

Theoretical study of deuterium kinetic isotope effect in peroxidation of phenol and toluene

Victor B. Luzhkov *

Department of Cell and Molecular Biology, Uppsala University, Biomedical Center, Husargatan, 3, P.O. Box 596, S-751 24 Uppsala, Sweden

Received 25 April 2005; accepted 9 June 2005

Available online 1 August 2005

Abstract

Reaction mechanisms of hydrogen abstraction from phenol and toluene by the hydroperoxyl radical are probed by theoretical calculations of deuterium kinetic isotope effect (KIE). In experiment the given free-radical reactions have nearly equal reaction heats and rates differing by 6 orders of magnitudes, yet demonstrate high H/D KIEs. The mechanism of phenol–peroxyl reaction is described by the proton-coupled electron transfer (PCET), while the toluene–peroxyl reaction follows the non-polar H-atom transfer (HAT). In present work, the H/D KIEs are assessed for several isotopomers of phenol and toluene using the DFT B3LYP/6-311+G(2d,2p) calculations and the post-processing Bigeleisen treatment with one-dimensional tunnel corrections. Differing patterns of bending vibrations are noted for the PCET and HAT TSs considered. The computed KIEs are 10.7 and 17.0 (at 65 °C) for the phenol and toluene reactions, respectively, that agrees with the available experimental results. The corresponding semi-classical contributions are 4.5 and 5.1, whereas the tunnel correction computed for unsymmetrical Eckart function yields the factors of 2.4 and 3.3 for phenol and toluene, respectively. The advantage of using Bigeleisen formula for reaction intermediates with low-frequency internal rotation modes is discussed.

© 2005 Elsevier B.V. All rights reserved.

Keywords: Kinetic isotope effect; Tunneling; Hydrogen abstraction; Antioxidants; Hydroperoxyl radical

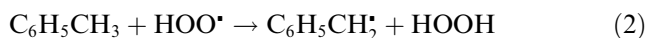
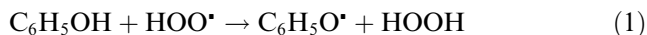
1. Introduction

The chain reactions of hydrocarbon (RH) auto-oxidation by the oxygen-derived peroxy radicals (ROO[•]) underlie important damaging effects in oils and biological lipids. These processes involve hydrogen abstraction from RH and can effectively be inhibited by trapping the reactive oxygen radicals with special compounds – antioxidants (InH). Among many known inhibitors, phenols play especially important role in protection of biological systems (e.g. [1–5]), in which case phenolic InH react with ROO[•] several orders faster than RH. The large difference between the peroxi-

dation rates of RH and phenolic InH is noted even for equal C–H and O–H bond energies (e.g. [6–8]). The high reactivity of phenols toward peroxy radicals was explained by several factors, including triplet repulsion terms and polar effects [7–10]. The role of polar effect (charge transfer) in the hydrogen transfer reactions of phenols was noted in a number of experimental works (e.g. [5,11,12]), however, the initial electron transfer as a rate-limiting step was ruled out [11]. The mechanisms of electron/charge transfer in radical reactions were also explored in the computational density functional theory (DFT) studies [13,14], which in particular showed that the phenol–phenoxyl and toluene–benzyl self-exchange reactions follow the proton-coupled electron transfer (PCET) [13,14] and the non-polar hydrogen atom transfer (HAT) [14] mechanisms, respectively:

* Tel.: +46 18 471 5055; fax: +46 18 536 971.

E-mail address: vluz@xray.bmc.uu.se.



An important and illustrative case of peroxidation of a phenolic inhibitor and hydrocarbon substrate is provided by model reactions (1) and (2). The toluene-peroxyl reaction can be viewed as a prototype model for oxidation of polyunsaturated fatty acids – the essential building blocks of biological lipids, in which case hydrogen atom is abstracted from the methylene group, $-\text{CH}=\text{CH}-\text{CH}_2-\text{CH}=\text{CH}-$, flanked by the carbon-carbon double bonds. The hydroperoxyl radical $\text{HOO}\cdot$ considered formally differs from the lipid-derived peroxy radicals. However, being a protonated form of superoxide radical, $\text{HOO}\cdot$ most probably belongs to the species directly involved in peroxidation of biological lipids [2]. Reactions (1) and (2) have nearly equal reaction heats, whereas their rates differ by a factor of 10^6 [6]. Similar and even closer to lipid oxidation case of kinetically controlled competitive hydrogen exchange is given by oxidation of bis(4-hydroxy-phenyl)methane by *tert*-ButO \cdot , where the bond dissociation energy of the methylene C–H is 13–19 kJ/mol lower than of the phenolic O–H, and yet the phenoxyl radicals are formed [15]. The potential energy surfaces and electron mechanisms of the reactions (1) and (2) have recently been studied by means of molecular dynamics empirical valence bond and DFT methods [16,17]. The DFT calculations successfully reproduce experimentally observed high difference of the reaction rates and predict that the phenol-peroxyl reaction follows the PCET mechanism, whereas the toluene-peroxyl reaction is described by the non-polar HAT mechanism [17]. Valuable information about reaction mechanisms can be obtained from the studies of deuterium kinetic isotope effect (KIE). The aim of the present work is to calculate and examine the nature of the H/D KIE for the reactions considered by means of computational theoretical methods. High values of deuterium KIE are observed in reactions of both compounds with peroxy and nitroxyl radicals [18–21]. In this respect, reactions (1) and (2) provide a well-defined test case for the studies of KIE for hydrogen transfer reactions with differing mechanisms.

2. Computational methods

The H/D kinetic isotope effect (KIE) in the reactions considered is evaluated in the framework of equilibrium statistical mechanics and Eyring transition state (TS) theory with the inclusion of one-dimensional tunnel correction (e.g. [22–25])

$$\begin{aligned} \text{KIE} &= \frac{k_{\text{H}}}{k_{\text{D}}} = q_{\text{t}} \times \text{KIE}_{\text{s}} \\ &= q_{\text{t}} \times \frac{v_{\text{i}}^{\text{H}}}{v_{\text{i}}^{\text{D}}} \times \prod_m^{3M-6} \frac{u_m^{\text{D}} \sinh(u_m^{\text{H}}/2)}{u_m^{\text{H}} \sinh(u_m^{\text{D}}/2)} \prod_n^{3N-7} \frac{u_n^{\text{H}} \sinh(u_n^{\text{D}}/2)}{u_n^{\text{D}} \sinh(u_n^{\text{H}}/2)} \end{aligned} \quad (3)$$

The semi-classical KIE_{s} term (also known as Bigeleisen formula) is based on quantization of harmonic vibrational frequencies ν at the reaction stationary points. The indexes m and n refer to the vibrational frequencies of the separated reactants and the TS, respectively. M and N is the number of atoms in the reactants and the TS, respectively. H and D denote the normal and deuterium hydrogen isotopes. v_{i} is the imaginary frequency for the activated complex and $u = h\nu/kT$. The term $q_{\text{t}} = \frac{Q_{\text{t}}^{\text{H}}}{Q_{\text{t}}^{\text{D}}}$ describes quantum mechanical tunnelling of the transferred atom across the potential barrier. The transmission coefficients Q_{t} , which give the ratio of the quantum and classical rates of the barrier crossing, are evaluated in this work either from Wigner approximation $Q_{\text{t}} = 1 + \frac{u_{\text{t}}^2}{24}$ [26], or from numerical integration of transmission probability across the barrier, modelled by unsymmetrical Eckart function [27,28]. Eckart potential $V(x)$ is given by the formula $V(x) = \frac{(V_1 - V_2)y}{1+y} + \frac{(V_1^{1/2} + V_2^{1/2})^2 y}{(1+y)^2}$, where $y = e^{2\pi x/L}$. In the expression for $V(x)$ the terms V_1 and V_2 are the heights of energy barrier in the forward and backward directions, respectively, the parameter $L = \frac{2\pi(2/|F^*|)^{1/2}}{(V_1^{-1/2} + V_2^{-1/2})}$ is the characteristic width of the potential barrier, and F^* is the curvature at the maximum of the potential barrier [28].

The structures and energies of the reaction intermediates are taken from the earlier reported unrestricted DFT B3LYP/6-311+G(2d,2p) calculations [17]. The computed harmonic vibrational frequencies (program Gaussian-98 [29]) for the reaction intermediates and their isotopomers are scaled using coefficients of [30]. The molecular graphics is prepared using MOLDEN [31] and ChemWindow from Bio-Rad (www.bio-rad.com).

3. Results

The hydrogen exchange reactions (1) and (2) involve three elementary steps, i.e., formation of the prereactive complex of reactants, hydrogen atom transfer, and dissociation of the product complex. Both reactions have multiple TSs [17], however, only the lowest energy TSs are considered here further. Fig. 1 gives the qualitative picture of the computed potential energy profiles and the electronic orbital rearrangement in the considered reaction pathways (the corresponding quantitative analysis of electronic parameters and TS geometries is given earlier [17]). The attack of $\text{HOO}\cdot$ at $\text{C}_6\text{H}_5\text{OH}$ first leads to the prereactive H-bonded complex and then proceeds as hydrogen transfer step. The phenolic proton is trans-

Download English Version:

<https://daneshyari.com/en/article/9575124>

Download Persian Version:

<https://daneshyari.com/article/9575124>

[Daneshyari.com](https://daneshyari.com)