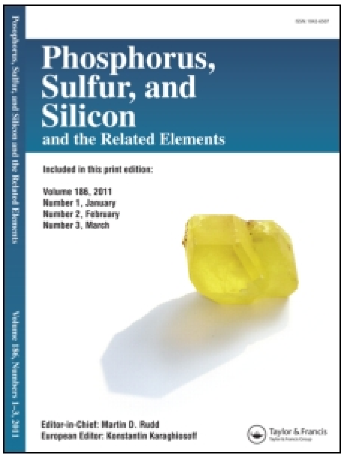

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M. M. Heravi[a]; H. R. Khademalfoghara[b]; M. M. Sadeghi[a]; Sh. Khaleghi[a]; M. Ghassemzadeh[c]
[a] Department of Chemistry, Azzahra University, Vanak, Tehran, Iran [b] Department of Chemistry, Azad University, Yazd, Iran [c] Chemistry and Chemical Engineering Research Center of Iran, Tehran, Iran

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M. M. Heravi
Department of Chemistry, Azzahra University, Vanak, Tehran, Iran

H. R. Khademalfoghara
Department of Chemistry, Azad University, Yazd, Iran

M. M. Sadeghi
Sh. Khaleghi
Department of Chemistry, Azzahra University, Vanak, Tehran, Iran

M. Ghassemzadeh
Chemistry and Chemical Engineering Research Center of Iran,
Tehran, Iran

3-mercapto-1,2,4-triazoles were condensed with allyl bromide in the presence of a base to afford the corresponding 3-allyl compounds 2. The latter were cyclized regioselectively to give 2,3-dihydro-3-methylthiazolo[3,2-b]1,2,4-triazoles ***3***.

Keywords 1,2,4-triazole; microwave irradiation; silica gel; sulfuric acid; thiazole; thiazolotriazole

Many compounds bearing five-membered rings such as thiazole[1] and triazoles[2] have been synthesized and evaluated for biological activities.[3] Thiazolo[3,2-*b*]1,2,4-triazoles also shows significant biological and pharmacological potentiality.[4]

Recently, we have described the synthesis of thiazolo[3,2-*b*]1,2,4-triazole.[5] In a previous article we described the regioselective cyclization of 3-crotylmercapto-1,2,4-triazine.[6] With a view to extending the synthetic utility of allylic type compounds, we have investigated the heterocyclization of 3-allylmercapto-1,2,4-triazoles.

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Address correspondence to Majid M. Heravi, Azzahra University, Department of Chemistry, School of Sciences, Vanak, Tehran, Iran. E-mail: mmh1331@yahoo.com

5-substituted-1,2,4-triazole-3(2H)-thiones[7] (**1**, R = H, Me, Ph) were condensed with allyl bromide in the presence of KOH to afford the corresponding 3-allylmercapto derivatives (**2**, R = H, Me, Ph).

We have recently reported on solid state heterocyclization using zeolite[8] and sulfuric acid adsorbed on silica gel.[9] We have also used sulfuric acid adsorbed on silica gel in solvent free tetrahydropyranylation of alcohols and phenols.[10]

Armed with these experiences and in continuation of our attempts to develop selective and preparatively useful methodology based on the use of solid acids as promoters[8–10] and microwave irradiation as a source of energy,[11] we have treated compound **2** (R = H) with sulfuric acid adsorbed on silica gel under microwave irradiation.

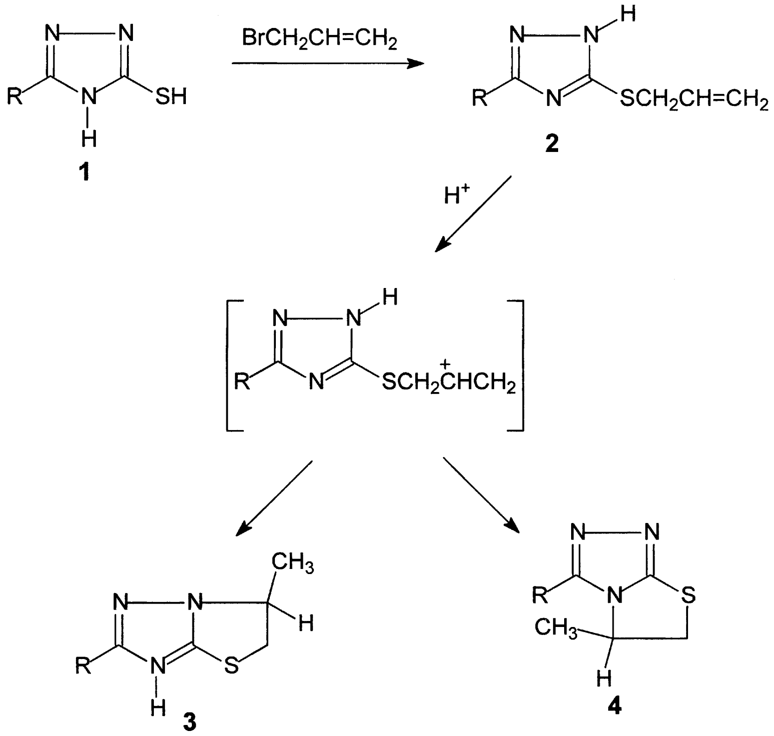
From this reaction a single crystalline product was obtained. In the mass spectrum, both **2** (R = H) and **3** (R = H), have the same parent peak. The IR spectrum of **3** (R = H) showed a carbonyl absorption band but no NH vibrations. The ^{1}HNMR spectrum of **3** (R = H) showed the disappearance of the olifinic protons and the appearance of a new doublet signal due to methyl protons adjacent to CH. These results clearly indicate the exclusive fusion of the thiazole ring to the 1,2,4-triazole ring via a carbocation intermediate, generated from sulfuric acid on allylmercapto-1,2,4-triazine (Scheme 1). However, fusion of the thiazolo and 1,2,4-triazole nuclei can be effected in two different ways represented by thiazolo[3,2-*b*]1,2,4-triazole **3** and thiazolo[2,3-c]1,2,4-triazole **4**.

It has been shown, due to the α-effect, that the nitrogen 2 of 1,2,4-triazole is more reactive than the nitrogen 4 leading to the cyclization around the b bond to give **3** rather than **4**.[5a,b] We have recently proved the reactivity of N2 relative to N4 in 1,2,4-triazole by X-ray structural determination.[5c]

In conclusion, we have developed a facile and ecofriendly method for the synthesis of thiazolo[3,2-*b*]1,2,4-triazoles. These compounds have a chiral center. Although we did not have a chiral media for the chiral induction, it is a good model for the asymmetric synthesis of thiazolo[3,2-*b*]1,2,4-triazoles.

EXPERIMENTAL

Melting points obtained on a Büchi 530 apparatus are uncorrected. ^{1}HNMR spectra were recorded on a Bruker AC 100 spectrometer. IR spectra were recorded on a Perkin-Elmer model 883 using a KBr disc, and mass spectra were obtained on a Varian CH-7.



SCHEME 1

Synthesis of 6-Substituted-3-methyl-3H-thiazolo[3,2-*b*]1,2,4-Triazoles 3: General Procedure

An appropriate 3-mercapto-1,2,4-triazole **1** (0.56 mmol) was dissolved in ethanolic solution of potassium hydroxide (0.03 g, 0.56 mmol). To this solution, allyl bromide (0.07 g, 0.56 mmol) was added slowly at r.t. The progress of the reaction was monitored by TLC. Upon the completion of the reaction, the solvent was evaporated to dryness under reduced pressure and the crude residue was disolved in chloroform (15 mL). The solvent was then evaporated and the residue was directly treated with sulfuric acid supported onto silica gel (1.5 g), and placed in an unmodified microwave oven for 8 min. The residue was dissolved in methanol and was filtered. The filtrate was evaporated to dryness under reduced pressure to obtain the titled compound.

Selected Data for 3 ($R = H$)

Yield: 88%, ^{1}HNMR, δ ($CDCl_3$) 1.2 (d, $J = 6$ Hz, 3H, Me), 3.5–4 (q, 1H, diasterotopic CH), 3.1–3.5 (q, 1H, diasterotopic CH), 4.1–4.6 (m, 1H, CH), 7.4 (s, 1H, CH of triazole); IR $\tilde{\upsilon}$ (KBr disc) 1688, 1459, 1382 cm^{-1}, MS, m/z, M^+ 141; UV λ (MeOH) 226 nm.

Selected Data for 3 ($R = CH_3$)

Yield: 50%. ^{1}HNMR, δ ($CDCl_3$) 1.5 (d, $J = 6$ Hz, 3H, Me), 2.2 (s, 3H. Me), 3.2–6 (q, 1H, diasterotopic CH), 3.7–4.1 (q, 1H, diasterotopic CH), 4.1–4.6 (m, 1H, CH); IR $\tilde{\upsilon}$ (KBr disc) 2980, 1141, 1377 cm^{-1}, MS, m/z, M^+ 155; UV λ (MeOH) 237 snm.

Selected Data for 3 ($R = Ph$)

Yield: 74% m.p. = 79–80°C, ^{1}HNMR, δ ($CDCl_3$) 1.5 (d, $J = 6$ Hz, 3H, Me), 3–3.5 (q, 1H, diasterotopic CH), 3.5–4 (q, 1H, diasterotopic CH), 4–4.6 (m, 1H, CH), 7.5 (s, 2H, aromatic), 8.0 (s, 2H, aromatic); IR $\tilde{\upsilon}$ (KBr disc) 2929, 1637, 1473, 1431 cm^{-1}; MS, m/z, -M^+ 217; UV λ (MeOH) 265, 238, 218 nm.

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