Nitration of alkanes with nitric acid catalyzed by N-hydroxyphthalimide

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Catalytic nitration of alkanes with nitric acid was first successfully achieved by the use of N-hydroxyphthalimide (NHPI) under mild conditions; the key to the present nitration was found to be the in situ generation of NO2 and phthalimide N-oxyl radical by the reaction of NHPI with nitric acid.

Nitration of saturated hydrocarbons using nitric acid is usually carried out at fairly high temperature (250–400 °C) because of difficulty in generating NO2 from HNO3.1 The nitration under such severe conditions resulted in not only the homolysis of C–H bonds but also the cleavage of the C–C bonds of hydrocarbons. As a consequence, the reaction is messy and often difficult to control, and exhibits poor product selectivity. To carry out the nitration selectively, in situ generations of alkyl radicals from alkanes and NO2 from HNO3 must be achieved under mild conditions. Recently, we have developed a novel catalytic method for the nitration of aliphatic hydrocarbons with NO2 using NHPI as the catalyst under mild conditions.2 We now find that alkanes can be nitrated with nitric acid through the in situ generation of NO2 and alkyl radicals by the use of NHPI as a catalyst under mild conditions.

The nitration of adamantane (1) was chosen as a model reaction and carried out in the presence of nitric acid and a catalytic amount of NHPI in trifluorotoluene, affording 1-nitroadamantane (2) (64%) and 1,3-dinitroadamantane (3) (3%) along with oxygenated products, adamantanol-1-ol (4) (9%) and adamantan-2-one (5) (5%) [eqn. (1), Table 1 entry 1]. In a previous paper, we showed that the nitration of 1 with NO2 as a nitrating reagent affords 2 in 66% yield.2 The nitration of 1 with HNO3 which is easier to handle than NO2 was found to be almost as same as that with NO2.

Table 1 shows the catalytic nitration of 1 with nitric acid by the NHPI under several reaction conditions.3 Among the solvents examined, trifluorotoluene and acetic acid were found to be good solvents. Acetonitrile and ethyl acetate considerably retarded the nitration (entries 3 and 4). No reaction took place in the absence of NHPI (entry 5). The present nitration under air afforded oxygenated products, 4 and 5, rather than nitro compounds (entry 6).

Upon treatment of NHPI with nitric acid at 60 °C, we found that the nitric acid was easily converted into NO2 in the presence of NHPI is known to be easily oxidized with Pb(OAc)4 to the N-oxyl radical (PINO).3 In the present reaction, nitric acid serves as a good oxidizing agent of the NHPI to form the PINO and NO2 [eqn. (2)].

In order to obtain further insight into the present nitration, 1 was allowed to react with nitric acid in the presence of copper metal. 1-nitro-3,5-dimethyladamantane (6) was obtained in 67% selectivity at 77% conversion (entry 1). When the NHPI used was increased from 0.1 mmol to 0.2 mmol, 7 was obtained in higher conversion and selectivity (entry 2). The nitration under relatively mild conditions, although it is known that the nitration of alkane with HNO3 must be carried out at high temperature because of the difficulty in decomposing HNO3 to NO2,4,6 From EPR measurements, it was found that the phthalimide N-oxyl radical (PINO) was formed with the evolution of NO2 by the reaction of the NHPI with nitric acid. NHPI is known to be easily oxidized with Pb(OAc)4 to the PINO.3 In the present reaction, nitric acid serves as a good oxidizing agent of the NHPI to form the PINO and NO2 [eqn. (2)].

Table 2 summarizes the representative results for the nitration of various saturated hydrocarbons and their derivatives with nitric acid under the influence of the NHPI in trifluorotoluene at 60 °C for 15 h. 1,3-Dimethyladamantane (6) reacted with nitric acid under these conditions to give 1-nitro-3,5-dimethyladamantane (7) in 67% selectivity at 77% conversion (entry 1). When the NHPI used was increased from 0.1 mmol to 0.2 mmol, 7 was obtained in higher conversion and selectivity (entry 2). The nitration

Table 1. Nitration of adamantane (1) with HNO3 by NHPI under various conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Conv. (%)</th>
<th>Select. (%)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>PhCF3</td>
<td>87</td>
<td>64</td>
</tr>
<tr>
<td>2</td>
<td>AcOH</td>
<td>93</td>
<td>62</td>
</tr>
<tr>
<td>3</td>
<td>CH3CN</td>
<td>55</td>
<td>38</td>
</tr>
<tr>
<td>4</td>
<td>AcOEt</td>
<td>34</td>
<td>24</td>
</tr>
<tr>
<td>6</td>
<td>PhCF3</td>
<td>40</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

*1 (1 mmol) was reacted with HNO3 (1.5 mmol) in the presence of NHPI (0.1 mmol) at 60 °C for 15 h. * In the absence of NHPI. ** Under air.
On the other hand, the nitration of cyclohexane (14%) as well as a small amount of cyclooctanone (5%) was obtained. Cyclooctane (10%) at 75% conversion. Cyclohexane was difficult to nitrate using excess HNO₃ from NHPI and nitric acid, respectively. The resulting PINO abstracts the hydrogen atom from alkanes to give NHPI and alkyl radicals which are readily trapped by NO₂ to form nitroalkanes.

In conclusion, the present alkane nitration with nitric acid provides a facile method for the preparation of nitroalkanes, by the use of cheap and easily available nitric acid compared with NO₂. This work was partially supported by the Research for the Future program, JSPS and DAICEL Chemical Industries, Ltd.

Notes and references

1 A typical reaction was carried out as follows: economic grade concentrated nitric acid (60% over) was used without any treatment. The reaction was carried out as follows: to a two necked flask was added adamantan-1-ol (1 mmol), NHPI (0.1 mmol) and nitric acid (1.5 mmol) in trifluorotoluene (3 mL), and the mixture was reacted under argon at 60 °C for 15 h. After evaporation of the solvent under reduced pressure, the reaction mixture was extracted with diisopropyl ether and the extracts were washed with aq. NaHCO₃. After separation of the organic phase, the reaction mixture was subjected to silica gel chromatograph, giving 1-nitroadamantane (57%).

The nitration is initiated by the in situ generation of PINO and NO₂ from NHPI and nitric acid, respectively. The resulting PINO abstracts the hydrogen atom from alkanes to give NHPI and alkyl radicals which are readily trapped by NO₂ to form nitroalkanes.

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On the basis of these results, a possible reaction path for the present catalytic nitration of alkanes with nitric acid by the NHPI is shown in Scheme 1.

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