

# SYNLETT Spotlight 340

## *N*-Hydroxyphthalimide: What Else Can You Ask For?

Compiled by Leonardo X. Alvarez



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

Leonardo X. Alvarez got his first chemistry degree (Licenciatura en Química) in 1997 from the University of Costa Rica. He passed the following years working in the Costa Rican chemical industry where he got trained on large-scale synthesis and in chemical formulation. In 2005, he moved to Lyon (France), to get a M.Sc. in Organic Synthesis from the Université Claude Bernard and finally, in 2006, he joined Dr. Andrew E. Greene's group at the Université Joseph Fourier in Grenoble where he is currently doing research on the synthesis of new aerobic oxidation catalysts under the supervision of Dr. Jacques Einhorn and Dr. Bernard Bessières

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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,<sup>1</sup> the functionalization of alkenes,<sup>2</sup> the halogenation of alkanes,<sup>3</sup> the Ritter-type reactions of alkylbenzenes,<sup>4</sup> and for the oxidation of alkylbenzenes,<sup>5</sup> acetals,<sup>6</sup> alkenes,<sup>7</sup> and sulfides<sup>8</sup>. Some other applications are described below.

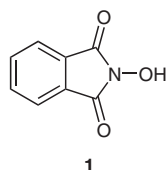
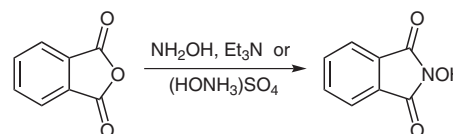


Figure 1

This reagent is not very expensive, it is air-stable, and does not need particular conditions for storage, but precautions must be taken for its manipulation, because it can be very irritating to the eyes and the skin.

### Preparation

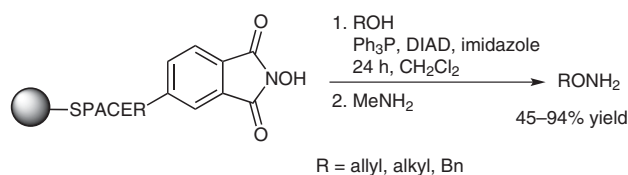
This phthalimide derivative can be prepared by treating phthalic anhydride with hydroxylamine or hydroxylammonium sulphate under basic<sup>9</sup> or neutral conditions.<sup>10</sup>



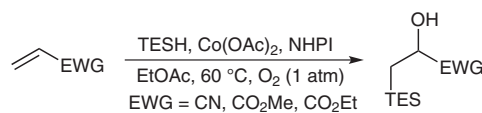
Scheme 1

### Abstracts

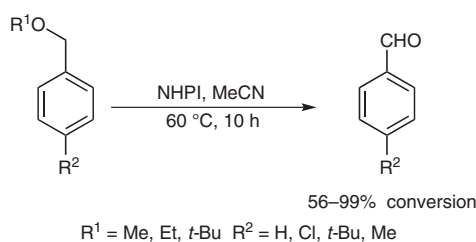
(A) The 'Mitsunobu-like' reaction between a supported NHPI derivative using imidazole as a base followed by treatment with methylamine gives the corresponding primary or secondary *O*-alkyl hydroxylamines isolated in very high purity and in good yields.<sup>11</sup>



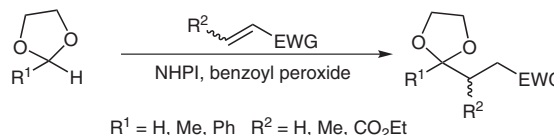
(B) The silyl-hydroxylation of olefins bearing electron-withdrawing groups is accomplished by the reaction of NHPI with a silane. The trialkylsilyl radical adds to the olefin to form an intermediate that, when trapped by molecular oxygen, forms the corresponding alcohol. The silyl-hydroxylation of olefins takes place with yields ranging from 61–99% and with very good selectivity.<sup>12</sup>



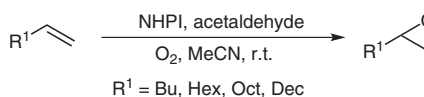
(C) The difficult oxidation of ethers to the related oxygen-containing compounds is accomplished with *N*-hydroxyphthalimide under an NO atmosphere. This reaction gives good and selective conversion of benzylic ethers to the corresponding aldehydes.<sup>13</sup>



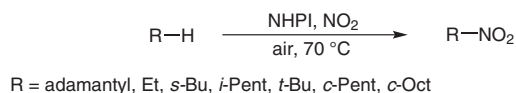
(D) The radical addition of masked aldehydes (1,3-dioxolanes) to electron-deficient alkenes is achieved using NHPI and benzoyl peroxide as polarity reversal catalyst in yields ranging from 46–88%. The tandem version of the reaction was also carried out using the same mild conditions.<sup>14</sup>



(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%.<sup>7</sup>



(F) The direct nitration of aliphatic C–H bonds is performed under mild conditions by reacting NHPI with alkanes in a NO<sub>2</sub> 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.<sup>15</sup>



## References

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