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Generation of 1,2-Dioxetane Decomposition Products in the Oxidation of 3-Phenyl-2-methylbenzofuran Epoxide by Dimethyldioxirane and the Oxodiperoxomolybdenum Complex

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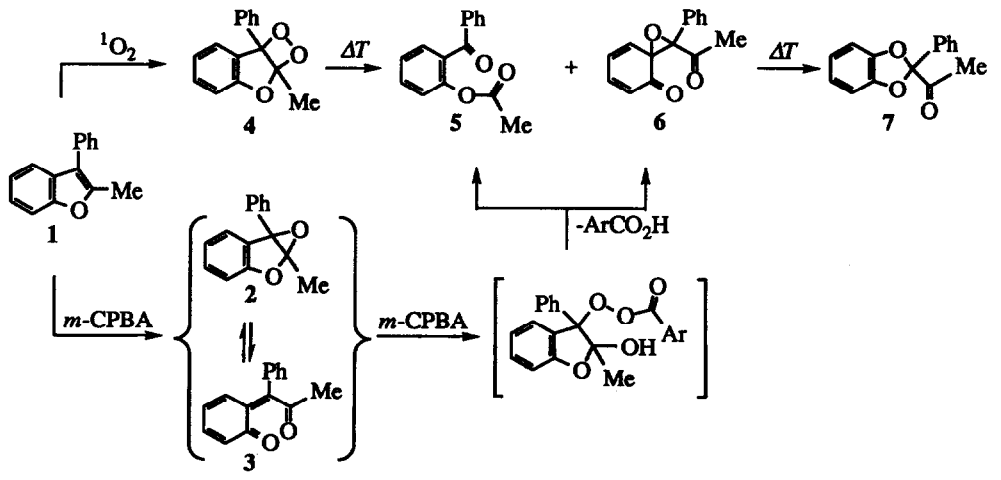
Abstract: Oxygen transfer reaction of dimethyldioxirane (DMD) and the oxodiperoxomolybdenum complex [HMPA-$MoO(O_2)_2$] on 3-phenyl-2-methylbenzofuran epoxide (**2**) affords the 1,2-dioxetane decomposition products, namely the keto ester **5** and the 1,3-benzodioxole **7**, the latter through rearrangment of the intermediary spiroepoxide **6**; neither the dioxetane **4** nor the 1,2,4-trioxane **8** serve as precursors.

Oxidation of the benzofuran **1** with two equivalents of *m*-CPBA afforded the keto ester **5** and the 1,3-benzodioxole **7**, the decomposition products of the 1,2-dioxetane **4** (Scheme 1).[1] This was explained in

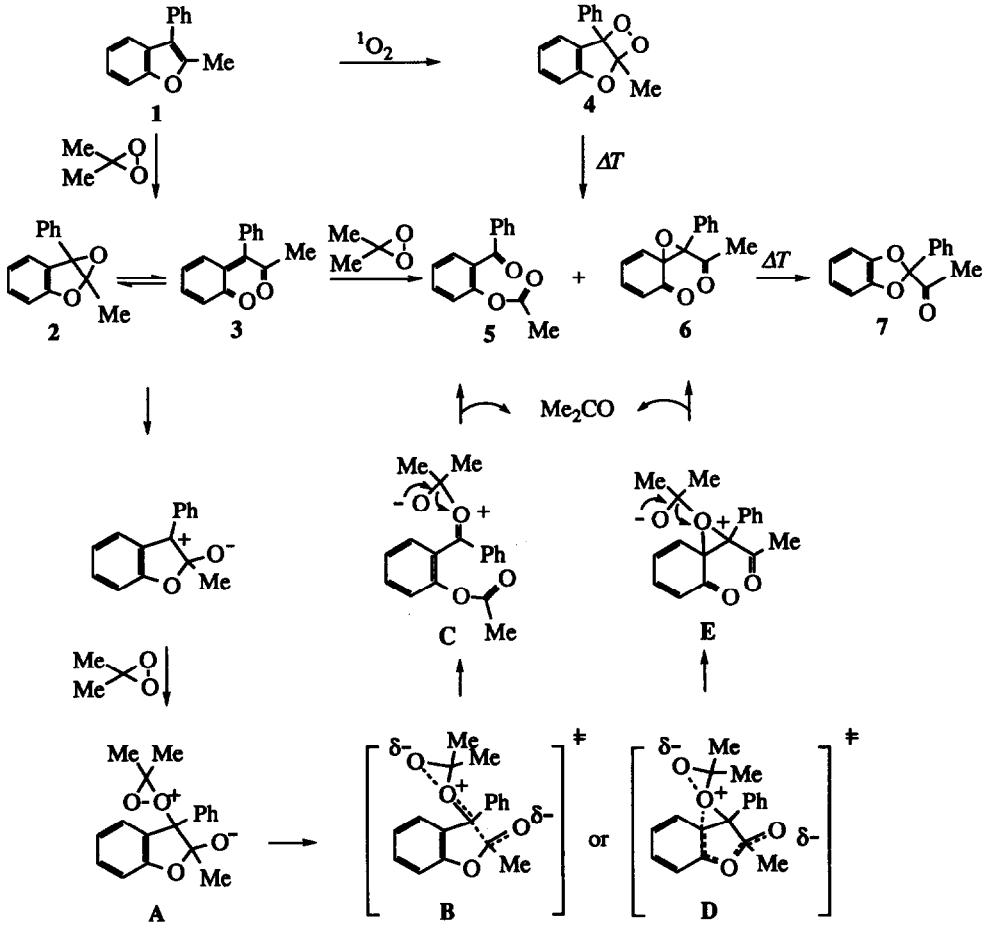
SCHEME 1



terms of epoxidation of the benzofuran **1** by the peroxy acid, the resulting epoxide **2** is in equilibrium with its valence-isomeric quinone methide **3**.[2] Subsequent nucleophilic trapping of another molecule of *m*-CPBA by the epoxide **2** and/or the quinone methide **3** generates the labile β-hydroxy peroxy ester, which subsequently cleaves to the keto ester **5** and the benzodioxole **7**, the latter by rearrangement of the intermediary spiroepoxide **6**.[3] When only one equivalent of $ArCO_3H$ is used, approximately one half of the benzofuran **1** is converted to a mixture of the dioxetane decomposition products **5** and **7**; thus, nucleophilic trapping of $ArCO_3H$ by the epoxide is faster than epoxidation of benzofuran **1**.

Presently we report that on treatment of the benzofuran **1** with an excess (ca. three equivalents) of the selective oxidant[4] DMD at -20 °C, within two days also a mixture (84:16) of the dioxetane decomposition products **5** and **7** is obtained (Scheme 2). In contrast, previously we observed[4c,d] that when the oxidation of

SCHEME 2

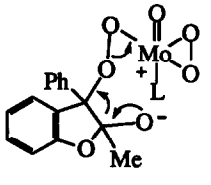


the benzofuran **1** was performed with one equivalent of dimethyldioxirane[5] (DMD as acetone solution[6]) at -70 to -20 °C, within 8 h the epoxide **2** was produced nearly quantitatively, as revealed by ^1H and ^{13}C NMR spectroscopy (Scheme 2). Moreover, in a control experiment, treatment of the isolated epoxide **2** with DMD (1.5 equivalents) at 0 °C gave within one day the keto ester **5** and the benzodioxole **7** as well. This constitutes the first oxygen transfer reaction of DMD on an epoxide!

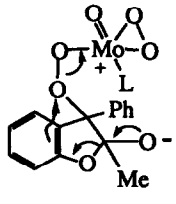
To explain these unusual results, it must be recalled that the benzofuran epoxides are the most reactive ones known to date; for example, the latter are subject to nucleophilic addition of MeOH at -78 °C without acid or base catalysis[2] and dipolar reaction with tetracyanoethylene.[2,4c] Therefore, we propose that the transient dipolar form of the epoxide **2** is trapped by DMD to generate the intermediate **A**, whose major reaction mode engages C-C bond cleavage to the keto ester **5** through transition state **B** and elimination of acetone from intermediate **C**. As minor pathway, C-O bond scission generates through transition state **D** the intermediate **E** which on loss of acetone yields spiroepoxide **6**. The rearrangement of the spiroepoxide **6** to the benzodioxole **7** is known.[3] In this novel way, the dioxetane decomposition products **5** and **7** are formed in ca. 85:15 ratio; however, the dioxetane **4** was not observed nor is its formation required (Scheme 2). Indeed, a control experiment revealed that the authentic dioxetane **4** persisted under these reaction conditions and, thus, had it been formed, it should have been detected.

Related oxygen transfer reactions have been reported in the oxidation of enol ether epoxides by (Py)$MoO(O_2)_2$.[7] In fact, in the case of the epoxide derived from the adamantylidene enol ether, the very stable dioxetane was isolated in ca. 80 % yield. Dioxetane formation was explained in terms of an electron transfer reaction through the epoxide radical cation and the metal diperoxo radical anion to afford the corresponding metalla-1,2,4-trioxane and subsequent elimination of the metal fragment. Furthermore, the analogous oxidation of heterocyclic substrates by HMPA-$MoO(O_2)_2$ has been observed.[8]

When epoxide **2** was treated with one equivalent of HMPA-$MoO(O_2)_2$[9] in $CDCl_3$ at room temperature for seven days, a 52:48 mixture of the keto ester **5** and the benzodioxole **7** was isolated in 28 % yield. Again, the benzofuran dioxetane **4** could not be detected under these conditions, not even by NMR analysis directly of the crude reaction mixture. The transition states **F** and **G** presumably operate in this oxygen transfer



F

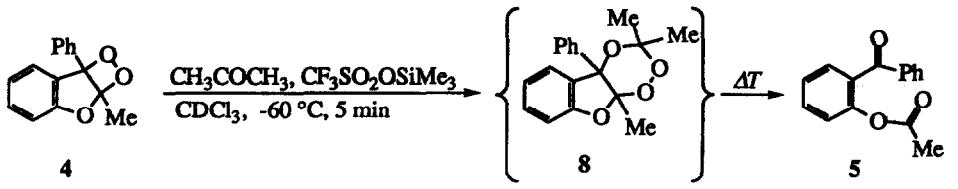


G

reaction and lead to the dioxetane decomposition products **5** and **7**, the latter by *in situ* rearrangement of the spiroepoxide **6**.

To probe, whether the reaction of the benzofuran epoxide **2** with DMD trespasses through the corresponding benzofuro-1,2,4-trioxane **8**, the latter was prepared by treatment of the dioxetane **4** with acetone (two equivalents) and trimethylsilyl trifluoromethanesulfonate, as shown in Scheme 3. The proposed structure for trioxane **8** is in good agreement with the observed spectral data. Although

SCHEME 3



4 8 5

the latter persists in solution at room temperature for a few days, attempts to purify it by silica gel column chromatography at -20 °C led to decomposition to the keto ester **5** (Scheme 3), but the benzodioxole **7** was not detected. Thus, the 1,2,4-trioxane **8** is an unlikely intermediate in the dioxirane oxidation of the benzofuran epoxide **2** (Scheme 2).

In conclusion, it was shown that dimethyldioxirane and HMPA-$MoO(O_2)_2$ oxidation of 2-methyl-3-phenylbenzofuran epoxide (**2**) engages oxygen transfer to generate the formal 1,2-dioxetane decomposition products, namely the keto ester **5** and the 1,3-benzodioxole **7**, the latter by subsequent rearrangement of the spiroepoxide **6**. However, neither the dioxetane **4** nor the 1,2,4-trioxane **8** appear to intervene in this unusual oxidation of epoxides.

Experimental

^1H and ^{13}C NMR spectra were run on a Bruker AC 200 (200 MHz) spectrometer. Chemical shifts refer to CDCl3 in TMS. Dimethyldioxirane (as acetone solution) was prepared according to the published procedure.[6b] The dimethyldioxirane solutions were stored over molecular sieves (4Å) at -20 °C.

Reaction of Benzofuran 1 with One Equivalent of Dimethyldioxirane (DMD):

a) *One Equivalent of DMD: Formation of 2,3-Dihydro-2,3-epoxy-2-methyl-3-phenylbenzofuran (2).*

10 mL (1.00 mmol) of a cooled (-78 °C) solution of dimethyldioxirane in acetone (0.1 M), dried over molecular sieves at -20 °C, was rapidly added to a cooled (-78 °C), stirred solution of 208 mg (1.00 mmol) benzofuran **1** in 2 mL dry CH_2Cl_2 under a N_2 atmosphere. The stirring was continued for 8 h until complete

consumption of the benzofuran **1** (monitored by TLC), while the reaction temperature was allowed to increase to -10 °C. The solvent was evaporated (-10 °C at 0.01 Torr) to yield quantitatively the epoxide **2** in high purity (by ^{1}H NMR). The spectral data were identical to those reported.[4d]

b) ***Three Equivalents of DMD: Formation of 2-Acetyloxy-benzophenone (5) and 2-acetyl-2-phenyl-1,3-benzodioxole (7).***
208 mg (1.00 mmol) of benzofuran **1** was treated with 30 mL (3.00 mmol) of dimethyldioxirane (0.1 M) for 2 d at -20 °C. The crude product was purified by column chromatography (20 g silica gel; 1:3 ether/pentane) to afford 181 mg (75 %) of **5** and 34.0 mg (14 %) of **7**, both as colorless oils, in a total yield of 89 %. The spectral data were identical to those reported.[1]

Reaction of Epoxide 2 with Dimethyldioxirane: ***Formation of 2-Acetyloxy-benzophenone (5) and 2-acetyl-2-phenyl-1,3-benzodioxole (7)***
224 mg (1.00 mmol) of epoxide **2** was treated with 15 mL (1.50 mmol) of dimethyldioxirane (0.1 M) for 1 d at 0 °C. The crude product was purified by column chromatography (20 g silica gel; 1:3 ether/pentane) to afford 172 mg of **5** and 30.0 mg of **7**, both as colorless oils, in a total yield of 84 %. The spectral data were identical to those reported.[1]

Reaction of Epoxide 2 with the Oxodiperoxomolybdenum Complex [HMPA-MoO(O$_2$)$_2$].
A solution of 23.0 mg (0.100 mmol) of epoxide **2** in 1 mL $CDCl_3$ was treated with 37.0 mg (0.100 mmol) of HMPA-MoO(O$_2$)$_2$ at 20 °C for 7 d. ^{1}H NMR showed 32 % conversion of the epoxide **2** to ester **5** and dioxole **7** in a ratio of 52:48. The spectral data of **5** and **7** were identical to those reported.[1]

5a-Phenyl-1a,4,4-trimethylbenzofuro-2,3,5-trioxane (8)
A solution of 50.0 mg (0.208 mmol) dioxetane **4**, prepared according to ref.[1] in 1 mL $CDCl_3$, was treated at -60 °C with 24.0 mg (0.416 mmol) acetone and one drop of trimethylsilyl trifluoromethanesulfonate for 5 min. ^{1}H NMR showed total conversion of the dioxetane **4** to the trioxane **8** and ester **5** in a ratio of 65:35. On the attempt to purify **8** by column chromatography (silica gel or alumina) at -30 °C, it rearranged to ester **5** on elimination of acetone. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.01 (s, 3 H), 1.05 (s, 3 H), 1.62 (s, 3 H), 6.87 - 7.44 (m, 9 H).- ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.9 (q), 24.6 (q), 25.7 (q), 83.1 (s), 104.9 (s), 109.3 (d), 115.8 (s), 121.3 (d), 125.8 (d), 126.7 (d), 127.8 (2xd), 128.7 (s), 129.6 (2xd), 130.3 (d), 148.6 (s), 158.9 (s).

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