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Experimental Detection of One Case of Benzene Epoxidation by a Peroxy Radical and Computational Prediction of Another

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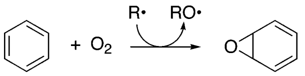

Reaction of the β-styryl radical with O_2 in benzene results in a low yield of benzene oxide, which is shown by isotopic labeling to arise from the solvent. Ab initio and DFT calculations elucidate the mechanism of this reaction, and identify the properties of other radicals that should be more effective promoters of the reaction. The CN radical is found to be one candidate.

The synthetically versatile[1−7] compound benzene oxide/oxepin has been proposed as an intermediate in several oxidative reactions of benzene.[8−11] However, to our knowledge, the only reported reactions of benzene affording the epoxide as an isolable product are those from photochemically generated oxygen atoms.[12,13] A strain of fungus has been found to epoxidize some substituted benzenes,[14] but the parent hydrocarbon has not been reported to participate in this biotransformation. In this note we describe the serendipitous discovery of a reaction that converts benzene + O_2 to benzene oxide/oxepin. Thus far it occurs only in very low yield, but the accompanying computational work predicts the existence of analogues with much higher efficiency.

The experimental detection of the reaction occurred during a study of the β-styryl (2-phenylethenyl) radical with O_2. The β-styryl radical is believed to play an important role in polycyclic aromatic hydrocarbon (PAH) formation during hydrocarbon combustion.[15−18] We have been studying its interception by O_2 to ascertain whether the resulting β-styrylperoxy radical is susceptible to unimolecular degradations that could divert it from the undesirable PAH and soot-forming pathway toward the preferred formation of CO_2 and H_2O.

One set of experiments involved the generation of the β-styryl radical from *trans*-cinnamoyl peroxide[15] at 100 °C, in O_2-saturated benzene, in a glass-lined stainless steel pressure vessel.[19] Among the several products detected and identified from this reaction was benzene oxide. It was characterized by comparison of its *N*-phenylmaleimide Diels−Alder adduct with an authentic sample, and shown to arise from the solvent rather than the cinnamoyl peroxide by isotopic labeling. Specifically, the use of C_6D_6 as solvent yielded only fully deuterium labeled benzene oxide. No benzene oxide was detected if either the cinnamoyl peroxide or oxygen was omitted. Significantly, use of benzoyl peroxide in place of cinnamoyl peroxide also failed to result in benzene oxide formation. The yield of benzene oxide was only about 1%, based on cinnamoyl peroxide as the limiting reagent. However, the computational results summarized below suggest that other radicals could be much more efficient promoters of the oxidation, and lead to the proposal of a candidate for that role.

The intuitively obvious mechanism for the reaction is supported by the calculations; it involves reversible addition of the peroxy radical to benzene, followed by intramolecular attack of the cyclohexadienyl radical on the O−O bond in the adduct. A schematic standard free energy profile[20] for this sequence (Figure 1) highlights the energetic factors that would favor formation of benzene oxide over competing decomposition reactions of the ROO$^\bullet$ radical. In general, one would clearly like to reduce ΔG°_2 with respect to ΔG°_1, the effective transition-state free energy for the summed decomposition reactions. However, that effort would be of no value if the conversion of the ROO-benzene adduct to products (ΔG°_4) became rate limiting for the benzene oxidation.

In terms of the bonding in the ROO$^\bullet$ adduct with benzene, these requirements suggest that one would like the newly formed C−O bond to be as strong as possible, but the O−O bond to be as weak as possible. A stronger

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(19) CAUTION: Reactions involving organic peroxides or O_2 in organic solvents are potentially explosive.

(20) Free energy differences (298.15 K) are computed with respect to a standard state of 11.3 M, appropriate for reactions in neat liquid benzene.

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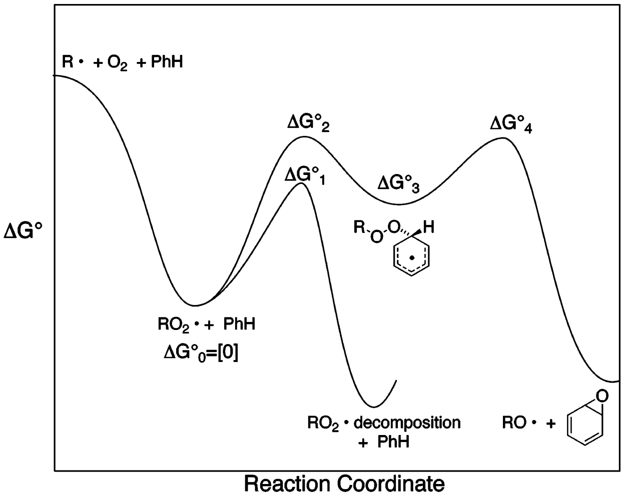

FIGURE 1. Schematic standard free energy profile for benzene oxidation by peroxy radical ROO•.

TABLE 1. Experimental (ref 22) and/or Calculated O−H and O−O Bond Dissociation Enthalpies (298 K) for Selected Organic Hydroperoxides, ROOH[a]

R	exptl O−H	calcd O−H	exptl O−O	calcd O−O
H	87.8 ± 0.5	87.8	50.3 ± 0.7	51.3
$(CH_3)_3C$	84 ± 2	84.8	46 ± 2	47.2
CH_3	88 ± 1	86.2	44 ± 2	45.6
Ph		87.2		23.4
$H_2C{=}CH$		86.4		21.0
E-PhHC=CH		86.0[b]		14.9[b]
NC		97.6		16.5
BH_2		98.6		36.9

[a] Values are in kcal/mol. Calculations used the CBS-QB3 model (ref 23), except where noted. [b] G3(MP2,B3) result (ref 24).

C−O bond would, by definition, reduce the energy of the adduct with respect to ROO• + PhH, and so presumably keep $\Delta G°_2$ as low as possible with respect to $\Delta G°_1$. A weak O−O bond in the adduct would help to ensure that $\Delta G°_4 \leq \Delta G°_2$. Assuming the entropic contribution to $\Delta G°_2$ to be roughly constant for all R groups, and assuming also a proportionality of C−O and O−O bond dissociation enthalpies (BDEs) in the benzene adduct respectively to those of the O−H and O−O bonds in ROOH,[21] one could use experimental or computational values of the latter quantities as measures of the suitability of a given ROO• for benzene oxidation. Some representative data are given in Table 1.

The BDEs in Table 1 show that the O−O bond is >20 kcal/mol stronger in the saturated organic hydroperoxides than in the unsaturated ones. That fact tends to make the unsaturated derivatives better potential O-atom donors. With the exceptions of NCOOH and H_2BOOH the O−H bonds of the hydroperoxides considered here all have dissociation enthalpies of 86 ± 2 kcal/mol. The 10 kcal/mol stronger O−H bond in NCOOH presumably derives from overlap of a low-lying π^* orbital of the nitrile with the p-type lone pair of the proximal oxygen, which would be expected to reduce the stabilizing effect of that lone pair in the NCOO• radical. That explanation is supported by the calculated 98.6 kcal/mol BDE for the O−H bond of H_2BOOH.

The ability (albeit marginal) of the β-styrylperoxy radical to effect epoxidation of benzene, but the failure of the phenylperoxy radical to carry out the reaction correlate, as expected, with the differences in O−H and O−O BDEs of the corresponding hydroperoxides. DFT calculations[25] on the epoxidation reaction suggested how those factors come into play. At the UB3LYP/6-31+G(d,p) level, $\Delta G°_2$, $\Delta G°_3$, and $\Delta G°_4$ (Figure 1) were calculated to be respectively 25.1, 20.6, and 24.9 kcal/mol for oxidation of benzene by *E*-PhHC=CHOO•,[26] but 24.6, 20.1, and 27.0 for the corresponding reactions of PhOO•. Thus the addition steps for the two peroxy radicals face similar activation barriers, and lead to adducts of similar stability with respect to the reactants. However, for the PhOO• addition, the stronger O−O bond in the adduct makes its decomposition to the products rate limiting and raises the overall barrier by 2.4 kcal/mol over that for addition.

These results made it interesting to explore the additions of NCOO•and H_2BOO• to benzene, since the strong O−H bonds in the corresponding hydroperoxides suggested that the adducts of these radicals to benzene might be relatively stable, and that the barriers to addition might consequently be lower than those for the additions of *E*-PhHC=CHOO• or PhOO•. However NCOO• and H_2BOO• were not expected to be equally effective oxidants of benzene. The much weaker O−O bond in NCOOH suggested that NCOO• should have the lower overall barrier for the oxidation reaction. The density functional calculations turned out to support that analysis, at least qualitatively, yielding values for $\Delta G°_2$ to $\Delta G°_4$ of 14.5, 6.2, and 17.3 kcal/mol, respectively, for the H_2BOO• reaction, and 10.8, 5.0, and 11.1 kcal/mol, respectively, for the NCOO• reaction. To assess the reliability of the DFT results, the calculations on the NCOO• reaction were repeated at the G3(MP2,B3) level.[24] That model gave values for $\Delta G°_2$ to $\Delta G°_4$ of 13.2, 3.3, and 14.4 kcal/mol, respectively. Thus the calculations suggest that oxidation of benzene by NCOO• should be substantially faster than the observed reaction effected by the β-styrylperoxy radical.

Of course, the apparently desirable properties of NCOO• for benzene oxidation would be misleading if the radical had an unusually low barrier to unimolecular decomposition, and so that issue was also explored computationally. The lowest barrier on the doublet potential energy surface[27] that could be found was the one for closure to a dioxirane ring, as has been previously

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[21] The justification for such proportionalities, as well as independent estimates of some of the BDEs in Table 1, can be found in: Sebbar, N.; Bozzelli, J. W.; Bockhorn, H. *J. Phys. Chem. A* **2004**, *108*, 8353−66.

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[26] Only the *E* stereoisomer of PhHC=CHOO• was considered because the *Z* stereoisomer has a decomposition pathway that is the intramolecular version of the benzene oxidation described here. It was the search for the intramolecular aromatic oxidation that prompted this study in the first place.

reported for this radical[28] and also for vinylperoxy[29] and phenylperoxy radicals.[29a,30] UB3LYP/6-31+G(d,p) and G3-(MP2,B3) calculations gave activation free energies for this reaction of 23.2 and 24.3 kcal/mol, respectively, suggesting that it would not compete significantly with the bimolecular reaction in neat benzene.

Despite its apparently favorable characteristics, it may be that NC$^\bullet$ is not the most practicable promoter for the oxidation of benzene with O_2, since it is not very convenient to generate. Nevertheless, the experimental results with the β-styrylperoxy radical show that conversion of benzene to its oxide with radical promoters is possible, and the calculations suggest that there are other radicals that should be able to do a much better job. The properties to be sought in any other candidate radicals have also been identified as a result of the computations. Specifically, the radical should be unsaturated to weaken the O−O bond in the benzene adduct, and should have a low-energy LUMO to strengthen the new O−C bond in the adduct. Determination of the O−O and O−H BDEs in the corresponding hydroperoxides provides a convenient way to screen for the effectiveness of these properties.

Experimental Section

Benzene oxide/oxepin was generated by a literature procedure[31] and trapped in situ with *N*-phenylmaleimide to generate the known Diels−Alder adduct.[31]

^1H NMR (400 MHz, $CDCl_3$) δ 3.12 (m, 2H), 3.42 (m, 2H), 3.71 (m, 2H), 5.93 (m, 2H), 7.14 (m 2H), 7.37 (m, 1H), 7.43 (m, 2H).

MS (EI) 267 (28), 222 (5), 173 (14), 119 (18), 91 (100).

trans-Cinnamoyl peroxide[15] (60 mg) was dissolved in benzene (5 mL) with *N*-phenylmaleimide (70 mg). The solution was placed in a glass-lined, stainless steel calorimetry bomb, charged with O_2 (10 atm), and the whole assembly was submerged in boiling water for 4 h.[19] The vessel was then cooled and vented, and the solvent was removed on a rotary evaporator. The residue was purified by chromatography on a 15 cm × 20 mm column of silica gel. Elution was conducted first with 9:2 chloroform: diethyl ether (60 mL) and then with pure diethyl ether (80 mL). The solvent was removed from the diethyl ether eluate by rotary evaporation, and the residue was subjected to NMR and GCMS comparison with the authentic Diels−Alder adduct prepared as above.

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Supporting Information Available: Details of calculations, including Cartesian coordinates of stationary points and literature citations. This material is available free of charge via the Internet at http://pubs.acs.org.

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[27] Calculations at a variety of levels up to CBS-QB3 (ref 23) suggest that a C_{2v} structure, N(CO)O, has a quartet state that is lower in energy than the doublet ground state of NCOO$^\bullet$. If the crossing of doublet and quartet surfaces happened to occur on the reactant side of the transition state for dioxirane ring closure of NCOO$^\bullet$, there could, in principle, be a spin-forbidden unimolecular reaction of NCOO$^\bullet$ with a lower PE barrier than that calculated for the spin-conservative ring closure.

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