COMMUNICATION

ChemComm
www.rsc.org/chemcomm

Mechanism of the catalytic oxidation of hydrocarbons by *N*-hydroxyphthalimide: a theoretical study†

Ive Hermans,*[ab] Luc Vereecken,[b] Pierre A. Jacobs[a] and Jozef Peeters[b]

[a] *Centre for Surface Science and Catalysis, Department of Interphase Chemistry, Kasteelpark Arenberg 23, B-3001 Heverlee, Belgium. E-mail: ive.hermans@chem.kuleuven.ac.be; Fax: **32 16 321998; Tel: **32 16 327356*

[b] *Division of Physical and Analytical Chemistry, Department of Chemistry, Celestijnenlaan 200F, B-3001 Heverlee, Belgium. E-mail: jozef.peeters@chem.kuleuven.ac.be; Fax: **32 16 327992; Tel: **32 16 327356*

Received (in Cambridge, UK) 22nd January 2004, Accepted 27th February 2004
First published as an Advance Article on the web 25th March 2004

The mechanism of the recently proposed catalytic oxidation of hydrocarbons by oxygen in the presence of *N*-hydroxyphthalimide (NHPI) was established by quantum chemical calculations, consistent with experiments.

Oxidation of saturated hydrocarbons by oxygen under mild conditions is of considerable scientific and industrial interest.[1,2] The products (alcohols and ketones) are extremely desirable as feedstock for the chemical industry. Recently, Ishii and coworkers,[3,4] followed by other groups, proposed *N*-hydroxyphthalimide (NHPI) as a catalyst for the aerobic oxidation of such hard to oxidize substrates as hydrocarbons,[5–7] as well as alcohols,[8,9] ketones and amides.[10] It is assumed that peroxyl radicals (ROO$^\cdot$) abstract an H-atom (>NO-**H**) from NHPI to form the PINO$^\cdot$ radical[4] (phthalimide *N*-oxyl). Apparently, this PINO$^\cdot$ radical can abstract a hydrogen atom from a hydrocarbon substrate (RH) (see Fig. 1).

In the present study, the energy barrier for abstraction of secondary alkane hydrogens by PINO$^\cdot$ and (>NO$^\cdot$) analogues is evaluated for the first time and compared with that by peroxyl radicals. Also the Potential Energy Surface (PES) of the subsequent ROO$^\cdot$ + NHPI $\rightleftharpoons$ ROOH + PINO$^\cdot$ reaction is characterized, and the influence of the solvent discussed. All calculations were carried out using the GAUSSIAN98 program.[11] At the DFT level we use the Becke three-parameter exchange functional[12,13] combined with the Lee–Yang–Parr correlation functional:[14] B3LYP-DFT. The B3LYP-DFT/6-31G(d_5,p) Zero Point Energies (ZPE) were scaled by 0.9814 as recommended for the B3LYP-DFT/6-31G* level.[15] Frequency analyses and Intrinsic Reaction Coordinate (IRC) calculations identified the located stationary points on the PES as true minima or as saddle-point Transition States (TS) connecting the reactants and products by paths of steepest descent.

Table 1 lists the barrier heights for secondary H-abstraction—reaction (1)—from propane (as a model compound for cyclohexane) by several PINO$^\cdot$-like radicals, calculated at increasingly higher levels of theory.

$$>NO^\cdot + RH \rightarrow >NOH + R^\cdot \qquad (1)$$

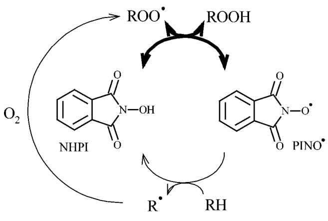

Fig. 1 Cycling of NHPI and PINO$^\cdot$ in the aerobic oxidation of hydrocarbons (RH). Below, NHPI + ROO$^\cdot$ $\rightleftharpoons$ PINO$^\cdot$ + ROOH is shown to be a fast equilibrium that drives the catalytic activity of NHPI.

Table 1 indicates that B3LYP/6-31G(d_5,p) underestimates the barrier by 13 ± 3 kJ mol^{-1} with respect to the high CCSD(T)//B3LYP-DFT level, which should be amply adequate for this kind of H-abstraction reaction.

The B3LYP/6-31G(d_5,p) barriers $(E)_1$ for H_{sec}-abstraction from propane by the >NO$^\cdot$ radicals from NHSI (*N*-hydroxysuccinimide) and NHPI are calculated to be 56 and 67 kJ mol^{-1} respectively. Increasing these values by 13 kJ mol^{-1} gives the approximate CCSD(T)//B3LYP-DFT barriers as 69 and 80 kJ mol^{-1} respectively. These are close to the H_{sec}-abstraction barriers from RH by ROO$^\cdot$ radicals,[16] consistent with similar experimental rate constants found for these two types of H-abstraction.[17]

Before addressing the formation of PINO$^\cdot$ in the catalytic cycle (Fig. 1) by the NHPI + ROO$^\cdot$ $\rightarrow$ PINO$^\cdot$ + ROOH reaction, we first examined the reaction of the smaller NHPI analogue $(O{=}CH)_2NOH$ with $CH_3OO^\cdot$. A full IRC analysis indicates that such reactions proceed through H-bonded pre- and post-reaction complexes, resulting in a substantial depression of the transition state energy as depicted in Fig. 2, which clearly reveals this reaction as very fast in both directions. The forward and reverse rate constants of the forward and reverse reactions for such a process are determined essentially by the relative energies and partition functions of the reactants, the TS and the products, whereas the precise energies of the pre- and post-reaction complexes are of negligible influence. As the reverse reaction of >NO$^\cdot$ + ROOH will be so much faster than the reaction of >NO$^\cdot$ radicals with RH, reaction (2) should be in

Table 1 ZPE-corrected barriers, E_1 (kJ mol^{-1}), for H_{sec}-abstraction by various >NO$^\cdot$ radicals from propane at different levels of theory

>NO$^\cdot$ radical	B3LYP/ 6-31G(d_5,p)	B3LYP/ 6-311++G-(2df,2pd)	CCSD(T)/ cc-pVDZ/ /B3LYP/ 6-311++G-(2df,2pd)
$H_2NO^\cdot$	103	109	115
$(O{=}CH)NHO^\cdot$	78	79	92
$(O{=}CH)N(CH_3)O^\cdot$	83	86	92
$(O{=}CH)_2NO^\cdot$	49	49	66

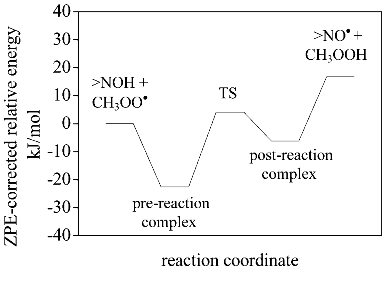

Fig. 2 ZPE-corrected PES of the $(O{=}CH)_2NOH$ + $CH_3OO^\cdot$ reaction at the B3LYP/6-31G(d_5,p) level.

DOI: 10.1039/b401050g

---

† Electronic supplementary information (ESI) available: all discussed TS and important intermediates (geometries, energies, ZPE, rotational constants and frequencies). See http://www.rsc.org/suppdata/cc/b4/b401050g/

near-perfect equilibrium at any instant during the hydrocarbon oxidation in the presence of an $>$NOH compound:

$$>\mathrm{NOH} + \mathrm{ROO}^\bullet \rightleftharpoons\ >\mathrm{NO}^\bullet + \mathrm{ROOH} \qquad (2)$$

The same conclusions can be drawn for the cases of NHSI and NHPI, for which the B3LYP/6-31G(d_5,p) relative energies of the TS with respect to the reactants are -2 and -13 kJ mol^{-1} respectively—although these are again likely underestimates by some 8 to 20 kJ mol^{-1}. The above remains valid in acetonitrile as solvent, even though CH_3CN forms H-bonded complexes with NHPI (analogues) and with ROOH that are stable for ~23 and ~18 kJ mol^{-1} respectively (at the B3LYP/6-311++G(d,p) level), such that the effective activation energies required for reactions (2) and (-2) are both raised by an additional ~21 kJ mol^{-1}. Still, in the NHPI case this leaves the activation energy required for reaction (1) at least 40 kJ mol^{-1} higher than that for reactions (2) and (-2), which therefore should both remain much faster than (1). This is at odds with Amorati *et al.*'s proposition[17] of reaction (2) as the rate-determining step in the catalytic cycle in acetonitrile.

As reaction (2) conserves the numbers of degrees of freedom of translation, vibration and rotation, the entropy change can be ignored ($<$ 12 J mol^{-1} K^{-1}) and the equilibrium constant $K_2 \equiv \{[>\mathrm{NO}^\bullet][\mathrm{ROOH}]\}/\{[>\mathrm{NOH}][\mathrm{ROO}^\bullet]\}$ will be entirely controlled by $\Delta_r H(2)$; *i.e.* $K_2 \approx \exp(-\Delta_r H/RT)$.

Defining the Catalytic Enhancement, C.E., as the ratio of the RH oxidation rate in the presence of $>$NOH catalyst over the rate without catalyst, one has:

$$\begin{aligned}\mathrm{C.E.} &\equiv \frac{\left\{k_p\left[\mathrm{ROO}^\bullet\right]_c + k_1\left[>\mathrm{NO}^\bullet\right]_c\right\}[\mathrm{RH}]}{k_p\left[\mathrm{ROO}^\bullet\right]_0[\mathrm{RH}]}\\ &= \frac{\left[\mathrm{ROO}^\bullet\right]_c}{\left[\mathrm{ROO}^\bullet\right]_0}\left\{1 + \frac{k_1}{k_p}\times\frac{\left[>\mathrm{NO}^\bullet\right]_c}{\left[\mathrm{ROO}^\bullet\right]_c}\right\}\end{aligned} \qquad (3)$$

where the c and 0 subscripts refer to concentrations in the presence and absence of $>$NOH catalyst, respectively, at identical concentrations of the ROOH chain-initiator ($\mathrm{ROOH} \rightarrow \mathrm{RO}^\bullet + {}^\bullet\mathrm{OH}$). k_1 is the rate constant of the H-abstraction by PINO$^\bullet$ from RH, k_p is the classical propagation rate constant ($\mathrm{ROO}^\bullet + \mathrm{RH} \rightarrow \mathrm{ROOH} + \mathrm{R}^\bullet$) in autoxidations. For a given [ROOH], the termination rate and hence the [ROO$^\bullet$] concentration are found equal with and without catalyst. Indeed, radical quasi-steady-state gives: $k_{term}[\mathrm{ROO}^\bullet]^2 = k_{ini}[\mathrm{ROOH}]$, both with and without catalyst (k_{term} and k_{ini} representing the rate constants of ROO$^\bullet$ termination and initiation, respectively), because there are no likely termination channels for PINO$^\bullet$ radicals at high enough [O_2] to capture the alkyl radicals. The combination of PINO$^\bullet$ radicals is endothermic by 14 kJ mol^{-1} at the B3LYP/6-31G(d_5,p) level, and O_2 elimination from the resulting $>$NO–ON$<$ faces such a huge barrier ($>$170 kJ mol^{-1}) that any dimer formed will promptly redissociate into PINO$^\bullet$ radicals. The combination of PINO$^\bullet$ with a isopropylperoxyl radical is exothermal for only 7 kJ mol^{-1} at the B3LYP/6-31G(d_5,p) level; again, redissociation will far outrun both the high-barrier O_2-elimination and the 105 kJ mol^{-1} endothermal PINOO$^\bullet$ + RO$^\bullet$ formation. Thus, $[\mathrm{ROO}^\bullet]_c = [\mathrm{ROO}^\bullet]_0$ and eq. 3 can be rewritten, using the definition of K_2, as:

$$\mathrm{C.E.} = 1 + (k_1/k_p) \times K_2 \times \{[>\mathrm{NOH}]/[\mathrm{ROOH}]\} \qquad (4)$$

The B3LYP/6-311++G(2df,2pd) $\Delta_r H$(0 K) of reaction (2) for $CH_3OO^\bullet$ + NHSI and NHPI were found to be +9 and -11 kJ mol^{-1}, respectively. As DFT underestimates the X–H BDE for a class of compounds in a systematic way, the *difference* in $\Delta_r H$(0 K) of these two reactions should be reliable, even in a polar solvent. Our $\Delta_r H$ data yield *e.g.* a K_2(383 K) of 0.06 for NHSI and of 32.4 for NHPI. Therefore, at 383 K, even though k_1 is ~30 times smaller for PINO$^\bullet$ than for SINO$^\bullet$ radicals (succinimide *N*-oxyl), the C.E. is still ~18 times larger for NHPI than for NHSI as the 383 K [$>$NO$^\bullet$]/[ROO$^\bullet$] ratio is 545 times larger in the case of NHPI. Our experimental observations confirm that NHPI is a much more active catalyst for the aerobic oxidation of cyclohexane than NHSI: at 383 K, 50 mL cyclohexane + 10 mL acetonitrile + 1 mol% NHPI or NHSI and 3 MPa O_2 in a 100 mL Parr reactor, require 6.6 and 14.2 hours respectively to reach 3% conversion. The temperature of 383 K was chosen arbitrarily, but low enough to prevent un-catalyzed autoxidation contributions to the observed activity.

The driving force of the catalytic activity of NHPI is that equilibrium (2) is shifted towards the non-terminating PINO$^\bullet$ chain propagation radicals. Therefore, at a given initiator concentration, the total radical concentration is much larger in the presence of NHPI as catalyst. Equation 4 shows that the rate constant of reaction (1) and the equilibrium constant of reaction (2) together determine the catalyst efficiency.

In pure acetonitrile as solvent the energy barrier E_1 for H_{sec}-abstraction from propane by SINO$^\bullet$ was found to increase by about 9.6 kJ mol^{-1} as calculated at the B3LYP/6-31G(d_5,p)//B3LYP/6-31G(d_5,p) level using the Polarized Continuum Model (PCM).[18] The higher E_1, together with the possible ionic dissociation of NHPI (into PINO$^-$ + H$^+$), can account for the observed decrease in catalytic activity with increasing concentrations of acetonitrile.[17]

This work is performed in the frame of a Belgian IAP-PAI network and a Flanders GOA (03/03) project. Ive Hermans is grateful to the Fonds voor Wetenschappelijk onderzoek, Flanders for a PhD grant. The authors thank Prof. D. De Vos, Dept. Interphase Chemistry for useful comments.

Notes and references

1 R. A. Sheldon and J. K. Kochi, *Metal-Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, 1981.
2 C. A. Tolman, J. D. Druliner, M. J. Nappa and N. Herron, in *Activation and Functionalization of Alkanes*, ed. C. L. Hill, John Wiley & Sons, New York, 1989.
3 Y. Ishii and S. Sakaguchi, *Catal. Surveys Jpn.*, 1999, **3**, 27.
4 Y. Ishii, S. Sakaguchi and T. Iwahama, *Adv. Synth. Catal.*, 2001, **5**, 393.
5 Y. Tashiro, T. Iwahama, S. Sakaguchi and Y. Ishii, *Adv. Synth. Catal.*, 2001, **2**, 343.
6 T. Iwahama, K. Syojyo, S. Sakaguchi and Y. Ishii, *Org. Process Res. Dev.*, 1998, **2**, 255.
7 I. W. C. E. Arends, M. Sasidharan, A. Kühnle, M. Duda, C. Jost and R. A. Sheldon, *Tetrahedron*, 2002, **58**, 9055.
8 T. Iwahama, Y. Yoshino, T. Keitoku, S. Sakaguchi and Y. Ishii, *J. Org. Chem.*, 2000, **65**, 6502.
9 F. Minisci, C. Punta, F. Recupero, F. Fontana and G. F. Pedulli, *Chem. Commun.*, 2002, 688.
10 F. Minisci, C. Punta, F. Recupero, F. Fontana and G. F. Pedulli, *J. Org. Chem.*, 2002, **67**, 2671.
11 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle and J. A. Pople, Gaussian 98 (Revision A.9), Gaussian, Inc., Pittsburgh PA, 1998.
12 A. D. Becke, *Phys. Rev. A*, 1988, **38**, 3098.
13 A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648.
14 C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785.
15 A. P. Scott and L. Radom, *J. Phys. Chem.*, 1996, **100**, 16502.
16 I. Hermans, L. T. Nguyen, P. A. Jacobs and J. Peeters, *ChemPhysChem*, 2004, submitted.
17 R. Amorati, M. Lucarini, V. Mugnaini and G. F. Pedulli, *J. Org. Chem.*, 2003, **68**, 1747.
18 *E.g.* S. Miertus, E. Scrocco and J. Tomasi, *Chem. Phys.*, 1981, **55**, 117.