

SYNLETT Spotlight 281

Bromonitromethane: A Versatile Reagent in Organic Synthesis

Compiled by Jun-min Zhang

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

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Dedicated to my dear research advisor Professor Ming Yan.

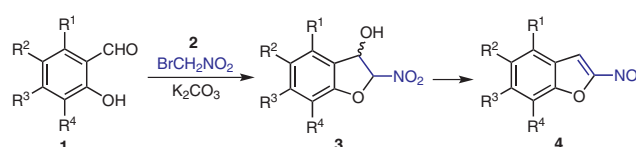


Introduction

Bromonitromethane (BrCH_2NO_2) has received considerable attention as a one-carbon synthon for the synthesis of a variety of important organic intermediates.¹ For examples, it was used in the synthesis of 2-nitrobenzofuran and 2-nitro-2,3-dihydrobenzofuran-3-ols,² nitrobenzothiophenes, and nitrothiazoles,³ polyfunctionalized nitrocyclopropanes.⁴ It has also been utilized in the synthesis of 1-bromo-1-nitroalken-2-ols⁵ and aryl nitromethanes. In addition, it could be used as a bromine donor.⁶

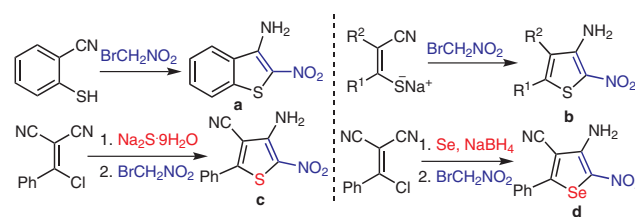
Abstracts

(A) 2-Nitrobenzo[*b*]furans **4** are prepared by reacting 2-hydroxybenzaldehydes **1** and bromonitromethane **2** at low temperature. The intermediate **3** is then quantitatively dehydrated by heating in acetic anhydride to provide **4** in good yields.²

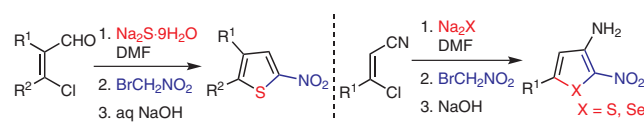


Scheme 1

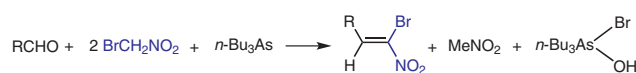
(B) Fishwick and co-workers described the preparation of 3-amino-2-nitrobenzo[*b*]thiophene (**a**) starting from 2-sulfanylbenzonitrile and bromonitromethane.³ Several 3-amino-2-nitrothiophenes were prepared starting from the sodium salt of disubstituted 3-sulfanyl-2-propenenitriles and bromonitromethane.³ The compounds **b** were obtained in the yields ranging from 30% to 70%. In another paper, thiophene **c** was synthesized by Gewald and Hain, starting from disubstituted β -chloroacrylonitrile, sodium sulfide and bromonitromethane.⁷ The formation of 5-phenyl-3-amino-2-nitroselenophene (**d**) was also observed.



(C) Recently, Kirsch and co-workers described a one-pot procedure to prepare new 2-aryl-5-nitrothiophenes efficiently from bromonitromethane and 3-chloro-3-aryl-propenals,^{1a} and to prepare substituted 3-amino-2-nitrothiophenes and selenophenes from β -chloroacrylonitriles and bromonitromethane.^{1b}



(D) Shen and co-workers described a reaction of aldehydes and bromonitromethane in the presence of tri-*n*-butylarsine. The reaction provided substituted 1-bromo-1-nitroalkenes in good yields.⁸



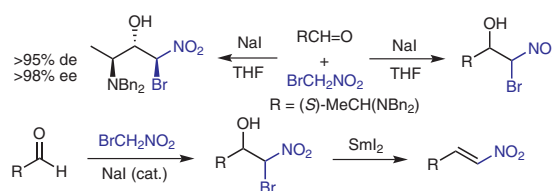
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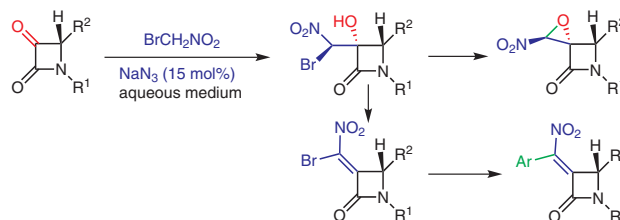
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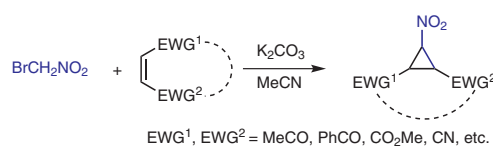
(E) Concellón and co-workers described an efficient synthesis of 1-bromo-1-nitroalkane-2-ols. The reaction of bromonitromethane and a variety of aldehydes was catalyzed by NaI under mild conditions. While chiral *N,N*-dibenzyl alanine was used, the corresponding (1*S*,2*S*,3*S*)-3-dibenzylamino-1-bromo-1-nitrobutan-2-ol was obtained with excellent stereoselectivity.⁵ In addition they also reported a samarium-promoted synthesis of (*E*)-nitroalkenes from 1-bromo-1-nitroalkane-2-ols in good yields.⁹



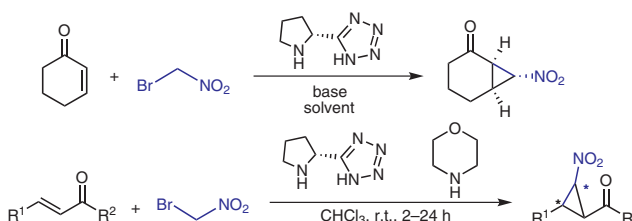
(F) Alcaide and co-workers reported a coupling reaction of azetidine-2,3-diones (α -oxo- β -lactams) and bromonitromethane in aqueous media and in the presence of catalytic amounts of sodium azide. The stereoselectivity of the process was generally good and reasonable *anti/syn* ratios were achieved by substrate control. Based on the reaction, a simple and efficient synthesis of the potentially bioactive 3-substituted 3-hydroxy- β -lactam moiety has been developed. 2-Azetidinone-tethered 1-halo-1-nitroalkane-2-ols are highly useful building blocks. For example, they can be converted into spiro and fused bicyclic- β -lactams.¹⁰



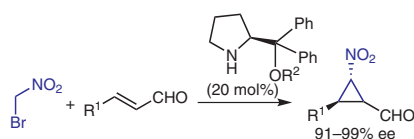
(G) Nitrocyclopropane has been successfully prepared by the reaction of bromonitromethane, potassium carbonate and electrophilic alkenes bearing electron-withdrawing groups both in the α - and β -positions. The method provided good yields and moderate to good diastereoselectivity for linear alkenes. The *exo*-products were exclusively formed for *N*-alkylmaleimides.^{4b}



(H) Ley and co-workers reported the first organocatalytic enantioselective nitrocyclopropanation of 2-cyclohexen-1-one and bromonitromethane with good yields and enantioselectivities. 5-(Pyrrolidin-2-yl)-1*H*-tetrazole was used as the efficient catalyst.¹¹ Recently, the same group developed a general organocatalytic synthesis of chiral nitrocyclopropanes from bromonitromethane and a variety of cyclic and acyclic enones.¹² Wang and co-workers reported the same reaction catalyzed by chiral primary amines. Good yields and excellent enantioselectivities were achieved.¹³ Very recently, Yan and co-workers reported an efficient synthesis of chiral 4-bromo-4-nitroketones via the asymmetric conjugate addition of bromonitromethane to alkyl vinyl ketones.¹⁴



(I) Córdova and co-workers described a novel organocatalytic nitrocyclopropanation of α,β -unsaturated aldehydes with bromonitromethane. 1-Nitro-2-formylcyclopropanes were obtained in good yields and with excellent enantioselectivities.¹⁵ Recently, Yan and co-workers used MeOH-AcONa instead of CHCl₃-Et₃N resulting in better yields for a variety of substrates.¹⁶



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