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[12] Crystal data for **6** $\cdot BF_4$ ($C_{47}H_{53}BF_4MnO_4P_3S$): $M_r = 948.61$, triclinic, space group $P1$, $a = 11.771(2)$, $b = 13.909(2)$, $c = 16.416(4)$ Å, $\alpha = 67.69(1)$, $\beta = 82.86(2)$, $\gamma = 81.43(1)^\circ$, $V = 2452.8(8)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.285\ g\,cm^{-3}$, $F(000) = 988$, $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å), $\mu(Mo_{K\alpha}) = 0.191\ mm^{-1}$; crystal dimensions $0.10 \times 0.28 \times 0.40$. Diffraction data were collected on an Enraf-Nonius diffractometer at 293 K. The structure was solved by direct methods and refined using full-matrix least-squares on F^2 with all non-hydrogen atoms anisotropically defined. The hydrogen atoms were placed in calculated positions, isotropically refined with common thermal parameters and allowed to ride on their parent carbon atoms. For 4866 observed reflections with $I > 2\sigma(I)$ and 551 parameters, the conventional R is 0.081 and $wR2 = 0.252$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-145733. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

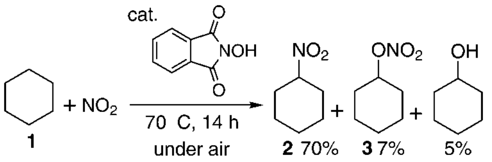
Efficient Catalytic Alkane Nitration with NO_2 under Air Assisted by *N*-Hydroxyphthalimide[**]

Satoshi Sakaguchi, Yoshiki Nishiwaki,
Takaaki Kitamura, and Yasutaka Ishii[*]

In contrast to the nitration of aromatic hydrocarbons, which is easily performed using nitric acid in the presence of sulfuric acid, the selective nitration of aliphatic hydrocarbons is very difficult because of the exceedingly low reactivity of the latter. Currently, nitrations of aliphatic hydrocarbons are carried out at fairly high temperatures (250–400 °C) using nitrogen dioxide or nitric acid, and they proceed by free radical chain reactions involving C–H bond homolysis.[1, 2] Under such high temperatures, higher alkanes undergo not only homolysis of C–H bonds but also cleavage of the C–C skeleton. Therefore, large-scale nitration of alkanes has been limited to lower alkanes such as methane and ethane.[2] For instance, the nitration of propane produces all of the possible nitroparafins, namely, nitromethane, nitroethane, 1-nitropropane, and 2-nitropropane.[1, 3] The development of selective nitration of cyclohexane is very attractive, since nitrocyclohexane is easily converted into cyclohexanone oxime, the raw material of ε-caprolactam, which in turn leads to nylon-6.[4–6]

Recently we developed a catalytic method for the generation of alkyl radicals from saturated hydrocarbons using *N*-hydroxyphthalimide (NHPI), which serves as the radical catalyst.[7] The phthalimide *N*-oxyl (PINO) radical generated in situ from NHPI and O_2, which lies in a triplet state, abstracts the hydrogen atom from the saturated hydrocarbons, forming the corresponding alkyl radicals. These radicals are readily trapped by O_2 under aerobic conditions to give oxygen-containing compounds such as alcohols, ketones, and carboxylic acids. These results led us to become interested in the nitration of alkanes with NO_2 by the use of NHPI as a catalyst.

In the first trial, NHPI was added at room temperature to a stirred benzene solution containing dissolved NO_2. The ESR measurement of the solution indicated a triplet signal, which is assigned to the PINO radical.[8] This is believed to be due to the fact that NO_2 is a stronger oxidant than O_2. Thus, the nitration of cyclohexane (**1**) was examined using NO_2 in the presence of a catalytic amount of NHPI under several reaction conditions ([Eq. (1)], Table 1).



(1)

The nitration of **1** with NO_2 by NHPI proceeded smoothly at 70 °C to give nitrocyclohexane (**2**, 70 % based on NO_2 used; Table 1, run 1) and cyclohexyl nitrite (**3**, 7 %) along with a small amount of an oxygenated product, cyclohexanol (5 %).

Table 1. NHPI-catalyzed nitration of **1** with NO_2 under selected conditions.[a]

Run	NHPI [mmol]	*T* [°C]	Yield of **2** [%][b]
1	0.6	70	70
2[c]	0.6	70	43
3	–	70	< 2
4	0.6	60	58
5	0.6	50	39
6	0.3	70	56
7[d]	0.6	70	63
8[e]	9	70	53

[a] Reactions were run as described in the Experimental Section. [b] Yields are average values obtained from several runs and are based on NO_2 used. [c] Under argon. [d] Recovered catalyst from run 1 was used. [e] The reaction was carried out using **1** (50 mL) and NO_2 (33 mmol). The yield of **2** is based on isolated product.

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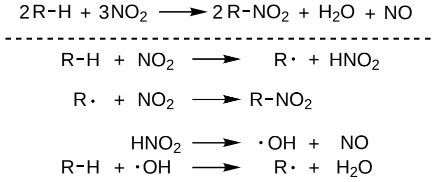
As discussed below, it is important that the NHPI-catalyzed nitration is conducted under air, since NO generated in the course of the reaction can be reoxidized to NO_2 by O_2. For the analogous nitration of **1** in the absence of air, the yield of **2** decreased to 43 % (run 2). Needless to say, the nitration of **1** was difficult to carry out without NHPI under these conditions (run 3). The nitration took place even at 50 °C to give **2** in 39 % yield (run 5). When the amount of NHPI was halved (0.3 mmol), **2** was formed in slightly lower yield (56 %, run 6). The nitration of **1** using recovered NHPI produced **2** in 63 % yield (run 7). The large-scale nitration allowed the isolation of **2** in 53 % yield (run 8).

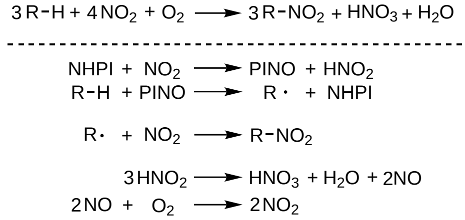
Scheme 1 shows the reaction pathway for the vapor-phase nitration of alkanes by NO_2.[2] According to this mechanism, one-third of the NO_2 employed is converted into NO via HNO_2. Hence, the maximum yield of nitroalkanes by this method cannot, in theory, be higher than 66.7 %. In fact, the nitration of **1** by NO_2 under argon led to **2** in 43 % yield (Table 1, run 2). It is noteworthy that the present nitration of **1** by NO_2 (under air, catalyzed by NHPI) afforded **2** in 70 % yield, that is, greater than the theoretical yield of 66.7 % for the conventional nitration by NO_2 alone. Owing to the complexities of the present nitration, the reaction pathway is uncertain at this stage. A plausible pathway is proposed in Scheme 2.



$$2\,R\text{-}H + 3\,NO_2 \longrightarrow 2\,R\text{-}NO_2 + H_2O + NO$$

$$R\text{-}H + NO_2 \longrightarrow R\cdot + HNO_2$$
$$R\cdot + NO_2 \longrightarrow R\text{-}NO_2$$
$$HNO_2 \longrightarrow \cdot OH + NO$$
$$R\text{-}H + \cdot OH \longrightarrow R\cdot + H_2O$$

Scheme 1. The reaction pathway for the conventional alkane nitration with NO_2.



$$3\,R\text{-}H + 4\,NO_2 + O_2 \longrightarrow 3\,R\text{-}NO_2 + HNO_3 + H_2O$$

$$NHPI + NO_2 \longrightarrow PINO + HNO_2$$
$$R\text{-}H + PINO \longrightarrow R\cdot + NHPI$$
$$R\cdot + NO_2 \longrightarrow R\text{-}NO_2$$
$$3\,HNO_2 \longrightarrow HNO_3 + H_2O + 2\,NO$$
$$2\,NO + O_2 \longrightarrow 2\,NO_2$$

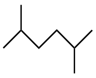
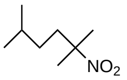
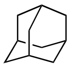
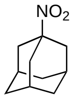
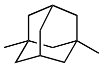
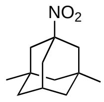
Scheme 2. A possible reaction pathway for the NHPI-catalyzed alkane nitration with NO_2 under air.

The nitration may be initiated by hydrogen-atom abstraction from the hydroxyimide group of NHPI by NO_2 to generate a PINO radical as described previously. The PINO radical readily abstracts the hydrogen atom from an alkane to form an alkyl radical, which undergoes nitration with NO_2 to give a nitroalkane. It has been reported that HNO_2 is converted into HNO_3, H_2O, and NO.[9] Under our conditions, the NO formed is expected to be oxidized by O_2 to NO_2, and the generated NO_2 is reused in the nitration. Therefore, the yield of nitrocyclohexane is over 66.7 %. In fact, when the reaction mixture was extracted with water after the reaction, the aqueous phase was acidic, probably because of the formation of HNO_3.

The most promising feature of the NHPI-catalyzed nitration of alkanes by NO_2 is that the nitration is conducted in the presence of air (O_2) under mild conditions. Owing to the higher concentration of NO_2 than air, the alkyl radicals formed can react selectively with NO_2 rather than O_2 to give nitroalkanes in preference to oxygenated products. In contrast, the conventional nitration is difficult to carry out in the presence of air, since under the high temperatures used (250 – 400 °C) the resulting alkyl radicals react not only with NO_2 but also with O_2 to provide a complex mixture of products.[2b]

The results of the nitration of other alkanes by the present method are shown in Table 2. The reaction of cyclooctane (**4**) afforded nitrocyclooctane (**5**, 50 %; run 1) and cyclooctyl nitrate (2 %) along with oxygenated products, such as cyclooctanone (**6**, 17 %) and cyclooctanol (**7**, 7 %). Owing to the potent oxidizing ability of NO_2 and the susceptibility of **4** to oxidation, the nitration of **4** with NO_2 led to oxygenated products **6** (8 %) and **7** (5 %), even in the absence of air.[10] Hexane afforded a 3:53:44 regioisomeric mixture of 1-nitrohexane, 2-nitrohexane, and 3-nitrohexane in 54 % yield (run 3) and the corresponding hexylnitrites (10 %). Only the tertiary position was attacked in the nitration of substituted alkanes such as isobutane, 2,5-dimethylhexane, and adamantanes to form the corresponding nitroalkanes (runs 4 – 7).

Table 2. NHPI-catalyzed nitration of alkanes with NO_2 under selected conditions.[a]

Run	Substrate	Product	Method	Yield [%]
1	cyclooctane (**4**)	nitrocyclooctane (**5**)	A	50
2[b]	cyclooctane (**4**)	nitrocyclooctane (**5**)	A	44
3	*n*-hexane	nitrohexane	A	54[c]
4	isobutane	2-methyl-2-nitropropane	B	46
5			C	46
6			C	66
7			C	70

[a] Reactions were carried out under air (1 atm) at 70 °C for 14 h. Method A: Alkane (5 mL), NO_2 (115 mg, 2.5 mmol), and NHPI (0.6 mmol) were used. Method B: Isobutane (2 mL) was treated with NO_2 (2.5 mmol) in the presence of NHPI (0.6 mmol) in $PhCF_3$ (3 mL) in a glass autoclave. Method C: The alkanes (3 mmol) were allowed to react with NO_2 (3.3 mmol) in the presence of NHPI (0.6 mmol) in $PhCF_3$ (5 mL). Yields are based on alkanes used. [b] Under argon. [c] 1-Nitrohexane:2-nitrohexane:3-nitrohexane = 3:53:44.

In conclusion, we have achieved the first catalytic nitration of higher alkanes with nitrogen dioxide under air using NHPI as a catalyst. This is the first procedure for catalytic nitration under mild conditions, and by further improvement of the methodology it may become possible to change the industrial process for alkane nitration.

1433-7851/01/4001-0223 $ 17.50+.50/0

Experimental Section

Representative procedure: NO_2 was used as a liquid at 0 °C. To a pear-shaped flask (100 mL) were added NHPI (98 mg, 0.6 mmol) and cyclohexane (5 mL). The flask was closed with a glass stopper and weighed. Then NO_2 (0.75 mL) was quickly added using a Hamilton gas-tight syringe, and the flask was reclosed with the glass stopper. The flask was weighed again in order to measure the NO_2 added (115 mg, 2.5 mmol). The flask was cooled in an ice bath and then quickly attached to a condenser, and the mixture was stirred at 70 °C for 14 h. After the reaction, GC and GC-MS analyses were performed. The yields of the products were estimated from the peak areas based on the internal standard technique using GC. The products were isolated by column chromatography on silica gel with hexane/ethyl acetate (10/1 – 3/1, v/v), and were identified by comparison of their analytical data with those of authentic samples.

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[5] Although ε-caprolactam is currently produced by the reaction of cyclohexanone with hydroxyl amine followed by a Beckmann rearrangement with sulfuric acid, the efficiency for the production of cyclohexanone by aerobic oxidation of cyclohexane is not high. Usually, the aerobic oxidation of cyclohexane is operated under 10 – 20 atm of air (150 – 200 °C) in the presence of a cobalt salt to form a ca. 1:2.5 – 1:4 mixture of cyclohexanone and cyclohexanol in only 3 – 5 % yield.

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[10] In the NHPI-catalyzed aerobic oxidation of cycloalkanes, cyclooctane (**4**) was more easily oxidized than cyclohexane (**1**).[7]

Immobilization of Redox-Active Ligands on an Electrode: The Dendrimer Route**

Franck Le Derf, Eric Levillain, Gaëlle Trippé,
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Macrocyclic systems that respond electrochemically when interacting with a guest ion have been extensively studied,[1] notably in connection with their potential applications as chemosensors. In such host molecules, the complexing ability of the ligand can be tuned by the electrochemical potential applied. Most of these compounds are built by covalent grafting of a receptor subunit onto a redox-active component. Thus, in the case of metal-cation recognition, various ligating fragments, for example, crown ethers, have been attached to an electroactive moiety such as a metallocene or a quinone derivative.[1] Alternatively, the ability of the tetrathiafulvalene (TTF) core to act as the redox-active subunit is now well established.[2] Indeed, TTF derivatives are able to exist in three different stable redox stages (neutral, radical cation, and dication) and therefore allow the electrochemical release of metallic cations to be controlled.

A further exciting challenge, less explored, lies in the preparation of sensing devices that can transfer the above-mentioned recognition properties, observed in solution, at the interface of a solid electrode and a liquid.[3] Results in this direction have been obtained thanks to a) electropolymerization of suitably substituted redox-responsive ligands (e.g., a pyrrole- or a thiophene-based monomer),[3, 4] and b) preparation of self-assembled monolayers.[5] Modified electrodes were also recently obtained by Casado et al. by electrodeposition of organometallic-containing silicon dendrimers.[6] On the other hand, TTF dendrimers, possessing 21 TTF moieties in the highest generation, were described by Bryce et al.,[7] but no mention was made of their immobilization on an electrode surface.

We describe here the synthesis of a series of dendrimers with up to 96 redox-active TTF moieties on the periphery, which allow the generation of polycationic species bearing up to 192 positive charges on the surface. Modified electrodes incorporating these electroactive TTF dendrimers were

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