

# X-ray Structure Analysis of Ozonides by the Crystalline Sponge Method

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**S** Supporting Information

**ABSTRACT:** The crystalline sponge method was used for the X-ray structure analysis of ozonide compounds. As this new technique requires only microgram quantities of the samples, structural analysis can be conducted without product isolation, isomer separation, or crystallization and most importantly without any risk of explosion.

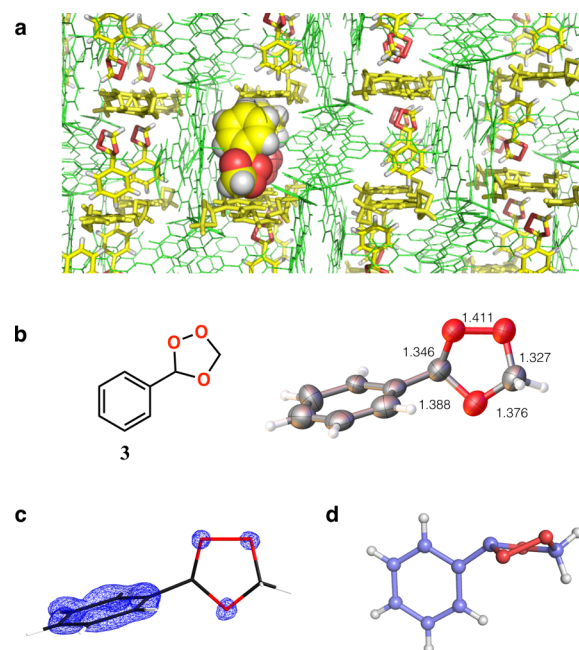
Ozonolysis represents an effective method to convert alkenes or alkynes into their oxidized congeners. The reaction intermediate, ozonide, is known to be a highly explosive compound and seldom isolated. When formed by reaction of olefins with ozone gas at low temperature, they are usually treated *in situ* with reducing reagents at low temperature in order to convert them into alcohols or aldehydes.<sup>1,2</sup> For safety reasons, concentration and heating of ozonide solutions should be strictly avoided even if the ozonolysis is carried out on a milligram scale.<sup>3</sup> These restrictions are a major issue in the study of these intriguing five-membered heterocyclic structures containing three oxygen atoms, and the structural study of ozonides by X-ray crystallography is particularly difficult. In fact, the crystal structures of ozonides found in the Cambridge Structural Database (CSD) are, in most cases, limited to those that are kinetically stabilized with bulky substituents. The crystal structures of sterically nonbiased ozonides are quite rare.<sup>4</sup>

Here, we report the X-ray crystallographic analysis of ozonides by using the crystalline sponge method that we recently developed for the micro- to the nanogram scale X-ray structure analysis of noncrystalline compounds without crystallization.<sup>5–7</sup> Several ozonide structures are successfully solved under safe treatment of the compounds, and even the stereochemistry of ozonide diastereomers can be discussed based on X-ray analysis. Through the crystallographic analysis of several ozonides, we also demonstrate that product isolation is unnecessary in the crystalline sponge method if the reactions occur cleanly and quantitatively.

A porous coordination network [(ZnI<sub>2</sub>)<sub>3</sub>(tpt)<sub>2</sub>·x(solvent)]<sub>n</sub> (**1**; tpt = tri(4-pyridyl)-1,3,5-triazine)<sup>8</sup> was used as the crystalline sponge throughout this study. An *n*-pentane solution of styrene (2, 24 mM, 4 mL) was bubbled with ozone gas (0.4 L min<sup>-1</sup>; 400 ppm) from an ozone generator at -78 °C. After 2 h, only a 5 μL aliquot was taken from the reaction solution and directly added to a capped microvial containing a sponge crystal and 20 μL of cyclohexane and equipped with a needle as a vapor outlet. Considering the thermally degradable nature of

ozonides,<sup>9</sup> the solvent was slowly evaporated through the needle at 4 °C over 2 d, and the resulting guest-included crystal was subjected to single crystal X-ray analysis.

In the crystallographic analysis, the most intense Q-peaks could be reasonably assigned to oxygen atoms of the product, and the refined crystal structure clearly showed ozonide structure **3** embedded in the pore of **1** (Figure 1). Oxygen and carbon atoms are clearly assigned from the electron density (Figure 1c) as well as by reasonable bond lengths in the five-membered ring (Figure 1b). The puckered conformation of the peroxide C–O–O–C part, which is dominant in common peroxides due to lone pair–lone pair repulsion, was observed.<sup>10</sup>



**Figure 1.** X-ray crystal structure of the styrene ozonide **3** determined by the crystalline sponge method. (a) Inclusion complex **1·3**, where styrene ozonide (**3** in yellow and red for carbon and oxygen, respectively) is embedded in the host framework **1** (green). (b) ORTEP drawing (30% probability) of **3**. (c) Electron density map  $F_0$  (contour  $0.8\sigma$ ), superimposed on the refined structure of **3**, from which oxygen and carbon atoms are easily distinguishable. (d) A ball-and-stick presentation that clarifies the puckered conformation of the peroxide C–O–O–C part.

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We believe that the data quality was sufficient to discuss the conformation of **3** in the pores.

It is also noteworthy that neither crystallization nor isolation of the target compound is necessary in the crystalline sponge method. Thus, the reaction solution can be directly subjected to guest soaking without isolation and purification procedures.

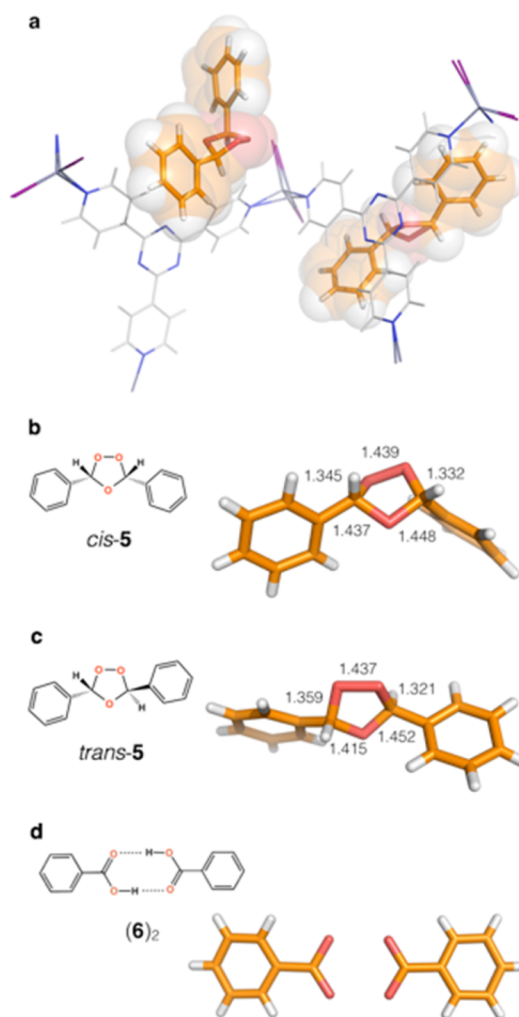
We next examined the X-ray analysis of a disubstituted ozonide derived from an internal olefin, stilbene (**4**), for which stereochemical issues will be concerned in the product. From *cis*-stilbene (*cis*-**4**), the formation of two diastereomers (*cis*- and *trans*-**5**) has been previously reported.<sup>11</sup> The stereochemistry of the two isomers has been tentatively assigned based on the chemical shifts in the <sup>1</sup>H NMR spectrum, but unambiguous structural determination by X-ray crystallography is still required. We analyzed the structures of the ozonide diastereomers derived from *cis*-**4**. The ozonolysis of *cis*-**4** was carried out in a similar manner to that of **2**, and the product inclusion into crystalline sponge **1** was conducted at 4 °C for 2 d. The X-ray crystal structure revealed two crystallographically independent molecules (one *cis*-**5** + one *trans*-**5**) in an asymmetric unit of the inclusion complex with the refined occupancies of 66% and 71% for the *cis* and *trans* isomers, respectively (Figure 2a–c). Similar to structure **3**, we also successfully analyzed the five-membered heterocyclic ring in *cis*-**5** and *trans*-**5** with converged C–O and O–O bond lengths (Figure 2b,c).

The observation of the two diastereomers (*cis* and *trans*-**5**) in the pores demonstrates the unique potential of the crystalline sponge method to analyze a mixture of compounds. The two compounds are independently analyzed provided that every component in the mixture finds its own binding site that does not overlap with the others. For safety reason, the separation and purification of the two isomers are difficult, but the crystalline sponge method enabled the direct crystallographic analysis of the mixture.

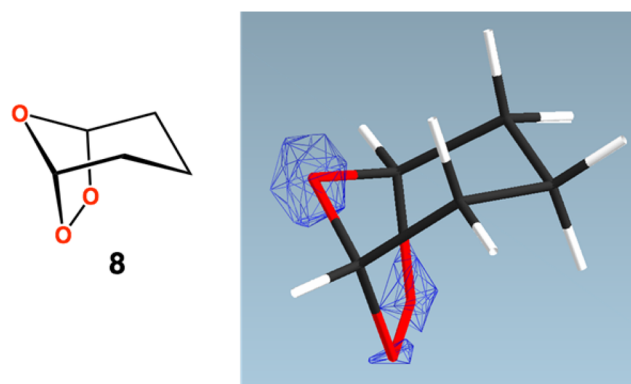
The product **5** is a relatively stable ozonide as a result of the steric and electronic effects of the two phenyl groups. Nevertheless, the compound should be treated with special care as thermally decomposed compounds were observed in the crystal when the guest inclusion was carried out at 50 °C. Crystallographic analysis of the sponge after guest uptake at 50 °C revealed only benzoic acid (**6**) dimer trapped in the pores of **1** (Figure 2d). This result indicates the explosive nature of ozonide **5** even at 50 °C. The microgram-scale structural analysis by the sponge method can therefore predict the stability of explosive compounds under safe conditions.

Finally, the crystalline sponge method was applied to the structure analysis of an ozonide derived from a low molecular weight olefin, cyclopentene **7**. Appropriate guest soaking conditions were found: 5 μL of reaction mixture and 30 μL of *n*-hexane (4 °C, 2 d). Because of its anticipated volatile and noncrystalline nature, the crystallographic analysis of the ozonide **8** from **7** is impossible by conventional X-ray studies. Furthermore, the high oxygen content of 41 wt% indicates the highly explosive nature of **8**. Nevertheless, by virtue of the crystalline sponge method that requires only a microgram quantity of the sample, we were able to analyze ozonide structure **8** without any risk of explosion (Figure 3).

Based on a reasonable quality data set of cyclopentene ozonide **8**, crystallographic analysis suggested the ozonide framework with an envelope-type conformation, which has been previously elucidated by theoretical calculation and microwave spectroscopy.<sup>12</sup> Our experimental observation



**Figure 2.** (a) X-ray crystal structure of the inclusion complex **1**-(*trans*-**5**)-(cis-**5**). Note that *cis*-**5** lies on the special positions and overlaps its symmetrically operated structure, which is omitted for clarity. Cyclohexane molecules are also omitted for clarity. (b) and (c) Stick models of *cis*-**5** and *trans*-**5**. (d) Stick models of benzoic acid dimer (**6**)<sub>2</sub> observed when the guest soaking was carried out at 50 °C.



**Figure 3.** Stick model presentation of cyclopentene ozonide **8**. Electron density at 0.70  $\sigma$  level is overlaid, from which three oxygen atoms are distinguished from carbon atoms.

underlies the fact that the reported reasonable quality data set is because of the highly reactive nature of ozonide **8**, therefore we could not improve data quality even further.

In summary, we have demonstrated an application of the crystalline sponge method for the structural determination of explosive ozonide compounds. As very small quantity of target samples is required, the risk of explosion is fully eliminated. The crystal structure of inclusion complex **1**·[(*cis*-5)·(*trans*-5)] shows one of the advantages of the method, namely that product isolation and isomer separation are unnecessary and the structures of more than one target compounds can be determined at once when the reaction mixture is directly analyzed. We believe that the crystalline sponge method is also applicable for the structural analysis of other harmful compounds (e.g., extremely explosive, toxic, or lachrymatory compounds), for which crystallographic studies have been avoided.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b05817.

Experimental and characterization details; experimental conditions, NMR data sets and crystallographic tables (CCDC nos. 1011446–1011449) (PDF)

Crystallographic data (CIF)

Crystallographic data (CIF)

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### Notes

The authors declare no competing financial interest.

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