2-(1,3-Benzothiazol-2-yl)ethanethioamides in Heterocyclic Synthesis: Novel Synthesis of Pyridine, Pyrido[2,3-*d*]pyrimidine, Coumarin, Thiazolone and Triazole Derivatives

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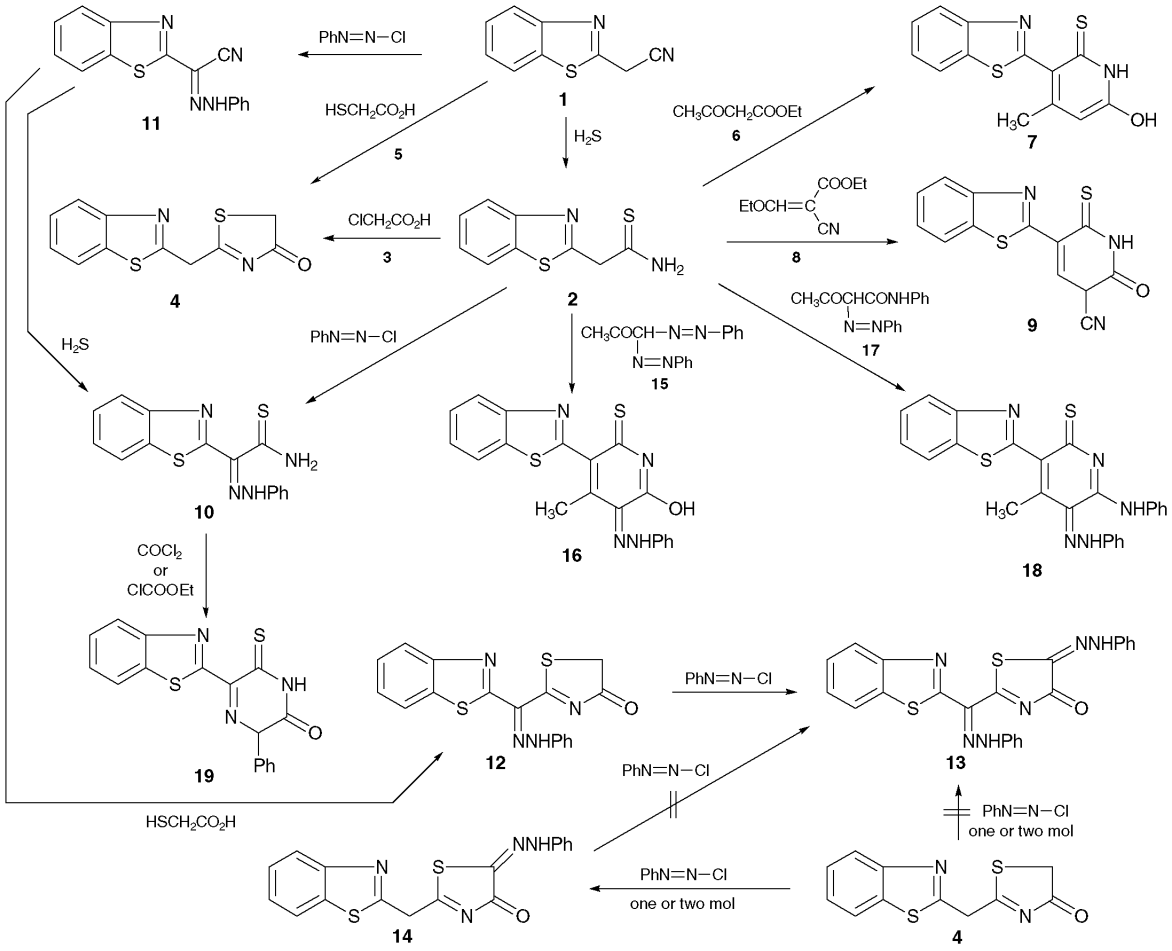
Syntheses of pyridine, pyrido[2,3-*d*]pyrimidine, coumarin, thiazolone and triazole derivatives by using 2-(1,3-benzothiazol-2-yl)ethanethioamide as starting material are described.

In a continuation of previous work[1] dealing with the reactions of 2-cyanomethylbenzothiazole with *N*-arylmaleimides, we report here the utility of 2-(1,3-benzothiazol-2-yl)ethanethioamide (**2**) in the synthesis of pyridine, annelated pyridine, thiazolone, coumarin, pyrimidine and triazole derivatives, which contain a benzothiazol-2-yl moiety. In view of the considerable biological importance of pyridine[2–4] and thiazolones[5–7] the synthesized compounds containing this structural moiety could possess interesting, useful biological and pharmaceutical properties.

It has been found that 2-(1,3-benzothiazol-2-yl)acetonitrile (**1**) reacts with hydrogen sulfide to afford 2-(1,3-benzothiazol-2-yl)ethanethioamide (**2**). Treatment of **2** with chloroacetic acid (**3**) afforded 2-(1,3-benzothiazol-2-ylmethyl)-1,3-thiazol-4(5*H*)-one (**4**). Compound **2** also reacts with ethyl acetoacetate (**6**) to afford the corresponding benzothiazolylpyridinethione derivative (**7**). Moreover, **2** reacted with the acetate **8** and gave the corresponding 1,3-benzothiazol-2-ylpyridine-3-carbonitrile (**9**) (Scheme 1).

Our investigation was also extended to study the reaction of **2** with benzenediazonium chloride to give the hydrazone derivative **10**. Compound **10** also reacted with chloroacetic acid (**3**) to furnish the recyclized thiazolyl hydrazone derivative **12**. Treatment of the thiazolone **12** with benzenediazo-



Scheme 1

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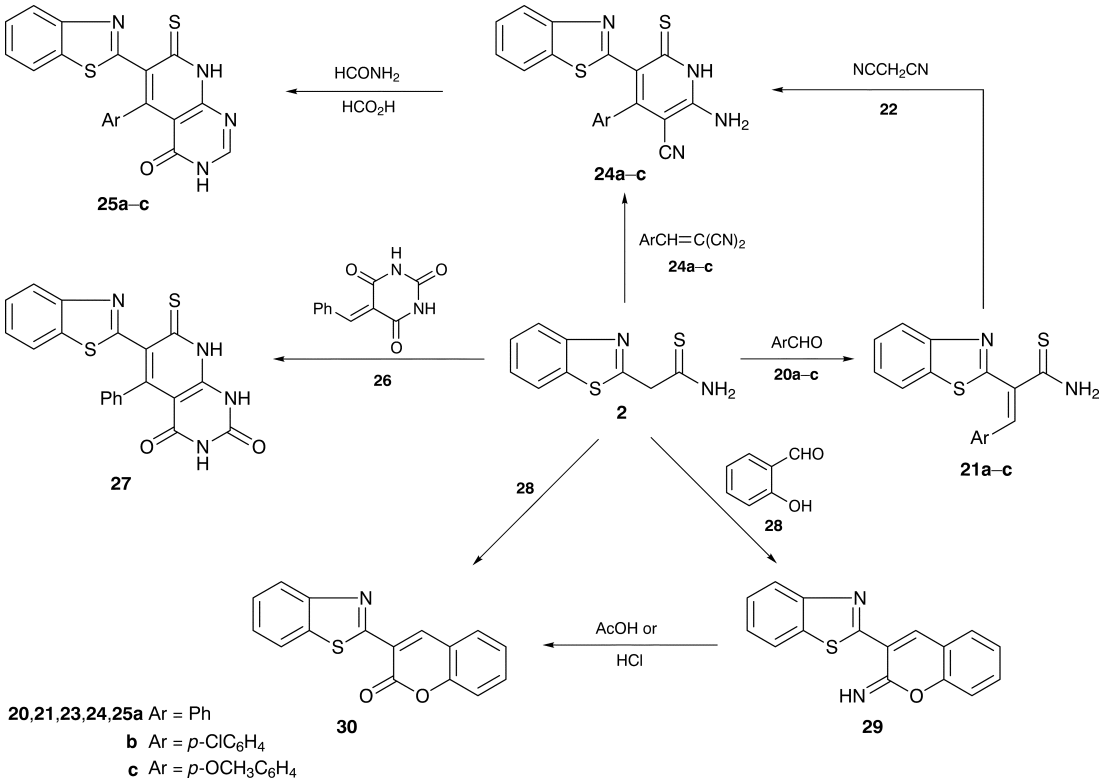

Scheme 2

nium chloride, in methanol in the presence of sodium acetate, afforded 2{1,3-benzothiazol-2-yl[(*Z*)-2-phenylhydrazono]methyl}-1,3-thiazole-4,5-dione 5-(*N*-phenylhydrazone) (**13**).

On the other hand, compound **4** reacts with benzenediazonium chloride to give the corresponding hydrazone derivative **14**.

Compound **2** reacted with ethyl 2-phenylazoacetoacetate (**15**) and gave the corresponding 5-(1,3-benzothiazol-2-yl)-2-hydroxy-4-methyl-6-thionopyridin-3(6*H*)-one *N*-phenylhydrazone (**16**). Treatment of compound **2** with phenylazoacetoacetanilide (**17**) afforded a product that was identified as the *N*-phenylhydrazone derivative (**18**).

Compound **10** also reacts with phosgene or ethyl chloroformate to give the corresponding 6-(1,3-benzothiozol-2-yl)-2-phenyl-5-thiono-4,5-dihydro-1,2,4-triazin-3(2*H*)-one (**19**).

Furthermore, the synthetic potential of **2** was demonstrated *via* its facile condensation with benzaldehyde (**20a**) to give the thioamide **21a**. Treatment of **21a** with malononitrile (**22**) in methanol afforded the pyridinethione derivative **24a** (Scheme 2). In the same manner, **2** reacts with each of **20b**,**c** to afford the corresponding thioamides **21b**,**c**, respectively, which were further reacted with **22** to give the corresponding pyridinethione derivatives **24b**,**c**, respectively. Compound **24a** was also prepared *via* another route, by reacting **2** with the cinnamonitrile derivative (**23a**) in methanol in the presence of triethylamine. Similarly, **2** also reacts with each of **23b**,**c** to afford **24b**,**c**, respectively. Further support for the proposed structure of **24a** was achieved by its reaction with formic acid and formamide to afford the corresponding pyrido[2,3-*d*]pyrimidine derivative **25a**. Analogously, compounds **24b**,**c** react with formic acid and formamide to give the corresponding pyrido[2,3-*d*]-pyrimidine derivatives **25b**,**c** respectively (Scheme 2). The reaction of **2** with the ylidene of barbituric acid **26** leads to the formation of **27**. Compound **2** also reacted with salicylaldehyde (**28**) to yield the corresponding chromenimine derivative **29**. The latter product was converted into the coumarin derivative **30** by treatment with hydrochloric acid or boiling acetic acid. The coumarin derivative **30** was also prepared by the reaction of **2** with salicylaldehyde (**28**) in acetic acid (Scheme 2).

Techniques used: ^{1}H NMR and IR

References: 7

Schemes: 2

Table 1: Characterization data of the newly synthesized compounds

Table 2: IR and ^{1}H NMR spectral data of the newly synthesized compounds

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