Photosensitized Oxidation of Furans; VIII[1]. 3a,6a-Dihydrofuro[2,3-*b*]furan-2(3*H*)-ones, a New Class of Furo[2,3-*b*]furans

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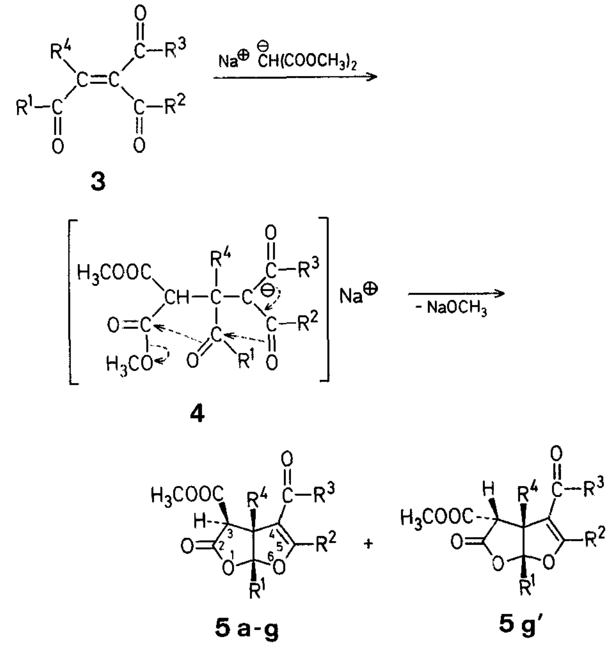
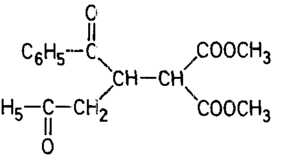
In connection with a study on the reactivity of 2,3,7-trioxabicyclo[2.2.1]hept-5-enes[2-5], we describe here a facile synthesis of 3a,6a-dihydrofuro[2,3-*b*]furan-2(3*H*)-ones **5** by reaction of functionalized endo-peroxides **2** with dimethyl malonate. Compounds **5** are structurally related to naturally occurring and synthetic derivatives showing insect anti-feeding activity[6].

The endo-peroxides **2** are formed by photosensitized oxidation of the furans **1** with singlet oxygen in tetrahydrofuran at −15°C. At this temperature compounds **2** are stable[1-5] and can be handled without isolation. Addition of a tetrahydrofuran solution of **2** to a suspension of 2.5 equivalents of sodium dimethyl malonate in tetrahydrofuran at −15°C affords, after aqueous work-up and chromatography on silica gel, 3a,6a-dihydrofuro[2,3-*b*]furan-2(3*H*)-ones (**5**) in good yields (Table).

Comparable yields of compounds **5b–d** are obtained by the reaction of triacylethylenes **3b–d**[5] with 1.1 equivalents of sodium dimethyl malonate. Derivatives **3a**[5] and **3g**[5] are unstable under the reaction conditions and give only polymeric materials. On the other hand, the yields of **5** are about halved when the endo-peroxides are treated with 1.1 equivalents of sodium dimethyl malonate.



These experiments indicate that, in the first reaction step, the peroxidic oxygen in **2** is displaced by the malonate anion to form *in situ* triacylethylenes **3**[7]. Intermediates **3** react with a second equivalent of malonate to give the enolate anions **4** which, on cyclization, yield the dihydrofurofurans **5**. Cyclization of **4** requires that the anions are sufficiently stabilized by resonance to avoid the formation of Michael-type adducts. In the case of 1,2-dibenzoylethylene, the cyclization of the corresponding enolate is repressed in favour of the formation of adduct **6**.



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The structures of compounds **5** were confirmed by microanalysis and spectroscopic data (Table). In particular, the ^{13}C-N.M.R. spectrum (CDCl$_3$/TMS) of **5b** shows characteristic signals at $\delta = 52.79$ and 53.42 (2d, C-3 and C-3a), 104.73 (s, C-4), 115.28 (s, C-6a), and 164.71, 166.76, 167.14, and 169.71 ppm (4s, C-5 and 3COO). It is noted that when $R^4 = H$, only the isomers **5a–f** are formed, whose stereochemistry has been assigned on the basis of the low value of the coupling constant of the 3-H[12] and nuclear Overhauser effect studies. In fact, in the ^{1}H-N.M.R. spectrum of **5e** irradiation at $\delta = 1.84$ ppm (6a-CH$_3$) caused the enhancement of the multiplet at $\delta = 3.97$ ppm (3a-H) and left the doublet at $\delta = 3.73$ ppm (3-H) unchanged. When $R^4 \neq H$, the mixture of inseparable configurational isomers **5g** and **5g'** is formed in a ~1:2 molar ratio as deduced by the ^{1}H-N.M.R. spectrum of the mixture on the basis of relative areas of 6a-CH$_3$ singlets. The stereochemistry of **5g** and **5g'** was assigned by comparison of the chemical shifts of 3-H and 6a-CH$_3$ with those of **5a–f** and **5a, c, e**, respectively.

The conversion of furans **1** into furofurans **5** has a wide range of applicability and represents an easy, one-step procedure which does not require the isolation of intermediates **2** and **3**.

3a,6a-Dihydrofuro[2,3-*b*]furan-2(3*H*)-ones (5); General Procedure:

A 2% solution of the furan **1** (1 mmol) and tetraphenylporphine ($3.6 \cdot 10^{-4}$ mmol) in dry tetrahydrofuran is irradiated with a halogen-superphot lamp (Osram 650 W). During the irradiation dry oxygen is bubbled through the solution which is cooled at −15°C. The reaction is monitored by T.L.C. (silica gel, chloroform) for the disappearance of **1**. When the reaction is complete (1 h), the photooxidation solution is slowly added dropwise at −15°C to a stirred suspension of sodium dimethyl malonate, prepared from sodium hydride (2.5 mmol) and dimethyl malonate (2.5 mmol) in dry tetrahydrofuran (8 ml). The mixture is allowed to warm to room temperature and kept at this temperature under stirring. After 6 h the solvent is removed under reduced pressure, the residue treated with water (10 ml) and extracted with chloroform (5 × 10 ml). The organic layer is washed with water (3 × 10 ml), dried with anhydrous calcium sulfate, and the solvent is removed under reduced pressure. The resulting oil is chromatographed on silica gel (20 g). Elution with light petroleum/ether (3:2) affords pure **5**; for **5e** and **f**, light petroleum/ether (3:7) is used.

3a,6a-Dihydrofuro[2,3-*b*]furan-2(3*H*)-ones (5b–d) from Alkyl 1,2-Diacylethylene-1-carboxylates (3b–d); General Procedure:

A 2% solution of diacylethylenes **3b–d** (1 mmol) in dry tetrahydrofuran is added at room temperature to a stirred suspension of sodium dimethyl malonate, prepared from sodium hydride (1.1 mmol) and dimethyl malonate (1.1 mmol) in dry tetrahydrofuran (8 ml), and the mixture is stirred for 6 h. The solvent is removed under reduced pressure, the residue is treated with water (10 ml) and extracted with chloroform (3 × 10 ml). The organic layer is washed with water (3 × 10 ml), dried with anhydrous calcium sulfate, and the solvent is removed un-

Table. 3a,6a-Dihydrofuro[2,3-*b*]furan-2(3*H*)-ones (**5**) prepared

Product	R^1	R^2	R^3	R^4	Yield[a] [%]	m.p. [°C]	Molecular formula[b]	I.R. ($CHCl_3$)[c] ν_{max} [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS)[d] δ [ppm]
5a	CH_3	CH_3	OCH_3	H	55	64–65°[e]	$C_{12}H_{14}O_7$ (270.2)	1795, 1740, 1712, 1695, 1655	1.57 (s, 3H, 6a-CH_3); 1.91 (d, 3H, J = 1.5 Hz, 5-CH_3)[f]; 3.27 and 3.35 (2s, 6H, 2OCH_3); 3.75 (dq, 1H, J = 1.5, 2.2 Hz, 3a-H)[g,h]; 3.86 (d, 1H, J = 2.2 Hz, 3H)[i]
5b	C_6H_5	CH_3	OCH_3	H	56	oil	$C_{17}H_{16}O_7$ (332.3)	1805, 1745, 1718, 1700, 1658[j]	2.34 (d, 3H, J = 1.5 Hz, 5-CH_3)[f]; 3.72 (s, 6H, 2OCH_3); 3.88 (d, 1H, J = 2.9 Hz, 3-H); 4.28 (dq, 1H, J = 1.5, 2.9 Hz, 3a-H)[g,h]; 7.40–7.60 (m, 5H_{arom})
5c	CH_3	C_6H_5	OC_2H_5	H	60	91–92°[e]	$C_{18}H_{18}O_7$ (346.3)	1788, 1735, 1710, 1680, 1630	1.21 (t, 3H, J = 7.0 Hz, X part of ABX_3-system); 1.95 (s, 3H, 6a-CH_3); 3.86 (s, 3H, OCH_3); 3.95 (d, 1H exchangeable with D_2O/NaOD, J = 2.6 Hz, 3-H); 4.13 (dq, J = 10.6, 7.0 Hz, B part of ABX_3-system); 4.19 (d, J = 2.6 Hz, 3a-H)[g], and 4.22 (dq, J = 10.6, 7.0 Hz, A part of ABX_3-system) together 3H; 7.35–7.86 (m, 5H_{arom})
5d	C_6H_5	C_6H_5	OCH_3	H	45	116–117°[e]	$C_{22}H_{18}O_7$ (394.4)	1800, 1745, 1718, 1690, 1632	3.72 and 3.80 (2s, 6H, 2OCH_3); 4.02 (d, 1H exchangeable with D_2O/NaOD, J = 3.3 Hz, 3-H); 4.54 (d, 1H, J = 3.3 Hz, 3a-H)[g]; 7.35–8.10 (m, 10H_{arom})
5e	CH_3	CH_3	CH_3	H	62	oil	$C_{12}H_{14}O_6$ (254.2)	1795, 1748, 1685, 1635	1.84 (s, 3H, 6a-CH_3); 2.29 (d, J = 1.5 Hz, 5-CH_3)[f] and 2.31 (s, $COCH_3$) together 6H; 3.73 (d, J = 2.2 Hz, 1H, 3-H); 3.84 (s, 3H, OCH_3); 3.97 (dq, 1H, J = 1.5, 2.2 Hz, 3a-H)[g,h]
5f	C_6H_5	CH_3	CH_3	H	60	oil	$C_{17}H_{16}O_6$ (316.3)	1800, 1745, 1685, 1635, 1608	2.35 (s, 3H, $COCH_3$); 2.40 (d, 3H, J = 1.6 Hz, 5-CH_3)[f]; 3.78 (s, OCH_3) and 3.82 (d, J = 3.2 Hz, 3-H) together 4H; 4.38 (dq, 1H, J = 1.6, 3.2 Hz, 3a-H)[g,h]; 7.40–7.65 (m, 5H_{arom})
5g + **5g′**	CH_3	CH_3	OCH_3	$COOCH_3$	63[k]	oil[k]	$C_{14}H_{16}O_9$ (328.3)	1805, 1748, 1700, 1665[k]	**5g**: 1.93 (s, 3H, 6a-CH_3); 2.32 (s, 3H, 5-CH_3); 3.75, 3.77 and 3.84 (3s, 9H, 3OCH_3); 4.15 (s, 1H, 3-H) **5g′**: 1.65 (s, 3H, 6a-CH_3); 2.33 (s, 3H, 5-CH_3); 3.66, 3.71 and 3.82 (3s, 9H, 3OCH_3); 4.80 (s, 1H, 3-H)

[a] Yield of pure isolated product.

[b] Satisfactory microanalyses obtained: C, ±0.26; H, ±0.11. Analyses were performed by Mikroanalytisches Laboratorium E. Thommen, CH-4126 Bettingen, Switzerland.

[c] Perkin-Elmer 399 spectrophotometer.

[d] Bruker WH 270 spectrometer.

[e] Recrystallization solvent, light petroleum (b.p. 40–70 °C).

[f] Homoallylic coupling[8].

[g] In naturally occurring furofuran derivatives, the 3a-H signal resonates at δ = 3.5–3.6 ppm[9,10]. In the compounds **5**, the proton suffers an additional large deshielding effect due to the substituents in the ring.

[h] The multiplicity of this signal, which really appears as broad signal, was assigned by double resonance experiments.

[i] In C_6D_6. The remarkable shift variations of the CH_3 signals are induced by the aromatic solvent[2,11].

[j] In CCl_4.

[k] Mixture of **5g** and **5g′** in ~1:2 molar ratio by ^{1}H-N.M.R. spectrometric analysis.

der reduced pressure. The resulting oil is chromatographed on silica gel (15 g). Elution with light petroleum/ether (3:2) affords pure **5b–d** in 45%, 50%, and 40% yields, respectively.

Reaction of Dimethyl Malonate with 1,2-Dibenzoylethylene:
To a stirred suspension of sodium dimethyl malonate, prepared from sodium hydride (1.1 mmol) and dimethyl malonate (1.1 mmol) in dry tetrahydrofuran (8 ml), is added a 2% solution of 1,2-dibenzoylethylene (1 mmol) in dry tetrahydrofuran. The mixture is refluxed under stirring for 3 h. Work up, as described above, gives a residue which is chromatographed on silica gel (15 g). Elution with light petroleum/ether (3:2) affords pure **6**; yield 65%; m.p. 116–117 °C [from light petroleum (40–70 °C)].

$C_{21}H_{20}O_6$	calc.	C 68.47	H 5.47
(368.4)	found	68.32	5.49

I.R. ($CHCl_3$): $\nu = 1755, 1735, 1685$ cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 3.38$ (ddd, AB part of ABX system, $J_{AB} = 18.0$ Hz, $J_{AX} = J_{BX} = 5.9$ Hz); 3.49 (s) and 3.53 (s) [together 8 H]; 3.84 (d, $J = 8.8$ Hz, 1 H); 4.82 (m, $J_{AX} = 5.9$ Hz, $J = 8.8$ Hz, 1 H); 7.35–8.05 ppm (m, 10 H_{arom}).

2,3,7-Trioxabicyclo[2.2.1]hept-5-enes (2):

The previously unreported endo-peroxides **2e, f** can be obtained in quantitative yields according to the procedure used for **2a**[2], by singlet oxygen oxidation of furans **1e**[13] and **1f**[14], respectively.

5-Acetyl-1,4-dimethyl-2,3,7-trioxabicyclo[2.2.1]hept-5-ene (**2e**); oil

$C_8H_{10}O_4$	calc.	O_{act} 9.4
(170.2)	found[15]	9.1

I.R. ($CHCl_3$): $\nu = 1680, 1605$ cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 1.89$ (s, 3 H, 1-CH_3); 2.02 (s, 3 H, 4-CH_3); 2.35 (s, 3 H, CO—CH_3); 6.82 ppm (s, 1 H, CH).

5-Acetyl-4-methyl-1-phenyl-2,3,7-trioxabicyclo[2.2.1]hept-5-ene (**2f**); oil

$C_{13}H_{12}O_4$	calc.	O_{act} 6.9
(232.2)	found[15]	6.7

I.R. ($CHCl_3$): $\nu = 1680, 1603$ cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 2.08$ (s, 3 H, CH_3); 2.37 (s, 3 H, $COCH_3$); 7.35–7.65 ppm (m + s, 6 H, CH + 5 H_{arom}).

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