Photosensitized Oxidation of Furans; XI[1]. A Simple General Method for the Synthesis of 3-, 4-, or 3,4-Functionalized 5-Hydroxyfuran-2 (5*H*)-ones (4-Hydroxy-2-butenolides)

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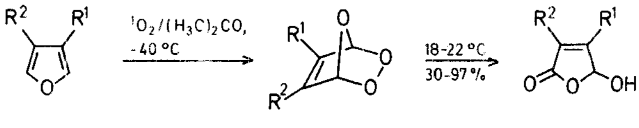
The title compounds 3 are prepared, in good yields, by methylene blue photosensitized oxidation of furans 1 in acetone and thermal conversion of the solutions of the intermediate *endo*- 2,5-peroxides 2.

5-Hydroxy- or 5-alkoxyfuran-2(5*H*)-ones are members of an important class of naturally occurring butenolides[2,3] and are reported to be starting materials for agricultural fungicides[4], antimicrobial compounds[5], and herbicides[6]. Moreover, they are useful intermediates in organic synthesis[7-10]. However, 3-, 4-, or 3,4-functionalized 5-hydroxyfuran-2(5*H*)-ones, other than the halogen derivatives, had been obtained only in a few particular cases[11,12] before our preliminary work on the thermal rearrangement of the 2,5-peroxide of methyl furan-3-carboxylate (**2a**)[13]. In that paper we described a convenient method for to the synthesis of functionalized furanones **3** and it was desirable to evaluate the best reaction conditions and their range of applicability. A serious limitation of the method was encountered in the difficult isolation of the furan *endo*-peroxides **2** which can be considered to be stable at – 40°C and rearrange at higher temperature in apolar solvents by a different route yielding furan diepoxides[12]. This problem can be eliminated by carrying out the photosensitized oxidation of the furans **1** in acetone (which conciliates the lifetime of singlet oxygen with the basicity required for the particular rearrangement) and by heating the solutions of the products to 18–22°C without isolation of the *endo*-peroxide intermediates **2**.

As shown in Table 1, the conversion of furans **1** into furanones **3** has a wide range of applicability even though attempts to isolate methyl 2(5*H*)-furanone-5-hydroxy-3-carboxylate, 3-benzoyl-5-hydroxyfuran-2(5*H*)-one, 3- and 4-acetyl-5-hydroxyfuran-2(5*H*)-one failed as these compounds polymerize spontaneously under the reaction conditions. It is interesting to note that generally furanones substituted at position 3 with electron-withdrawing group polymerize more easily than 4- or 3,4-substituted ones.



1a-g **2a-g** **3a-g**

1-3	R¹	R²
a	$COOCH_3$	H
b	$CO-N(C_2H_5)_2$	H
b'	H	$CO-N(C_2H_5)_2$
c	$CO-C_6H_5$	H
d	$COOCH_3$	$COOCH_3$
e	$CO-N(C_2H_5)_2$	$CO-N(C_2H_5)_2$
f	$CO-CH_3$	$CO-CH_3$
g	$CO-C_6H_5$	$CO-C_6H_5$

The previously unreported furans **1** were prepared starting from the corresponding furoyl chlorides; **1b** and **1e** by reaction with diethylamine; **1f** and **1g** according to the procedure previously used for **1c**[15] (Table 2).

5-Hydroxyfuran-2(5*H*)-ones 3; General Procedure:

A 0.1 molar solution of the furan **1** (1 mmol) and methylene blue (0.008 mmol) in dry acetone is irradiated with a halogen-superphot lamp (Osram 650 W). During the irradiation, dry oxygen is bubbled through the solution, which is cooled at – 40°C. Periodically, samples are syringed into a ¹H-N.M.R. tube and monitored for the conversion of furan **1** to *endo*-peroxide **2**. After completion of singlet oxygenation, the solution is warmed to room temperature (18–22°C) and kept until complete disappearance of **2** (¹H-N.M.R.). Removal of the solvent in vacuum gives the crude **3b–3g**, which are purified as reported in Table 1. In order to obtain furanone **3a** in the pure state, after completion of singlet oxygenation, acetone is removed in vacuum at – 40°C and the *endo*-peroxide **2a**, which in acetone partly rearranges into methyl 2,6-dioxabicyclo[3.1.0]hexane-3-oxo-5-carboxylate[13], is dissolved in dimethylformamide (5 ml). The solution is kept at room temperature for 5 min. Removal of the solvent in vacuo gives a mixture of **3a** and polymeric material which are separated by dissolution in ether. It is to be noted that **3a**, **3c**, **3d**, and **3f** cannot be purified by column chromatography as they polymerize on contact with the absorbent.

2,3,7-Trioxabicyclo[2.2.1]hept-5-enes 2; General Procedure:

The previously unreported compounds **2b–g** can be isolated after completion of singlet oxygenation and removal of the solvent at – 40°C in vacuum, in quantitative yields according to the procedure previously described for similar peroxides[14] (Table 2).

Table 1. 5-Hydroxyfuran-2(5*H*)-ones **3** prepared

Product	Irradiation time (min) at −40 °C	Conversion time (min) at 18–22 °C	Yield [%][a]	m.p. [°C]	Molecular Formula[b] or Lit. m.p.	^{1}H-N.M.R. (CDCl$_3$/TMS)[c] δ [ppm]	I.R. (CHCl$_3$)[d] ν [cm^{-1}]
3a	180	5[e]	54[f]	oil	oil[13]		
3b	180	45	30[g,h]	95–97[i]	$C_9H_{13}NO_4$ (199.2)	1.21 (t, 6H, J = 7 Hz, 2CH$_3$); 3.3–3.8 (m, 4H, 2CH$_2$); 6.10 (s, 1H, 5-H); 6.43 (s, 1H, 3-H); 6.60 (br. s, 1H, OH)	3300, 1760, 1620
3b′	180	45	42[g,j]	oil	$C_9H_{13}NO_4$ (199.2)	1.17, 1.19 (2t, 6H, J = 7 Hz, 2CH$_3$); 3.28, 3.46 (2q, 4H, J = 7 Hz, 2CH$_2$); 5.90 (br. s, 1H, OH); 6.20 (s, 1H, 5-H); 7.31 (s, 1H, 3-H)[k]	3300, 1765, 1611
3c	180	15	30[f,l]			5.02 (br. s, 1H, OH); 6.37 (s, 1H, 5-H); 6.62 (s, 1H, 3-H); 7.20–8.00 (m, 5H$_{arom}$)	3280, 1762, 1662, 1620
3d	480	60	80[f]	oil	$C_8H_8O_7$ (216.1)	3.88 (s, 6H, 2OCH$_3$); 5.15 (br. s, 1H, OH); 6.42 (s, 1H, 5-H)	3250, 1789, 1742, 1678
3e	150	30	92[g,j]	oil	$C_{14}H_{22}N_2O_5$ (298.3)	1.10 (t, 12H, J = 7 Hz, 4CH$_3$); 3.20–3.80 (m, 8H, 4CH$_2$); 6.45 (s, 1H, 5-H); 6.95 (br. s, 1H, OH)	3300, 1767, 1620
3f	150	10	85[f]	oil	$C_8H_8O_5$ (184.1)	2.50, 2.58 (2s, 6H, 2COCH$_3$); 5.37 (br. s, 1H, OH); 6.36 (s, 1H, 5-H)	3250, 1780, 1708, 1640
3g	150	30	97[g,m]	oil	$C_{18}H_{12}O_5$ (308.3)	5.84 (br. s, 1H, OH); 6.87 (s, 1H, 5-H); 7.20–8.00 (m, 10H$_{arom}$)	3580, 1778, 1665

[a] Yield of pure, isolated product except for **3c**.

[b] Satisfactory microanalyses obtained (C ±0.19, H ±0.14, N ±0.15), except for **3c**.

[c] Varian EM-360A spectrometer.

[d] Perkin-Elmer 399 spectrophotometer.

[e] In dimethylformamide.

[f] Obtained by dissolution in ether, filtration and removal of the solvent.

[g] Isolated by column chromatography over silica gel (ratio absorbant/crude product, 50/1).

[h] Eluent light petroleum/ether (1/4).

[i] From petroleum ether (b.p. 60–80 °C).

[j] Eluent: ether.

[k] Recorded on Bruker WH 270 spectrometer.

[l] Obtained in a purity of *ca.* 40% (^{1}H-N.M.R.).

[m] Eluent light petroleum/ether (1/1).

Table 2. Physical and Spectral Data of the New Products **1** and **2** prepared

Product[a]	m.p. [°C]	Molecular Formula[b]	^{1}H-N.M.R. (CDCl$_3$/TMS)[c] δ [ppm]	I.R. (CHCl$_3$)[d] ν [cm^{-1}]
1b	oil	$C_9H_{13}NO_2$ (167.2)	1.21 (t, 6H, J = 7 Hz, 2CH$_3$); 3.48 (q, 4H, J = 7 Hz, 2CH$_2$); 6.59 (d, 1H, J = 1.8 Hz, 5-H); 7.40 (dd, 1H, J = 1.8, 1.5 Hz, 4-H); 7.70 (d, 1H, J = 1.5 Hz, 2-H)[e]	1612
1e	80–83[f]	$C_{14}H_{22}N_2O_3$ (266.3)	1.19 (t, 12H, J = 7 Hz, 4CH$_3$); 3.47 (q, 8H, J = 7 Hz, 4CH$_2$); 7.55 (s, 2H, 2-H + 5-H)	1625
1f	63–65[g]	$C_8H_8O_3$ (152.1)	2.57 (s, 6H, 2CH$_3$); 7.90 (s, 2H, 2-H + 5-H)	1687
1g	118–122[f]	$C_{18}H_{12}O_3$ (276.3)	7.92, 7.20–8.10 (s + m, H$_{arom}$, 2-H + 5-H)	1660
2b	oil	$C_9H_{13}NO_4$ (199.2)	1.11 (t, 6H, J = 7 Hz, 2CH$_3$); 3.37 (q, 4H, J = 7 Hz, 2CH$_2$); 6.53 (s, 2H, 1-H + 4-H); 6.71 (s, 1H, 6-H)	1620, 1595
2c	oil	$C_{11}H_8O_4$ (204.2)	6.62 (s, 1H, 1-H); 6.85 (s, 2H, 4-H + 6-H); 7.40–8.00 (m, 5H$_{arom}$)	1645
2d	87–91[f]	$C_8H_8O_7$ (216.1)	3.87 (s, 6H, 2OCH$_3$); 6.68 (s, 2H, 1-H + 4-H)	1745, 1642
2e	64–67[g]	$C_{14}H_{22}N_2O_5$ (298.3)	1.16 (t, 12H, J = 7 Hz, 4CH$_3$); 3.15–3.75 (m, 8H, 4CH$_2$); 6.63 (s, 2H, 1-H + 4-H)	1627
2f	oil		2.50 (s, 6H, 2CH$_3$); 6.73 (s, 2H, 1-H + 4-H)	1715, 1637
2g	oil	$C_{18}H_{12}O_5$ (308.3)	6.86 (s, 2H, 1-H + 4-H); 7.20–8.00 (m, 10H$_{arom}$)	1655

[a] For R^1 and R^2 see Table 1. Compounds **2b**–**2g** are obtained in quantitative yield. Yield of compounds **1b** and **1e**–**g**: 80 and 83, 23, 20%, respectively.

[b] Satisfactory microanalyses obtained (C ±0.11, H ±0.02, N ±0.15, O$_{act}$[16] ±0.7), expect for the unstable **2f**.

[c] Varian EM-360A spectrometer.

[d] Perkin-Elmer 399 spectrophotometer.

[e] Recorded on Bruker WH 270 spectrometer.

[f] From petroleum ether (b.p. 60–80 °C).

[g] From light petroleum (b.p. 30–50 °C).

This work has been financially supported by Progetto Finalizzato del C.N.R. Chimica Fine e Secondaria. We thank Miss M. Marmorino for technical assistance.

Received: May 6, 1985

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