

Dihydrogen Trioxide (HOOOH) Is Generated during the Thermal Reaction between Hydrogen Peroxide and Ozone**

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In memory of Bernard (Bernie) M. Babior

The reaction between HOOH and O₃ has fascinated scientists for almost a century.^[1-3] The reactivity of O₃ is markedly increased by the presence of HOOH, although a clear mechanistic understanding of this phenomenon has thus far eluded researchers.^[4-8] In modern times, the reaction between HOOH and O₃ has received industrial utility and has been named both the peroxone process and an advanced oxidation reaction.^[9,10] It is one of the most potent antibacterial processes known and is a powerful chemical remediation tool utilized to treat soil, groundwater, and wastewater contaminated with poly-cyclic aromatic hydrocarbons, polychlorinated biphenyls (PCBs), methyl *tert*-butyl ether (MTBE), benzene, toluene, ethylbenzene and xylene (BTEX), trinitrotoluene (TNT), and other persistent organic pollutants.^[10]

Recently, the reaction between HOOH and O₃ has become of biological interest. It has been discovered that all antibodies have the ability to catalyze the oxidation of water by singlet oxygen (¹Δ_g), with the postulated intermediacy of HOOOH, to generate HOOH and detectable amounts of an oxidant with the chemical signature of O₃.^[11-13] The proposition of HOOOH as a key intermediate in the antibody-catalyzed reaction has led to an interest in the study of thermally accessible routes to HOOOH that may utilize biologically relevant components.

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A rigorous kinetic examination of the reaction between O_3 and HOOH was first performed by Rothmund and Burgstaller in 1917.^[1] Weiss^[14] first proposed a free-radical mechanism for this process, and subsequently Bray^[3] concluded that either free radicals, $\cdot OH$ and hydroperoxyl ($HO_2\cdot$), or HOOH were necessary to explain the observed kinetics of the process. Taube and Bray^[2] in 1940 then established the role of $\cdot OH$ and $HO_2\cdot$ as chain-initiating intermediates in a complex radical cascade (Table 1, entries 1–4). Subsequent detection of $\cdot OH$, the superoxide anion ($O_2^{\cdot-}$), and the ozonide radical anion ($O_3^{\cdot-}$) as intermediates in this process supported the free-radical mechanism proposed by Weiss.^[15–17] Thus, the contemporary view is that a common free-radical mechanism may account for the decomposition of O_3 by HOOH under all conditions, with the potential involvement of HOOH being largely ignored. Recently however, HOOH has been thrust into center stage as a plausible intermediate in the photochemical peroxone process. Engdahl and Nelander^[18] observed that mixing HOOH and O_3 in an argon matrix results in a complex that, when photolyzed at 266 nm, produces HOOH. However, there is no report of HOOH being detected from the strictly thermal peroxone reaction.

Herein we demonstrate the direct observation of HOOH formed during the thermal reaction between HOOH and O_3 . Passage of a stream of ozone/oxygen gas through a solution of aqueous hydrogen peroxide (ca. 96 %

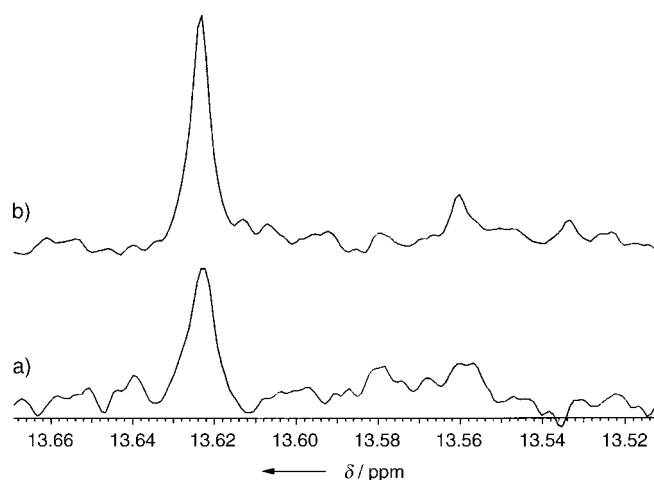


Figure 1. 1H NMR spectra (600 MHz recorded at $-60^\circ C$) of the peroxone reaction between $\delta = 13.50$ and 13.70 ppm downfield from phenyltrimethylsilane (PhTMS) in $[D_4]$ methanol (99%, external reference). a) $H_2O_2 + O_3/O_2$ (20 s), b) $H_2O_2 + O_3/O_2$ (20 s) + H_2O_3 (authentic sample). The authentic HOOH used as an additive in (b) was generated by the ozonation of a resin-supported 1,2-diphenylhydrazine (hydrazobenzene) derivative.^[19] An aliquot of this HOOH solution (100 μL) was added with a glass syringe and needle to the teflon-valved NMR tube at $-60^\circ C$. Note that no signal at about 13.60 ppm was present in the following control NMR spectra: 1) After O_3/O_2 was bubbled through $[D_6]$ acetone (99.9%) for 20 s and 2) HOOH (28 M) in $[D_6]$ acetone (99.9%).

Table 1: Selected equations from the reaction between ozone and hydrogen peroxide (in aqueous media unless otherwise stated).

Entry	Equation	Comment
1 ^[a]	$O_3 + H_2O_2 \rightarrow \cdot OH + HO_2\cdot + O_2$	$k_1 = 6.5 \times 10^{-2} M^{-1} s^{-1}$
2 ^[b]	$O_3 + \cdot OH \rightarrow HO_2\cdot + O_2$	$k_2 = 1.1 \times 10^8 M^{-1} s^{-1}$
3 ^[c]	$O_3 + \cdot O_2^- + H^+ \rightarrow \cdot OH + 2 O_2$	$k_3 = 1.6 \times 10^9 M^{-1} s^{-1}$
4 ^[d]	$H_2O_2 + \cdot OH \rightarrow HO_2\cdot + H_2O$	$k_4 = 2.7 \times 10^7 M^{-1} s^{-1}$
5 ^[e]	$O_3 + H_2O_2 \rightarrow H_2O_3 + {}^3O_2$	$\Delta H_f = -32.3 \text{ kcal mol}^{-1}$
6 ^[f]	$O_3 + HO_2\cdot \rightarrow HO_3\cdot + O_2$	$k_6 = 2.8 \times 10^6 M^{-1} s^{-1}$
7 ^[g]	$H_2O_3 \rightarrow O_2 + H_2O$	$\Delta H_f = -16.2 \text{ kcal mol}^{-1}$, $\Delta H_a(0 H_2O) = 45.1 \text{ kcal mol}^{-1[h]}$, $\Delta H_a(1 H_2O) = 12.7 \text{ kcal mol}^{-1}$, $\Delta H_a(2 H_2O) = 0.2 \text{ kcal mol}^{-1}$

[a] Ref. [2, 33]. [b] Ref. [34]. [c] Ref. [35]. [d] Ref. [36, 37]. [e] Gas-phase calculation: Ref. [31]. [f] Ref. [32]. [g] Ref. [21, 38]. [h] The number of water molecules (in parentheses) signifies the molar equivalents of water participating as a catalyst in the reaction.

w/w), generated either by vacuum distillation of commercially available HOOH (containing stabilizers) or pure HOOH generated by reduction of O_2 ^[19] in $[D_6]$ acetone or $[D_{10}]$ tetrahydrofuran at $-78^\circ C$ produced an intermediate that could be characterized by 1H NMR analysis ($-60^\circ C$) as having a typical OOOH resonance at $\delta = 13.6 \pm 0.2$ ppm relative to tetramethylsilane (Figure 1 b).

This signal disappeared upon warming the $[D_6]$ acetone and $[D_{10}]$ tetrahydrofuran solutions to room temperature and did not reappear upon recooling. The 1H NMR chemical shift and thermal instability of this intermediate are both in line with the wealth of physical data available for HOOH.^[18, 20–23]

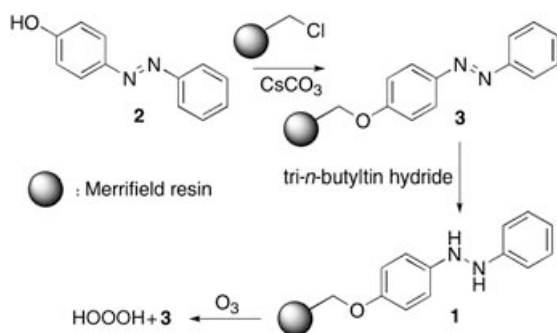
To add support to the notion that this 1H NMR resonance at $\delta = 13.6 \pm 0.2$ ppm in the peroxone reactions corresponds

to HOOH, an authentic solution of HOOH in $[D_6]$ acetone was required as a control. Neither of the two main chemical routes for the preparation of HOOH (pulsed radiolysis of air-saturated perchloric acid solutions^[24, 25] or reduction of ozone by reducing agents such as 2-ethylanthrahydroquinone^[20] and 1,2-diphenylhydrazine^[20, 21, 23]) were suitable for this control sample. The lifetime of HOOH in acid solutions (ca. 200 ms in perchlorate pH 2) precludes the pulsed radiolysis method as being viable for NMR analysis (a single pulse sequence in

a typical 1H NMR experiment shown in Figure 1 is > 25 s). Plesnicar et al.^[26] have shown that HOOH is always contaminated with a number of oxidation products of 1,2-diphenylhydrazine and HOOH when the low-temperature ozonation of 1,2-diphenylhydrazine in an organic solvent is employed. Therefore a new methodology was required for the generation of a pure solution of HOOH.

The development of polymer-supported methodologies to facilitate solution-phase chemistry has exploded over the past decade in response to the stringent requirements of high-throughput solution-phase combinatorial and parallel synthesis.^[27–30] We rationalized that HOOH could be prepared free of the contamination products arising from the oxidation of 1,2-diphenylhydrazine (1,2-DPH) if the 1,2-DPH was on a

resin support. Thus, resin-supported 1,2-DPH derivative **1** was prepared (Scheme 1).^[19]



Scheme 1. Preparation of resin-bound diphenylhydrazine **1** and its use to prepare HOOOH from O₃.

The resin-supported hydrazine **1** was prepared in two steps by an initial addition of 4-phenylazophenol (**2**) to low cross-linked (1% divinylbenzene) chloromethylpolystyrene followed by reduction of the orange azo resin derivative **3** with tri-*n*-butyltin hydride in refluxing toluene. Low-temperature ozonation (−78 °C) of resin-1,2-DPH **1** in [D₆]acetone or [D₁₀]tetrahydrofuran with a stream of ozone/oxygen led to the formation of HOOOH in solution, with the only contaminant being HOOH (Figure 2). The oxidized resin turns bright orange during the ozonation, as it becomes oxidized in part to **3**, and can then be removed by filtration.

Addition of the solution of HOOOH in [D₆]acetone to the NMR tube containing the peroxone reaction resulted in an increase in the area of the OOH resonance (13.6 ± 0.2 ppm, Figure 1a), thus strengthening the hypothesis that the unknown resonance corresponds to HOOOH.

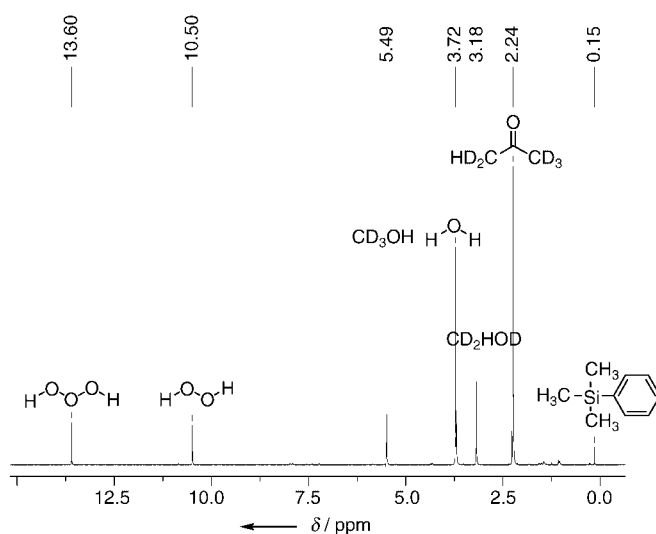


Figure 2. ¹H NMR spectrum (600 MHz recorded at −60 °C) of the filtrate following low-temperature ozonation (−78 °C) of resin-1. Note PhTMS in [D₄]methanol is present as an external standard for quantification of HOOOH.

The amount of HOOOH generated during the peroxone reaction was determined from an analysis of the relationship between the area of the OOH resonance (13.6 ± 0.2 ppm) and the amount of HOOOH present in the NMR sample. This relationship was determined by a standard method involving interpolation of the ratio of the peak areas of the OOH resonance at 13.6 ± 0.2 ppm and the methyl protons of an external standard (phenyltrimethylsilane) to a standard calibration curve. This analysis revealed that approximately 29 μmol of HOOOH (corresponding to a concentration of 2.9 mM in the [D₆]acetone solution) was formed in this specific peroxone reaction (10 mL reaction volume). This quantity of H₂O₃ was reproducibly generated when the peroxone reaction was repeated under identical conditions of HOOH concentration and O₃ flow. This amount of H₂O₃ generated in the peroxone process is significant, and therefore the chemistry of the peroxone reaction may now have to be revised to not only consider ozone and HOOH chemistry, but also that of H₂O₃.

There are at least two mechanistically viable possibilities for the origin of HOOOH in the peroxone reaction. By using quantum chemical methods Xu and Goddard^[31] have calculated that the enthalpy of reaction (ΔH_r) for the thermal reaction of HOOH and O₃ to yield HOOOH and ³O₂ in the gas phase is −32.3 kcal mol^{−1}, with the highest enthalpy of activation (ΔH_a) being 4.8 kcal mol^{−1} (Table 1, entry 5). The process involves two sequential single electron transfer reactions that is formally the redox reaction between O₃ and HOOH. Xu and Goddard^[31] have proposed that the reaction proceeds via a planar seven-membered-ring biradical intermediate (with the spin multiplicity of the triplet and singlet states being almost degenerate) to yield HOOOH and ³O₂ (Figure 3 and Table 1, entry 5). More recently, to explain hydrogen isotope effects on the reaction kinetics of the peroxone reaction in water, Lesko et al.^[32] have concluded that HO₃[−], the conjugate base of H₂O₃, may be generated from a reaction between the anion of hydrogen peroxide and O₃ (Table 1, entry 6).

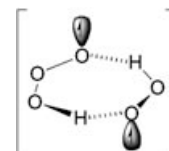


Figure 3. Postulated seven-membered-ring triplet biradical intermediate on the pathway from H₂O₂ and O₃ into H₂O₃ and ³O₂.

The observation that HOOOH is generated in the thermal peroxone reaction in low-water-content organic solvents at low temperature brings with it clear questions. These include the as yet, unknown generation of HOOOH under totally aqueous conditions at room temperature of a peroxone mixture. Bielski^[24,25] has shown that HOOOH, detected chemically and spectroscopically, is quasistable under totally aqueous conditions ($t_{1/2}$ = ca. 2 s at pH 1.5, 298 K). Koller and Plesnicar^[21] and Xu and Goddard^[31] have independently calculated that HOOOH decomposes to yield ¹O₂ and H₂O in a water-catalyzed reaction (Table 1 entry 7). Thus, although not yet reported, ¹O₂ may well be generated during the peroxone reaction in aqueous systems from the known decomposition of H₂O₃. In addition, further reactions of HOOOH with either itself, HOOH, ¹O₂, or O₃ to yield, as yet, undefined products will add further complexity to this rich and complex reaction process.

Experimental Section

Reaction between O₃ and HOOH: All samples were prepared as solutions in [D₆]acetone (99.9%) or [D₁₀]tetrahydrofuran (99.9%, 10 mL). The experiments were carried out by using Schlenk techniques. In brief, a stream of O₃ in O₂ was bubbled through an HOOH solution (28M) in [D₆]acetone (99.9%) or [D₁₀]tetrahydrofuran (99.9%, 10 mL) precooled to -78 °C for 20 s. The hydrogen peroxide used in these studies was prepared either by the resin method described in the Supporting Information or by vacuum distillation of an aqueous H₂O₂ (50% w/v containing stabilizers) solution to approximately one-third volume. These ozonolyzed solutions were then degassed briefly by bubbling argon through the solution of H₂O₂ and transferred to a teflon-valved NMR tube. The samples were then warmed to -60 °C and ¹H NMR spectra were measured. Each experiment was repeated at least twice and gave essentially the same amount of HOOOH.

Generation of HOOOH in [D₆]acetone with **1**: Resin-supported 1,2-diphenylhydrazine **1** was suspended in [D₆]acetone (5 mL) and cooled to -78 °C. A stream of ozone/oxygen gas was passed through the suspension for 2 min. The resin was then removed by filtration under argon and the filtrate was quickly transferred to an NMR tube under a positive argon pressure.

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