Synthesis of 5,6-Unsubstituted 1,3-Dioxin-4-ones

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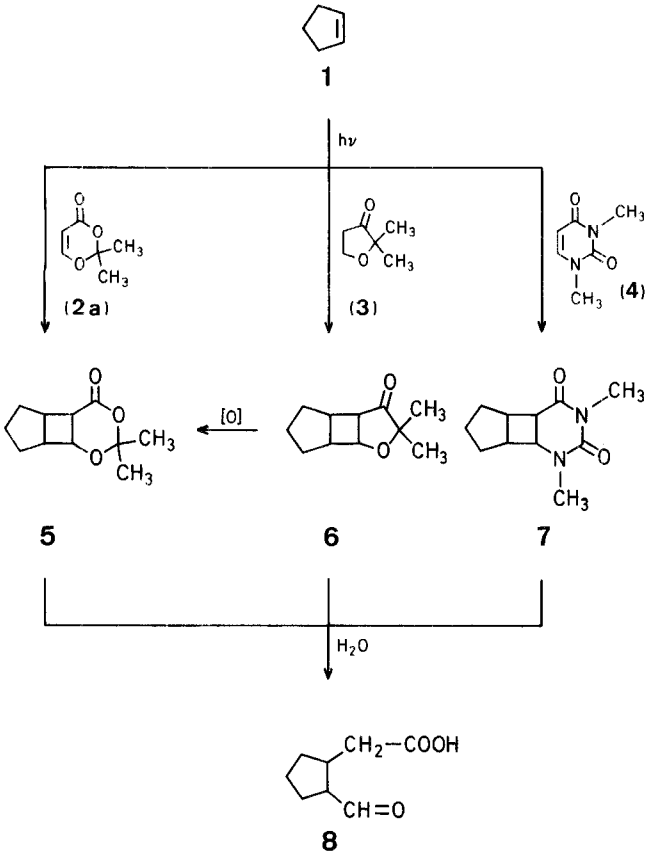
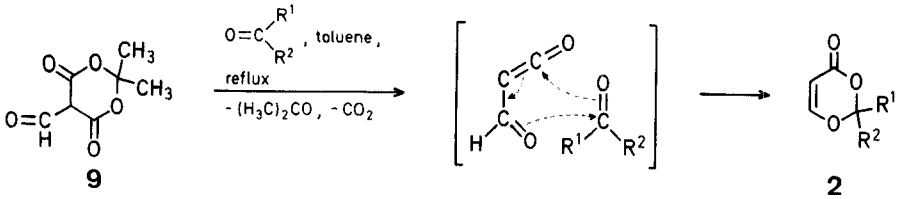
1,3-Dioxin-4-ones unsubstituted in positions 5 and 6 (e.g. **2a**) are potential equivalents of formylacetic esters. Therefore, these compounds are of interest for the introduction of formyl and carboxymethyl groups at the vicinal positions of al-

kenes such as **1** by the De Mayo reaction[1]. Recently, we prepared 2,2-dimethyl-1,3-dioxin-4-one (**2a**) in 31% yield by heating formylated Meldrum's acid (**9**)[2] in toluene in the presence of acetone[3].

It was shown that a variety of formylacetic esters do not add photochemically to alkenes[4]. Up to now the only synthetic alternatives to formylacetic esters that can add to alkenes known are uracils (e.g. **4**)[5] and 2,2-dimethyl-3(2*H*)-furanone (**3**)[6]. However, the adduct **7** requires drastic conditions for the subsequent hydrolysis to **8** and the adduct **6** requires Baeyer-Villiger oxidation before hydrolysis. In preliminary experiments it has been found that **2a** can be added efficiently to alkenes by irradiation at 300 nm[7]. Thus, the utility of compounds of type **2** as synthetic equivalents of formylacetic esters has now become obvious.



We now describe a general method for the synthesis of 5,6-unsubstituted 1,3-dioxin-4-ones **2** from formylated Meldrum's acid (**9**), which raises the yield of **2a** to 67%.



2	R^1	R^2
a	CH_3	CH_3
b	$-(CH_2)_4-$	
c	$-(CH_2)_5-$	
d	H	n-C_7H_{15}
e	H	c-C_6H_{11}
f	H	C_6H_5

Furthermore, the procedure is compatible with a variety of ketones and aldehydes.

2,2-Dimethyl-1,3-dioxin-4-one (2a):
To a refluxing solution of acetone (2.0 g, 50 mmol) in toluene (300 ml) is added portionwise finely powdered formyl-Meldrum's acid[2] (**9**; 8.6 g, 50 mmol). When the addition is complete (2 h), the solution is refluxed for an additional h. The solvents are removed on a rotary evaporator (the bath temperature should be maintained below 30°C) and the residual oil is distilled at reduced pressure: yield: 4.3 g (67%); b.p. 59°C/4 torr[8] (Ref.[3], b.p. 65°C/1 torr).

H.R.M.S.: $C_6H_8O_3$ (M^+) calc. 128.0473, found 128.0483.

I.R. ($CHCl_3$): ν = 1730 (C=O); 1620 cm^{-1} (C=C).

^{1}H-N.M.R. (CCl_4): δ = 1.70 [s, 6H, $C(CH_3)_2$]; 5.28 (d, J = 6 Hz, 1H, 5-H), 7.07 ppm (d, J = 6 Hz, 1H, 6-H).

9-Oxo-6,10-dioxaspiro[4.5]dec-7-ene (2b):
To a refluxing solution of cyclopentanone (4.2 g, 50 mmol) in toluene (20 ml) is added slowly finely powdered formyl-Meldrum's acid (**9**; 1.72 g, 10 mmol). When the addition is complete (15 min), the solution is refluxed for additional 30 min. After evaporation of the solvent, the residue is subjected to column chromatography (silica gel, 30 g) with hexane/ethyl acetate (6/1) as eluent to give **2b**; yield: 0.75 g (49%); b.p. 47°C/0.2 torr[8]. The use of xylene instead of toluene in this reaction lowers the yield of **2b** to 35%.

$C_8H_{10}O_3$ calc. C 62.32 H 6.54
(154.2) found 62.03 6.49

M.S.: m/e = 154 (M^+); 85; 84; 70.

I.R. ($CHCl_3$): ν = 1730 (C=O); 1615 cm^{-1} (C=C).

^{1}H-N.M.R. ($CDCl_3$): δ = 1.6–2.5 (m, 8H); 5.47 (d, J = 6 Hz, 1H, 5-H); 7.25 ppm (d, J = 6 Hz, 1H, 6-H).

1,3-Dioxin-4-ones (2c–f); General Procedure:
To a refluxing xylene solution (20 ml) containing the appropriate ketone or aldehyde (50 mmol), is added portionwise finely powdered formyl-Meldrum's acid (**9**, 1.72 g, 10 mmol). When the addition is complete (15 min), the solution is refluxed for additional 20 min. After evaporation of the solvent and an excess of ketone or aldehyde, the residue is subjected to column chromatography on silica gel (40 g) with hexane/ethyl acetate (6/1) as eluent.

4-Oxo-1,5-dioxaspiro[5.5]undec-2-ene (**2c**); yield: 1.12 g (67%); m.p. 39–42°C. An analytical pure sample is obtained by recrystallization from pentane; m.p. 40–42°C.

$C_9H_{12}O_3$ calc. C 64.27 H 7.19
(168.2) found 64.11 7.23

M.S.: m/e = 168 (M^+); 98; 71; 70.

I.R. ($CHCl_3$): ν = 1730 (C=O); 1615 cm^{-1} (C=C).

^{1}H-N.M.R. ($CDCl_3$): δ = 1.3–2.3 (m, 10H); 5.45 (d, J = 6 Hz, 1H, 5-H); 7.22 ppm (d, J = 6 Hz, 1H, 6-H).

2-n-Heptyl-1,3-dioxin-4-one (**2d**); yield: 1.49 g (75%); b.p. 75°C/0.001 torr[8].

$C_{11}H_{18}O_3$ calc. C 66.64 H 9.15
(198.3) found 66.39 9.16

M.S.: m/e = 199 ($M^+ + 1$); 129; 128; 127; 72; 71; 70.

I.R. ($CHCl_3$): ν = 1735 (C=O); 1608 cm^{-1} (C=C).

^{1}H-N.M.R. ($CDCl_3$): δ = 0.6–2.2 (m, 15H); 5.47 (d, J = 6 Hz, 1H, 5-H); 5.52 (t, J = 5 Hz, 1H, 2-H); 7.32 ppm (d, J = 6 Hz, 1H, 6-H).

2-Cyclohexyl-1,3-dioxin-4-one (**2e**); yield: 1.2 g (66%); m.p. 32–33°C (pentane).

$C_{10}H_{14}O_3$ (182.2) calc. C 65.91 H 7.74 found 65.66 7.78

M.S.: *m/e* = 111; 83; 71; 70.

I.R. ($CHCl_3$): ν = 1735 (C=O); 1610 cm^{-1} (C=C).

^{1}H-N.M.R. ($CDCl_3$): δ = 1.0–2.2 (m, 11 H); 5.33 (d, J = 4 Hz, 1 H, 2–H); 5.50 (d, J = 6 Hz, 1 H, 5–H); 7.40 ppm (d, J = 6 Hz, 6–H).

2-Phenyl-1,3-dioxin-4-one (**2f**); yield: 1.1 g (63%); m.p. 57–58°C (hexane ether).

$C_{10}H_8O_3$ (176.2) calc. C 68.18 H 4.58 found 67.85 4.76

M.S.: *m/e* = 176 (M^+); 107; 106; 105; 77; 71; 70.

I.R. ($CHCl_3$): ν = 1745 (C=O); 1605 cm^{-1} (C=C).

^{1}H-N.M.R. ($CDCl_3$): δ = 5.63 (d, J = 6 Hz, 1 H, 5–H); 6.47 (s, 1 H, 2–H); 7.47 (d, J = 6 Hz, 1 H, 6–H); 7.52 ppm (brs, 5 H_{arom}).

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[8] Oil bath temperature of bulb to bulb distillation.