

SYNLETT Spotlight 152

N-Bromosuccinimide – A Selective, Mild Substitute for Bromine

Compiled by Taraknath Kundu



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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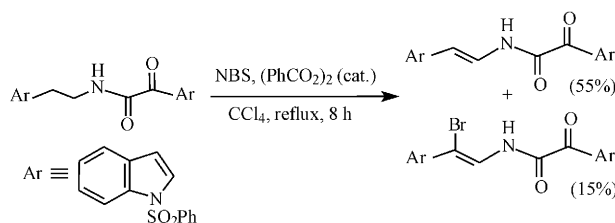
Introduction

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 CCl₄.^{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

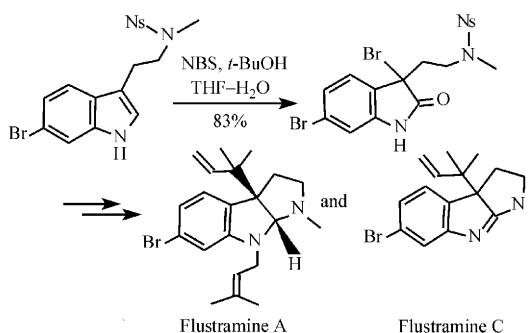
E-alkene isomerisation.^{2c} Cook and co-workers demonstrated the regioselectivity of bromination by NBS under different conditions with indoles.^{2a} In many instances, NBS has been used as an activator, for example in stereoselective glycosidation,^{3a} protection^{3b} and deprotection of ketals^{3c} or THP ethers,^{3d} and in the synthesis of diindolyl-alkanes.^{3e} NBS is also widely used as a mild oxidant⁴ 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 NaHSO₄–SiO₂,^{6c} or TMSOTf.^{6d}

Abstracts

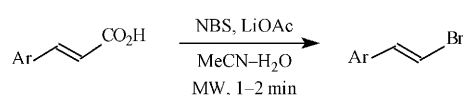
(A) Chakrabarty et al. recently reported the formation of an enamide double bond under benzylic bromination conditions with NBS in a concise synthesis of coscinamide B, an *anti*-HIV bis-indolic enamide.⁷



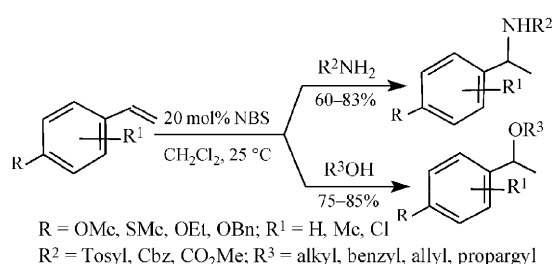
(B) Oxidation of indoles to isatins has also been accomplished by NBS; the reaction is thought to proceed via a 3,3-dibromooxindole as an intermediate.^{8a} Indeed, Fuchs and Funk have isolated and used a 3-alkyl-3-bromooxindole as a key intermediate in the elegant syntheses of (\pm)-flustramines A and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



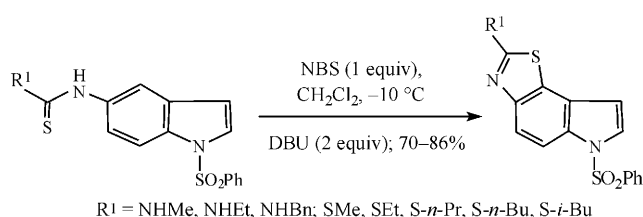
(C) Decarboxylative bromination with NBS in the presence of LiOAc under MWI has provided a stereoselective synthesis of (*E*)- β -arylvinyl bromides by a Hunsdiecker-type reaction.⁹



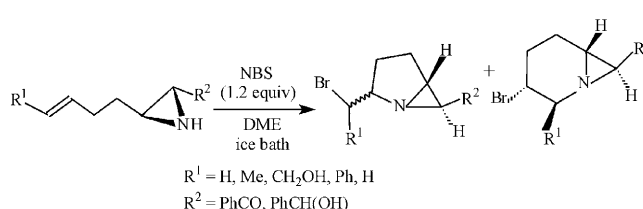
(D) Recently, NBS was used to catalyse both hydroamination and hydroalkoxylation of activated styrenes to afford amino and ether derivatives, respectively.¹⁰



(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



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



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