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On the Mechanism of the Ozonation of Isopropyl Alcohol: An Experimental and Density Functional Theoretical Investigation. ^{17}O NMR Spectra of Hydrogen Trioxide (HOOOH) and the Hydrotrioxide of Isopropyl Alcohol

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The mechanism of ozonation of the C−H bond of saturated organic compounds (R−H) is still controversial.[1] A concerted 1,3-dipolar insertion mechanism to form the corresponding hydrotrioxide, ROOOH, has been proposed.[2] The mechanistic possibility involving hydrogen atom abstraction by ozone to form the radical pair, $[R^\bullet\ {}^\bullet OOOH]$, that collapses to ROOOH has also been suggested.[3] More recently, a hydride ion transfer to form a carbenium ion and hydrotrioxide anion pair, $[R^+\ {}^-OOOH]$, has been proposed.[4] We now report that the hydrotrioxide of isopropyl alcohol and hydrogen trioxide (HOOOH) are formed in the low-temperature ozonation of the alcohol. Both polyoxides were characterized for the first time by ^{17}O NMR. These observations, together with the results of a density functional theoretical investigation of the ozonation of isopropyl alcohol, support the "radical" mechanism of this reaction.

Ozonation of isopropyl alcohol (**1**) (1 M) with ozone−oxygen or ozone−nitrogen mixtures in acetone-d_6 at −78 °C produced the corresponding hydrotrioxide, $Me_2C(OH)(OOOH)$ (**2**), characterized by the OOOH ^{1}H NMR absorption at 12.9 ppm (δ CH_3, 1.44) and ^{13}C NMR absorptions at 25.7 (δ CH_3) and 104.3 (δ C) ppm downfield from Me_4Si (−10 °C) in yields of 40−50%. Still, another OOOH absorption at 13.1 ppm, belonging to another polyoxide species with exchangeable protons (fast exchange with CH_3OD at −60 °C), was, on the basis of ^{17}O NMR of the species, highly enriched with ^{17}O,[5] assigned to HOOOH.[6] This assignment was confirmed by GIAO/MP2/6-311++G** calculations[7] of ^{17}O NMR chemical shifts for this species, which are in excellent agreement with the experimentally obtained values (Table 1). Similar observations were also made in methyl acetate and *tert*-butyl methyl ether as solvents.[8] **2** and HOOOH were formed in molar ratio of roughly 1:0.6 in all solvents investigated.

Table 1. ^{17}O NMR Chemical Shifts (δ) of the Hydrotrioxide of Isopropyl Alcohol (**2**) and Hydrogen Trioxide (HOOOH) in Acetone-d_6 at −10 °C[a−c]

	^{17}O NMR		
	δO(1)	δO(2)	δO(3)
$(H_3C)_2C(OH)(O_1{-}O_2{-}O_3{-}H)$	368 (840)[d,e]	445 (3470)[d,e]	305 (350)[d,e]
$H{-}O_1{-}O_2{-}O_3{-}H$	305 (350)[d−f]	421 (3680)	305 (350)
	306 (calcd)[c]	433 (calcd)	306 (calcd)
$H{-}O_1{-}O_2{-}H$	187 (320)[g]	187 (320)	
	192 (calcd)[c]	192 (calcd)	

[a] Values in parts per million downfield from the internal standard $H_2{}^{17}O$. [b] ^{17}O NMR data were obtained on Varian Unity Inova-600 spectrometer operating at 81.37 MHz. [c] The calculated GIAO/MP2/6-311++G** absolute shielding for H_2O is 343.9 ppm. Experimental values: $H_2O(g)$, 344 ppm; $H_2O(l)$, 307.9 ppm (Wasylishen, R. E.; Mooibroek, S.; Macdonald, J. B. *J. Chem. Phys.* **1984**, *81*, 1057). [d] Area ratio of peaks O(1):O(2):O(3) was 1:1:1 (2:1 for HOOOH). [e] Line widths of the resonances at half-height ($\Delta\nu_{1/2}$), ±5%. [f] Identical ^{17}O NMR chemical shifts were observed in the spectra of HOOOH, generated by the ozonation of hydrazobenzene in acetone-d_6 (see footnote 8). [g] For a pioneering study, see: Olah, G. A.; Berrier, A. L.; Prakash, G. K. S. *J. Am. Chem. Soc.* **1982**, *104*, 2373.

A detailed investigation of the products in the decomposition mixture after warming up the ozonized solutions of **1** in *tert*-butyl methyl ether by GC/MS and NMR revealed acetone (37 ± 5%), peroxyacetic acid (11 ± 2%), acetic acid (39 ± 5%), formic acid (7 ± 2%), hydrogen peroxide (11 ± 3%), water, isopropoxymethanol ($H_2C(OH)OCH(CH_3)_2$) (5 ± 1%), and oxygen ($\Sigma\,{}^3O_2/\Delta\,{}^1O_2$[6d]). Peroxyacetic and formic acids, as well as isopropoxymethanol, were already present in the ozonized solutions of **1** at −78 °C, and their concentrations did not change significantly during the decomposition of **2**/HOOOH.

To gain mechanistic insight and to accommodate the above observations, ab initio density functional calculations at the B3LYP/6-31G* + ZPE level[9,10] were used to fully optimize the stationary points on the singlet potential energy surface of the title reaction.[11] Upon going from the reactants to the product, ROOOH, two stationary points were calculated which were found

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(1) For reviews, see: (a) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, 1982; Vol. II, Chapter 9. (b) For a review on polyoxides, see: Plesničar, B. In *Organic Peroxides*; Ando, W., Ed.; Wiley: New York, 1992; Chapter 10. (c) Olah, G. A.; Molnar, A. *Hydrocarbon Chemistry*; Wiley: New York, 1995; Chapter 8.

(2) (a) Tal, D.; Keinan, E.; Mazur, Y. *J. Am. Chem. Soc*. **1979**, *101*, 502. (b) Bailey, P. S.; Lerdal, D. A. *J. Am. Chem. Soc*. **1978**, *100*, 5820. (c) Teillefer, R. J.; Thomas, S. E.; Nadeau, Y.; Fliszar, S.; Henry, H. *Can. J. Chem*. **1980**, *58*, 1138. (d) Giamalva, D. H.; Church, D. F.; Pryor, W. A. *J. Org. Chem*. **1988**, *53*, 3429.

(3) (a) Hellman, T. M.; Hamilton, G. A. *J. Am. Chem. Soc*. **1974**, *96*, 1530. (b) Whiting, M. C.; Bolt, A. J. N.; Parish, J. H. *Adv. Chem. Ser*. **1968**, *77*, 4. (c) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon: Oxford, 1983; Chapter 2.

(4) (a) Nangia, P. S.; Benson, S. W. *J. Am. Chem. Soc*. **1980**, *102*, 3105. (b) For the thermochemistry of polyoxides, see: Benson, S. W.; Cohen, N. In *Peroxyl Radicals*; Alfassi, Z., Ed.; Wiley: New York, 1997; Chapter 4.

(5) ^{17}O-enriched ozone was generated by flowing ^{17}O-enriched oxygen (58% $^{17}O_2$, ISOTEC) through an ozonator.

(6) For the previous studies on HOOOH, see: (a) Giguere, P. A.; Herman, K. *Can. J. Chem*. **1970**, *48*, 3473. (b) Bielski, B. H. J.; Schwartz, H. A. *J. Phys. Chem*. **1968**, *72*, 3836. (c) Cremer, D. *J. Chem. Phys*. **1978**, *69*, 4456. (d) Plesničar, B.; Cerkovnik, J.; Koller, J.; Kovač, F. *J. Am. Chem. Soc*. **1991**, *113*, 4946. (e) Jackels, C. F. *J. Chem. Phys*. **1993**, *99*, 5768. (f) Cerkovnik, J.; Plesničar, B. *J. Am. Chem. Soc.* **1993**, *115*, 12169. (g) Koller, J.; Plesničar, B. *J. Am. Chem. Soc*. **1996**, *118*, 2470. (h) Speranza, M. *Inorg. Chem*. **1996**, *35*, 6140. (i) Fujii, T.; Yashiro, M.; Tokiwa, H. *J. Am. Chem. Soc*. **1997**, *119*, 12280. (j) Mckay, D. J.; Wright, J. S. *J. Am. Chem. Soc*. **1998**, *120*, 1003.

(7) (a) GIAO/MP2/6-311++G** ^{17}O NMR chemical shifts were calculated by using ACESII package of programs (Stanton, J. F.; Gauss, J.; Watts, J. D.; Lauderdale, W. J. Bartlett, R. J. *Quantum Theory Project*, University of Florida, Gainesville, 1994). For some relevant references, see: Gauss, J. *Chem. Phys. Lett.* **1992**, *191*, 614 (GIAO/MP2). Raghavachari, K.; Trucks, G. W.; Pople, J. A.; Head-Gordon, M. *Chem. Phys. Lett.* **1989**, *157*, 479. Bartlett, R. J.; Watts, J. D.; Kucharski, S. A.; Noga, J. *Chem. Phys. Lett*. **1990**, *165*, 513 (CCSD(T)). (b) HOOOH, MP2/6-311++G** (CCSD(T)/6-311++G**, for comparison): R(H−O) = 0.969 Å (0.969), R(O−O) = 1.421 Å (1.433), ∠HOO = 101.4°(101.3), ∠OOO = 107.2°(107.1), ∠HOOO = 80.4°(81.7).

(8) HOOOH, generated in this way, decomposed somewhat faster than **2** in all solvents investigated, thus enabling unambiguous ^{17}O NMR assignments. For example, kinetic and activation parameters for the decomposition of the polyoxides obtained by following the decay of the OOOH (CH_3) absorption(s) in *tert*-butyl methyl ether are: **2**, $k_1 = 1.2 \times 10^{-4}$ s^{-1} (−10 °C), $E_a = 25.6 \pm 1.0$ kcal/mol, log $A = 17.3 \pm 0.5$ (−15 to +5 °C); HOOOH, $k_1 = 2.9 \times 10^{-4}$ s^{-1} (−15 °C), $E_a = 16.7 \pm 1.0$ kcal/mol, log $A = 10.2 \pm 1.0$. The values for HOOOH are in good agreement with those for the decomposition of HOOOH, generated by the ozonation of hydrazobenzene ($E_a = 15.3 \pm 1.0$ kcal/mol, log $A = 8.3 \pm 1.0$ (−10 to +25 °C). The latter procedure yields solutions of HOOOH without the interfering presence of other hydrotrioxides.[6f,g]

(9) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *GAUSSIAN 94, Revision B.3*; Gaussian, Inc.: Pittsburgh, PA, 1995.

(10) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785. (b) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

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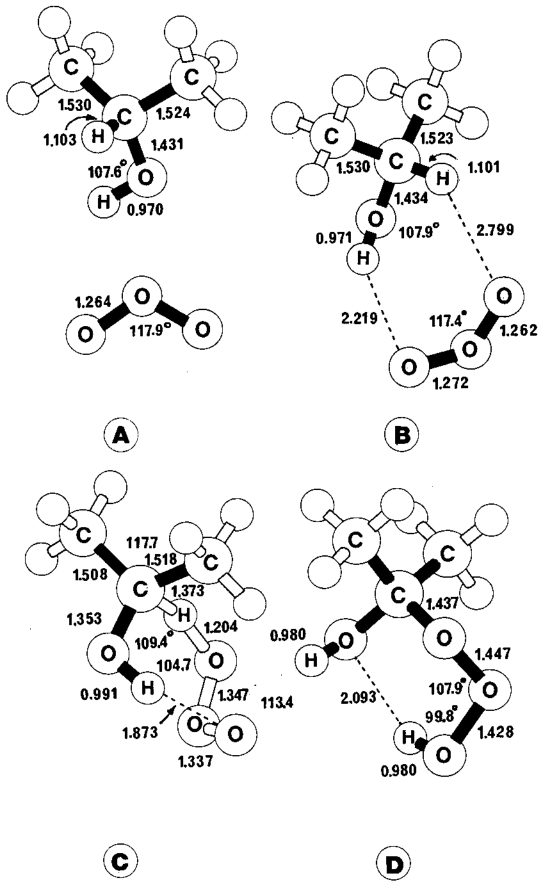
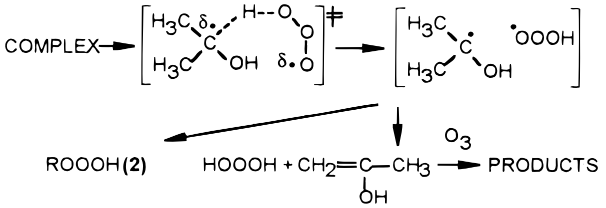


Figure 1. Relevant geometrical parameters for the fully optimized structures (B3LYP/6-31G*) of isopropyl alcohol and ozone (A), the complex (B), the transition state (C), and the hydrotrioxide of isopropyl alcohol (D).

to be an intermediate complex and a transition state (TS) (Figure 1). A complex is formed in a fairly early stage of the reaction and is held together by a stabilization energy of 3.1 kcal/mol. The TS, calculated to be 7.4 kcal/mol less stable than that of the isolated reactants and 10.6 kcal/mol[12] less stable than that of the complex, apparently does not involve synchronous C−O and O−H bond formation to form ROOOH. Rather, a highly asymmetric TS with considerable O−H bond (but not C−O bond) formation is indicated.

A concerted insertion mechanism involving a transition state with the O−H bond formation preceding C−O bond formation has already been proposed for ozonations of C−H bonds.[2d] However, it is unclear how the calculated TS could accommodate the formation of HOOOH in terms of a concerted 1,3-dipolar insertion mechanism. Therefore, we were left with two remaining mechanistic possibilities. (1) The radical pair at a sufficiently large separation was formed after the transition state of the rate-limiting step, thus allowing both the collapse (with less than unit efficiency) of the pair to ROOOH[3a,b] and the abstraction of the hydrogen atom from the 2-hydroxy-2-propyl radical to form the enol, i.e., 2-hydroxypropen,[3b] and HOOOH. (2) The ion pair[3,4] that produces the same products was formed along the reaction path. The energies of the radical and ion pair at infinite separation

Scheme 1



are 3.3 and 127.3 kcal/mol, respectively, above the energy of the isolated reactants. However, solvation of these species (particularly ions) could dramatically lower the endothermicity of these reactions.[4,13] Overall, the ozonation of **1** to form the intramolecularly hydrogen-bonded ROOOH (**2**) is exothermic by 55.8 kcal/mol, while the adduct, 2-hydroxypropen-HOOOH, is 33.3 kcal/mol below the energy of the isolated reactants.

The Mulliken population analysis indicates that the migrating hydrogen does not behave as a hydride ion in this reaction. Also, the geometry of the TS resembles that of the forming hydrotrioxide radical more than does that of the hydrotrioxide anion.[6j,14] The extraordinary long HO−OO bond in the anion calculated in the present study (1.73 Å) is in accord with the calculations on this species at higher levels of sophistication.[6g,14] Therefore, it seems unlikely (but not impossible) that such a loosely bound species could exist as a distinguished molecular entity in solutions of organic solvents containing water (decomposition into HO^- and O_2) and undergo the above-mentioned reactions.

In summary, the present calculations have clarified the transition structure for the ozonation of isopropyl alcohol and have, together with the formation of HOOOH (and some other products[15]), indicated the involvement of radical intermediates in the reaction (Scheme 1). The origin of the experimentally observed rate acceleration of the formation of ROOOH[16] (and HOOOH as well) in polar aprotic solvents, could be attributed to the enhanced polarization of the TS relative to the reactants (**1**, μ = 1.56 D; O_3, 0.61 D; C, 1.15 D; TS, 4.50 D). The increased reactivity of the alcohol, compared to that of simple hydrocarbons, might be due to the additional stabilization of the TS by hydrogen bonding between the forming OOOH radical and the OH group (O−H···O).

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Supporting Information Available: B3LYP/6-31G*-optimized geometries and energies (B3LYP/6-31G* + ZPE) of the structures reported (4 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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[11] The ozone molecule is best described as a diradical with two unpaired electrons on the terminal oxygens in orbitals, pointing out of the plane of the molecule (π direction), that are weakly coupled in a singlet pair (Meredith, C.; Quelch, G. E.; Schaefer, H. F. *J. Am. Chem. Soc.* **1991**, *113*, 1186, and references therein.).

[12] For example, the activation parameters for the ozonation of isopropyl ether in CCl_4 are: $E_a = 10.0$ kcal/mol, $\log A = 7.9$. (Giamalva, D. H.; Church, D. F.; Pryor, W. A. *J. Am. Chem. Soc.* **1986**, *108*, 7678.).

[13] By using known heats of formation for the radicals and molecules, as taken from Benson and Cohen,[4] $\Delta_r H$(g) = 21 ± 1.5 kcal/mol, and $\Delta_r H$(l) = 13 ± 2.0 kcal/mol were calculated for the reaction: $O_3 + Me_2CHOH \rightarrow HO_3 + Me_2COH$. The $\Delta_r H$(l) value is now close to the estimated 9 kcal/mol for the experimental activation energy to make the hydrogen atom abstraction plausible. We thank one of the reviewers for this information.

[14] HOOO•: UB3LYP/6-31G*, $R(H-O_1) = 0.981$ Å, $R(O_1-O_2) = 1.503$ Å, $R(O_2-O_3) = 1.262$ Å, $\angle HO_1O_2 = 98.8°$, $\angle O_1O_2O_3 = 112.2°$, $\angle HO_1O_2O_3 = 0°$. $E = -226.035\,175$ au. $HOOO^-$, B3LYP/6-31G* (CCSD(T)/6-311++G**), $R(H-O_1) = 0.972$ Å (0.966), $R(O_1-O_2) = 1.734$ Å (1.882), $R(O_2-O_3) = 1.336$ Å (1.315), $\angle H_1O_1O_2 = 87.6°$(85.1), $\angle O_1O_2O_3 = 108.5°$ (110.1), $\angle HO_1O_2O_3 = 0°$ (−43.7). $E = -226.058\,174$ au (−225.682 552 au).

[15] Peroxyacetic and formic acids are presumably formed by the ozonolysis of the enol.[1a,3b] The initially formed formaldehyde is oxidized further (O_3/O_2), and also reacts with isopropyl alcohol to form isopropoxymethanol.

[16] Kovač, F.; Plesničar, B. *J. Am. Chem. Soc.* **1979**, *101*, 2677. Pryor, W. A.; Ohto, N.; Church, D. F. *J. Am. Chem. Soc.* **1983**, *105*, 3614. Zarth, M.; de Meijere, A. *Chem. Ber.* **1985**, *118*, 2429. Plesničar, B.; Kovač, F.; Schara, M. *J. Am. Chem. Soc.* **1988**, *110*, 214.