## Regioselective Synthesis of 2-Hydroperoxy-2-methylenebutanoic Acid Derivatives via Photooxygenation of Tiglic Acid Derivatives**

Waldemar ADAM*, Axel GRIESBECK

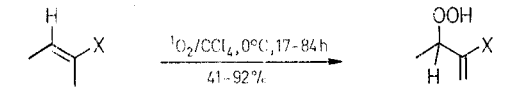
Institut für Organische Chemie der Universität Würzburg, Am Hubland D-8700 Würzburg, West Germany

Photooxygenation of (*E*)-2-methyl-2-butenoic acid derivatives (tiglic acid derivatives) in tetrachloromethane in the presence of catalytic amounts of tetraphenylporphine affords 3-hydroperoxy-2-methylenebutanoic derivatives in generally high yields. Acid-catalyzed cyclodehydration of the 3-hydroperoxy-2-methylenebutanoic acid thus obtained readily gives 5-methyl-4-methylene-3-oxo-1,2-dioxolane, a peroxylactone, in 61% yield. The analogous cyclodehydration of 3-hydroperoxy-2-methylenebutanal [generated *in situ* by oxygenation of (*E*)-2-methyl-2-butenal] leads to the formation of 3-hydroxy-5-methyl-4-methylene-1,2-dioxolane.

The ene reaction of singlet oxygen with olefins bearing electron-donating substituents is an efficient method for the synthesis of allylic hydroperoxides[1]. Subsequent transformation permits convenient the preparation of allylic alcohols[2] and epoxy alcohols[3]. Comparatively little work has been published on the use of electron-deficient olefins as ene components[4,5,6]; examples are tiglic acid (**1a**)[6] and its methyl ester (**1b**)[5].

In this communication, we report a convenient synthesis of further 3-hydroperoxy-2-methylenebutanoic acid derivatives (**2**) by photooxygenation of a broad range of (*E*)-2-methyl-2-butenoic (tiglic) acid derivatives (**1**). The oxygenations were carried out in tetrachloromethane in the presence of catalytic amounts (0.0005–0.0008 molar) of tetraphenylporphine as sensitizer. Reaction times were normally 24–36 h, except for the cyano derivative **2i**, which required four- to fivefold longer irradiation times for complete reaction.

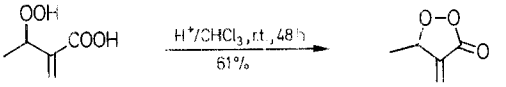
Products **2** were isolated by Kugelrohr distillation, flash chromatography, or crystallization. Only one of the two possible regioisomeric oxygenation products of compounds **1**, i.e., the allylic hydroperoxide **2**, was detected by $^1$H- and $^{13}$C-NMR spectrometry immediately after completion of the reaction.




**1a-d,f-i** **2a-d,f-i**

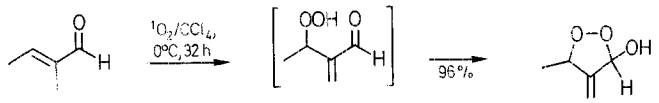
| 1/2 | X |
|---|---|
| a | COOH |
| b | $COOCH_3$ |
| c | $COOC_2H_5$ |
| d | $COOC(H)(CH_3)COOC_2H_5$ |
| f | $CONH_2$ |
| g | CON(CH$_2$)$_4$ |
| h | 2-(4,4-dimethyl-2-oxazolinyl) |
| i | CN |

A wide variety of (*E*)-2-methyl-2-butenoic acid derivatives **1** (all of them having electron-withdrawing functional groups) underwent this highly regioselective ene reaction. The hydroperoxy acid **2a** was readily dehydrated using catalytic amounts of mineral acids to give 5-methyl-4-methylene-3-oxo-1,2-dioxolane[6] (**3**), a new type of β-peroxylactone.




**2a** **3**

Oxygenation of (*E*)-2-methyl-2-butenal (tiglic aldehyde, **1e**) under the same conditions gave the hydroperoxy aldehyde **2e** which underwent cyclization *in situ* to afford *cis*- and *trans*-3-hydroxy-5-methyl-1,2-dioxolane (**4**) in the ratio 65:35 as determined by $^{13}$C-NMR spectrometry. This result is analogous to the photooxygenation of 3,4-dimethyl-3-penten-2-one[4].




**1e** **2e** **4**

*Caution!* Peroxides are potentially dangerous substances and all precautions must be taken when working with them.

**3-Hydroperoxy-2-methylenebutanoic Acid Derivatives (2); General Procedure:**

A tetrachloromethane solution 0.85 molar in the (*E*)-2-methyl-2-butenoic acid derivative **1** and 0.0006 molar in tetraphenylporphine[7], is irradiated at 0°C with a 150 W sodium lamp (Philips G/98/2) under continuous purging with dry oxygen. The reaction is monitored by TLC and $^1$H-NMR. Reaction times required for complete conversion are 16–84 h (see Table 1). After evaporation of the solvent at 10°C/10 torr, the residue is purified by either Kugelrohr distillation (A) at 0.1 torr, or by flash chromatography (B) on silica gel with dichloromethane as solvent, or by recrystallization from dichloromethane (C).

**Table 1.** Photooxygenation of (*E*)-2-Methyl-2-butenoic (Tiglic) Acid Derivatives **1**

| Starting Material | Product | Reaction Time [h] | Yield[a] [%] | Isolation Method[b] | b.p. [°C]/torr or m.p. [°C] | Molecular Formula[c] |
|---|---|---|---|---|---|---|
| **1a** | **2a** | 50 | 92 | A | b.p. 64–67/0.1 | $C_9H_8O_4$ (132.1) |
| **1b** | **2b** | 26 | 81 | A | b.p. 52–57/0.08 | $C_6H_{10}O_4$ (146.1) |
| **1c** | **2c** | 17 | 89 | A | b.p. 58–62/0.08 | $C_7H_{12}O_4$ (160.2) |
| **1d** | **2d** | 26 | 81 | A | b.p. 111–113/0.1 | $C_{10}H_{16}O_6$ (232.2) |
| **1e** | **4**[d] | 32 | 96 | A | b.p. 58–62/0.1 | $C_5H_8O_3$ (116.1) |
| **1f** | **2f** | 30 | 68 | C | m.p. 79–81 (needles) | $C_5H_9NO_3$ (131.1) |
| **1g** | **2g** | 24 | 75 | B | b.p. 132–134/0.1 | $C_9H_{15}NO_3$ (185.2) |
| **1h** | **2h** | 18 | 84 | C | m.p. 68–70 (needles) | $C_9H_{15}NO_3$ (185.2) |
| **1i** | **2i** | 84 | 41 | A | b.p. 58–61/0.1 | $C_9H_7NO_2$ (113.1) |

[a] Yield of isolated product; optimized.
[b] A: Kugelrohr distillation; B: flash chromatography; C: crystallized from dichloromethane.
[c] Satisfactory microanalysis obtained: C ± 0.42, H ± 0.27, N ± 0.30 (exception **1i**: C + 0.78, N − 0.84).
[d] *cis*/*trans*-Ratio: 65 : 35 ($^{13}$C-NMR).

**Table 2.** Spectral Data of Products **2** and **4**

| Compound | IR (film) $\nu$[cm$^{-1}$] | $^1$H-NMR ($CDCl_3$)[a] $\delta$[ppm] | $^{13}$C-NMR ($CDCl_3$)[b] $\delta$[ppm] |
|---|---|---|---|
| **2a** | 3300 (s); 2990 (m); 1700 (s); 1628 (m); 1272 (m); 1178 (m) | 1.35 (d, 3H, $J$ = 6.2 Hz); 4.95 (q, 1H, $J$ = 6.2 Hz); 6.02 (s, 1H); 6.48 (s, 1H); 9.67 (s, 2H, OOH and COOH) | 18.34 (q); 79.13 (d); 128.32 (t); 139.91 (s); 171.90 (s) |
| **2b** | 3400 (s); 2995 (s); 1720 (s); 1630 (m); 1440 (m); 1030 (m) | 1.17 (d, 3H, $J$ = 6.2 Hz); 3.57 (s, 3H); 4.73 (q, 1H, $J$ = 6.2 Hz); 5.75 (s, 1H); 6.13 (s, 1H); 9.17 (s, 1H, OOH) | 18.34 (q); 51.82 (q); 79.15 (d); 125.75 (d); 140.45 (s); 166.72 (s) |
| **2c** | 3402 (s); 2982 (s); 1718 (s); 1631 (m); 1345 (s); 1150 (s) | 1.14 (d, 3H, $J$ = 6.3 Hz); 1.23 (t, 3H, $J$ = 7.6 Hz); 4.07 (q, 2H, $J$ = 7.6 Hz); 4.73 (q, 1H, $J$ = 6.3 Hz); 5.74 (s, 1H); 6.13 (s, 1H); 8.55 (s, 1H, OOH) | 14.95 (q); 19.39 (q); 61.68 (t); 80.11 (d); 126.03 (t); 141.86 (s); 167.01 (s) |
| **2d** | 3420 (s); 2960 (m); 1755 (s); 1721 (s); 1220 (s); 1140 (m) | 1.28 (t, 3H, $J$ = 6.6 Hz); 1.37 (d, 3H, $J$ = 6.6 Hz); 1.55 (d, 3H, $J$ = 7 Hz); 4.20 (q, 2H, $J$ = 6.6 Hz); 4.96 (q, 1H, $J$ = 6.6 Hz); 5.18 (q, 1H, $J$ = 7 Hz); 5.95 (s, 1H); 6.41 (s, 1H); 9.00 (s, 1H, OOH) | 13.97 (q); 16.79 (q); 18.23 (q)*; 18.43 (q)**; 61.53 (t); 68.98 (d); 79.52 (d)*; 79.57 (d)**; 126.14 (d)*, 126.47 (d)**; 140.21 (s)*, 140.39 (s)**; 165.36 (s)*, 165.41 (s)**; 170.89 (s)[c] |
| **2f** | 3408 (m); 3160 (s); 1820 (m); 1795 (s); 1457 (s); 1380 (s)[e] | 1.18 (d, 3H, $J$ = 6.5 Hz); 4.73 (q, 1H, $J$ = 6.5 Hz); 5.52 (s, 1H); 5.83 (s, 1H); 7.06 (s, 1H, NH); 7.47 (s, 1H, NH); 11.49 (s, 1H, OOH)[d] | 18.51 (q); 78.29 (d); 118.34 (t); 144.50 (s); 168 (s)[d] |
| **2g** | 3405 (s); 2943 (s); 1799 (s); 1465 (s); 1374 (s); 1035 (m) | 1.20 (d, 3H, $J$ = 6.2 Hz); 1.80 (m, 4H); 3.38 (m, 4H); 4.51 (q, 1H, $J$ = 6.2 Hz); 5.07 (s, 1H); 5.27 (s, 1H); 8.28 (s, 1H, OOH) | 17.61 (q); 23.97 (t); 25.57 (t); 45.06 (t); 48.50 (t); 80.92 (d); 116.02 (t); 145.99 (s); 168.63 (s) |
| **2h** | 3380 (m); 2998 (s); 1611 (s); 1470 (m); 1372 (s); 1082 (s)[e] | 1.32 (2s, 6H); 1.34 (d, 3H; $J$ = 6.8 Hz); 4.01 (m, 2H); 4.94 (q, 1H, $J$ = 6.8 Hz); 5.69 (s, 1H); 6.01 (s, 1H); 8.67 (s, 1H, OOH) | 18.25 (q); 28.11 (q); 28.18 (q); 67.53 (s); 78.76 (t); 80.78 (d); 122.16 (t); 138.26 (s); 162.08 (s) |
| **2i** | 3380 (m); 2214 (s); 1730 (m); 1450 (m); 1376 (m); 1240 (m) | 1.37 (d, 3H, $J$ = 6.2 Hz); 4.58 (q, 1H, $J$ = 6.2 Hz); 6.04 (s, 1H); 6.10 (s, 1H); 9.23 (s, 1H, OOH) | 22.09 (q); 81.13 (d); 116.40 (s); 124.35 (s); 132.72 (t) |
| **4** | 3405 (s); 2982 (m); 1680 (s); 1498 (s); 1419 (s); 1311 (s); 1060 (s); 955 (s); 921 (s) | *trans*: 1.30 (d, 3H, $J$ = 6.2 Hz); 4.59 (m, 1H); 5.06 (m, 1H); 5.31 (m, 1H); 5.77 (s, 1H); 4.55 (s, 1H, OH) | *trans*: 14.95 (q); 78.12 (d); 97.68 (d); 108.86 (t); 156.89 (s) |
| | | *cis*: 1.25 (d, 3H, $J$ = 6.3 Hz); 4.81 (m, 1H); 5.11 (m, 1H); 5.30 (m, 1H); 5.71 (s, 1H); 4.55 (s, 1H, OH) | *cis*: 20.49 (q); 77.47 (d); 96.74 (d); 108.86 (t); 157.41 (s) |

[a] 400 MHz (Bruker WM 400).
[b] 100.6 MHz (Bruker WM 400).
[c] For **1d**, a 1 : 1 ratio of diastereoisomers was observed, marked by * and **.
[d] In DMSO-$d_6$.
[e] In $CDCl_3$.

**5-Methyl-4-methylene-3-oxo-1,2-dioxolane (3):**
3-Hydroperoxy-2-methylenebutanoic acid (**2a**; 1.00 g, 7.60 mmol) is dissolved in chloroform (30 ml) containing conc. sulfuric acid (3 drops) at 0 °C. This solution is stirred for 48 h at room temperature. Then, water (30 ml) is added and the organic phase is separated and dried with sodium sulfate. The solvent is evaporated and the residue distilled in vacuo to give product **3** as a colorless oil with a penetrating odor; yield: 530 mg (61%); b.p. 32–36 °C/0.08 torr.

$C_5H_6O_3$ (114.5) calc. C 52.63 H 5.30
found 52.85 5.58

IR (film, NaCl): 2990 (w); 1790 (s); 1672 (w); 1410 (s), 1246 (s); 1132 (s); 960 (s).

$^1$H-NMR ($CDCl_3$, 100.6 MHz): $\delta$ = 1.53 (d, 3H, $^3J$ = 6.2 Hz); 5.42 (ddq, 1H, $^3J$ = 6.2 Hz, $^4J$ = 2.5 Hz, 3.0 Hz); 5.77 (dd, 1H, $^4J$ = 2.5 Hz, $^2J$ = 0.75 Hz); 6.30 ppm (dd, 1H, $^4J$ = 3.0 Hz, $^2J$ = 0.75 Hz).

$^{13}$C-NMR ($CDCl_3$, 100.6 MHz): $\delta$ = 17.76 (q); 81.27 (d); 122.11 (t); 138.66 (s); 168.48 ppm (s).

***cis*, *trans*-3-Hydroxy-5-methyl-4-methylene-1,2-dioxolane (4):**
A solution of (*E*)-2-methyl-2-butenal (**1e**; 600 mg, 7.10 mmol) in tetrachloromethane (38 ml) 0.0006 molar in tetraphenylporphine[7] is irradiated at 0 °C for 32 h with a 150 W sodium lamp (Philips G/98/2) with continuous purging of dry oxygen. The solvent is then evaporated and the residue distilled in vacuum to give product **4** as a colorless oil with pleasant odor; yield: 790 mg (96%); b.p. 58–62 °C/0.1 torr.

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* Address for correspondence.
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