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# Alcoholysis of malonyl peroxides to give peracids

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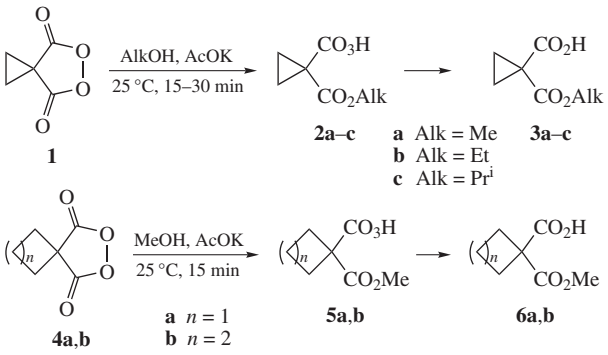
**Potassium acetate catalyzed alcoholysis of spirocycloalkyl malonyl peroxides affords 1-alkoxycarbonylcycloalkane-1-percarboxylic acids which are suitable for epoxidation of olefins.**

Cyclic diacylperoxides, malonyl peroxides (MPOs) in particular, are promising reagents for heavy metal-free *cis*-dihydroxylation of olefins.[1] Much earlier, MPOs were successfully used for generation of low-stability α-lactones[2] and malonic anhydrides,[3] and recently for oxidative C–O coupling with 1,3-dicarbonyl compounds.[4]

Little is known about other chemical properties of MPOs. Slow solvolysis of dibutyl-MPO with methanol or ethanol at 22–80 °C and 140 °C gave dibutylmalonic acid, its monoesters and products of their subsequent decarboxylation.[5] Reaction of spirocyclobutyl-MPO with sodium methoxide in methanol afforded methyl hydrogen cyclobutane-1,1-dicarboxylate,[6(a)] however, this transformation was explained as a fast reaction of MPO with methanol.[1(b)] Dihydroxylation of olefins with MPOs does not occur in methanol,[1(b),(d)] but the presence of 1 equiv. of methanol does not interfere with this reaction in chloroform.[1(f)]

In terms of chemical structure, MPOs are mixed anhydrides of a carboxylic and peroxy acids, hence MPOs can in principle undergo alcoholysis to give esters (by the carboxyl group) of substituted monopermalonic acids. We have found that the most reactive MPO,[1(a)] spirocyclopropyl-MPO (**1**, Scheme 1), does not react with 0.2 M solution of methanol in $CDCl_3$ for 72 h at 25 °C, but is partially (by 20–30%) converted in methanol solution, first to give peracid **2a** along with other products. In the course of reaction, unstable peracid **2a** is gradually converted into acid **3a**, which is completed within 24 h. The methanolysis of peroxide **1** is efficiently catalyzed by potassium acetate. In the presence of 1 mol-equiv. AcOK in methanol, peroxide **1** is converted nearly quantitatively to yield peracid **2a** in 15 min. Subsequent acidification of the reaction mixture to pH 1–6 somewhat stabilizes the peracid, however, peracid **2a** can be isolated only with an admixture of monoester **3a** (71:29, respectively).† Peracid **2a** is more stable in a solution in $CDCl_3$ wherein deoxygenation in 24 h at 4 °C did not exceed 10%.




**Scheme 1**

The reaction of peroxide **1** with ethanol catalyzed by AcOK occurs similarly to produce homologous peracid **2b** which was isolated with much monoester **3b** (45:55, respectively).† Although the reaction of peroxide **1** with propan-2-ol under the same conditions is completed in 30 min, the major product is a polymer with unknown structure that is soluble in water but insoluble (and nonrecoverable) in chloroform, so the isolated yield of the mixture of peracid **2c** and isopropyl monoester **3c** (in 43:57 ratio) does not exceed 20%.† Active oxygen quickly disappears in a solution of peroxide **1** and AcOK in *tert*-butanol.

This readily occurring alcoholysis of peroxide **1** is not due to the presence of a cyclopropane moiety in its structure. Homologous MPOs **4a**,**b** with four- and five-membered rings equally readily react with methanol on catalysis by AcOK to give peracids **5a**,**b**, which were isolated with an admixture of monoesters **6a**,**b** (70:30 and 95:5, respectively).† Note that dibenzoyl peroxide does not react in 24 h under these conditions.

The structure of peracids **2** and **5** obtained was confirmed by spectral data‡ and by their complete conversion to the corre-

† *1-Alkoxycarbonylcycloalkane-1-carboxylic peracids* **2** *and* **5** *(general procedure)*. A solution of peroxide **1** or **4** and an equivalent amount of anhydrous AcOK in an alcohol (5–15 ml $mmol^{-1}$) was kept for 15 min at 25 °C (complete peroxide conversion according to TLC). The resulting solution (in MeOH) or suspension (in EtOH or $Pr^iOH$) with pH 7 was acidified with $CF_3COOH$ to pH 1–2, diluted with water and extracted with $CHCl_3$. The extract was dried with $MgSO_4$ and evaporated to dryness *in vacuo* at 25 °C to give almost quantitative yields (except in the reaction with $Pr^iOH$) of a mixture of peracids **2a**,**b** and **5a**,**b** with the corresponding monoesters of cycloalkane-1,1-dicarboxylic acids **3a**,**b** and **6a**,**b** containing no other components according to $^1H$ NMR spectra. The compositions of these mixtures are given in the text. They depend both on the peracid structure and on the isolation conditions. The mixture of monomolecular products obtained in 25–35% yields from **1** + $Pr^iOH$ contains ~2/3 (by mass) **2c** + **3c** (in 43:57 ratio) and ~1/3 of other products.

‡ **2a**: $^1H$ NMR (hereinafter, 300 MHz, $CDCl_3$) δ: 1.57–1.67 [m, AA′BB′, 4H, $(CH_2)_2$], 3.78 (s, 3H, OMe), 10.7 (br. s, 1H, OH). $^{13}C$ NMR (hereinafter, 75 MHz, $CDCl_3$) δ: 17.7 [$(CH_2)_2$], 25.8 (C), 53.0 (OMe), 168.9 ($CO_3H$), 170.7 (COO). Mass spectra could not be obtained for peracids **2** and **5**, like for peroxides **1** and **4**.[1(a),(e)]

**2b**: $^1H$ NMR, δ: 1.29 (t, 2H, Me, *J* 7.2 Hz), 1.56–1.67 [m, AA′BB′, 4H, $(CH_2)_2$], 4.23 (q, 2H, $OCH_2$, *J* 7.2 Hz), 10.7 (br. s, 1H, OH). $^{13}C$ NMR, δ: 14.0 ($OCH_2$*Me*), 17.7 [$(CH_2)_2$], 26.0 (C), 62.3 ($OCH_2$Me), 168.6 ($CO_3H$), 172.7 (COO).

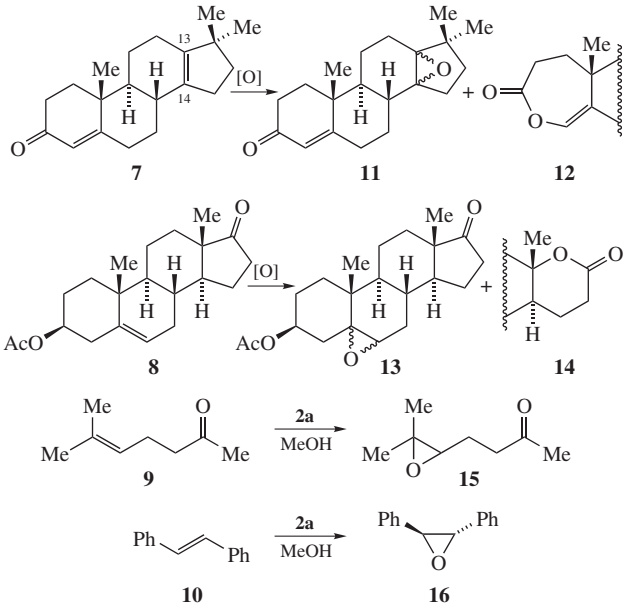
**2c**: $^1H$ NMR, δ: 1.27 (d, 6H, 2Me, *J* 6.3 Hz), 1.54–1.65 [m, AA′BB′, 4H, $(CH_2)_2$], 5.06 (sept, 1H, OCH, *J* 6.3 Hz), 7.9 (br. s, 1H, OH).

**5a**: $^1H$ NMR, δ: 2.07 (quint, 2H, $CH_2$, *J* 8.1 Hz), 2.65 (t, 4H, $2CH_2$, *J* 8.1 Hz), 3.79 (s, 3H, OMe), 10.2 (br. s, 1H, OH). $^{13}C$ NMR, δ: 16.6 [$CH_2(CH_2)_2$], 29.2 [$CH_2(CH_2)_2$], 50.6 [$C(CH_2)_2$], 53.2 (OMe), 170.7 ($CO_3H$), 172.7 (COO).

**Table 1** Oxidation of olefins with peracids **2a**,**b** generated *in situ* from peroxide **1** and MCPBA.

| Entry | Olefin | Method[a] | Peracid | Mol-equiv. | Solvent | Time/h | Olefin conversion (%) | Products, ratio |
|---|---|---|---|---|---|---|---|---|
| 1 | **7** | A | **2a** | 1.5 | MeOH | 2.5 | 100 | **11** + **12**, 98:2[b] |
| 2 | **7** | C | MCPBA | 3 | MeOH | 1.25 | 100 | **11**, ~100[b] |
| 3 | **8** | A | **2a** | 1.5 | MeOH | 24 | 87 | **13** + **14**, 76:24[c] |
| 4 | **8** | A | **2a** | 3 | MeOH | 24 | 94 | **13** + **14**, 48:52[c] |
| 5 | **8** | A | **2b** | 1.5 | EtOH | 24 | 75 | **13** + **14**, 75:25[c] |
| 6 | **8** | C | MCPBA | 1.7 | MeOH | 48 | 98 | **13** + **14**, 77:23[d] |
| 7 | **9** | A, B | **2a** | 1.5 | MeOH | 1 | 94, 100 | **15** |
| 8 | **10** | A | **2a** | 1.5 | MeOH–$CHCl_3$ (39:1) | 24 | 13 | **16** |
| 9 | **10** | A | **2a** | 5 | MeOH–$CHCl_3$ (39:1) | 24 | 43 | **16** |

[a] *Method A*. To a solution of an olefin and AcOK in an alcohol, peroxide **1** was added (in an amount equimolar to AcOK). After 15 min the mixture was acidified with acetic acid to pH 6 and the solution was kept until the olefin or peroxides disappeared. After dilution with water, the products were extracted with $CH_2Cl_2$. The extract was washed with saturated aqueous $KHCO_3$ solution, dried with $MgSO_4$ and concentrated. The residue (~100% with respect to the substrate) was dissolved in $CDCl_3$ and analyzed by $^1$H NMR spectroscopy. For the parameters of the spectra, see Online Supplementary Materials. *Method B*. An olefin was added to the peracid solution obtained from peroxide **1** by the general procedure (pH 7), then the process was carried out as in method A. *Method C*. Same as method A, but MCPBA was used instead of peroxide **1**. [b] The α : β stereoisomer ratio was 37:63. [c] The α : β stereoisomer ratio was 77:23. [d] The α : β stereoisomer ratio was 74:26.




**Scheme 2**

sponding monoesters of substituted malonic acids **3** and **6** upon addition of tetramethylethylene to solutions of the peracids, which readily epoxidate it.

The reasonable yields of reactive peracids **2a**,**b** generated *in situ* as solutions was a challenge of their use for epoxidation of olefins **7**–**10** (Scheme 2, Table 1).§ For reactions of highly reactive tri- and tetrasubstituted olefins **7** and **8** with peracids **2a** and **2b** (entries 1, 3–5), the rate, stereoselectivity and extent of Baeyer–Villiger side oxidation of existing carboxyl groups (formation of lactones **12** and **14**) are close to the similar epoxidation characteristics of *m*-chloroperoxybenzoic acid (MCPBA) (entries 2 and 6). Owing to neutrality of the medium, the epoxidation of olefin **9** with peracid **2a** to furnish epoxide **15** (entry 7) occurs exceptionally smoothly, without traces of the well known easy intramolecular cyclization of this valuable keto epoxide under conditions of its synthesis using MCPBA.[7] However, the instability of peracid **2a** noted above prevents complete epoxidation of electron-deficient stilbene **10**, even with a large excess of the peracid (entries 8 and 9).

The discovered fast reaction of spirocycloalkyl malonyl peroxides with alcohols can serve as the mechanism of some reactions[4,5] of MPOs in alcohol media. These peracids are generated from relatively stable MPOs in neutral buffer media, which makes it possible to use them for convenient preparation of acid-labile epoxides.

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*Online Supplementary Materials*

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2016.01.006.

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**5b**: $^1$H NMR, δ: 1.69–1.80 [m, 4 H, $(CH_2)_2$], 2.22–2.31 (m, 4 H, 2 $CH_2$), 3.75 (s, 3 H, OMe), 11.3 (br. s, 1H, OH). $^{13}$C NMR, δ: 25.4 [$CH_2(CH_2)_2CH_2$], 34.9 [$CH_2(CH_2)_2CH_2$], 53.18 (OMe), 58.5 [$C(CH_2)_2$], 171.5 ($CO_3H$), 173.8 (COO).

§ For the sources or syntheses of comparison specimens of products **3**, **5**–**8** and **11**–**15** as well as the corresponding spectral data, see Online Supplementary Materials.