SYNLETT
Spotlight 281

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

Bromonitromethane: A Versatile Reagent in Organic Synthesis

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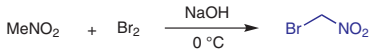
Dedicated to my dear research advisor Professor Ming Yan.

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-nitroalkan-2-ols[5] and aryl nitromethanes. In addition, it could be used as a bromine donor.[6]

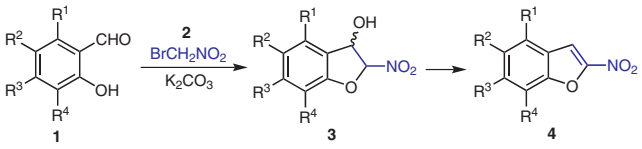
Bromonitromethane is commercially available and can also be easily prepared according to the procedures reported by Fishwick et al. (Scheme 1).[3] A typical procedure is as following: freshly distilled nitromethane was stirred at 0 °C and bromine was dropped in 5 seconds. The resulted bromonitromethane could be used without further purification.[1a]



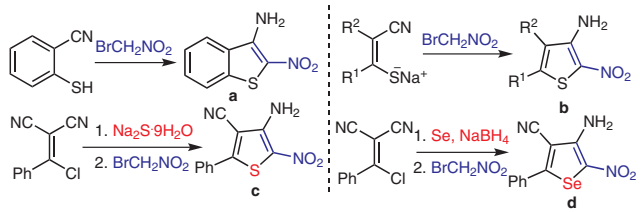
Scheme 1

Abstracts

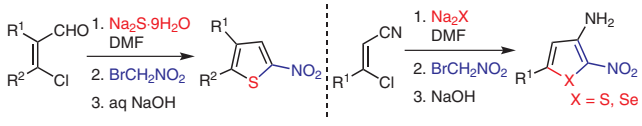
(A) 2-Nitrobenzo[*b*]furans **4** are prepared by reacting 2-hydroxybenzaldehydes **1** and bromonitromethane **2** at low temperature. The intermediate **3** is then quantitatively dehydrated by heating in acetic anhydride to provide **4** in good yields.[2]



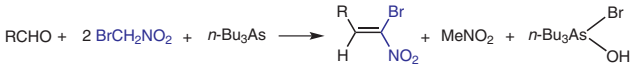
(B) Fishwick and co-workers described the preparation of 3-amino-2-nitrobenzo[b]thiophene (**a**) starting from 2-sulfanylbenzonitrile and bromonitromethane.[3] Several 3-amino-2-nitrothiophenes were prepared starting from the sodium salt of disubstituted 3-sulfanyl-2-propenenitriles and bromonitromethane.[3] 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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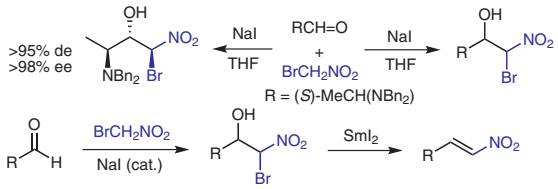
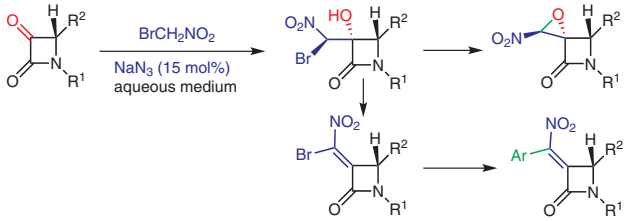
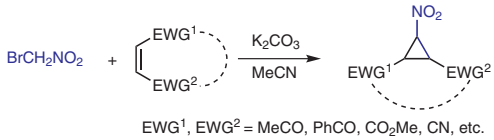
(E) Concellón and co-workers described an efficient synthesis of 1-bromo-1-nitroalkan-2-ols. The reaction of bromonitromethane and a variety of aldehydes was catalyzed by NaI under mild conditions. While chiral *N*,*N*-dibenzyl alaninal was used, the corresponding (1*S*,2*S*,3*S*)-3-dibenzylamino-1-bromo-1-nitrobutan-2-ol was obtained with excellent stereoselectivity.[5] In addition they also reported a samarium-promoted synthesis of (*E*)-nitroalkenes from 1-bromo-1-nitroalkan-2-ols in good yields.[9]



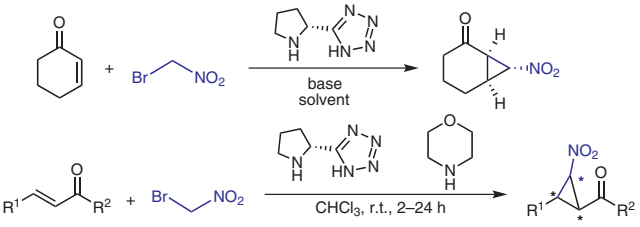
(F) Alcaide and co-workers reported a coupling reaction of azetidine-2,3-diones (α-oxo-β-lactams) and bromonitromethane in aqueous media and in the presence of catalytic amounts of sodium azide. The stereoselectivity of the process was generally good and reasonable *anti*/*syn* ratios were achieved by 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-nitroalkan-2-ols are highly useful building blocks. For example, they can be converted into spiro and fused bicyclic-β-lactams.[10]



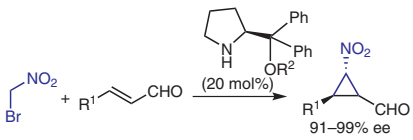
(G) Nitrocyclopropane has been successfully prepared by the reaction of bromonitromethane, potassium carbonate and electrophilic alkenes bearing electron-withdrawing groups both in the α- and β-positions. The method provided good yields and moderate to good diastereoselectivity for linear alkenes. The *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)-1H-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 $CHCl_3$–Et_3N resulting in better yields for a variety for substrates.[16]



References

(1) (a) Rodríguez Dominguez, J. C.; Thomae, D.; Seck, P.; Kirsch, G. *Synlett* **2008**, 286. (b) Thomae, D.; Rodríguez Dominguez, J. C.; Kirsch, G.; Seck, P. *Tetrahedron* **2008**, *64*, 3232.

(2) (a) Ohishi, Y.; Doi, Y.; Nakanishi, T. *Chem. Pharm. Bull.* **1984**, *32*, 4260. (b) Tromelin, A.; Demerseman, P.; Royer, R. *Synthesis* **1985**, 1074.

(3) Fishwick, B. R.; Rowles, D. K.; Stifling, C. J. M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1171.

(4) (a) Braish, T. F.; Castaldi, M.; Chan, S.; Fox, D. E.; Keltonic, T.; McGarry, J.; Hawkins, J. M.; Norris, T.; Rose, P. R.; Sieser, J. E.; Sitter, B. J.; Watson, H. J. r. *Synlett* **1996**, 1100. (b) Ballini, R.; Fiorini, D.; Palmieri, A. *Synlett* **2003**, 1704.

(5) Concellón, J. M.; Rodríguez-Solla, H.; Concellón, C.; García-Granda, S.; Díaz, M. R. *Org. Lett.* **2006**, *8*, 5979.

(6) Sherrill, M. L. *J. Am. Chem. Soc.* **1924**, *46*, 2753.

(7) Gewald, K.; Hain, U. *Monatsh. Chem.* **1992**, *123*, 455.

(8) Shen, Y.; Yang, B. *Synth. Commun.* **1993**, *23*, 1.

(9) Concellón, J. M.; Bernad, P. L.; Rodríguez-Solla, H.; Concellón, C. *J. Org. Chem.* **2007**, *72*, 5421.

(10) Alcaide, B.; Almendros, P.; Luna, A.; Torres, M. R. *Org. Biomol. Chem.* **2008**, *6*, 1635.

(11) Hansen, H. M.; Longbottom, D. A.; Ley, S. V. *Chem. Commun.* **2006**, 4838.

(12) Wascholowski, V.; Hansen, H. M.; Longbottom, D. A.; Ley, S. V. *Synthesis* **2008**, 1269.

(13) Lv, J.; Zhan, J.; Wang, Y. *Chem. Eur. J.* **2009**, *15*, 972.

(14) Dong, L.-t.; Lu, R.-j.; Du, Q.-s.; Zhang, J.-m.; Liu, S.-p.; Xuan, Y.-n.; Yan, M. *Tetrahedron* **2009**, *65*, 4124.

(15) Vesely, J.; Zhao, G. L.; Bartoszewicz, A.; Córdova, A. *Tetrahedron Lett.* **2008**, *49*, 4209.

(16) (a) (a) Zhang, J.-m.; Hu, Z.-p.; Zhao, S.-q.; Yan, M. *Tetrahedron* **2009**, *65*, 802. (b) (b) Zhang, J.-m.; Hu, Z.-p.; Dong, L.-t.; Xuan, Y.-n.; Lou, C.-l.; Yan, M. *Tetrahedron: Asymmetry* **2009**, *20*, 355.