SYNLETT
Spotlight 444

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

Methallyl Isothiocyanate

Compiled by Maksym Fizer

Maksym Fizer was born in Ukraine, in 1987. He obtained his B.Sc. in chemistry and his M.Sc. in organic chemistry (2009) from the Uzhgorod National University, Ukraine. He is currently working towards his Ph.D. under the supervision of Dr. Mikhail Slivka at the same institution. His research interest focusses on studying the synthesis of alkenyl-substituted bisthioureas, their alkaline cyclization into alkenylaminotriazolthiones, and their biological action.

Laboratory of Organic Chemistry, Department of Organic Chemistry, Chemical Faculty, Uzhgorod National University, Fedynets St. 53/1, 88000 Uzhgorod, Ukraine
E-mail: mmfizer@rambler.ru

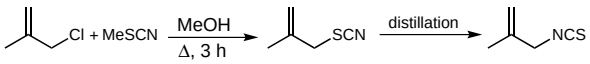
Introduction

Methallyl isothiocyanate (MAITC) is a flammable, colorless liquid with a boiling point of 169–170 °C (760 mm),[1] a flash point of 57 °C, and a density of 0.993 g/cm^3 at 25 °C. It has a special, onion-like odor and is insoluble in water. MAITC is a lachrymator and may be harmful if inhaled, swallowed, and absorbed through the skin; it may cause respiratory tract, skin and eye irritation.

MAITC is commercially available and can be synthesized by the reaction of methallyl chloride with an alkali metal thiocyanate or with ammonium thiocyanate to give methallyl thiocyanate which readily rearranges under heating (usually with distillation) to the desired product (Scheme 1).[1] In addition, it is the product of the reaction of thiocyanogen with isobutylene.[2]

Recent literature has shown the anti-inflammatory action of MAITC through (i) the irreversible inhibition of the macrophage migration inhibitory factor[3] and (ii) the inhibition of the caspase-1 activity through the inhibition of intracellular calcium levels.[4] Polymerized MAITC is used to obtain oral care compositions comprising a polymeric dye.[5]

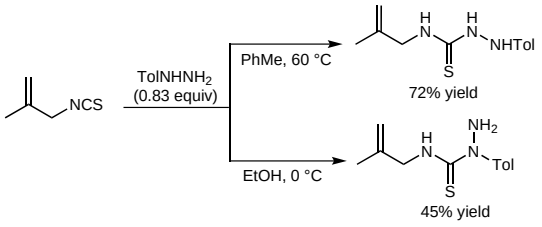
MAITC has several applications in organic synthesis because of two highly reactive centers which provide the basis for numerous applications of the compound as an organic intermediate. MAITC is a versatile building block in the hands of the organic chemist because of the ease with which reactions can be initiated at either center without losing the reactive possibilities of the other center.



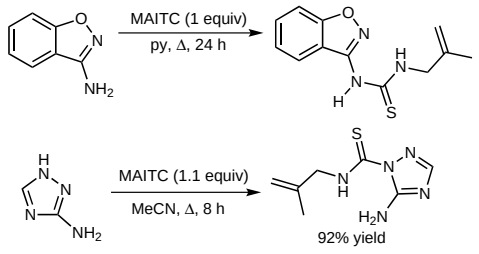
Scheme 1

Abstracts

(A) *Reaction with Arylhydrazines:*
Richter and co-workers found that MAITC reacts with substituted arylhydrazines to 1,4- or 2,4-disubstituted thiosemicarbazides, depending on the reaction conditions and the nature of the aryl group.[6] A derivative of methallyl thiosemicarbazide can be used as sensor element suitable for colorimetric detection of anions.[7]



(B) *Derivatization of Heterocycles:*
Merla and co-workers patented a method for the synthesis of substituted benzo[*d*]isoxazol-3-yl-*N*′-methallyl thioureas which exhibit an strong affinity for the KCNQ2/3 K^+ channel and which are suitable for relieving pain.[8] MAITC is a reagent for the synthesis of thioureido-substituted spiro compounds which can be used for the production of producing pain-relief medicaments.[9] A new thiourea derivative of 1,2,4-triazole has been synthesized and tested as a possible drug. It was shown that the thiourea with the endocyclic *N*-atom forms selectively.[10]



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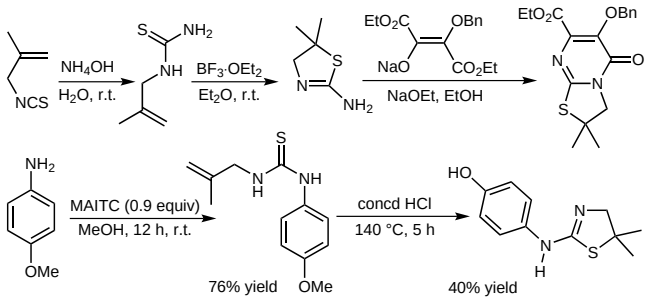
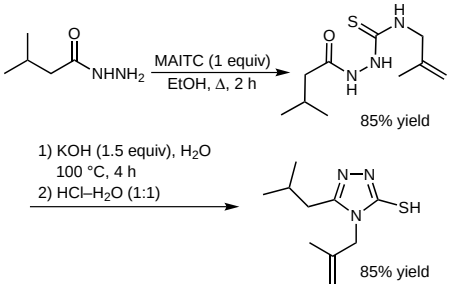
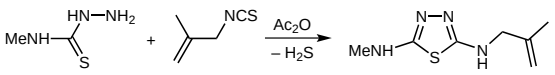
(C) *Production of Substituted and Condensed Thiazoles:*
Novel bicyclic thiazolopyrimidinone compounds, which inhibit HIV integrase, were synthesized using methallyl thiourea.[11] MAITC is a general reagent for the synthesis of thiazole compounds which have an excellent inhibitory action on melanin production and which are useful as skin whitening agents. The first step of the synthesis is the formation of *N*-aryl-*N*′-methallyl-thioureas. The second stage is the cyclization to thiazoles by the action of hydrochloric acid in a steel tube.[12]



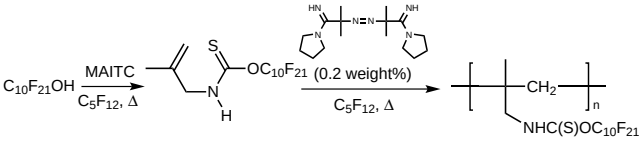
(D) *Synthesis of Triazoles:*
New 1,2,4-triazoles have been synthesized by the alkali cyclization of acyl thiosemicarbazides which can be obtained from MAITC and hydrazides. The obtained compound exhibited a stabilizing effect on cell membranes, and antioxidant activity with respect to erythrocytes under oxidative stress conditions was demonstrated.[14]



(E) *Diaminothiadiazoles Formation:*
Cyclization of substituted thiosemicarbazides with methallyl isothiocyanate in the presence of acetic anhydride gave diaminothiadiazoles.[14]



(F) *Synthesis of Polymers:*
MAITC can be used to synthesize fluoropolymers via the formation of urethanes with an appropriate fluorinated alcohol under the action of water-soluble azo-initiator.[15]



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