SYNLETT
Spotlight 428

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Mercaptoacetic Acid

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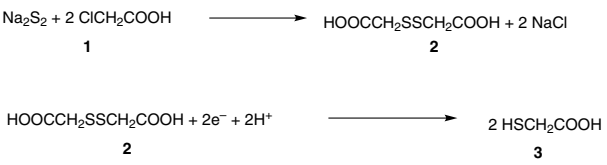
Introduction

Mercaptoacetic acid (**3**), also known as thioglycolic acid, is a liquid miscible with water and with most organic solvents such as alcohols, ether, chloroform and benzene.[1] It is widely described in the literature, especially as a substrate for the synthesis of pharmacologically active heterocycles[2] including 1,3-thiazolidin-4-ones,[3] 1,4-thiazepines[4] and thiazoles.[5] It is also used for the formation of spiro derivatives,[6] in multicomponent reactions, and in removing the nosyl protecting group from amine functions of α-amino acids.[7]

Preparation

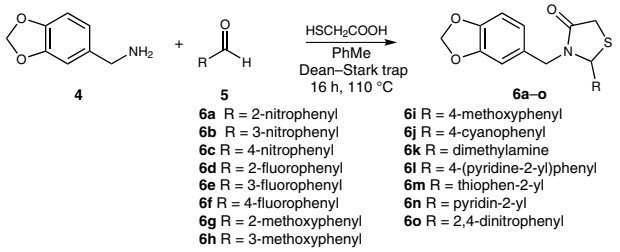
This reagent can be prepared under eco-friendly conditions by condensation of chloroacetic acid (**1**) with sodium disulfide followed by electrochemical reduction of dithiodiglycolic acid (**2**) leading to **3** with a yield of 92–97%.[8]



Scheme 1 Eletrochemical synthesis of mercaptoacetic acid (**3**)

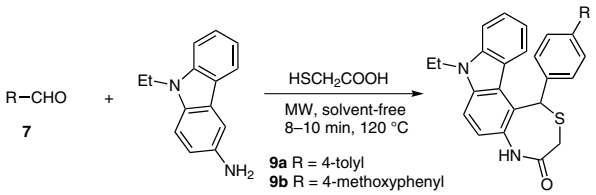
Abstracts

(A) Gomes and co-workers obtained fifteen new 1,3-thiazolidin-4-one derivatives through one-pot cyclocondensation reactions of piperonylamine (**4**), arenealdehyde (or heteroaromatic aldehyde) **5** and mercaptoacetic acid in refluxing toluene, using a Dean–Stark trap. The derivatives **6a–o** were obtained with moderate to excellent yield (51–91%). These novel compounds have been assessed as antibacterial agents against *Mycobacterium tuberculosis* $H_{37}Rv$.[3]



6a R = 2-nitrophenyl
6b R = 3-nitrophenyl
6c R = 4-nitrophenyl
6d R = 2-fluorophenyl
6e R = 3-fluorophenyl
6f R = 4-fluorophenyl
6g R = 2-methoxyphenyl
6h R = 3-methoxyphenyl
6i R = 4-methoxyphenyl
6j R = 4-cyanophenyl
6k R = dimethylamine
6l R = 4-(pyridine-2-yl)phenyl
6m R = thiophen-2-yl
6n R = pyridin-2-yl
6o R = 2,4-dinitrophenyl

(B) Shi et al. reported the design and synthesis of novel 1,4-thiazepine derivatives **9a–f** embedding the carbazole motif via microwave irradiation multicomponent reactions of several arenealdehydes (or heteroaromatic aldehydes) **7**, mercaptoacetic acid and 3-amino-9-ethylcarbazole (**8**) under solvent-free conditions, thus providing a green and facile access to the desired derivatives with prominent features of high structural diversity, short reaction times, minimal environmental impact and high yield (76–93%). These novel compounds have been assessed with respect to their *in vitro* antioxidant and cytotoxic activities.[4]



9a R = 4-tolyl
9b R = 4-methoxyphenyl
9c R = benzo[d][1,3] dioxol-6-yl
9d R = 3,4-dimethoxyphenyl
9e R = thiophen-2-yl
9f R = 4-bromophenyl

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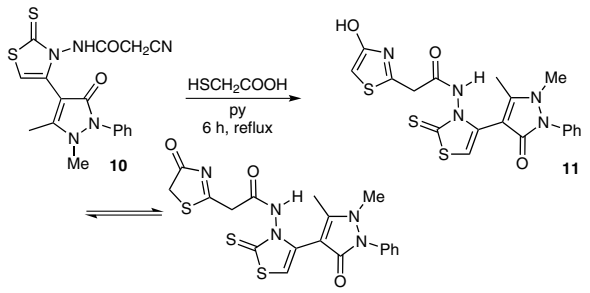
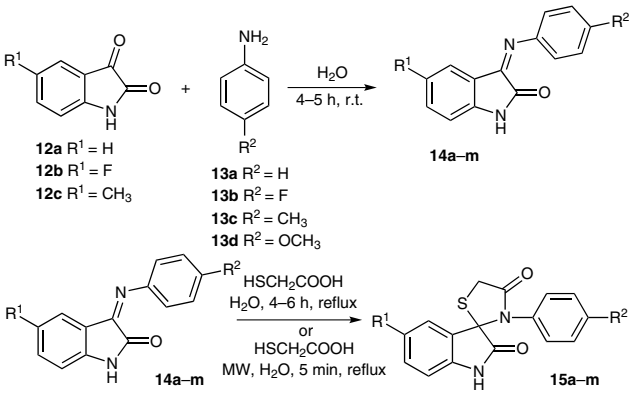
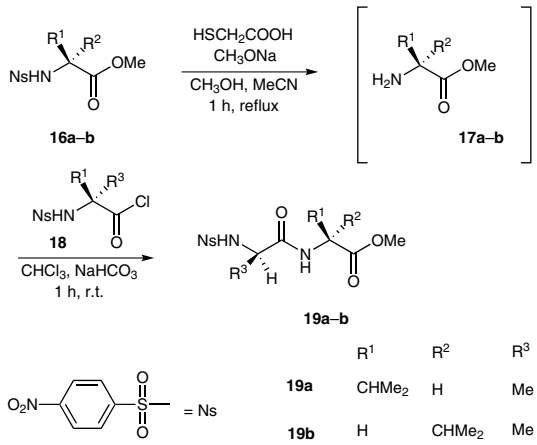
(C) Recently, Ayyad and co-workers reported the reaction between acetamide **10** and mercaptoacetic acid allowing the synthesis of 2-(4-oxo-4,5-dihydrothiazol-2-yl)acetamide (**11**) in acceptable yield (60%). Compound **11** belongs to a new class of thiazole derivatives carrying an antipyrinyl moiety.[5]



(D) Panda and Jain developed a protocol 'on water' for the synthesis of new Schiff bases **14a–m** starting from 1*H*-indol-2,3-diones **12a–c** and *p*-substituted anilines **13a–d** in high purity and excellent yield (92–98%). These derivatives (**14a–m**) were converted by cyclocondensation with mercaptoacetic acid into spiro derivatives **15a–m** under MW irradiation as well as in water in good yield and pure form.[6]



(E) Leggio et al. described an efficient and practical alternative strategy for carrying out peptide synthesis using the *p*-nitrobenzenesulfonyl (nosyl) group for protection of the amino function of α-amino acids. Aiming at the deprotection of the amino functionality, compounds **16a–b** were treated with mercaptoacetic acid in the presence of sodium methoxide in an acetonitrile–methanol solution under reflux. Products **17a–b** were coupled, without further purification, with *N*-nosyl-D-alanine chloride (**18**) in a chloroform solution containing aqueous $NaHCO_3$ to obtain the corresponding diastereomeric dipeptides Ns-D-Ala-L-Val-OMe (**19a**) and Ns-D-Ala-D-Val-OMe (**19b**) with 71% and 78% yield, respectively. In order to extend the peptide chain, the same methodology to deprotect the amino function can be applied.[7]



References

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