SYNLETT
Spotlight 340

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

N-Hydroxyphthalimide: What Else Can You Ask For?

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Introduction

N-Hydroxyphthalimide (1, NHPI, Figure 1) is a white crystalline powder that has been used for the preparation of O-alkyl hydroxylamines, the functionalization of alkenes, the halogenation of alkanes, the Ritter-type reactions of alkylbenzenes, and for the oxidation of alkylbenzenes, acetics, alkenes, and sulfides. Some other applications are described below.

Figure 1

Preparation

This phthalimide derivative can be prepared by treating phthalic anhydride with hydroxylamine or hydroxylammonium sulphate under basic or neutral conditions.

Abstracts

(A) The ‘Mitsunobu-like’ reaction between a supported NHPI derivative using imidazole as a base followed by treatment with methylamine gives the corresponding primary or secondary O-alkyl hydroxylamines isolated in very high purity and in good yields.

(B) The silyl-hydroxylation of olefins bearing electron-withdrawing groups is accomplished by the reaction of NHPI with a silane. The trialkylysilyl radical adds to the olefin to form an intermediate that, when trapped by molecular oxygen, forms the corresponding alcohol. The silyl-hydroxylation of olefins takes place with yields ranging from 61–99% and with very good selectivity.
(C) The difficult oxidation of ethers to the related oxygen-containing compounds is accomplished with N-hydroxyphthalimide under an NO atmosphere. This reaction gives good and selective conversion of benzyl ethers to the corresponding aldehydes.13

\[ \text{R}_1O\text{R}_2 \xrightarrow{\text{NHPi, MeCN, 60 °C, 10 h}} \text{CHO} \]

56–99% conversion

\( \text{R}_1 = \text{Me, Et, t-Bu}; \text{R}_2 = \text{H, Cl, t-Bu, Me} \)

(D) The radical addition of masked aldehydes (1,3-dioxolanes) to electron-deficient alkenes is achieved using NHPI and benzoyl peroxide as polarity reversal catalyst in yields ranging from 46–88%. The tandem version of the reaction was also carried out using the same mild conditions.14

\[ \text{R}_1\text{H} \xrightarrow{\text{NHPI, benzoyl peroxide}} \text{R}_1\text{R}_2 \]

\( \text{R}_1 = \text{H, Me, Ph}; \text{R}_2 = \text{H, Me, CO}_2\text{Et} \)

(E) The metal-free catalytic aerobic oxidation of primary olefins by the in situ generation of peracetic acid from acetaldehyde is carried out by mixing all the reagents in the presence of N-hydroxyphthalimide and under an atmospheric pressure of oxygen. The isolated yield of the epoxides goes up to 96%.7

(F) The direct nitration of aliphatic C–H bonds is performed under mild conditions by reacting NHPI with alkanes in a NO₂ atmosphere at 70 °C and in the presence of air. A variety of alkanes were successfully nitrated by this NO/NHPI system in very useful yields.15

References
