SYNLETT
Spotlight 46

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

3-Mercaptopropionic Acid (3-MPA)

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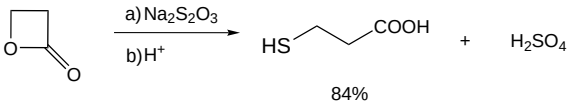
Introduction

3-Mercaptopropionic acid (3-MPA) belongs to the family of mercaptans. 3-MPA is known for a long time and was already synthesized by Lovén[1] in 1884. All major chemical suppliers sell the compound for a reasonable price nowadays. A convenient preparation is possible by the procedure of Gresham et al,[2] who employed MPA for various organic syntheses. This interesting bifunctional compound is also known as a versatile chain transfer reagent in the telomerization of short oligomers for biotechnological applications.[3]

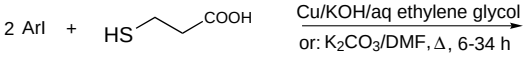
Preparation

β-Propiolactone and sodium thiosulfate react easily to a stable thiosulfate intermediate. By the following acidification the desired product, mercaptopropioinc acid (3-MPA) and sulfuric acid, are isolated in good yields.

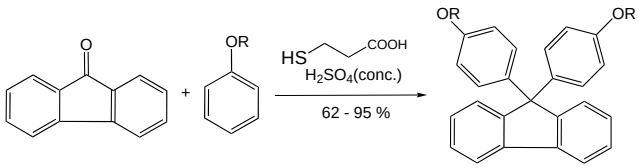


Abstracts

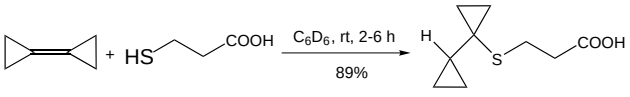
3-MPA serves as a sulfur-transfer reagent[4] in this reaction. With the procedure a wide range of aryliodides are transformed into bis aryl sulfides in fair to good yields.



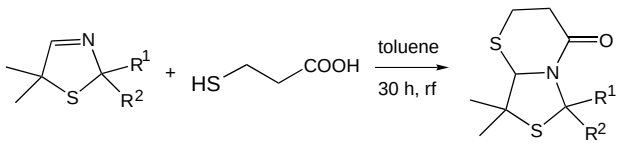
The transformation of fluorene to fluorenebisphenoxy derivatives is co-catalyzed by 3-MPA.[5] The observed results indicate that the thiol group adds to the fluorenes carbonyl C-atom. The positively charged intermediate is easily replaced by two phenoxy substituents and 3-MPA is liberated and reused in a next cycle. The reaction is driven by concentrated sulfuric acid, which acts as the main catalyst.



The thiol group of 3-MPA is easily added to the double bond of bicyclopropylidene. This reaction was also investigated in d_6-benzene at room temperature[6] and according to recorded ^{1}H NMR is a quantitative process. The reaction performs in the dark and therefore no radical mechanism is involved. The reaction is possible due to the remarkable reactivity, which is based on the strain in bicyclopropylidene.



3-Thiazolines contain a C=N double bond, which perform a ring closure reaction with 3-MPA under azeotropic conditions.[7] The bicyclic product is isolated as a racemate. If R^1, R^2 carry protons almost no diasteroselectivity (52,5: 47,5) is observed but if R^2 is replaced by a isopropyl group a diasteromeric *cis-trans* ratio 95:5 is found.



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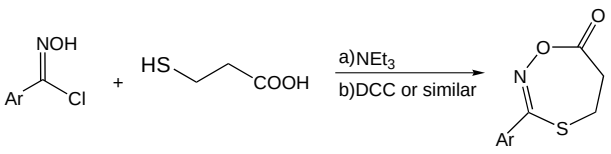
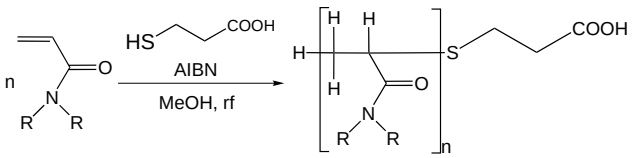
The heterocyclic system 5,6-dihydro-7-1,4,2-oxathiazepin-7-one was prepared[8] by the reaction of hydroxymoyl chlorides with 3-mercaotopropionic acid in a first step. The following ring closure was achieved with 1,3-dicyclohexylcarbodiimide or 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide.



For the telomerization process, 3-mercaptopropionic acid is often used as a chain transfer reagent due to its high transfer reactivity and because the isolated polymer contains a single specific functional end group. AIBN is used as initiator to transform the thiol into a radical. By the variation of the concentration of the chain transfer reagent the telomer length is easily adjusted to a convenient molecular average weight (2000–2500 g/mol). Structures with a lower critical solution temperature are often used for bioconjugates.[3]



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