Mercaptoacetic Acid
Compiled by Eliza de Lucas Chazin

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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 \(\alpha\)-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%.\(^8\)

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\text{Na}_2S_2 + 2 \text{CICH}_2\text{COOH} \rightarrow \text{HOOCCH}_2\text{SSCH}_2\text{COOH} + 2 \text{NaCl}
\]

\[
\text{HOOCCH}_2\text{SSCH}_2\text{COOH} + 2e^- + 2\text{H}^+ \rightarrow 2 \text{HSCH}_2\text{COOH}
\]

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* H₃₇Rv.\(^3\)

(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.\(^4\)
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.

Panda and Jain developed a protocol ‘on water’ for the synthesis of new Schiff bases 14a–m starting from 1H-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.

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 NaHCO3 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.

References