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A new type of anomalous ozonolysis in strained allylic bicycloalkan-1-ols

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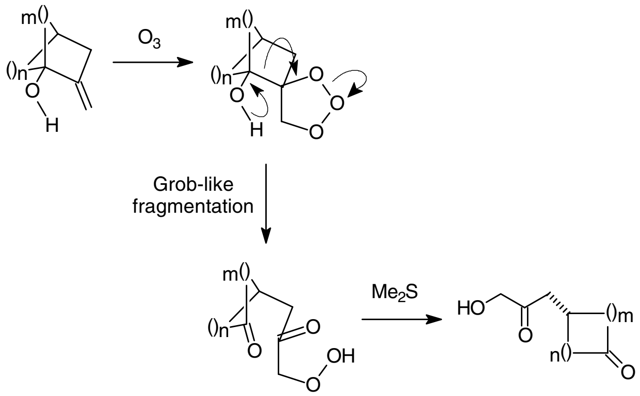
Abstract—7,7-Dimethyl-2-methylenenorbornan-1-ol, a fenchone-derived strained allylic bicycloalkan-1-ol, undergoes an unexpected new type of anomalous ozonolysis to yield a mixture of a rearranged β-hydroxyketone and a fragmented carboxylic acid. The proposed mechanisms involves two unusual different trappings for two different key Criegee's intermediates.

Ozonolysis reaction has a great interest in synthetic organic chemistry since it constitutes one of the most efficient tools for the oxidative cleavage of carbon–carbon double bonds.[1] Nevertheless, some unsaturated compounds such as allylic alcohols,[2] methylenecyclobutanes,[3] α,β-unsaturated carbonyl compounds,[4] α,β-unsaturated phosphonic esters,[5] etc. are known to undergo anomalous ozonolysis. In this sense, Jung and Davidov have recently demonstrated that several strained allylic bicycloalkan-1-ols undergo a general anomalous ozonolysis to synthetically-valuable cycloalkanone-based α-hydroxymethylketones (Scheme 1).[2c]

This anomalous ozonolysis takes place by a required formation of a key Criegee's primary ozonide (1,2,3-trioxolane), which undergoes an unusual Grob-like-fragmentation (Scheme 1), instead of the expected dissociation into the subsequent Criegee's intermediates towards normal ozonization.[2c] The process occurs under standard ozonization conditions (CH_2Cl_2, −78 °C, O_3 and Me_2S) with good-to-high yields, providing an efficient tactic for the stereocontrolled preparation of cycloalkanone-based α-hydroxymethylketones from several strained allylic bicycloalkan-1-ols, such as bicyclo[2.2.1]heptane-, bicyclo[3.2.0]heptane- and bicyclo[4.2.0]octane-based ones.[2c]



Scheme 1. General anomalous ozonolysis of strained allylic bicycloalkan-1-ols to fragmented cycloalkanone-based α-hydroxymethylketones.

In this letter we demonstrate that such anomalous ozonolysis of strained allylic bicycloalkan-1-ols to cycloalkanone-based α-hydroxymethylketones (Scheme 1) is not a general process, being possible by other types of anomalous ozonolysis for such kind of allylic alcohols.

Keywords: Ozonolysis; Cleavage reactions; Bicycles; Substituent effects.

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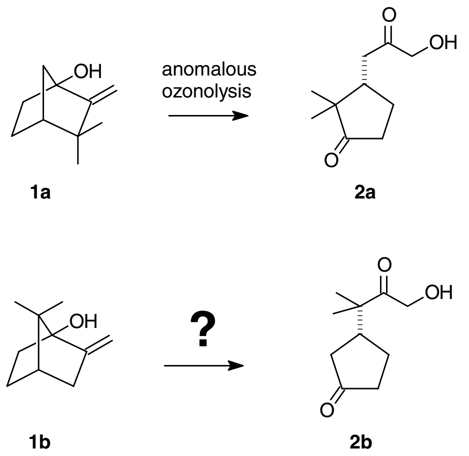


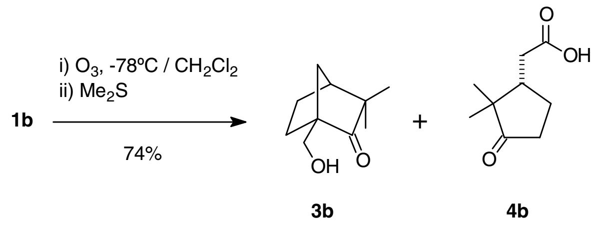
Scheme 2. Previously described anomalous ozonolysis of **1a** and expected anomalous ozonolysis for analogue **1b**.

In the course of our investigations on the synthetic applications of several fenchone-derived C1-substituted 2-methylenenorbornanes,[6] we were interested in obtaining cyclopentanone-based α-hydroxymethylketone **2b** using the anomalous ozonolysis of fenchone-derived 7,7-dimethyl-2-methylenenorbornan-1-ol **1b** (Scheme 2), as the same form that analogue **2a** can be easily obtained by simple ozonization of camphor-derived 3,3-dimethyl-2-methylenenorbornan-1-ol **1a** (Scheme 2).[2c]

Surprisingly, when **1b**[6a] was submitted to ozonization under standard conditions,[7] a mixture of rearranged norbornane-based β-hydroxyketone **3b**[8] and fragmented cyclopentanone-based carboxylic acid **4b**,[9] in ca. 4:1 ratio,[7] was obtained instead of the expected **2b** (Scheme 3).

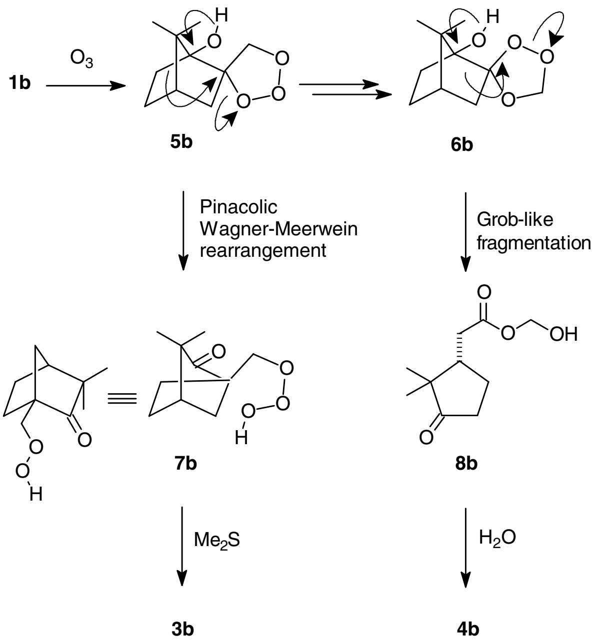
We have considered the next mechanism to account for this new type of anomalous ozonolysis: (1) key participation of the Criegee's primary and secondary ozonides **5b** and **6b**, respectively, (2) partial trapping of **5b** through a pinacolic Wagner–Meerwein rearrangement process involving intermediate **7b**[10,11] and (3) partial trapping of **5b** through a Grob-like-fragmentation process involving intermediate **8b** (Scheme 4).

We are convinced that the different behaviour of allylic bicycloalkan-1-ols **1a** and **2a** towards ozonizations is due to a crucial stereocontrol of the possible cascades of reactions occurring in the ozonization process.[12] This control must be present in the overall process from the first individual cycloaddition step of ozone to the starting substrate.[13]



3b / **4b** = *ca.* 4/1

Scheme 3. Anomalous ozononlysis of **1b**.



Scheme 4. Proposed mechanism.

In summary, a new type of anomalous ozonolysis in strained allylic bicycloalkan-1-ols is reported. The process involves two different and unusual trappings for two different key ozonide intermediates (primary and secondary ones, respectively). Further investigations on a plausible stereochemical control in the anomalous ozonolysis of 2-methylenebicycloalkan-1-ols are in progress.

Acknowledgment

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7. Ozone was burbled through a cooled (−78 °C) solution of 162 mg (1.06 mmol) of **1b** in 10 mL of dry CH_2Cl_2 for 4 h. After that, a stream of argon was passed through the cooled solution for 10 min to eliminate the excess of ozone. The cooled reaction mixture was then quenched with excess of Me_2S (0.3 mL), allowed to warm up to room temperature and treated with water (10 mL). After standard work up, the obtained residue was analyzed by RMN (**3b**/**4b** in an approximately 4:1 ratio); 74 % yield. Spectroscopic data of **3b** are coincident with the previously described by the same compound in Ref. 8, whereas the corresponding data of **4b** are coincident with the previously described by us for such compound in Ref. 9.
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10. Some related pinacolic Wagner–Meerwein rearrangements (e.g., in the treatment of alcohol **1b** with *m*-CPBA) are described in Ref. 6a. Paukstelis has also reported partial formation of analogue 10-hydroxycamphor **3a** in the ozonization of **1a** under unreported conditions Paukstelis, J.; Macharia, B. W. *Chem. Commun.* **1970**, 131.
11. As an example on the final O_2 disengagement of **7b**, see: Danieli, B.; Lesma, G.; Palmisano, G.; Gabetta, B. *J. Chem. Soc., Chem. Commun.* **1981**, 908.
12. At this stage, crude attempts to rule out the claimed stereocontrol empirically (in the base of the restricted disposable experimental data) have resulted to be highly speculative.
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