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SUPPLEMENTARY MATERIAL

Baeyer-Villiger Oxidations with Hydrogen Peroxide in Fluorinated Alcohols: Lactone Formation by a Novel, Non-Classical Mechanism

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Experimental

1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP) was purchased from Aldrich or ABCR, HFIP- d_2 was supplied by Deutero, Kastellaun. Hydrogen peroxide was used as 50 % aqueous solution. ^{18}O -enriched water (95 %) was purchased from Aldrich. ^1H -NMR spectra were taken at 300 MHz, ^{13}C -NMR spectra at 75 MHz on a Bruker DPX 300 instrument. GC-MS measurements were carried out on a Hewlett-Packard HP 6890

Series II instrument, equipped with a HP 5973 mass selective detector and a 30 m HP 5 column. IR thermography was done using an Inframetrics Thermacam SC 1000 and Thermagram 95, Dynamite 97 software. 7,8,15,16-Tetraoxa-dispiro[5.2.5.2]hexadecane (**3**) was prepared according to ref. 1, mp. 128 °C (mp. ref. 1: 128-129 °C). CAUTION: DTG-analysis of the peroxide **3** showed no decomposition below melting temperature. When the melting point is reached, rapid but not explosive exothermic decomposition sets in. Nevertheless, this material should be handled with care since ref. 15 (main manuscript) reports explosive decomposition upon mechanical impact.

NMR-Monitoring of the reaction of cyclohexanone (1) and cyclopentanone with hydrogen peroxide: At ca. 20 °C, hydrogen peroxide (50 %, 33 µl, 573 µmol, 1.3 eq.) was added to a solution of 46 µl (441 µmol) cyclohexanone (**1**) (or cyclopentanone) in 0.7 ml HFIP-*d*₂ in an NMR-tube. In the case of cyclohexanone (**1**), the ¹³C-NMR spectrum of this solution clearly showed the typical resonance of the bis-peroxide **3**, i.e. at δ = 110 ppm (see main manuscript, Figure 1, trace a). In the case of cyclopentanone, the resonance of the bis-peroxide spiro-C was found at δ = 124.6 ppm. One crystal of *p*-toluenesulfonic acid monohydrate was added and the ¹³C-NMR spectrum was recorded again. In the case of cyclohexanone (**1**), the peroxide signals were replaced by the resonances of ε-caprolactone (**2**, C=O-resonance at δ = 183.55 ppm) and ε-hydroxycaproic acid (**4**, C=O-resonance at δ = 174.64 ppm, see main manuscript, Figure 1, trace d). According to NMR-integration and GC-analysis, **2** and **4** were formed in a ration of 71:29. In the case of cyclopentanone, clean conversion to δ-valerolactone (C=O resonance at δ = 179.87 ppm) as the sole product was observed.

NMR-Monitoring of the reaction of cyclohexanone (1) with hydrogen peroxide-urea clathrate: The reaction monitoring was done as described above. However, 54.3 mg (570 μmol , 1.3 eq.) of solid hydrogen peroxide-urea clathrate were added instead of aqueous hydrogen peroxide. Again, the characteristic signal at $\delta = 110$ ppm indicated (partial) conversion to the bis-peroxide **3**. Upon addition of one crystal of *p*-toluene-sulfonic acid monohydrate, conversion to **3** was completed instantaneously, and partial conversion to the lactone **2** was observed. Quantitative conversion to the product lactone **2** required heating to 55 $^{\circ}\text{C}$ for ca. 10 h.

Acid-catalyzed rearrangement of the spiro-bisperoxide 3 in HFIP, anhydrous conditions: A solution of 50.3 mg (220 μmol) of the bis-peroxide **3** in 0.7 ml HFIP- d_2 was placed into an NMR-tube and one crystal of *p*-toluenesulfonic acid monohydrate was added. The reaction occurred spontaneously with evolution of heat. ^{13}C -NMR revealed the quantitative rearrangement of the peroxide **3** to ϵ -caprolactone (**2**, C=O-resonance at $\delta = 183.55$ ppm, see main manuscript, Figure 2, trace b).

Acid-catalyzed rearrangement of the spiro-bisperoxide 3 in HFIP, in the presence of added water: The reaction was carried out as described above, but D_2O (31 μl , 1.7 mmol) was added before the reaction was started by addition of *p*-TsOH. Less heat was evolved, and ^{13}C -NMR analysis revealed the complete conversion of the peroxide **3**, ϵ -caprolactone (**2**, 73 %), ϵ -hydroxycaproic acid (**4**, 10 %) and cyclohexanone (**1**, 17 %) were formed as products.

Acid-catalyzed rearrangement of the spiro-bisperoxide 3 in HFIP, in the presence of added $^{18}\text{OH}_2$: The reaction was carried out as described above, but 95 % $^{18}\text{OH}_2$ (20.6 μl , 1.15 mmol) was added before the reaction was started by addition of *p*-TsOH. The reaction mixture was either subjected to silylation using BSA (bis-trimethylsilylacetamide, 150 μl , 125 mg, 61.3 μmol) and triethylamine (50 μl , 36.3 mg, 36 μmol) or analyzed directly by GC/MS. Typical ions/fragments of the bis-silylated ϵ -hydroxycaproic acid (**4**): 276 (M^+), 186 ($\text{M}^+ - \text{Me}_3\text{SiOH}$); of non-silylated ϵ -hydroxycaproic acid (**4**): 114 ($\text{M}^+ - \text{H}_2\text{O}$), 86 ($\text{M}^+ - \text{HCO}_2\text{H}$), 73 ($\text{CH}_2 - \text{CH}_2 - \text{CO}_2\text{H}$). When the peroxide rearrangement was carried out in the presence of $^{18}\text{OH}_2$, M^+ of the bis-silylated acid **4** appeared at $m/z = 278$, ($\text{M}^+ - \text{Me}_3\text{SiOH}$) at 188. In the case of the non-silylated acid **4**, ($\text{M}^+ - \text{H}_2\text{O}$) shifted to 116, ($\text{CH}_2 - \text{CH}_2 - \text{CO}_2\text{H}$) shifted to 75, and ($\text{M}^+ - \text{HCO}_2\text{H}$) remained at 86. These data indicate that one oxygen atom of **4** stems from water and this oxygen atom is part of the carboxyl function.

Isolation of the spiro-bisperoxide 3 from the reaction of cyclohexanone (1) with hydrogen peroxide in HFIP: A 50 ml round-bottomed flask was charged with a solution of 2.00 ml (19.3 mmol) cyclohexanone (**1**) in 24 ml HFIP. *Para*-toluenesulfonic acid monohydrate was added (37.0 mg, 194 μmol , 1 mol-%). The flask was cooled by immersion into a water bath and 1.50 ml (25.0 mmol, 1.30 eq.) of 50 % aqueous hydrogen peroxide were added within 30 min with stirring. Excess hydrogen peroxide was decomposed by addition of a catalytic amount of MnO_2 , and stirring was continued at ca. 20 $^\circ\text{C}$ for 15 min. Potassium carbonate (ca. 200 mg) was added, and the mixture was filtered after additional stirring for ca. 10 min. When the filtrate was subjected to distillation at ca. 110 $^\circ\text{C}$ and 0.2 Torr, the bis-peroxide **3**

solidified in the condenser. Recrystallization from methanol afforded colorless needles, mp. 128 °C (mp. ref. 1: 128-129 °C). ¹H-NMR (toluene-*d*₈, -20 °C) δ = 1.11-1.57 (m; CH₂), 2.36 (mc; CH₂). ¹³C-NMR (toluene-*d*₈, -20 °C) δ = 22.0, 22.5, 25.5, 29.9, 32.0 (t; CH₂), 108.0 (s; spiro-C).

IR-Thermographic solvent screening: A 96-well Teflon plate was charged with solutions of the bis-peroxide **3** (18 mg, 78.8 μmol) in the following solvents: HFIP (250 μl), HFIP/H₂O (239 μl HFIP + 11 μl H₂O), CF₃CH₂OH (250 μl), dioxane (250 μl), acetonitrile (250 μl), chloroform (250 μl). After thermal equilibration, the reactions were started simultaneously by the addition of 20 μl (2 mol-% relative to peroxide) of a stock solution of *p*-TsOH (90 mg *p*-TsOH in 3 ml dioxane).

Reference

- [1] J. R. Sanderson, K. Paul, P. R. Story, D. D. Denson, J. A. Alford, *Synthesis* **1975**, 159-161.