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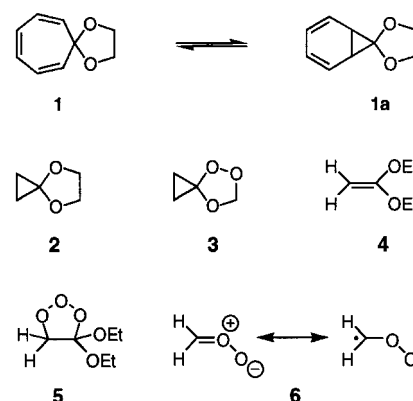
A Spontaneous Fragmentation: From the Criegee Zwitterion to Coarctate Möbius Aromaticity**

Christian Berger, Christian Bresler, Ulrich Dilger, Daniel Geuenich, Rainer Herges,* Herbert Röttele, and Gerhard Schröder*

Dedicated to Professor William von E. Doering on the occasion of his 80th birthday

Coarctate reactions^[1] are defined as those in which two bonds are simultaneously formed and broken at one or more atoms. Like the pericyclic reactions, they form an independent and coherent class of concerted reactions. Rules are available for predicting the stereochemical course of coarctate reactions,^[1] similar to the Woodward–Hoffmann rules for pericyclic reactions. We now describe an unusual fragmentation reaction which is in accordance with these stereochemical rules and for which such a coarctate transition state was confirmed by theoretical calculations.

Tropone ethylene acetal (**1**) is in equilibrium with the norcaradiene derivative **1a**. Above 100 °C **1** undergoes sigmatropic rearrangements ($E_a = 23.9 \text{ kcal mol}^{-1}$).^[2] Moreover, above 110 °C **1** decomposes via **1a** to give carbon dioxide, benzene, and ethene ($E_a = 31.6 \text{ kcal mol}^{-1}$).^[2] The fragmentation of **1a** was interpreted as a chelotropic cycloreversion to give benzene and 2-carbena-1,3-dioxolane. The authors speculate that the decomposition of the 2-carbena-1,3-dioxolane and the chelotropic cycloreversion might be part of a single concerted step.^[2] The parent structural element in the fragmentation of **1a** is the 4,7-dioxaspiro[2.4]heptane **2**. If a C–O bond in **2** is replaced by a O–O bond (**3**),



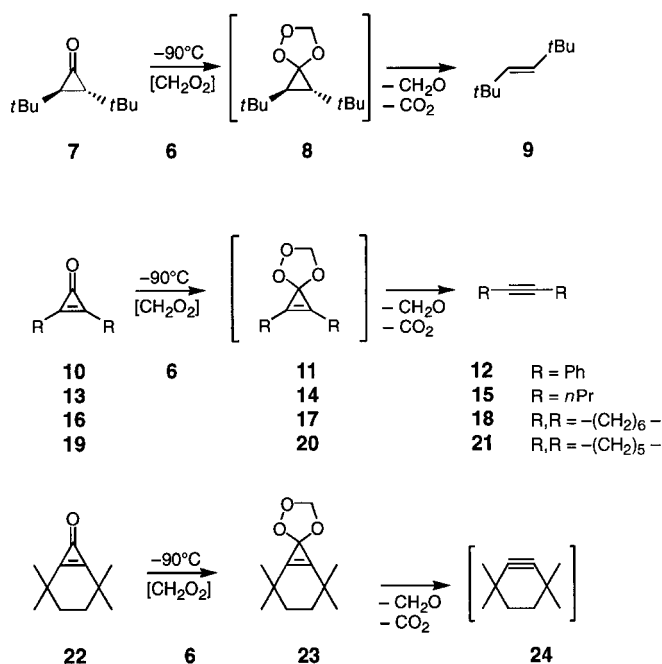
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the activation barrier for a concerted fragmentation should be lowered considerably relative to **1** or **2**. The bond energy of a C–O bond is about 85 kcal mol^{−1},^[3] and that of an O–O bond only 40 kcal mol^{−1}.^[4] Derivatives of **3** are generally accessible by 1,3-dipolar cycloaddition of formaldehyde *O*-oxide (**6**) to three-membered ring ketones under ozone-free conditions.^[5a] The primary ozonide **5**, generated from ozone and ketene diethyl acetal (**4**) at −110 °C was used as a source of **6**. Compound **5** decomposes between −90 and −80 °C in a [3+2] cycloreversion to give **6** and inert diethyl carbonate ($E_a = 12.5$ kcal mol^{−1}, $\Delta H^\ddagger = 11.5$ kcal mol^{−1}).^[5b]

The three-membered ring ketones **7**, **10**, **13**, **16**, **19**, and **22** are known. They were added at −110 °C to the primary



ozonide **5**, which was identified in the ¹H NMR spectrum at −110 °C by means of the methylene signal of the 1,2,3-trioxolane ring at $\delta = 4.35$ (s, 2H, in [D₁₄]methylcyclohexane), 3.9 (in [D₁₄]methylcyclohexane/[D₈]toluene 2/1), and 4.68 (in [D₁₀]diethyl ether). The [3+2] cycloreversion of **5**, which begins at −90 °C, can be monitored by following the decrease in intensity of this signal. We suggest^[6] that **6** reacts with **7**, **10**, **13**, **16**, **19**, and **22** to form the spiroozonides **8**, **11**, **14**, **17**, **20**, and **23**, which with the exception of **23** (see below) decompose spontaneously to carbon dioxide, formaldehyde, and the alkene **9** or the alkynes **12**, **15**, **18**, and **21**. Carbon dioxide can be extracted from the reaction mixture with a stream of nitrogen and precipitated as barium carbonate by passing it through a solution of barium hydroxide. Formaldehyde could not be detected by ¹H NMR spectroscopy.^[7] The characterization of the hydrocarbon products **9**, **12**, **15**, **18**, and **21** is described in the Experimental Section. The reactions of **7**, **10**, **13**, and **22** with **6**, which was generated from **5**, were monitored by low-temperature ¹H NMR spectroscopy. Results for the temperature range −90 to −80 °C are discussed below.

In the reaction of **7** with **6** in [D₁₄]methylcyclohexane,^[8] the decrease in the methylene proton signal of **5** at $\delta = 4.35$ (s, 2H) corresponds to the increase in the olefin proton signal at $\delta = 5.3$ (s, 2H) of *trans*-di-*tert*-butylethene (**9**). In the reaction of **10** with **6** in [D₁₀]diethyl ether/CD₂Cl₂ (8/1), the decrease in the signal for the *o,o'*-protons of **10** at $\delta = 8.05$ (sym. m, 4H) is in agreement with the increase in the signal for the *o,o'*-protons of the tolane **12** at $\delta = 7.53$ (sym. m, 4H). The reaction of **13** with **6** in [D₁₀]diethyl ether can be unambiguously monitored by means of the signals of the α -methylene protons of the *n*-propyl groups of the starting material **13** [$\delta = 2.62$ (t, 4H)] and of the product **15** [$\delta = 2.1$ (t, 4H)]. Decrease and increase of these signals are in agreement.

When **22** was treated with **6** in [D₁₄]methylcyclohexane/[D₈]toluene (2/1), we could not assign any ¹H NMR signals to 3,3,6,6-tetramethylcyclohex-1-yne (**24**) between −90 and −80 °C. This is in agreement with the literature.^[9] The behavior of **24** under the reaction conditions (in the presence of peroxide) was not investigated. In the presence of tetraphenylcyclopentadienone, no Diels–Alder product was formed. Above −90 °C the decrease in the methylene signal of **5** at $\delta = 3.9$ (s, 2H) was accompanied by an increase in a signal at $\delta = 4.88$ (s, 2H). After about 15 min a relative intensity maximum was reached at −85 °C (about 15%, relative to the four methylene protons of diethyl carbonate at 20 °C). At −80 °C the intensity of the signal at $\delta = 4.88$ decreases faster than that of the signal of **5** at $\delta = 3.9$. We interpret the former as unambiguous evidence for the intermediate spiroozonide **23**, the fragmentation of which forms the highly strained alkyne **24**. Therefore, **23** is more stable than the spiroozonides **8**, **11**, and **14**.

The substantially lower thermal stability which was expected for **3** relative to **2** was proved to be correct. The spiroozonides **8**, **11**, **14**, **17**, and **20** with the structural elements of 4,5,7-trioxaspiro[2.4]heptane (**3**) and of a 4,5,7-trioxaspiro[2.4]hept-1-ene undergo spontaneous fragmentation between −90 and −80 °C.^[10] The fragmentation of the spiroozonides fulfils the formal criteria for reactions with a coarctate transition state. In the course of the reaction two C–C bonds of the three-membered ring are broken at the central spiro C atom, and two C–O bonds are formed to generate CO₂. Eight electrons are involved in the reaction (the mechanism can be formally written with four electron-pushing arrows). A topological analysis shows that the transition state of the reaction is stabilized by coarctate Möbius aromaticity. According to the stereochemical rules of coarctate reactions, the π systems of the two terminators must be orthogonal in the transition state (Figure 1). This is realized in an ideal manner in the spiro arrangement of the three- and five-membered rings in the spiroozonides **8**, **11**, **14**, **17**, **20**, and **23**. In our nomenclature^[11] the fragmentation should be denoted as a [$\pi^2 + \chi^2 + \pi^4$] coarctate reaction.

The fragmentation of cyclopent-3-ene-1-one spiroozonide (1,2,4-trioxaspiro[4.4]non-7-ene) is homologous to that of the cyclopropanone spiroozonide **3** (4,5,7-trioxaspiro[2.4]heptane). According to the stereochemical rules of coarctate reactions involving ten electrons, this reaction must proceed via a flat transition state, which can not be realized in the spiro

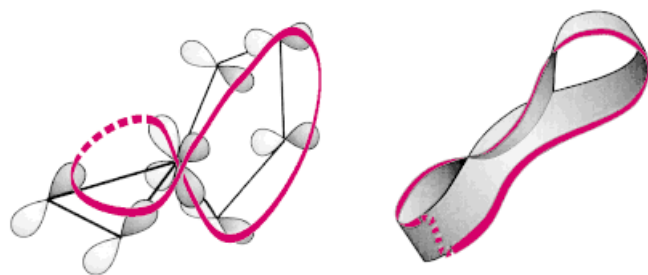


Figure 1. Orbital basis (left) and topology (right) of the transition state of the spiroozonide fragmentation. The orbital basis contains eight electrons in eight orbitals. The spiro C atom (coarctate center) participates in two basis orbitals, because two bonds are formed and broken simultaneously at this atom. The topology of orbital overlap is equivalent to a coarctate Möbius strip. For the resulting consequences for the stereochemical course of the reaction, see the text.

system. As a consequence, a coarctate fragmentation was not observed in this system.^[10]

We performed quantum-chemical calculations with semiempirical, ab initio, and density functional theory (DFT) methods^[12] (PM3,^[13] QCISD/6-31G, B3LYP/6-31G, B3LYP/6-31 + G*^[14, 15]) on the parent systems of the reactions presented above. We found such a transition state at all levels of theory. The transition states were characterized as first-order stationary points by harmonic frequency calculations (one imaginary frequency per transition state), and they were confirmed to be saddle points of a concerted fragmentation by intrinsic reaction coordinate (IRC) calculations. Figure 2

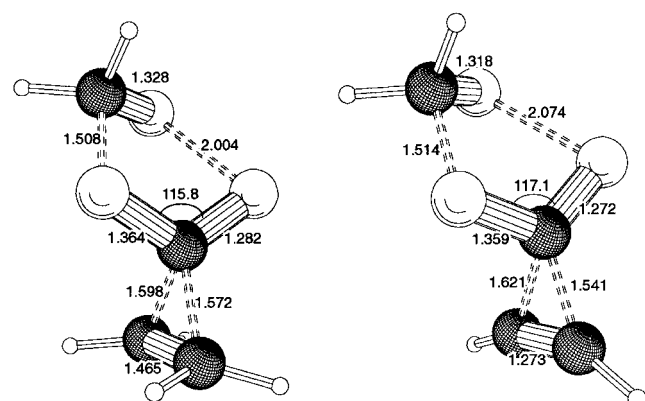


Figure 2. Transition state structures of both parent systems of the spiroozonide fragmentation calculated at the B3LYP/6-31 + G* level with bond lengths [Å] and angles [°].

shows the geometry of the two transition states, and Table 1 lists the energies of the starting materials, transition states, and products for the highest and most reliable theoretical level of the calculations. The transition states are not symmetrical. The calculated course of the reaction is not synchronous but concerted.^[16] A barrier of $\Delta H^\ddagger =$

11.3 kcal mol⁻¹ was calculated for the fragmentation of the spirocyclopropane, and $\Delta H^\ddagger = 16.4$ kcal mol⁻¹ for the fragmentation of the spirocyclopropene. As expected, the reactions are strongly exothermic: $\Delta H^\circ = -85.2$ and -84.8 kcal mol⁻¹, respectively.

Alternatively, the following two-step reaction is conceivable: In the first step the olefin or alkyne is eliminated, and in the second step the carbene (1,2,4-trioxolane-3-ylidene) fragments to give CO₂ and CH₂O. We did not find a stationary point corresponding to the carbene at any of the above-mentioned levels of theory. The corresponding structures fragment without a barrier to give CO₂ and CH₂O. The two-step mechanism therefore can be excluded with a high degree of certainty.

Table 1. Energies of the starting materials, transition states, and products of the fragmentation of both parent systems of the spiroozonide fragmentation calculated at the B3LYP/6-31 + G* level.^[a]

E_{abs} [a.u.]	-381.56811	-381.54647	-381.69250	-380.30805	-380.27665	-380.43233
ZPE [a.u.]	0.100789	0.09079	0.089423	0.076021	0.070694	0.065092
N_{imag}	0	1	0	0	1	0
$\tilde{\nu}$ [cm ⁻¹]	—	-397.5	—	—	-440.1	—
E_{rel} [kcal mol ⁻¹]	0.0	11.3	-85.2	0.0	16.4	-84.8

[a] E_{abs} = absolute energy, ZPE = zero-point energy, N_{imag} = number of imaginary frequencies according to a normal coordinate analysis, $\tilde{\nu}$ = wavenumber of the imaginary frequency, E_{rel} = energy relative to the starting materials.

The back reaction of the spontaneous fragmentation is a termolecular $[\pi^2 + \chi^2 + \pi^4]$ reaction, which will be difficult to realize unless preorganization of the components and high pressure are used.

Experimental Section

Procedure for the low-temperature ¹H NMR experiments: An excess of ozone was passed into a solution of ketene diethyl acetal **4** in a NMR tube at -110°C through a capillary. The precooled gas stream was adjusted such that single gas bubbles passed through the solution. After ozonization, a precooled stream of nitrogen was passed through the NMR tube until a moistened KI/starch paper remained colorless. A storage bottle, in which a solution of the three-membered ring ketone was precooled to -110°C , was connected to the glass joint on the top of the NMR tube. The contents were discharged by nitrogen pressure into the NMR tube, which was immediately introduced into the precooled ¹H NMR measuring cell.

7 + 6: 4 (14.1 mg, 0.121 mmol) in [D₁₄]methylcyclohexane (0.5 mL), **7** (7.4 mg, 0.044 mmol) in [D₁₄]methylcyclohexane (0.4 mL); **10 + 6: 4** (20.8 mg, 0.171 mmol) in [D₁₀]diethyl ether (0.45 mL), **10** (7.4 mg, 0.036 mmol) in [D₁₀]diethyl ether (0.35 mL) and CD₂Cl₂ (0.1 mL); **13 + 6: 4** (23.5 mg, 0.20 mmol) in [D₁₀]diethyl ether (0.45 mL), **13** (7.0 mg, 0.05 mmol) in [D₁₀]diethyl ether (0.45 mL); **22 + 6: 4** (18.2 mg, 0.157 mmol) in [D₁₄]methylcyclohexane (0.45 mL), **22** (8.2 mg, 0.05 mmol) in [D₁₄]methylcyclohexane (0.12 mL) and [D₈]toluene (0.33 mL).

The [3+2] cycloaddition of **6** with the three-membered ring ketones on a preparative scale is similar to the low-temperature ¹H NMR procedure. Ozonization was carried out in cold traps with an additional side flask.^[5] A precooled stream of ozone was passed through the solution of **4** at -110°C until the mixture turned blue. Excess ozone was expelled with a precooled

stream of nitrogen until a moistened KI/starch paper remained colorless. The solution of the ketone was transferred with a pipette into the side flask. After temperature equalization (5 min), the cold solution was discharged into the main flask with nitrogen pressure. During warm up above -65°C , a gentle stream of nitrogen was passed through the solution. In all cases, above -60°C we observed slight and above -50°C pronounced precipitation of barium carbonate on passing the gas through an aqueous solution of barium hydroxide.

7 + 6: 4 (132.4 mg, 1.14 mmol) in pentane (7 mL), **7** (63.0 mg, 0.37 mmol) in pentane (7 mL). The solvent was removed at 20°C and 200 mbar on a rotary evaporator. The residue was purified by chromatography (SiO_2 ; pentane/diethyl ether, 20/1) to give **9** (13.6 mg, 0.1 mmol, 26%). The ^1H NMR data were in agreement with the literature data.^[17] A yield of 51% was determined by ^1H NMR spectroscopy of the crude product (benzene as standard).

10 + 6: 4 (132.9 mg, 1.14 mmol) in diethyl ether (6 mL), **10** (47.2 mg, 0.23 mmol) in diethyl ether (5 mL) and CH_2Cl_2 (3 mL); for the workup, see above; the pressure was reduced to about 1 mbar. The residue was purified by chromatography (SiO_2 , CH_2Cl_2) to give colorless crystals (23.6 mg, 0.13 mmol, 58%) of the tolane **12**, m.p. 63°C (methanol). The yield of the crude product was 76%, as determined by ^1H NMR spectroscopy with toluene as standard.

13 + 6: 4 (149.0 mg, 1.28 mmol) in diethyl ether (7 mL), **13** (42.4 mg, 0.31 mmol) in diethyl ether (5 mL). The yield of the crude product was 67%, as determined by ^1H NMR spectroscopy with benzene as standard. The ^1H NMR data of **15** are in agreement with those of an independently synthesized sample.

16 + 6: 4 (165.3 mg, 1.42 mmol) in diethyl ether (6 mL), **16** (63.0 mg, 0.46 mmol) in diethyl ether (6 mL). The yield of the crude product was 83%, as determined by ^1H NMR spectroscopy with benzene as standard. The ^1H NMR data of **18** are in agreement with the literature data.^[18]

16 + 6 + tetraphenylcyclopentadienone: 4 (192.0 mg, 1.65 mmol) in pentane (13 mL), **16** (72.9 mg, 0.54 mmol) in pentane (6 mL) and toluene (2.5 mL). At 20°C tetraphenylcyclopentadienone (205.9 mg, 0.54 mmol) in CH_2Cl_2 (8 mL) was added, and the mixture stirred for 48 h. After the usual workup, the product was purified by chromatography (Al_2O_3 , activity level I, petroleum ether (b.p. $100\text{--}140^{\circ}\text{C}$)/benzene (7/3)) as colorless crystals (166 mg, 0.36 mmol, 67%), m.p. $222\text{--}223^{\circ}\text{C}$ (pentane/diethyl ether, 2/1; $224\text{--}225^{\circ}\text{C}$ ^[19]). The ^1H NMR data of the cyclooctanetetraphenylbenzene are in agreement with the literature data.^[19]

19 + 6: 4 (241.0 mg, 2.07 mmol) in pentane (14 mL) was ozonized at -110°C . Then **19** (62.7 mg, 0.51 mmol) in pentane (2 mL) and toluene (6 mL) was added, and the reaction flask was immersed in a cold bath at -78°C . After 15 min tetraphenylcyclopentadienone (200 mg, 0.52 mmol) in CH_2Cl_2 (8 mL) was introduced into the reaction flask from a separate flask with N_2 pressure. The mixture was kept for 48 h at -78°C , worked up as usual, and purified by chromatography as described above. Colorless crystals (120 mg, 0.27 mmol, 52%), m.p. $221\text{--}222^{\circ}\text{C}$ (petroleum ether); $222\text{--}223^{\circ}\text{C}$.^[20a] The ^1H NMR data of the cycloheptanetetraphenylbenzene are in agreement with the literature data.^[20b]

22 + 6: 4 (214 mg, 1.83 mmol) in pentane (8 mL), **22** (75.3 mg, 0.46 mmol) in pentane (2 mL) and toluene (6 mL). There were no ^1H NMR signals that could be assigned to 3,3,6,6-tetramethyl-1-(3,3,6-trimethyl-hept-6-en-1-ynyl)cyclohexene (isomer of the dimer of **24**)^[21] in the spectrum of the crude product.

22 + 6 + tetraphenylcyclopentadienone: 4 (239.5 mg, 2.06 mmol) in pentane (8 mL), **22** (84.4 mg, 0.51 mmol) and tetraphenylcyclopentadienone (202.4 mg, 0.53 mmol) both in pentane (2 mL) and toluene (6 mL). The mixture was kept for 15 min at -78°C and worked up as usual. There are no signals in the ^1H NMR spectrum that could be assigned to the Diels–Alder product. According to a control experiment, tetraphenylcyclopentadienone is virtually inert towards **6**.

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