Reaction of Carbon Disulfide with Cyanoacetic Acid Hydrazide: Novel Synthesis of Thiazole and Thiazolo[4,5-*c*]pyrazole

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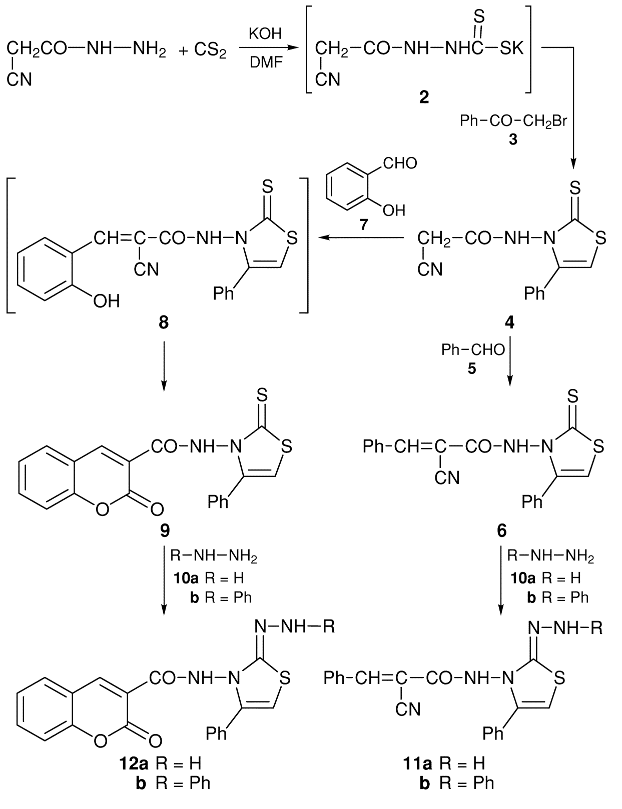
The reaction of cyanoacetic acid hydrazide with carbon disulfide in basic dimethylformamide afforded the potassium thiocarbamate **2** which underwent ready heterocyclization upon its reaction with α-haloketones to give the thiazole derivatives **4** and **23**.

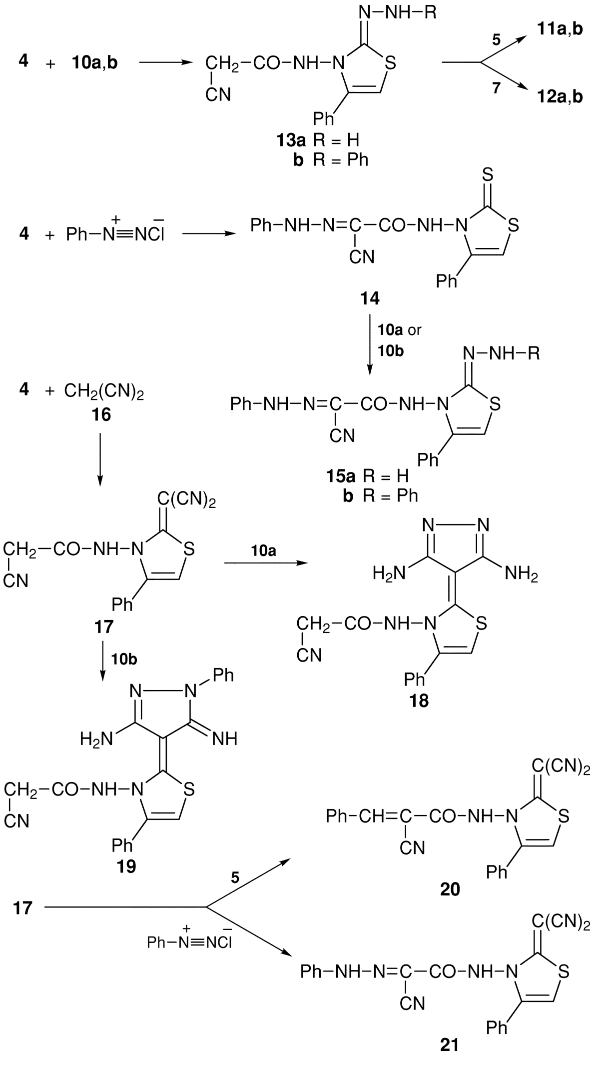
Recently our studies have been directed to studies of the reaction of carbon disulfide towards active methylenes as well as amino functional groups to afford thiazole and thiophene derivatives.[14,15] However, in this article we report the reaction of 2-cyanoacetic acid hydrazide **1** with carbon disulfide in dimethylformamide under basic conditions in KOH/DMF to afford a non-isolable intermediate, the N-potassium thiocarbamate salt **2**.[16] The reaction of **2** with phenacyl bromide **3** gave the thiazole derivative **4**. Confirmation for the structure of **4** was obtained through studying its reactivity towards chemical reagents. It was found that **4** reacts with benzaldehyde (**5**) in 1,4-dioxane that contains a catalytic amount of piperidine to afford the benzylidene derivative **6** (Scheme 1).

The reaction of **4** with salicylaldehyde (**7**) gave the benzo-[*b*]pyran derivative **9**.

The reaction of compound **6** or **9** with either hydrazine hydrate (**10a**) or phenylhydrazine (**10b**) afforded the corresponding hydrazone derivatives **11a**,**b** and **12a**,**b**, respectively (Scheme 1). The structures of the latter products were established on the basis of analytical and spectral data (see full text). Formation of **11a**,**b** and **12a**,**b** takes place through elimination of hydrogen sulfide. Further confirmation for the structures **11a**,**b** and **12a**,**b** was obtained through their synthesis *via* another reaction route. Thus, the reaction of **4** with either hydrazine hydrate **10a** or phenylhydrazine **10b** afforded the hydrazone derivatives **13a**,**b** (Scheme 2). The reaction of the latter products with either benzaldehyde (**5**) or salicylaldehyde (**7**) gave the same products as above, *i.e.* **11a**,**b** and **12a**,**b** respectively (identical IR, mp and mixed mp).



Scheme 1



Scheme 2

Similarly, the reaction of **4** with benzenediazonium chloride in ethanol that contained sodium acetate gave the phenylhydrazone derivative **14**. The structure of the latter

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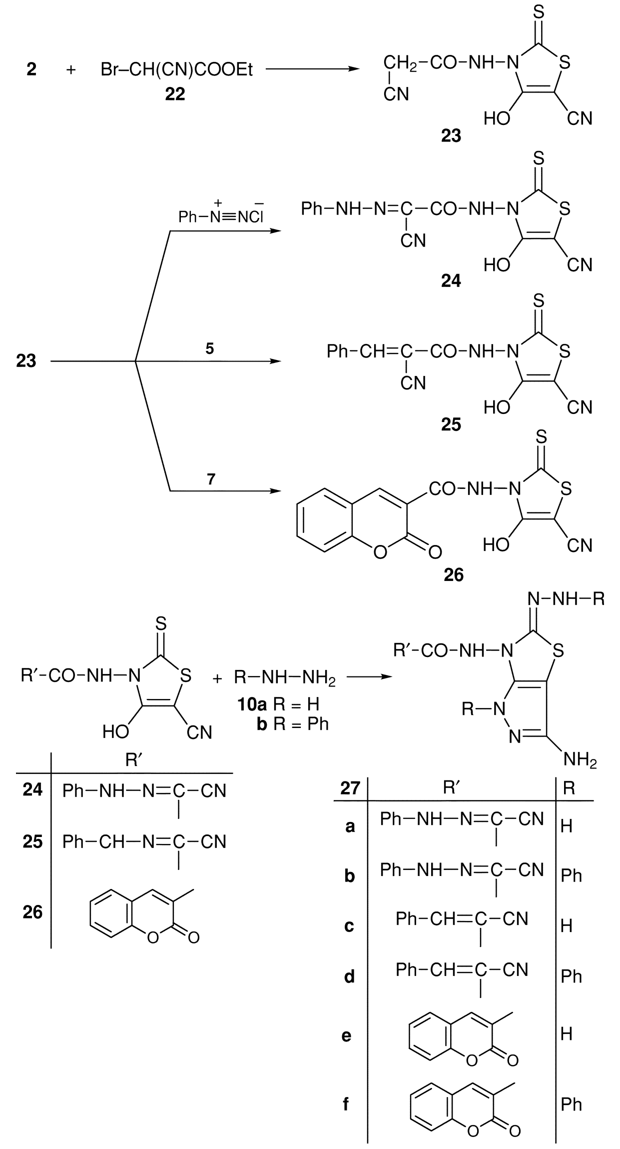
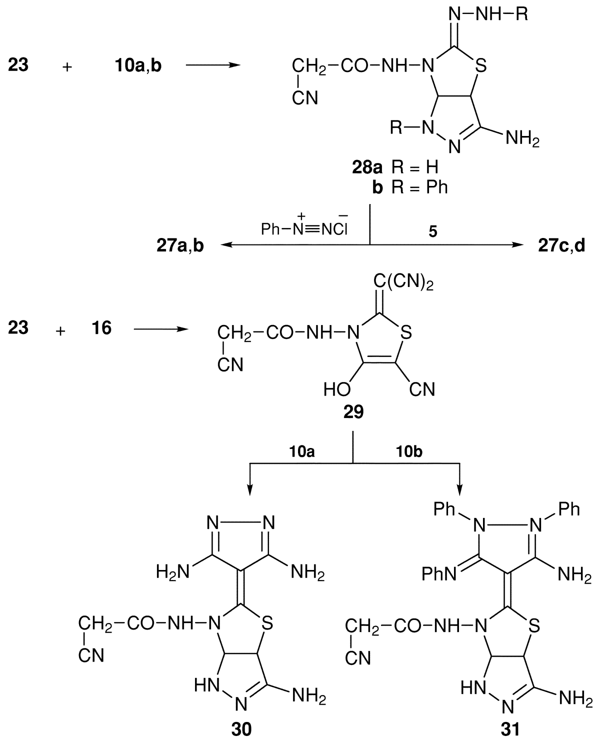


Scheme 3

product was based on the obtained analytical and spectral data. The reaction of **14** with either hydrazine hydrate **10a** or phenylhydrazine **10b** gave the hydrazone derivatives **15a** and **15b**, respectively. Confirmation for structures of **15a** and **15b** was obtained through their synthesis *via* another reaction route. Thus, the reaction of either **13a** or **13b** with benzenediazonium chloride gave the same hydrazone derivatives as before, **15a** and **15b**, respectively (identical IR, mp and mixed mp).

The reaction of **4** with active methylene reagents was studied to afford condensed products which will be ready for further cyclizations. Thus, the reaction of **4** with malononitrile **16** gave the condensed product **17**. The structure of **17** was based on analytical and spectral data (Scheme 2); its formation took place *via* elimination of hydrogen sulfide. The reaction of **17** with either hydrazine hydrate **10a** or phenylhydrazine **10b** afforded the pyrazole derivatives **18** or **19** respectively. The structures of compounds **18** and **19** were based on analytical and spectral data. The reaction of **17** with benzaldehyde afforded the benzylidene derivative **20**. On the other hand, the reaction of **17** with benzenediazonium chloride gave the phenylhydrazone derivative **21**.

The reaction of the intermediate thiocarbamate salt **2** with ethyl α-bromocyanoacetate **22** afforded the thiazole derivative **23** (Scheme 3).



Scheme 4

The reaction of **23** with benzenediazonium chloride gave the phenylhydrazone derivative **24**. On the other hand, compound **17** reacted with benzaldehyde (**5**) to give the benzal derivative **25**. The reaction of **23** with salicylaldehyde (**7**) afforded the benzo[*b*]pyran derivative **26**.

The reaction of **24**, **25** or **26** with hydrazine hydrate (**10a**) or phenyl hydrazine (**10b**) afforded the thiazolo[4,5-*c*]-pyrazol-5-hydrazone derivatives **27a**–**f**, respectively (Scheme 3). The formation of **27a**–**f** was proposed in terms of the formation of a simple hydrazone through the loss of H_2S and the addition of NH_2 to the CN group to form the corresponding amidrazone derivatives, followed by elimination of water. The reaction of **23** with either hydrazine hydrate (**10a**) or phenylhydrazine (**10b**) afforded the hydrazone derivatives **28a** and **28b** respectively. The reaction of any of the latter products with either benzenediazonium chloride or benzaldehyde (**5**) afforded the products **27a**,**b** and **27c**,**d**, respectively (identical mp and mixed mp). The reaction of **23** with malonitrile (**16**) afforded the dicyanomethino derivative **29**. Compound **29** reacted with either hydrazine hydrate (**10a**) or phenylhydrazine (**10b**) to form the pyrazole derivatives **30** and **31**, respectively. The structures of the latter products were based on analytical and spectral data (Scheme 4).

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Techniques used: ^1H and ^{13}C NMR, IR and elemental analysis

References: 21 Schemes: 4

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References cited in this synopsis

14 R. M. Mohareb and S. M. Sherif, *Heteroatom*, 1997, **8**, 77.
15 R. M. Mohareb and S. M. Sherif, *J. Chem. Res.* (*S*), 1994, 484.
16 M. T. Cocco, C. Congiu and V. Onnis, *J. Heterocycl. Chem.*, 1995, **32**, 463.