Reactions with hydrazonoyl halides XXIX: synthesis of some new 1,2,4-triazolo[4,3-*a*]benzimidazole, thiazolo[3,2-*a*]benzimidazole, and unsymmetrical azine derivatives

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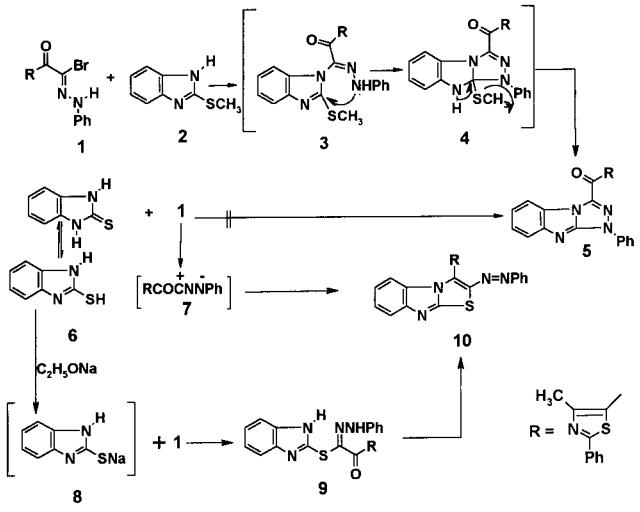
Triazolo[4,3-*a*]benzimidazole, thiazolo[3,2-*a*]benzimidazole, and unsymmetrical azines, were synthesized via reactions of C-thiazol-5-oyl-*N*-phenylhydrazonoyl bromide with each of 2-(methylthio)benzimidazole, benzimidazoline-2-thione, and alkyl carbodithioate, respectively.

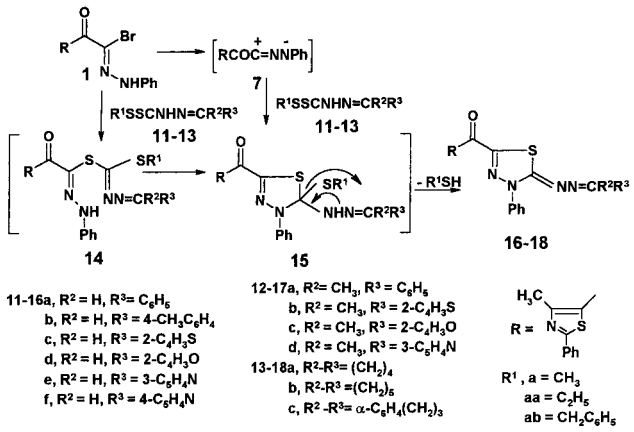
α-Ketohydrazonoyl halides have been widely employed for the synthesis of heterocyclic compounds. The reaction of equimolar amounts of *C*-thiazol-5-oyl-*N*-phenylhydrazonoyl bromide **1**[6] with 2-(methylthio)benzimidazole (**2**) in ethanolic triethylamine solution furnished exclusively the corresponding 1-phenyl-3-(4′-methyl-2′-phenylthiazol-5′-oyl)-1,2,4-triazolo[4,3-*a*]benzimidazole (**5**). Structure **5** was proposed on the basis of analytical and spectral data. The formation of **5** can be explained by a stepwise path involving substitution to give amidrazone **3**, which readily cyclized to give intermediate **4**. The latter converted into **5** by elimination of CH_3SH (*c.f.* Scheme 1).

On the other hand, benzimidazoline-2-thione (**6**) reacted with **1** in refluxing chloroform containing triethylamine to afford a product formulated as 2-phenylazo-3-(4′-methyl-2′-phenylthiazol-5′-yl)thiazolo[3,2-*a*]benzimidazole (**10**) based on the spectral data and elemental analyses. The IR spectrum of **10** revealed the absence of any bands between 1800 and 1600 cm^{-1} attributable to a CO group.[7] Its ^1H NMR spectrum showed signals at δ = 3.06 (s, 3H, CH_3 (thiazole C-4)) and 7.21–7.88 (m, 14H, ArH's). Its mass spectrum showed *m/z* = 451(M^+). In contrast, **6** reacted with hydrazonoyl bromide **1** in sodium ethoxide solution to afford 1-benzimidazol-2′-ylthio)-1-phenylhydrazono-2-(4′-methyl-2′-phenylthiazol-5′-oyl)ethane (**9**). Compound **9** was converted into **10** by treatment with sulfuric acid.



Scheme 1

Treatment of hydrazonoyl bromide **1** with the methyl carbodithioates **11a**, **11aa** or **11ab** in ethanolic triethylamine gave unsymmetrical azine **16a**. Structure **16** was proposed on the basis of elemental analyses, and spectral data. The formation of **16a** can be explained via elimination of alkyl mercaptan from cycloadduct **15**, which is assumed to be formed from the 1,3-dipolar cycloaddition of **7** to C=S double bond with the appropriate **11a**, **11aa**, **11ab** (*c.f.* Scheme 2). Alternatively, the formation of **16a** can be also explained by stepwise path involving substitution or 1,3-addition to give acyclic hydrazone **14**. Cyclization of the latter is achieved by elimination of alkyl mercaptan. Similarly, compounds **11b–f**, **12a–d** and **13a–c** reacted with hydrazonoyl bromide **1** in ethanolic triethylamine, to give the corresponding unsymmetrical azines **16b–f**, **17a–d** and **19a–c**, respectively.



Scheme 2

Treatment of methyl phenylthiocarbamate **19a** with hydrazonoyl bromide **1** in ethanolic triethylamine gave 2-phenylimino-2,3-dihydro-1,3,4-thiadiazole **22a** in good yield. In contrast, hydrazonoyl bromide **1** reacted with phenylthiourea (**24a**) in ethanolic triethylamine solution to give 5-phenylazothiazole derivative **23a**. The structure of **23** was elucidated on the basis of elemental analyses, spectral data, and alternative route by treatment of benzenediazonium chloride with thiazole **25a** (which was prepared by reaction of 5-bromoacetylthiazole[8] with phenylthiourea). Compound **1** reacted with methyl phenylhydrazinecarbodithioate **19b** in ethanolic triethylamine to give 2,3-dihydro-1,3,4-thiadiazole **22b**. On the other hand, compound **1** reacts with benzoyl thiosemicarbazide to give 5-phenylazothiazole **23b** (*c.f.* Scheme 3).

Hydrazonoyl bromide **1** reacted with 5-phenyl-1,3,4-oxadiazole-2-thione in boiling chloroform containing triethylamine to afford 2-benzoylhydrazino-1,3,4-thiadiazole **28**. Structure **28** was elucidated on the basis of elemental analyses, spectral data, and alternative method [by treatment of **1** with the appropriate alkyl benzoylhydrazinecarbodithioate **29a,b** in ethanolic triethylamine) (cf. Scheme 4).

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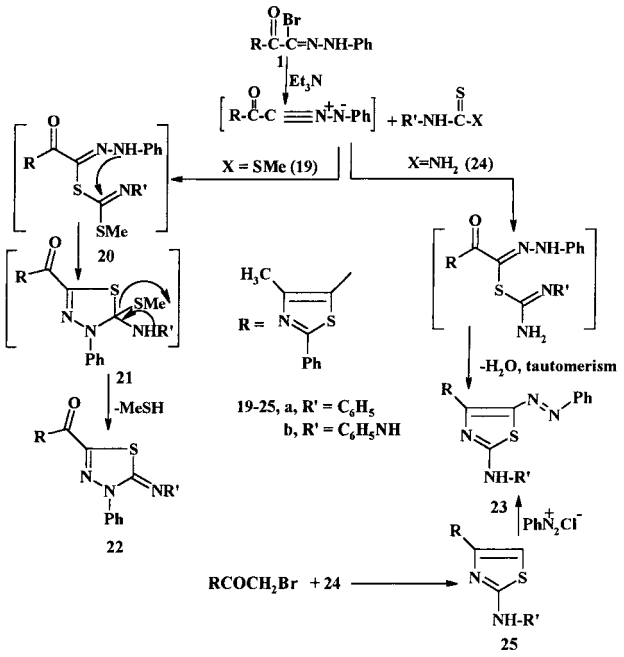
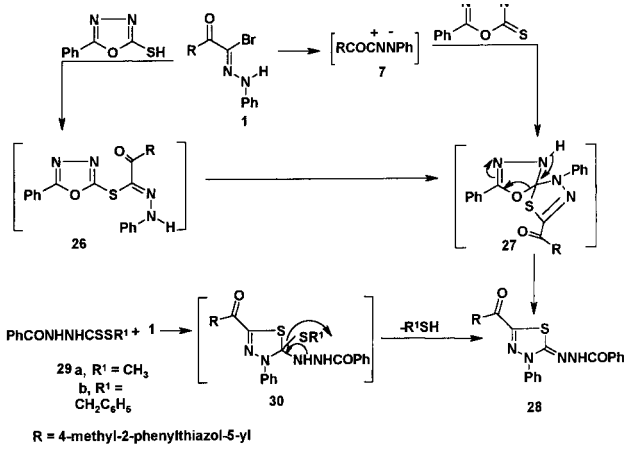


Scheme 3

In the light of the above results, the mechanism outlined in Scheme 4 seems to be the most plausible pathway for the formation of **28** from the reaction **1** with 5-phenyl-1,3,4-oxadiazole-2-thione. The reaction involves the initial formation of the thiohydrazonate ester **26**, which undergoes intramolecular cyclization as soon as it is formed to yield the spirothiadiazole intermediate **27**, or via 1,3-dipolar cycloaddition of nitrilum ylide **7** to the C=S double bond of the oxadiazolethione. The formation of **26** and **27** are similar to the reaction of hydrazonoyl chloride with 5-phenyl-1,3,4-thiadiazole-2(3*H*)-thione[9] and 1-phenyl-1,4-dihydrotetrazole-5-thione[10]. Ring-chain tautomerism of the spiro intermediate **27** leads to the end product **28**. Alternatively, the formation of **29** can be explained via elimination of alkyl mercaptain from cycloadduct **30**.

Techniques used: IR, 1H NMR and Mass spectra



Scheme 4

Tables: 2

Schemes: 4

References: 14

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