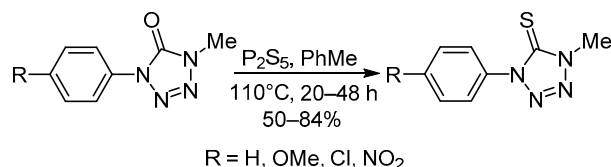
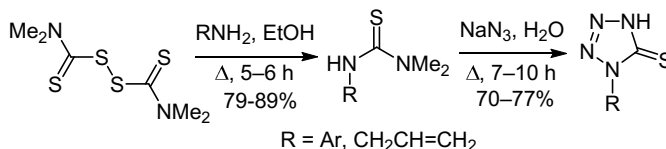
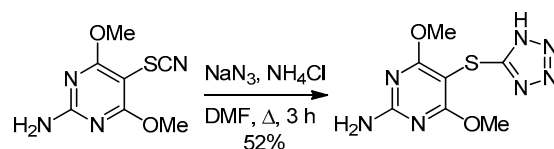


Synthesis of tetrazole-5-thiones (continued)

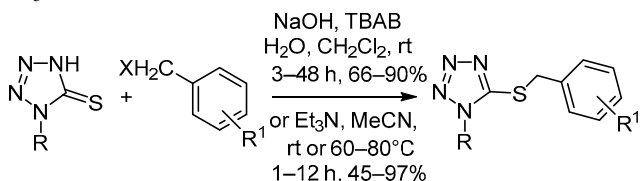
Substitution of isothiocyanates with arylthiocyanates in the reaction with NaN_3 allows for an easy one-step synthesis of *S*-aryl derivatives of 1*H*-tetrazole-5-thiones. Thus, 2-amino-4,6-dimethoxy-5-(1*H*-tetrazol-5-ylsulfanyl)pyrimidine was obtained by reacting thiocyanatopyrimidine with NaN_3 in the presence of NH_4Cl in DMF.⁹

Haidar et al. have developed a new technique for the synthesis of 1-aryl(alkyl)-1*H*-tetrazole-5-thiones from tetramethylthiuram disulfide *via* isolation of intermediate 3-substituted 1,1-dimethylthiourea.¹⁰

An alternative method of preparing tetrazolethiones involves the use of tetrazol-5-ones as precursors. A series of 1-substituted 4-methyl-1*H*-tetrazole-5-thiones was obtained by the action of P_2S_5 on the corresponding 4-methyl-1*H*-tetrazol-5-ones.¹¹ Lawesson's reagent is also used as a thiocarbonylating agent in such reactions.¹²

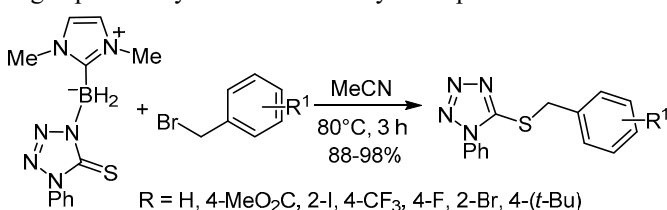
**Alkylation**

It is known that tetrazolethiones are ambident nucleophiles. However, in alkylation reactions with different alkyl halides they act solely as *S*-nucleophiles.^{1b,13} Thus, a series of 1-alkyl/aryl-5-benzylsulfanyl-1*H*-tetrazoles was synthesized *via* a reaction of 1-substituted 1*H*-tetrazole-5-thiones with the corresponding benzyl halides under phase-transfer catalysis conditions or in acetonitrile in the presence of Et_3N .^{1b}

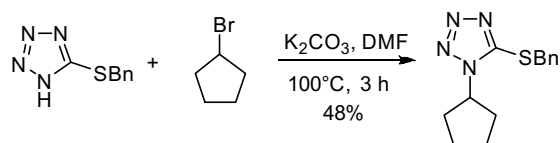


$\text{X} = \text{Cl}, \text{Br}$; $\text{R} = \text{Me}, \text{NH}_2, \text{hexyl}, 1\text{-Ad}, \text{Bn}, \text{Ph}, 2\text{-O}_2\text{NC}_6\text{H}_4, 4\text{-Et}_2\text{NC}_6\text{H}_4, 2\text{-MeOC}_6\text{H}_4, 3\text{-FC}_6\text{H}_4, \text{etc}$; $\text{R}^1 = \text{H}, 4\text{-NO}_2, 2,4\text{-(NO}_2)_2, 3,5\text{-(NO}_2)_2$

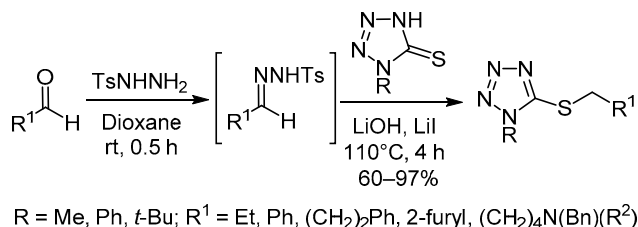
The reaction of *N*-boryltetrazolethione with benzyl bromides by heating in acetonitrile similarly proceeds regioselectively to form the *S*-alkylation products.^{13b}



Only further alkylation of 5-aryl/benzylsulfanyl-1*H*-tetrazoles with alkyl halides leads to the corresponding *N*-derivatives.^{9,14} 5-Benzylsulfanyl-1-cyclopentyl-1*H*-tetrazole was synthesized by the action of cyclopentyl bromide on benzylsulfanyltetrazole by heating in DMF in the presence of K_2CO_3 .¹⁴

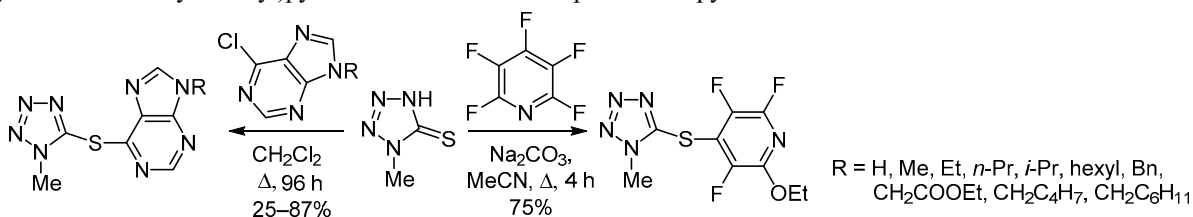


A fundamentally new, simple, convenient one-pot method for the synthesis of alkyl(1*H*-tetrazol-5-yl)thioethers has been developed, comprising condensation of aldehydes with *N*-tosylhydrazine to produce tosylhydrazones, which are then used *in situ* in reactions with 1*H*-tetrazole-5-thiones.¹⁵

**Arylation**

Methods for the synthesis of 9-alkyl-6-(1-methyl-1*H*-tetrazol-5-ylsulfanyl)-9*H*-purines¹⁶ and 2-ethoxy-3,5,6-trifluoro-4-(1-methyl-1*H*-tetrazol-5-ylsulfanyl)pyridine¹⁷ have been

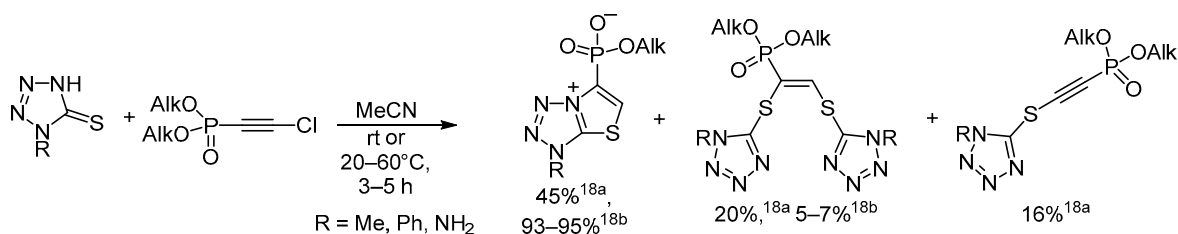
proposed based on the reaction of 1-methyl-1*H*-tetrazol-5-thione with respectively 9-alkyl-6-chloro-9*H*-purines or pentafluoropyridine.



Reactions with chloroethynylphosphonates

The reaction of 1-substituted 1*H*-tetrazole-5-thiones with an equimolar amount of dialkyl chloroethynylphosphonates in acetonitrile proceeds ambiguously. According to ¹H, ¹³C, and ³¹P NMR, the major reaction product is the cyclic

thiazolotetrazole zwitterion, whereas the phosphonate and thioethynylphosphonate are formed in negligible amounts.¹⁸



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