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Spotlight 404

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

Bromoacetyl Bromide

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Introduction

Bromoacetyl bromide is a versatile and widely used reagent for the synthesis of heterocyclic compounds, especially for the regioselective synthesis of heterocycles. It easily forms esters and amides used for the synthesis of many important intermediates to yield therapeutically active compounds, e.g. cefotetan and labetalol and is also utilized for the selective cleavage of ethers and acetals and exploited for the selective extension of carbon chains. Spectroscopic investigations have shown that bromoacetyl bromide in both gaseous and liquid phases is a mixture of two conformers, anti and gauche in the ratio of 40:60, respectively. Bromoacetyl bromide is prepared by reaction of acetic acid and bromine in the presence of red phosphorous at 140 °C. Bromoacetyl bromide is a colorless corrosive liquid (bp 296.6–302 °C) and hydrolyses readily in water. Some of the important uses of bromoacetyl bromide are depicted below.

Abstract

(A) Schneider et al. reported the selective cleavage of ethers and acetals with bromoacetyl bromide taking cyclic ethers and acetal as starting materials, also exploited for the selective extension of carbon chains.

(B) Klila et al. reported the regioselective synthesis of 2-alkyl(aryl)-imino-3-(anthracen-9-yl)-1,3-thiazolidin-4-ones on treatment of thiourea with bromoacetyl bromide. The reaction of thioureas with acyl halides gives the S-bound carbonyl product and in this instance the sulfur reacts with the more reactive of the electrophiles (the carbonyl carbon) to form the acylsulfinonium halide. Migration of the acyl group to nitrogen also occurs and has been studied in depth kinetically.

(C) G. Mendoza et al reported a new reaction which was carried out between oxazolidinethiones or thiazolidinethiones with bromoacetyl bromide to give N-substituted thiazolidinediones through intramolecular nucleophilic substitution.
(D) G. L. Sommen et al. reported a one-pot synthesis of selenium-containing five-membered heterocycles, 2-methylidene-1,3-selenazolidine derivatives, starting with isoselenocyanates as the building blocks.6

(E) A. Hamid et al. demonstrated the utility of 1,3-thiazolium-4-olate salts, derived from pyrrolidine-2-thione and isoindoline-1-thione, to create dipolarophiles, a set of diverse and new thiapyrrolizinones.7

(F) M. H. Bolli et al. reported the discovery, preparation and characterization of a novel class of 2-imino-thiazolidin-4-one derivatives and discussed the factors that influence the regioselectivity during the synthesis of 2-alkylimono-3-phenylthiazolidin-4-one.8

(G) M. Anzini et al. reported the synthesis of benzodiazepinone from 2-amino-5-chlorobenzonitrile 6, which was treated with Grignard’s reagent and 1-naphthylmagnesium bromide to afford the expected naphthyl derivative 7. Condensation of 7 with bromoacetamide in dichloromethane afforded the respective bromoacetamide, which in turn cyclized to the expected lactam 8.9

(H) Y. Qiao et al. reported the synthesis of piperazinedione-based peptide mimetic substrate analogues. Protected amino acid 9 was reacted with an aldehyde, followed by reduction using sodium borohydride. Compound 10 was then reacted with bromoacetamide to generate product 11 and later converted into the final product 12 through initial ammonolysis of methyl ester to give an amide, following a nucleophilic attack to knock out bromide as a good leaving group, leading to the formation of a stable six-membered ring.10

References