Permanganate Oxidation of 4,7-Dihydro-1,3-dioxepins: A New Method for the Preparation of Bis[carboxymethyl] Acetals via Acetalisation with (*Z*)-2-Butene-1,4-diol

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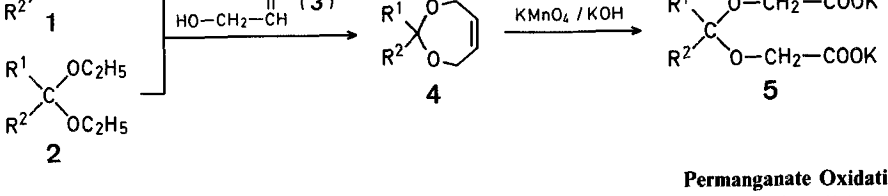
Several bis[carboxymethyl] acetals have been proposed as potential substitutes for phosphate in detergent formulation[1,2,3]. An important property of this type of compound is the low stability in acidic waste water, which facilitates degradation.

For the preparation of bis[carboxymethyl] acetals, the reaction of carbonyl compounds with sodium ethyl glycolate and ethyl bromoacetate and the reaction of geminal dihalogen compounds with sodium ethyl glycolate have been reported in the patent literature[1,3]. When applying solid acids, such as amorphous silica-alumina, as catalysts[4] in the reaction of carbonyl compounds with an alkyl glycolate, yields proved to be poor. This is possibly due to preferential adsorption of the alkyl glycolate or the reaction product on the catalyst. As an alternative we report here a convenient two-step synthesis of bis[carboxymethyl] acetals (Scheme A).

Firstly, the carbonyl compound (**1**) is converted to a 4,7-dihydro-1,3-dioxepin (**4**) by reaction with (*Z*)-2-butene-1,4-diol[5] (**3**) or by transacetalisation via diethyl acetals (**2**)[6]. Secondly, **4** is oxidized by potassium permanganate in aqueous potassium hydroxide solution to the respective potassium bis[carboxymethyl] acetal **5**.



1, 2, 4, 5	R^1	R^2
a	H	H
b	CH_3	H
c	CH_3	CH_3
d	H	$CH{=}CH_2$ (COOK in **5**)
e	CH_3	COOK

Scheme A

In the preparation of **5e**, reaction of pyruvic acid (**1e**) gave **4e** as the (*Z*)-2-butene-1,4-diol ester, which was saponified before the permanganate oxidation. The overall yield for **5a–e** was 45–90%. Permanganate oxidations of **4** occurred almost quantitatively at 0 °C in aqueous potassium hydroxide solution. In the present procedure potassium salts are obtained. Generally, preparation of the free acids with this method is not possible, due to low stability of the acetal bond at lower pH. Only the acetals **5d** and **5e**, which contain a stabilizing carboxylic group, could be obtained as the free acid by ion exchange at 0 °C.

4,7-Dihydro-1,3-dioxepins 4a–c from Acetals 2a–c:

A mixture of **2a–c** (125 mmol), (*Z*)-2-butene-1,4-diol (**3**; 23.3 g, 265 mmol) and *p*-toluenesulfonic acid hydrate (2 mg) is slowly distilled at atmospheric pressure. Redistillation of the distillate yields compounds **4** of >95% purity (G.L.C.). Structures were confirmed by ^{1}H-N.M.R., ^{13}C-N.M.R., and mass spectrometry.

4a; yield: 55%; b.p. 125–127 °C/760 torr (Ref.[7], b.p. 127°/760 torr);
4b; yield: 46%; b.p. 136–137.5 °C/760 torr (Ref.[8], b.p. 137–138 °C/760 torr);
4c; yield: 65%; b.p. 144–146.5 °C/760 torr (Ref.[6], b.p. 144.5–147 °C/760 torr).

2-Vinyl-4,7-dihydro-1,3-dioxepin (4d):

A mixture of propenal (**1d**; 14.0 g, 0.25 mol), (*Z*)-2-butene-1,4-diol (**3**; 22.0 g, 0.25 mol) and *p*-toluenesulfonic acid hydrate (5 mg) in benzene (150 ml) is boiled in a Dean and Stark equipment for 3 h to produce the theoretical amount of water (4.5 ml). The residue is distilled to give **4d**; yield: 18.8 g (60%); b.p. 155–159 °C/760 torr (Ref.[9], b.p. 154–155 °C/760 torr).

2-Carboxy-2-methyl-4,7-dihydro-1,3-dioxepin (4e):

A mixture of pyruvic acid (**1e**; 17.6 g, 0.20 mol), (*Z*)-2-butene-1,4-diol (**3**; 35.2 g, 0.4 mol), and *p*-toluenesulfonic acid hydrate (5 mg) in benzene (150 ml) is boiled in a Dean and Stark equipment for 12 h to produce the theoretical amount of water (7.2 ml). The reaction mixture is concentrated in vacuum and 1.5 normal potassium hydroxide solution (150 ml) is added. After 2 h, the pH is brought to 9 with Dowex AG-50W-X8 ($H^{\oplus}$) and water is evaporated at 45 °C. The residual syrup is extracted with acetone (3 × 200 ml) to remove (*Z*)-2-butene-1,4-diol. The remaining solid is dried in vacuo to give **4e** as the potassium salt; yield: 35.3 g (90%); m.p. 96–98 °C.

$C_7H_9O_4K$	calc.	C 42.84	H 4.62
(196.2)	found	42.28	4.96

^{1}H-N.M.R. (D_2O): δ = 1.47 (s, 3 H); 4.25 (AA'BB', 4 H); 5.73 ppm (m, 2 H).

^{13}C-N.M.R. (D_2O): δ = 19.8 (CH_3); 61.7 (CH_2); 102.2 (OCO); 128.1 (CH); 175.3 ppm (COO).

Permanganate Oxidation of 4c:

Compound **4c** (1.3 g, 10 mmol) is added within 0.5 h to a solution of potassium permanganate (4.8 g, 30 mmol) and potassium hydroxide (0.5 g, 9 mmol) in water (100 ml) at 0 °C. After 2 h, the reaction mixture is filtered, brought to pH 9 with Dowex AG-50W-X8 ($H^{\oplus}$), and freeze dried from water (200 ml) to give **5c** as a solid; yield: 2.9 g (95%); m.p. 145 °C (dec); see Table.

$C_7H_{10}O_6K_2 \cdot 2\,H_2O$	calc.	C 27.63	H 4.60
(304.4)	found	28.32	4.61

Compounds **4a, b, e** were oxidized similarly on a 4 mmol scale, see Table.

The potassium salt **5e** (0.67 g, 2 mmol) in water (50 ml) is treated with an excess of Dowex AG-50W-X8 ($H^{\oplus}$) (8 meq) at 0 °C. After 1 h the reaction mixture is filtered and freeze dried from water (70 ml). Recrystallization from acetone gives the free carboxylic acid corresponding to **5e**; yield: 0.36 g; m.p. 150 °C (dec).

$C_7H_{10}O_8$	calc.	C 37.85	H 4.54
(222.1)	found	38.45	4.62

^{1}H-N.M.R. (D_2O): δ = 1.78 (s, 3 H); 4.43 ppm (s, 4 H).

Permanganate Oxidation of 4d:

Compound **4d** (0.5 g, 4 mmol) is added within 0.5 h to a solution of potassium permanganate (3.8 g, 24 mmol) and potassium hydroxide (0.4 g, 7 mmol) in water (50 ml) at 0 °C. After 4 h, the reaction mixture is filtered and the filtrate treated with a slight excess of barium hy-

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Table. Bis[carboxymethyl] Acetals **5a–e** from Dioxepins **4a–e**

Product	Yield [%]	m.p. [°C]	Molecular formula[a]	^{1}H-N.M.R. (D_2O) δ [ppm][b]	^{13}C-N.M.R. (D_2O) δ [ppm][c]
5a	96	135° (dec)	$C_5H_6O_6K_2 \cdot 2H_2O$ (276.3)	4.05 (s, 4H); 4.82 (s, 2H)	65.7 (CH_2); 93.5 (OCO); 177.0 (COO)
5b	95	130° (dec)	$C_6H_8O_6K_2 \cdot 2H_2O$ (290.4)	1.38 (d, 3H, J=5 Hz); 4.00 (s, 4H); 4.80 (q, 1H, J=5 Hz)	17.7 (CH_3); 63.7 (CH_2); 99.0 (OCO); 176.8 (COO)
5c	95	145° (dec)	$C_7H_{10}O_6K_2 \cdot 2H_2O$ (304.4)	1.40 (s, 6H); 3.93 (s, 4H)	28.0 (CH_3); 64.9 (CH_2); 93.0 (OCO); 181.8 (COO)
5d	98	220° (dec)	—[d]	4.00 (s, 4H); 4.87 (1H)	64.3 (CH_2); 97.8 (OCO); 172.4 (COO); 176.3 (COO)
5e	94	220° (dec)	—[d]	1.50 (s, 3H); 3.96 (s, 4H)	20.2 (CH_3); 60.9 (CH_2); 100.2 (OCO); 175.1 (COO); 176.5 (COO)

[a] Satisfactory microanalyses obtained: C ±0.51, H ±0.15.

[b] 37 °C, sodium 2,2,3,3-tetradeutero-3-(trimethylsilyl)propionate as internal reference.

[c] 35 °C, tetramethylammonium chloride as internal reference.

[d] Converted to the free acid and characterized as such.

droxide octahydrate (0.66 g, 2.1 mmol) to remove formic acid. The solution is filtered again, brought to pH 9 with Dowex AG-50W-X8 ($H^{\oplus}$) and freeze dried from water (100 ml) to yield **5d** as a solid; yield: 0.78 g (98%); m.p. 220 °C (dec); see Table.

The potassium salt **5d** (0.32 g, 1 mmol) in water (50 ml) is treated with an excess of Dowex AG-50W-X8 ($H^{\oplus}$) (8 meq) at 0 °C. After 1 h, the reaction mixture is filtered and freeze dried from water (70 ml). Recrystallization from acetone gives the free acid corresponding to **5d**; yield: 0.15 g (72%); m.p. 135–137 °C (dec).

$C_6H_8O_8$	calc.	C 34.63	H 3.87
(208.1)	found	34.58	3.87

^{1}H-N.M.R. (D_2O): δ=5.10 (s, 1H); 4.27 ppm (s, 4H).

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