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Wagner–Meerwein rearrangement in the course of the ozonolysis of a bornene derivative

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ABSTRACT

The ozonolysis of the bicyclo[2.2.1]heptene derivative **1** or **2** gave the octaline derivative **6** (the structure was confirmed by X-ray crystallographic analysis) or **7**. The *exo*-addition of ozone to the double bond of **1** or **2** was followed by the fragmentation in carbonyl oxide and aldehyde. Then, the strong electrophilic character of the carbonyl oxide induces an unexpected Wagner–Meerwein rearrangement to give zwitterion **4**. Finally, a fragmentation reaction with elimination of dioxygen gave the tetrasubstituted C–C double bonds of **6** or **7**.

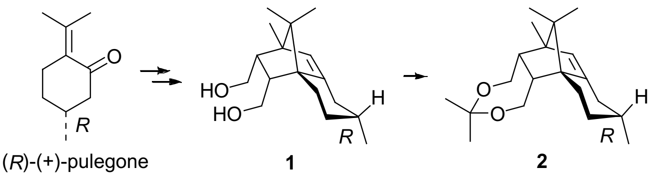
Ozone is a clean reagent useful both in academic synthesis and in industrial processes. It can now be employed safely on large scale reactions.[1] Ozonolysis is actually largely employed for the preparation of biologically active molecules. Therefore, the reactions of ozone with organic compounds[2] continue to be a subject of major interest from mechanistic, synthetic and also environmental aspects[3] (ozone is an efficient disinfectant with a greater specific lethality towards most microorganism types than chlorine-based disinfectants).[4]

According to the Criegee mechanism for alkene ozonolysis,[5] a primary ozonide (1,2,3-trioxolane), formed by addition of ozone to the alkene, is subject to fragmentation to give a carbonyl compound from one end of the starting alkene derivative and a carbonyl oxide from the other end. However, the detailed mechanism of these processes is somewhat uncertain.

In the course of the synthesis of new polydentate ligands, useful for palladium-catalysed cross-coupling reactions or allylic substitution,[6] we explored the ozonolysis of bicyclo[2.2.1]heptene derivatives arising from (*R*)-(+)-pulegone. In the present study, we describe results concerning the ozonolysis of the diol **1** or its acetonide **2** in methylcyclohexane/chloroform as solvent in the presence of pyridine (Scheme 1). We have already reported some unusual ozonolysis reactions using similar substrates, but we had employed other reaction conditions and ketone derivatives had been obtained.[7]

Here, we wish to report that the ozonolysis of **1** using methylcyclohexane/chloroform as solvent with a small amount of pyridine at −60 °C led to the hemiketal **6** (Scheme 2). The ^{13}C NMR spectra of **6** reveal the presence of a tetrasubstituted carbon–carbon double bond (signals at 136.1 and 128.5 ppm). A signal at 94.7 ppm corresponding to an hemiketal carbon atom was also observed.[8] However, the complete determination of the structure of **6** was not possible using only NMR spectra. Fortunately, **6** crystallises and its structure has been confirmed unambiguously by X-ray analysis (Fig. 1).

The Scheme 2 explains the mechanism of the formation of this unexpected structure. The *exo*-addition of ozone to the double bond of **1** was followed by the fragmentation in carbonyl oxide and aldehyde. The primary ozonide cleavage occurs to give the carbonyl oxide which is more stable.[9] The strong electrophilic character of the carbonyl oxide[10] induces a Wagner–Meerwein



Scheme 1. Preparation of diol **1** and acetonide **2** from (*R*)-(+)-pulegone.

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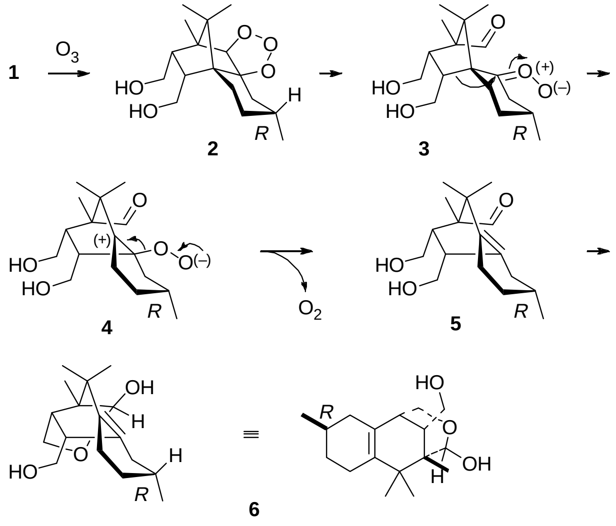
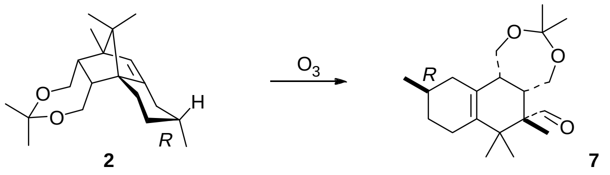
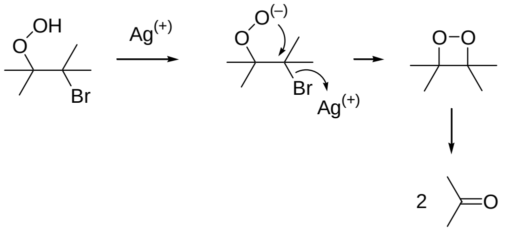


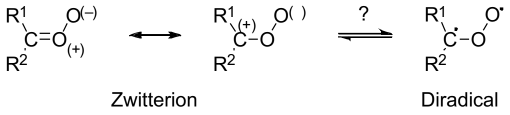
Scheme 2. Ozonolysis of **1** and formation of hemi-ketal **6**.



Scheme 3. Ozonolysis of **2**.



Scheme 4. Formation of tetramethyl-1,2-dioxetane.



Scheme 5. Electronic structures of carbonyl oxides.

rearrangement[11] to give zwitterion **4**. Next, a fragmentation reaction with elimination of an oxygen molecule (singlet ?) gave the tetrasubstituted C–C double bond. This proposed mechanism has some similarity with the Grob fragmentation reaction.[12] Finally, an intramolecular addition of one of the two hydroxymethyl groups to the aldehyde moiety gives the hemiketal **6**.

A very similar result has been obtained in the course of the ozonolysis of acetonide **2**. Again, using the same reaction conditions, the formation of the tetrasubstituted carbon–carbon double bond was observed. As the two hydroxymethyl groups of this substrate are protected, the aldehyde function remained untouched, and **7** was isolated (Scheme 3).[14]

We observed that, in the course of this reaction, the zwitterion **4** did not cyclise into a 1,2-dioxetane as the β-halohydroperoxydes generally do in basic medium.[15] 1,2-Dioxetanes are well known to undergo thermal decomposition into carbonyl compounds (Scheme 4).[16] The lack of formation of such 1,2-dioxetane can be explained by the non-discrete state of the carbocation **4**. The migration of the C–C bond and the fragmentation reaction can be synchronous reactions if the involved bonds are previously antiparallel (the singlet dioxygen appears as an electrofuge).[12]

The fact that the presence of a carbonyl oxide function induces a Wagner–Meerwein rearrangement gives interesting information on its electronic structure. In fact, the two electronic structures, zwitterion or diradical (Scheme 5), which can describe this type of short-lived species are subjects of debate.[17] In our case, the migration of the C–C bond is in accordance with a very polar carbonyl group of a zwitterion.

It should be noted that the Wagner–Meerwein rearrangement of 2-norbornanone derivatives has been very rarely described. To our knowledge, a similar rearrangement has been reported only once. It was in the presence of substituted 2-norbornanones and triflic anhydride as reagents via the formation of 2-bornylcarbonium ions (Scheme 6).[18]

To the best of our knowledge, a Wagner–Meerwein rearrangement in the course of the ozonolysis of bornene derivative has not been reported so far. We report here for the first time that the well known electrophilic character of a carbonyl oxide induces a C–C bond migration with concerted elimination of dioxygen. As the ozone chemistry has gained importance in recent years due to the ease with which such reactions can be conducted, to its broad scope and also of its significant role in atmospheric chemistry (degradation of the volatile organic compounds),[17c] this observation is of particular interest.

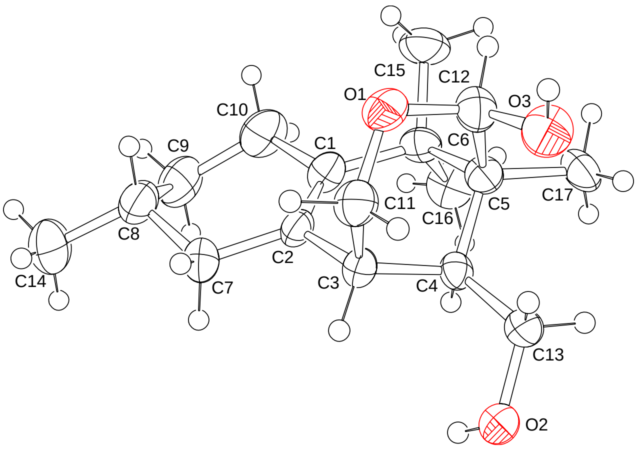
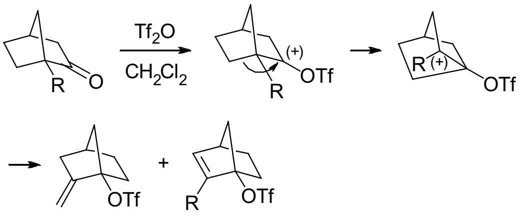


Figure 1. ORTEP drawing for **6**. Non-hydrogen atoms are drawn with 50% probability thermal ellipsoids.[13]



Scheme 6.

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8. Ozone in oxygen was bubbled through a stirred solution of **1** (528 mg, 2 mmol) in methylcyclohexane (30 mL) and chloroform (5 mL) containing 0.3 mL of pyridine and two drops of an ethanolic solution of 'Sudan III' (Eastman Kodak) (ozonizable red dye as internal standard)[19] at −60 °C until the red colour disappeared. The mixture was flushed with argon and cooled to −80 °C. A suspension of $NaBH_4$ (0.14 g, 3.7 mmol) in EtOH was slowly added. After stirring at room temperature overnight, the crude mixture was filtered on Celite®. After concentration in vacuo, the colourless residue was purified by flash-chromatography on silica gel eluting with petroleum ether/ethyl acetate 1:1 to give white crystals of **6** (168 mg, 0.6 mmol, 30% from **1**), mp 145 °C, $[\alpha]_D^{22}$ −12.0 (*c* 1.59, CH_2Cl_2). ^1H ($CDCl_3$, 300 MHz) δ 4.89 (br s, 1H), 4.13 (d, $J = 11.0$ Hz, 1H), 4.03 (m, 2H), 3.76 (d, $J = 11.3$ Hz, 1H), 3.15 (d, $J = 11.0$ Hz, 1H), 2.01 (m, 2H), 1.56 (m, 2H), 1.22 (td, $J = 7.1$ and 1.4 Hz, 1H), 1.05 (m, 2H), 0.96 (s, 3H), 0.90 (s, 6H), 0.89 (s, 3H).; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.1 (s), 128.5 (s), 94.7 (d), 62.5 (t), 57.6 (t), 42.3 (s), 42.1 (s), 39.1 (d), 39.0 (d), 37.4 (t), 32.1 (t), 29.3 (d), 25.7 (t), 23.8 (q), 22.2 (q), 20.7 (q), 16.5 (q).
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13. Crystal data and structure refinement. CCDC-703681 contains the supplementary crystallographic data. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44 1223 336 033; or e-mail: deposit@ccdc.cam.ac.uk]. Formula: $C_{68}H_{112}O_{12}$; M_w: 1121.58; Crystal colour: colourless; crystal size/mm³: 0.3 × 0.15 × 0.05; crystal system: triclinic; space group: *P*1; a/Å: 10.415(5); b/Å: 11.045(5); c/Å: 14.153(5); α/°: 101.675(5); β/°: 99.141(5); γ/°: 90.043(5);V/Å³: 1573.2(12); *Z*: 1; D_c/g cm^{-3}: 1.184; μ(Mo Kα)/cm^{-1}: 0.79; *N*° of unique data: 7437; *N*° parameters refined: 722; *N*° refl. in refinement: (7437; $F^2 > 4\sigma F^2$: 5187); *R*: 0.0804 [$F^2 > 4\sigma F^2$]; *wR*: 0.1956 [$F^2 > 4\sigma F^2$] ($w = 1/[\sigma^2(F_o{}^2) + (0.1354P)^2 + 0.654P]$ where $P = (F_o{}^2 + 2F_c{}^2)/3$; goodness of fit: 1.149; residual Fourier/e Å^{-3}: −0.731; 0.697.
14. Compound **2** (228 mg, 0.75 mmol) in methylcyclohexane (20 mL) containing 2 mL of pyridine was ozonolysed in the same conditions for **1**. The residue was purified by flash-chromatography on silica gel eluting with petroleum ether/ethyl acetate 4:1 to give yellow oil of **7** (108 mg, 0.34 mmol, 45% yield). ^1H ($CDCl_3$, 300 MHz) δ 9.91 (s, 1H), 4.05 (d, $J = 7.1$ Hz, 1H), 3.91 (dd, $J = 5.7$ and 9.5 Hz, 2H), 3.76 (dd, $J = 1.9$ and 5.7 Hz, 2H), 3.50 (m, 1H), 2.29 (m, 4H), 2.04 (m, 1H), 1.54 (m, 2H), 1.29 (s, 3H), 1.16 (s, 3H), 1.07 (s, 3H), 0.91 (s, 3H), 0.83 (d, $J = 4.5$ Hz, 3H), 0.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 206.2 (d), 135.6 (s), 125.1 (s), 101.5 (s), 61.8 (t), 60.2 (t), 53.5 (s), 51.8 (s), 43.3 (d), 41.1 (d), 37.2 (t), 31.6 (t), 28.5 (d), 28.6 (t), 24.5 (q), 24.1 (q), 23.7 (q), 21.8 (q), 21.5 (q), 17.5 (q).
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