A Convenient Synthesis of 4-Oxoalkanals

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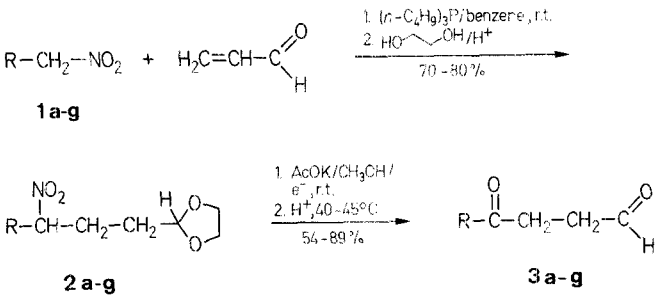
4-Oxoalkanals(γ-Ketoaldehydes), which are important intermediates for the syntheses of jasmonoids and pheromones, are prepared from the Michael reaction of nitroalkanes with acrolein catalyzed by tributylphosphine, followed by an electrochemical oxidative Nef reaction of the resultant 4-nitroalkanal ethylene acetals.

4-Oxoalkanals (γ-ketoaldehydes) are useful intermediates in organic synthesis. They are used for the preparation of pyrroles, furans, and thiophenes, as well as in the preparation of synthetic perfumes and drugs[1]. Recently[2], 4-oxoalkanals **(3)** were employed in the synthesis of cyclopentenones, e.g., methyl jasmonate. Numerous methods for preparing 4-oxoalkanals have been reported[3].

We needed an efficient and mild procedure for the preparation of 4-oxalkanals **(3)** in connection with our studies on the synthesis of pheromones. In a preceding paper, we described a useful novel method for the preparation of 1,4-diketones *via* Michael reaction of nitroalkanes with alkyl vinyl ketones in the presence of a catalytic amount of tributylphosphine[4] followed by Nef reaction. I describe here an analogous convenient synthesis of 4-oxoalkanals **(3)** *via* the Michael reaction of nitroalkanes with acrolein catalyzed by tributylphosphine.



1,2,3: **a** R = CH_3
b R = C_2H_5
c R = *n*-C_3H_7
d R = *i*-C_3H_7
e R = *n*-C_4H_9
f R = *i*-C_4H_9
g R = *i*-C_5H_{11}

The methods consists of stirring a mixture of nitroalkane **(1)** acrolein, and tributylphosphine in benzene for 20 min,

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Table 1. 4-Nitroalkanal 1,1-Ethanediyl Acetals (**2a–g**) Prepared

2	Yield[a] [%]	b.p. [°C/torr]	Molecular Formula[b]	IR[c] ν[cm⁻¹]	¹H-NMR (CCl_4)[d] δ[ppm]
a	72	95–97/2	$C_7H_{13}NO_4$ (175.2)	1540, 1140	1.53 (d, J = 6 Hz, 3H); 1.7–2.3 (m, 4H); 3.9 (m, 4H); 4.6 (m, 1H); 4.82 (t, J = 4.2 Hz, 1H)
b	70	102–104/2	$C_8H_{15}NO_4$ (189.2)	1540, 1140	0.97 (t, J = 7 Hz, 3H); 1.6–2.1 (m, 6H); 3.8 (m, 4H); 4.4 (m, 1H); 4.78 (t, J = 4.2 Hz, 1H)
c	72	106–107/2	$C_9H_{17}NO_4$ (203.2)	1540, 1140	0.97 (deformed t, 3H); 1.3–2.1 (m, 8H); 3.8 (m, 4H); 4.4H (m, 1H); 4.80 (t, J = 4.2 Hz, 1H)
d	73	98–100/2	$C_9H_{17}NO_4$ (203.2)	1540, 1140	0.97 (d, J = 6.7 Hz, 3H); 1.01 (d, J = 6.7 Hz, 3H); 1.5–2.2 (m, 5H); 3.8 (m, 4H); 4.4 (m, 1H); 4.80 (t, J = 4.2 Hz, 1H)
e	70	112–113/3	$C_{10}H_{19}NO_4$ (217.2)	1540, 1140	0.90 (deformed t, 3H); 1.3–2.1 (m, 10H); 3.8 (m, 4H); 4.4 (m, 1H); 4.80 (t, J = 4.2 Hz, 1H)
f	75	111–112/2	$C_{10}H_{19}NO_4$ (217.3)	1540, 1140	0.93 (d, J = 5.7 Hz, 3H); 0.97 (d, J = 5.7 Hz, 3H); 1.3–2.1 (m, 7H); 3.8 (m, 4H); 4.3 (m, 1H); 4.80 (t, J = 4.2 Hz, 1H)
g	80	116–118/2	$C_{11}H_{21}NO_4$ (231.3)	1540, 1140	0.95 (d, J = 5.7 Hz, 3H); 0.99 (d, J = 5.7 Hz, 3H); 1.3–2.1 (m, 9H); 3.8 (m, 4H); 4.4 (m, 1H); 4.80 (t, J = 4.2 Hz, 1H)

[a] Yield of isolated product.
[b] All compounds gave satisfactory microanalyses: C ±0.25, H ±0.25.
[c] Recorded on a Hitachi 260-30 spectrophotometer.
[d] Recorded on a Varian EM-390 spectrometer.

Table 2. 4-Oxoalkanals (**3a–g**) Prepared

3	Yield[a] [%]	b.p. [°C/torr]	Molecular Formula[b] or Lit. b.p. [°C/torr]	IR ν[cm⁻¹]	¹H-NMR (CCl_4) δ[ppm]
a	54	70/16	64–65/11[6]	2750, 1715, 1710	2.13 (s, 3H); 2.63 (s, 4H); 9.83 (s, 1H)
b	75	83–84/16	60–61/4.5[7]	Ref.[8]	Ref.[8]
c	80	94–95/16	93–94/15[9]	Ref.[10]	Ref.[10]
d	84	90–92/16	$C_7H_{12}O_2$ (128.2)	2750, 1710, 1705	1.10 (d, J = 6.6 Hz, 6H); 2.5 (m, 1H); 2.67 (s, 4H); 9.73 (s, 1H)
e	82	60–61/2	59–60/3[9]	2750, 1710, 1705	0.90 (deformed t, 3H); 1.3 (m, 4H); 2.37 (t, J = 7 Hz, 2H); 2.55 (s, 4H); 9.70 (s, 1H)
f	85	56–58/2	$C_8H_{14}O_2$ (142.2)	Ref.[11]	Ref.[11]
g	89	88–89/3	67/0.5[10]	Ref.[10]	Ref.[10]

[a] Yield of isolated product.
[b] All compounds gave satisfactory microanalyses: C ±0.28, H ±0.25.

acetalization of the resultant Michael adduct *in situ* with ethylene glycol in the presence of *p*-toluenesulfonic acid, treatment of the 1,1-ethanediyldioxy-4-nitroalkane (**2**) thus obtained with potassium acetate in methanol by an electrolytic procedure[5], and hydrolysis of the resultant 4-oxoalkanal 1-acetal by treatment with 4% hydrochloric acid.

1,1-Ethanediyldioxy-4-nitroalkanes (2a–g); General Procedure:
To a stirred solution of acrolein (2.8 g, 50 mmol) and the nitroalkane (**1**; 0.25 mol) in benzene (50 ml), a solution of tributylphosphine (40 mg, 0.2 mmol) in benzene (1 ml) is added with stirring. At the end of the addition, the temperature reaches 45–50 °C. The mixture is cooled and stirring is continued for 20 min. Then, a solution of *p*-toluenesulfonic acid monohydrate (100 mg, 0.5 mmol) in ethylene glycol (3.7 g, 60 mmol) is added over 10 min with stirring and the mixture is refluxed for 5 h. It is then washed with 5% sodium hydrogen carbonate solution (20 ml) and with saturated sodium chloride solution (50 ml). The organic solution is evaporated and the residue is distilled *in vacuo* (Table 1).

4-Oxoalkanals (3a–g); General Procedure (cf. Ref[5]):
Potassium acetate (0.5 g, 5 mmol) is added to a stirred solution of the 1,1-ethanediyldioxy-4-nitroalkane (**2**; 10 mmol) in methanol (40 ml) at 25 °C. The mixture is electrolyzed in Beaker-type cell at constant current (0.18 A, 8 V) using platinum electrodes (1 cm²) for 4 F/mol. Then, methanol is removed on a rotary evaporator, and to the residue is added 4% hydrochloric acid (100 ml). The mixture is stirred at 40–45 °C for 5 h under nitrogen, then cooled, and extracted with ethyl acetate (3 × 30 ml). The combined organic layers are washed with 5% sodium hydrogen carbonate solution (50 ml), and dried with sodium sulfate. The solvent is evaporated and the residue is distilled in vacuo (Table 2).

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[1] See, for example:
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