 8.4$ Hz), 9.94 (s, 1H); ^{13}C NMR 67.14, 119.68, 121.48, 127.82, 132.02, 133.78, 134.22, 134.27, 134.58, 138.29, 150.04, 151.06, 154.45, 159.09, 163.16; MS (EI, 70 eV): m/z (%) 404 (M^+, 57), 295 (43), 268 (29), 252 (37), 212 (48), 196 (36), 121 (50), 91 (49), 77 (100); IR 3426, 2924, 2683, 1609, 1536, 1477, 1438, 1352, 1319, 1256, 1208, 1138, 836, 804, 771, 698 cm^{-1}. Calcd. for $C_{21}H_{16}N_4O_3S$: C, 62.36; H, 3.99; N, 13.85; O, 11.87; S, 7.93. Found: C, 62.45; H, 4.13; N, 13.76.

4-[5-(Allylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl] phenol (5h). Mp 206–208 °C; ^{1}H NMR 3.75 (d, 2H, $J = 6.9$ Hz), 5.08 (d, 1H, $J = 10$ Hz), 5.20 (d, 1H, $J = 16.8$ Hz), 5.86 (m, 1H), 6.69 (d, 2H, $J = 8.4$ Hz), 7.15 (d, 2H, $J = 8.4$ Hz), 7.35 (m, 2H), 7.57 (m, 3H); ^{13}C NMR 36.87, 118.23, 119.83, 121.68, 132.14, 133.13, 133.88, 134.43, 138.52, 156.58, 159.04, 163.32; MS (EI, 70 eV): m/z (%) 309 (77), 294 (100), 196 (44), 157 (35), 121 (39), 77 (86); IR 3426, 2984, 2808, 1608, 1543, 1479, 1439, 1382, 1281, 1256, 1185, 1128, 819, 835, 770, 732, 696 cm^{-1}. Calcd. for $C_{17}H_{15}N_3OS$: C, 66.00; H, 4.89; N, 13.58; O, 5.17; S, 10.36. Found: C, 65.86; H, 4.68; N, 13.42.

4-[5-(Benzylthio)-4-phenyl-4*H*-1,2,4-triazol-3-yl] phenol (5i). Mp 258–260 °C; ^{1}H NMR 4.52 (s, 2H), 6.63 (d, 2H, $J = 8.0$ Hz), 6.78 (m, 3H), 6.90 (d, 2H, $J = 8.0$ Hz), 7.14–7.24 (m, 2H), 7.35 (m, 3H), 7.40 (m, 2H), 9.98 (s, 1H); MS (EI, 70 eV): m/z (%) 359 (45), 343 (11), 250 (48), 207 (48), 196 (20), 167 (29), 91 (100), 77 (49); IR 3423, 2924, 2683, 1609, 1477, 1438, 1319, 1268, 1208, 1136, 836, 804, 769, 692 cm^{-1}. Calcd. for $C_{21}H_{17}N_3OS$: C, 70.17; H, 4.77; N, 11.69; O, 4.45; S, 8.92. Found: C, 70.25; H, 4.53; N, 11.83.

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REFERENCES

1. (a) Kane, J. M.; Staeger, M. A.; Dalton, C. R.; Miller, F. P.; Dudley, M. W.; Ogden, A. M. L.; Kehne, J. H.; Ketteler, H. J.; McCloskey, T. C.; Senyah, Y.; Chmielewski, P. A.; Miller, J. A. 5-Aryl-3-(alkylthio)-4H-1,2,4-triazoles as selective antagonists of strychnine-induced convulsions and potential antispastic agents. *J. Med. Chem.* **1994**, *37*, 125–132; (b) Hosam, S. Synthesis of some pyridyloxymethyloxadiazoles, thiadiazoles and triazoles of expected pharmacological activity. *Indian J. Chem.* **1996**, *35B*, 980–984.
2. Hui, X. P.; Chu, C. H.; Zhang, Z. Y.; Wang, Q.; Zhang, Q. Synthesis and antibacterial activities of 1,3,4-oxadiazole derivatives containing 5-methylisoxazole moiety. *Indian J. Chem.* **2002**, *41B*, 2176–2179.
3. (a) Labanauskas, L.; Udrenaite, E.; Gaidelis, P.; Brukštus, A. Synthesis of 5-(2-,3- and 4-methoxyphenyl)-4*H*-1,2,4-triazole-3-thiol derivatives exhibiting anti-inflammatory activity. *Farmaco*. **2004**, *59*, 255–259; (b) Maxwell, J. R.; Wasdahl, D. A.; Wolfson, A. C.; Stenberg, V. I. Synthesis of 5-aryl-2*H*-tetrazoles, 5-aryl-2*H*-tetrazole-2-acetic acids, and [(4-phenyl-5-aryl-4*H*-1,2,4-triazol-3-yl)thio]acetic acids as possible superoxide scavengers and antiinflammatory agents. *J. Med. Chem.* **1984**, *27*, 1565–1570.

4. Foley, K. Triazole derivatives and their preparation and method for treating non-Hodgkin's lymphoma. US Patent 2006-808341, 2007.
5. Mullican, M. D.; Wilson, M. W.; Conner, D. T.; Kostlan, C. R.; Schrier, D. J.; Dyer, R. D. Design of 5-(3,5-di-*tert*-butyl-4- hydroxyphenyl)-l,3,4-thiadiazoles-1,3,4-oxadiazoles, and-1,2,4-triazoles as orally active, nonulcerogenic anti-inflammatory agents. *J. Med. Chem*. **1993**, *36*, 1090–1099.
6. Kane, J. M.; Dudley, M. W.; Sorensen, S. M.; Miller, F. P. 2,4-Dihydro-3*H*-1,2,4-triazole-3-thiones as potential antidepressant agents. *J. Med. Chem*. **1988**, *31*, 1253–1256.
7. Gulerman, N. N.; Dogan, H. N.; Rollas, S.; Johansson, C.; Celik, C. Synthesis and structure elucidation of some new thioether derivatives of 1,2,4-triazoline-3-thiones and their antimicrobial activities. *Farmaco*. **2001**, *56*, 953–958.
8. Foks, H. Synthesis and tuberculostatic activity of some 2-piperazinmethylene derivatives 1,2,4-triazole-3-thiones. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180*, 537–543.
9. Rigo, B.; Couturier, D. Studies on pyrrolidinones: Synthesis of 5-(5-oxo-2-pyrrolidinyl)-1,2,4-triazole-3-thione derivatives. *J. Heterocycl. Chem*. **1989**, *26*, 1723–1727.
10. Talawar, M. B.; Bennur, S. C.; Kankanwadi, S. K.; Patil, P. A. Anti-inflammatory activity of some new 3-substituted-4-amino-5-mercapto-4(H)-1,2,4-triazoles. *Indian J. Pharm. Sci*. **1995**, *57*, 194–197.
11. Hoggarth, E. Compounds related to thiosemicarbazide, I: 3-Phenyl-1,2,4-triazole derivatives. *J. Chem. Soc*. **1949**, 1160–1163.
12. Durant, G. J. The reaction of benzoyl isothiocyanate with hydrazine derivatives, I: Reaction with some alkyl hydrazines. *J. Chem. Soc. C* **1967**, 92–94.
13. Kane, J. M. The bis(tricyclohexylstannyl) sulfide thionation of 3*H*-1,2,4-triazol-3-ones. *Synthesis* **1987**, 912–913.
14. (a) Seneci, P. *Solid-Phase Synthesis and Combinatorial Chemistry*; Wiley Interscience: New York, 2000; (b) Dorwald, F. Z. *Organic Synthesis on Solid Phase*; Wiley-VCH: Weinheim, 2000.
15. (a) Wilson, M. W.; Hernandez, A. S.; Calvet, A. P.; Hodges, J. C. Solid-supported syntheses of 3-thio-1,2,4-triazoles. *Mol. Divers.* **1998**, *3*, 95–112; (b) Graybill, T. L.; Thomas, S.; Wang, M. A. A convenient 'catch, cyclize, and release' preparation of 3-thio-1,2,4--triazoles mediated by polymer-bound BEMP. *Tetrahedron Lett*. **2002**, *43*, 5305–5309.
16. (a) Liu, Z. X.; Zhao, J. L.; Huang, X. Solid-phase synthesis of 1,3,4-oxadiazoline-5-thione derivatives from resin-bound acylhydrazines. *Bioorg. Med. Chem. Lett*. **2006**, *16*, 1828–1830; (b) Liu, Z. X.; Mu, Y. Y.; Lin, J.; Chen, Y. Y. Traceless solid-phase synthesis of 1,2,3-thiadiazole derivatives from resin-bound acylhydrazine. *Synth. Commun*. **2008**, *38*, 4407–4414; (c) Liu, Z. X.; Mu, Y. Y.; Song, Z. S. Solid-phase synthesis of 4,5-disubstituted 1,2,4-triazol-3-one derivatives from resin-bound acylhydrazines. *J. Chem. Res.*, **2008**, 216–217.