Chinese Chemical Letters Vol. 10, No. 3, pp. 189–190, 1999

A Novel Tandem Reaction for the Synthesis of Thieno[2,3-C]Pyrazole

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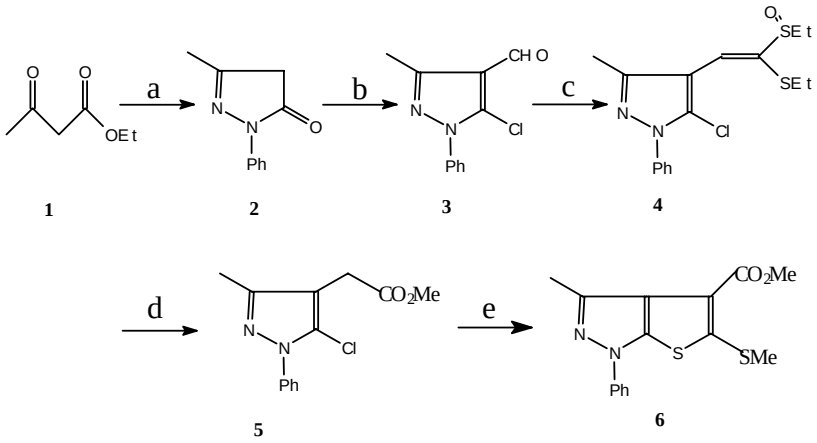
Abstract: A new method was found for the synthesis of pyrazoleacetate esters from pyrazolaldehyde. By a new tandem reaction, in which methyl 4-pyrazoleacetate reacted with carbon disulfide and iodomethane, thieno[2,3-c]pyrazole was synthesized. This was an easy method for the synthesis of this type of heterocycles.

Keywords: Thieno[2,3-c]pyrazole; heterocycles; synthesis.

In study on new pharmaceuticals and agrochemicals, the application of heterocycles is a very important method, which can improve the biological activities. In these years, more and more new agrochemicals have been synthesized which have the structures containing heterocycles, especially pyrazole. In our study on this type of compounds, we found that thieno[2,3-c]pyrazole had good biological activities. We are also interested on its synthesis. Thieno[2,3-c]pyrazole was seldom studied before. Kvitko[1,2] prepared 3-methyl-1-phenyl-5-thieno[2,3-c]pyrazolecarboxylic acid by treatment of 5-chloro-3-methyl-1-phenyl-4-pyrazolaldhyde with thioglycolic acid. They[3] also prepared this compound by the reaction of 4-dimethyaminomethylene-3-methyl-1-phenyl-5-thiopyrazolone with chloro-acetic acid. 5-Chloro-3-methyl-1-phenyl-4-cyanopyrazole reacted with N-phenylthioacetamide to afford 4-amino-3-methyl-1-phenyl-5-phenyl-amino-carbonylthienol [2,3-c]pyrazole[4]. Brown *et al.*[5] used dithiodipyrazolaldhyde to react with nitromethane to afford 3-methyl-5-nitro -1-phenylthieno[2,3-c]pyrazole.

In our study, we found a new method for the synthesis of this type of heterocycles (**Scheme**). Pyrazolone **2** was prepared by treatment of ethyl acetoacetate with phenylhydrazine[6]. Pyrazolaldehyde **3** was prepared by Vilsmeier-Haack reaction from pyrazolone **2**[7-10]. Using the method of Ogura[11-14], a yellow thick liquid **4** (Y=80%) was prepared, which was then converted to a colorless liquid **5** (Y=80%). This was a new method for the synthesis of pyrazoleacetate esters from pyrazolaldehyde. After ester **5**, CS_2, KOH and DMSO were stirred overnight and MeI was then added into, the ring-closure product **6** (Y=94%, mp: 138-139℃) was synthesized.

Scheme



1 **2** **3** **4** **5** **6**

a. $PhNHNH_2$; **b**. $DMF/POCl_3$; **c**. $FAESO^{13}$/NaH/THF; **d**. dry HCl/MeOH; **e. 1**, CS_2/KOH /DMSO; 2, MeI;

References and notes

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Received 29 July 1998