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Spotlight 152

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

N-Bromosuccinimide – A Selective, Mild Substitute for Bromine

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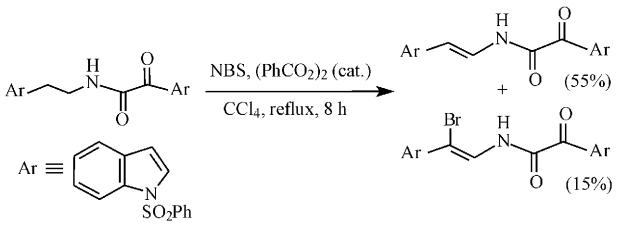
Introduction

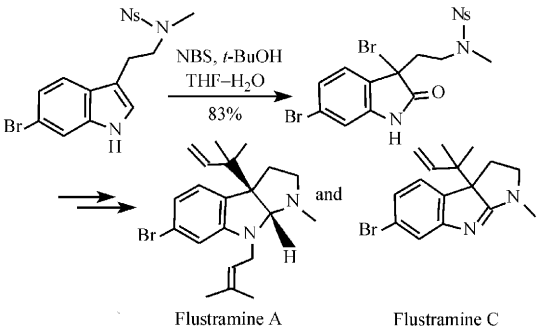
N-Bromosuccinimide (NBS) is commercially available but can also be prepared from succinimide by bromination under alkaline conditions. It is used as a mild source of bromine with higher selectivity, primarily due to its property of releasing of bromine in a low, steady-state concentration.[1] It is most widely used for benzylic and allylic brominations in the presence of a catalytic amount of a free-radical initiator such as benzoyl peroxide or AIBN in CCl_4.[2a] However, benzylic bromination in the absence of any free-radical initiator was recently achieved under microwave irradiation (MWI) in solid phase.[2b] The free-radical condition is also reported to bring about *Z*- to *E*-alkene isomerisation.[2c] Cook and co-workers demonstrated the regioselectivity of bromination by NBS under different conditions with indoles.[2a] In many instances, NBS has been used as an activator, for example in stereoselective glycosidation,[3a] protection[3b] and deprotection of ketals[3c] or THP ethers,[3d] and in the synthesis of diindolylalkanes.[3e] NBS is also widely used as a mild oxidant[4] as well as for oxidative cyclisations.[5] Recently, NBS was used for the mild, regioselective bromination of (hetero)aromatics in ionic liquid,[6a,b] or for α-bromination of carbonyl compounds in the presence of $NaHSO_4$–SiO_2,[6c] or TMSOTf.[6d]

Abstracts

(A) Chakrabarty et al. recently reported the formation of an enamide double bond under benzylic bromination conditions with NBS in a concise synthesis of coscinamide B, an *anti*-HIV bisindolic enamide.[7]



(B) Oxidation of indoles to isatins has also been accomplished by NBS; the reaction is thought to proceed via a 3,3-dibromooxindole as an intermediate.[8a] Indeed, Fuchs and Funk have isolated and used a 3-alkyl-3-bromooxindole as a key intermediate in the elegant syntheses of (±)-flustramines A and C,[8b] and (±)-perphoramidine.[8c]



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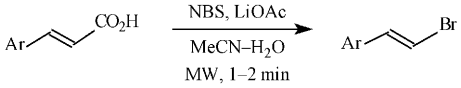
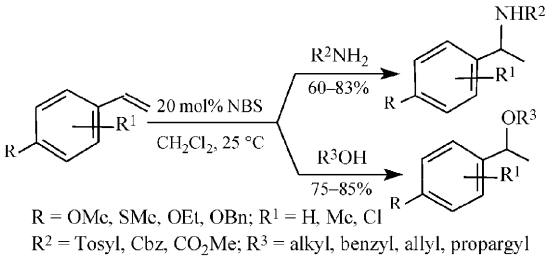
(C) Decarboxylative bromination with NBS in the presence of LiOAc under MWI has provided a stereoselective synthesis of (*E*)-β-arylvinyl bromides by a Hunsdiecker-type reaction.[9]

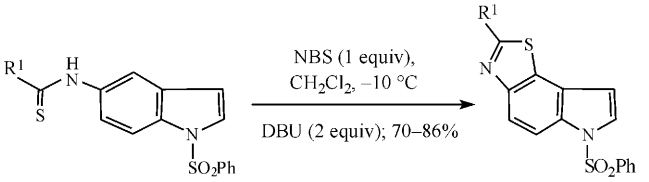


(D) Recently, NBS was used to catalyse both hydroamination and hydroalkoxylation of activated styrenes to afford amino and ether derivatives, respectively.[10]



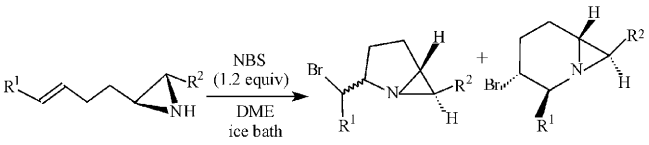
R = OMe, SMe, OEt, OBn; R1 = H, Me, Cl
R2 = Tosyl, Cbz, CO_2Me; R3 = alkyl, benzyl, allyl, propargyl

(E) Interestingly, NBS, along with DBU, promotes the cyclisation of *N*-alkylthioureidoindoles and alkyl *N*-(indol-5′-yl)dithiocarbamates to furnish only the corresponding 2-alkylamino- and 2-alkylthiothiazolo[5,4-*e*]indoles, regioselectively.[11]



R1 = NHMe, NHEt, NHBn; SMe, SEt, S-*n*-Pr, S-*n*-Bu, S-*i*-Bu

(F) NBS has also found application in the oxidative cycloamination of olefins with aziridines for the synthesis of saturated nitrogen-contaning heterocycles.[12]



R1 = H, Me, CH_2OH, Ph, H
R2 = PhCO, PhCH(OH)

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