

SYNLETT Spotlight 244

N-Chlorosaccharin (NCSac): A Useful and Alternative Reagent in Organic Synthesis

Compiled by Paola Ervatti Gama



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-Chlorosaccharin (NCSac) belongs to the class of *N*-haloimides and is of great importance in synthetic organic chemistry since its chloro substituent is more electrophilic than the chlorine in the structurally analogous *N*-chlorosuccinimide.¹ NCSac is stable, crystalline, soluble in most common organic solvents; it is a commercially available, relatively inexpensive reagent and commonly used in diverse organic transformations, such as halogenation,^{2,3} co-halogenation,^{1,2,4} addition,⁵ oxidation,^{6,7} allylic and benzylic halogenation.^{6a}

Preparation: NCSac can be easily prepared from sodium saccharinate in many different ways;⁶ only the green methodology is presented here.⁸ This route starts from sodium saccharinate and potassium chloride in the presence of oxone[®] and water as solvent, resulting in moderate yields.⁸

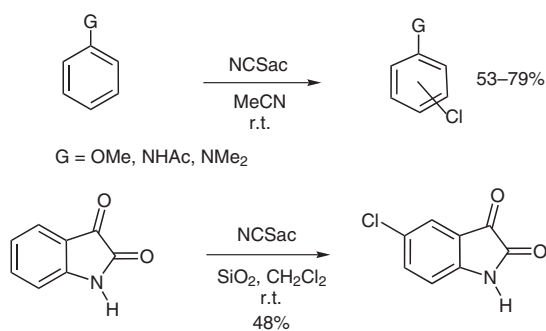


Oxone = 2 KHSO₅·KHSO₄·K₂SO₄

Scheme 1 Green route for NCSac synthesis

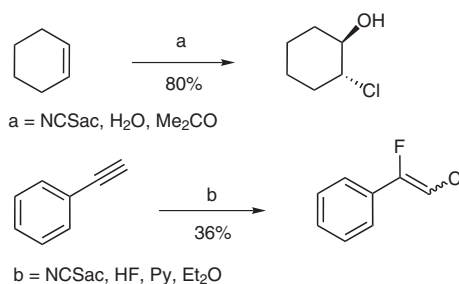
Abstracts

(A) de Souza and co-workers² described an efficient procedure for halogenation of electron-rich aromatic compounds (anisole, acetanilide, *N,N*-dimethylaniline) with NCSac, leading to a mixture of *ortho* and *para* isomers (*o/p* = 4:1–5:1) in moderate to high yields. The same group reported a convenient regiospecific preparation of 5-chloroisatin with NCSac mediated by SiO₂, which leads under mild conditions in moderate yields to the product.³

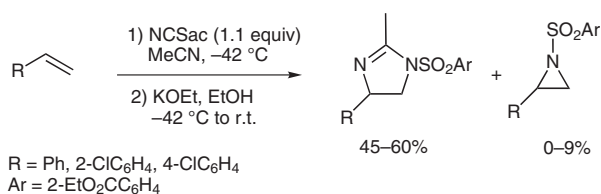


(B) de Souza and co-workers² described a co-halogenation procedure of alkenes which was easily achieved with NCSac in aqueous acetone at room temperature, leading to the corresponding chlorohydrins in high yields. The regioselectivity was very high and no regioisomeric products were detected.

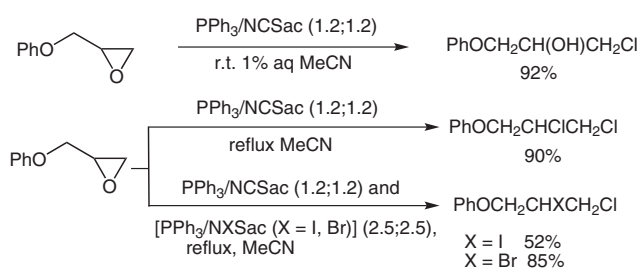
Dolenc and Sket⁴ reported a chlorofluorination of alkynes with NCSac, leading to products usually difficult to obtain.¹ The reagent is more reactive than other *N*-chloroimides, but requires long reaction times, affording a mixture of vicinal chloro-fluoroalkenes, but only Markovnikov products.



(C) Booker-Milburn and co-workers^{5a} described a one-pot electrophilic Ritter-type reaction of NCSac with alkenes in acetonitrile, leading to two different products, imidazolidine and aziridine, in moderate yields.

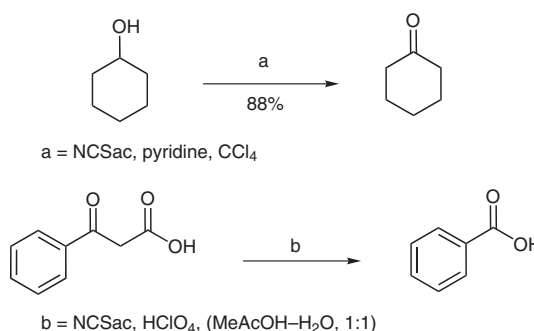


(D) Iranpoor and co-workers^{5b} reported a new, mild, regioselective and simpler methodology for the efficient conversion of epoxides into vicinal halo alcohols, symmetrical dichloride and unsymmetrical chloride compounds, using PPh₃/NCSac in acetonitrile in good yields. In this method the conversion depends on the molar ratio and the type of *N*-haloimide used.

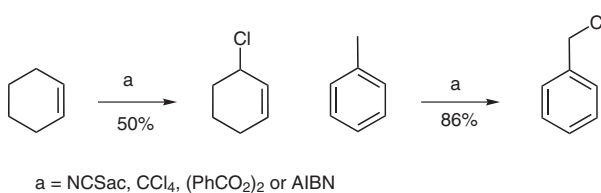


(E) Bachhawat and co-workers^{6a} described an oxidation methodology of alcohols and α -hydroxy acids to the corresponding aldehydes or ketones by NCSac. The oxidation reaction by chloronium ion, produced in situ, was carried out in CCl₄-pyridine at room temperature, leading to the corresponding products in high yields.

Farook⁷ reported the kinetic study of the oxidation of substituted and unsubstituted 4-oxo acids by NCSac in aqueous acetic acid catalyzed by HClO₄, leading to benzoic acid as major product. In this study, the presence of electron-releasing substitutes on the aromatic ring increases the reaction rate (4-MeO > 4-Me > 4-Ph > 4-H > 4-Cl > 4-Br > 3-NO₂).



(F) In addition to the previous cases, Bachhawat and co-workers^{6a} also described an allylic and benzylic chlorination of organic compounds with NCSac and benzoyl peroxide or AIBN, as free radical source, leading to the corresponding products in moderate yields.



References

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