

SYNLETT Spotlight 351

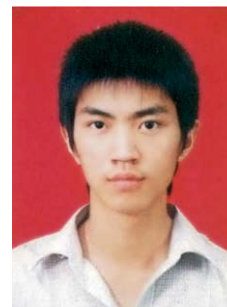
tert-Butyl Nitrite

Compiled by Yang Liu

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Dedicated to my mentor Dr. Ge Meng for the constant encouragement

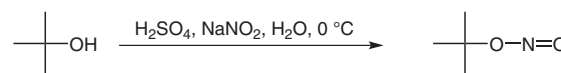


This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Introduction

tert-Butyl nitrite (TBN) is a very useful synthetic reagent with requisite chemical and physical properties, such as volatilizing with a low boiling point and favorable solubility, which leads to the feasibility of mixing or separating with other reagents. TBN is an efficient NO source, frequently used as the reagent for diazotization¹ and nitrosation of alcohols, thiols, amines and cycloalkanes.^{2–5} It is also a safe and chemoselective nitrating agent that provides preferentially mononitro derivatives.⁶ Besides, TBN is used in oxidations due to its ability to activate molecular

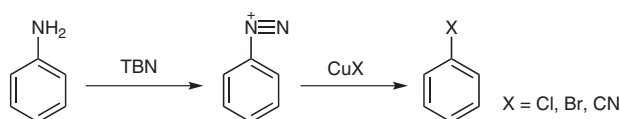
oxygen.⁷ TBN could be prepared in good to excellent yield by treating *tert*-butyl alcohol with nitrous acid or other nitrosating agents, such as nitrosyl chloride in pyridine and nitrosonium salts (NO⁺BF₄⁻, NO⁺ClO₄⁻). In the laboratory, usually sodium nitrite and sulfuric acid is used instead of nitrous acid (Scheme 1).⁸ An overview of the usage of TBN in organic synthesis is presented below.



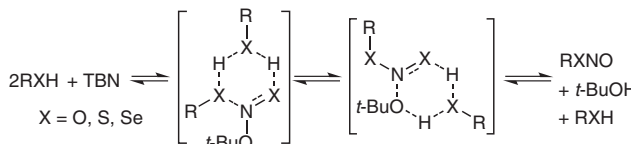
Scheme 1 Preparation of TBN

Abstract

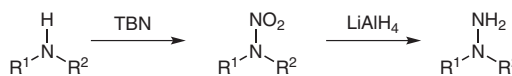
(A) TBN was used to prepare diverse substituted arenes by transforming aromatic amines into diazonium compounds, the diazonium group of which could be replaced by halogen or cyano in the presence of cuprous salts to form various products.¹



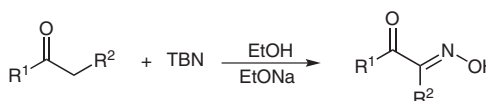
(B) Treatment of alcohols dissolved in chloroform with excess TBN resulted in the corresponding alkyl nitrites in quantitative yield. Simple thiols or selenols could also undergo this nitrosyl exchange with TBN.²



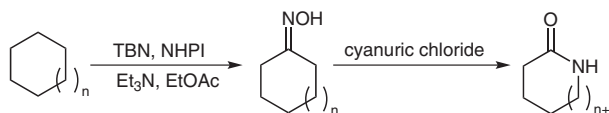
(C) Secondary amines were nitrosated with TBN to give quantitative formation of *N*-nitrosamine, which were used to prepare hydrazines by reduction with lithium aluminium hydride.³



(D) Introduction of the oximino group in α -position to the carbonyl group could be achieved by nitrosation with TBN in both acidic and alkaline condition.⁴



(E) Cycloalkanes were treated with TBN in the presence of *N*-hydroxyphthalimide (NHPI) followed by triethylamine to form the oxime, which could be transformed into the lactam with cyanuric chloride via Beckmann rearrangement.⁵



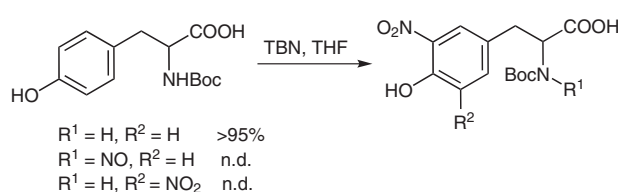
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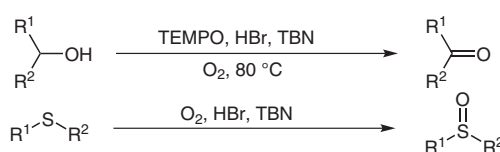
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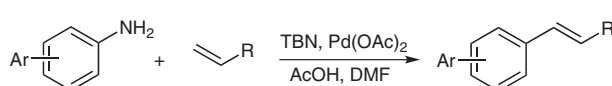
(F) TBN displayed exquisite chemoselectivity in the nitration of phenols, and the procedure yielded *tert*-butyl alcohol as the only byproduct.⁶



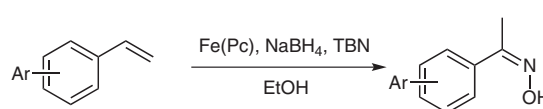
(G) Various alcohols were oxidized to carbonyl compounds with TEMPO, HBr and TBN as catalyst in high selectivity and yields. Similarly, thioethers could be oxidized to sulfoxides.⁷



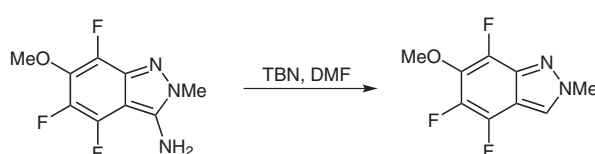
(H) The aniline derivatives were converted into the diazonium intermediates by TBN. A solution of Pd(OAc)₂ and the alkenes were then introduced to prepare the substituted alkenes via Heck reaction.⁹



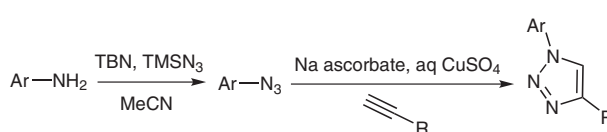
(I) Aryl-substituted olefins reacted with TBN and sodium borohydride in the presence of iron(II) phthalocyanine [Fe(Pc)] to give oximes in moderate to high yields.¹⁰



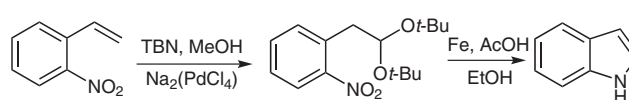
(J) Adding TBN to a solution of amine in DMF could result in deamination. The conversion from *N*-methyl-3-aminoindazoles into *N*-methylindazoles was adapted from this procedure.¹¹



(K) A variety of substituted aryl amines were transformed into aryl azides by using TBN and azidotrimethylsilane (TMSN₃) under mild conditions. The product reacted with terminal alkynes to produce 1,4-disubstituted-1,2,3-triazoles via Huisgen cycloaddition.¹²



(L) The mixture of 2-nitrostyrenes in methanol were treated with TBN in the presence of Na₂(PdCl₄) as a catalyst followed by iron in acetic acid to give indoles.¹³



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