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 alkylenzenes, and for the oxidation of alkylenbenzenes, acetals, alkenes, and sulfides. Some other applications are described below.

![Figure 1](image)

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.11

(B) The silyl-hydroxylation of olefins bearing electron-withdrawing groups is accomplished by the reaction of NHPI with a silane. The trialkysilyl 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.12
(C) The difficult oxidation of ethers to the related oxygen-containing compounds is accomplished with N-hydroxyphtalimide under an NO atmosphere. This reaction gives good and selective conversion of benzylic ethers to the corresponding aldehydes.¹³

(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

(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-hydroxyphtalimide 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