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Conversion of 3-Acetoxy-6-acetoxymethyl-2*H*-pyran-2-one to Cyclopentenone Derivatives and 1,3-Cyclopentanedione

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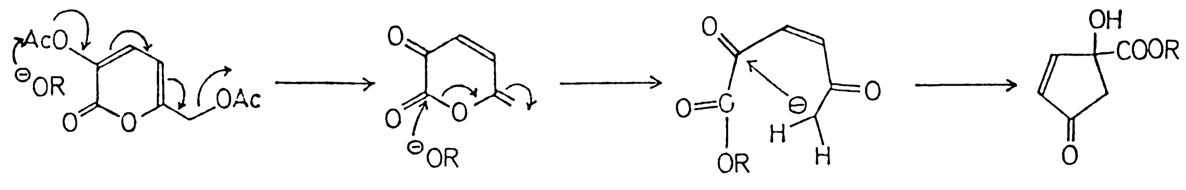
Simple synthetic routes to 2-cyclopentenone derivatives and 1,3-cyclopentanedione from 3-acetoxy-6-acetoxymethyl-2*H*-pyran-2-one were developed.

Degradation products obtained by heating carbohydrates in slightly acidic or basic aqueous solutions have been isolated and identified.1) A small amount of cyclopentenone derivatives have been also isolated from degradation products of carbohydrates.2)

Cyclopentenone derivatives have been known as biologically active natural products and a variety of methods have been developed for the construction of five membered ring. However, development of simple synthetic routes to them is still significant.

Such degradation reaction of carbohydrates as mentioned above can be considered as a complex of one-pot reactions. Consequently, if it is possible to control them, we can obtain useful compounds, for example cyclopentenone derivatives, from carbohydrates by one-pot or short step reactions.

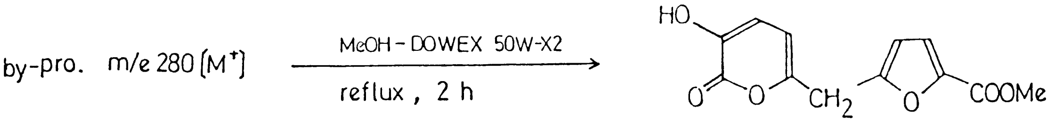
Based on these considerations, degradation product which could be used as a synthetic intermediate for conversion to cyclopentenone derivatives was searched, because control of the degradation reaction in one-pot process was assumed to be difficult. 3-Acetoxy-6-acetoxymethyl-2*H*-pyran-2-one(1) has been selectively obtained from D-glucono-1,5-lactone by treatment in acetic anhydride-pyridine at 80 °C for 1 h.3) This compound was expected to be converted to 4-alkoxycarbonyl-4-hydroxy-2-cyclopentenone(4) *via* reaction mechanism as shown below under alcoholysis condition.



1 2 3 4

Thus, methanolysis of 1 was tried by using various bases such as sodium methoxide, sodium hydroxide, 1,8-diazabicyclo[5.4.0]-undec-7-ene(DBU), triethylamine, 4-(dimethylamino)pyridine, etc. The reaction proceeded as we expected but side reactions were also found. One of them was dimerization to give a compound of m/e 280[M$^+$]. This by-product was converted to α-pyrone derivative

(7)[4] by treatment in MeOH-ion exchange resin (DOWEX 50W-X2) under reflux.



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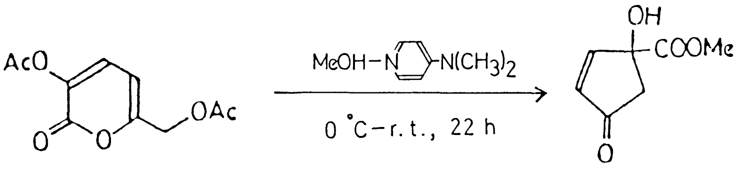
Dilution of reaction system was proved to be effective on improvement of yield of 4 as shown in Table 1.

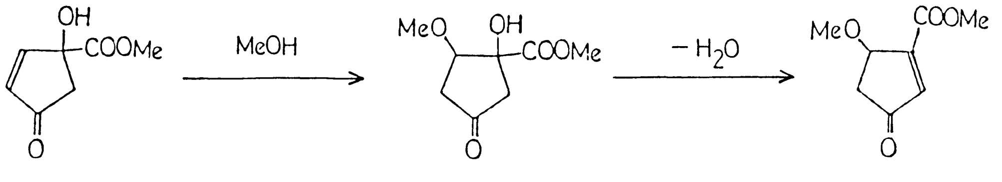
Table 1. Effect of Dilution of Reaction System on Improvement of Selectivity in Conversion of α-Pyrone(1) to Cyclopentenone(4) in MeOH-4-(dimethylamino)pyridine



1 4

Entry	MeOH(ml/1 mmol 1)	Yield of 4/%
1	0.2	trace
2	2.7	35.4
3	14.3	68.5
4	21.4	70.7

The other side reactions such as addition of alcohol to 4 leading to 5[6] or dehydration in 5 leading to 6[7] were controlled by using sodium hydroxide as a base and adding water to the system.



4 5 6

When the reaction was carried out by adding a solution of sodium hydroxide to a solution of 1 under ice cooling, by using various contents of water in the both solutions, and by changing periods of dropwise addition and stirring, yields of 4 and 5 were as shown in Table 2.

The best result was obtained in the following way: A solution of 0.064 g (1.60 mmol) of sodium hydroxide in 6.5 ml of water was added to a solution of 0.362 g(1.60 mmol) of 1 in 13 ml of methanol under ice cooling in a period of 4 min. The mixture was stirred additionally for more 4 min and then treated with a cation exchange resin (DOWEX 50W-X2) in methanol under ice cooling to neutralize sodium hydroxide. After evaporation of methanol under reduced

Table 2. Effect of Water on Selectivity in Conversion of α-Pyrone(1) to Cyclopentenone(4) in MeOH-NaOH

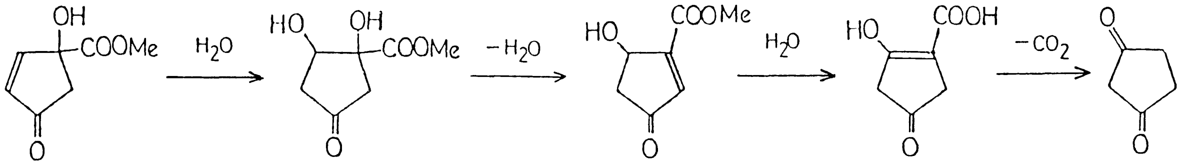
Soln. of 1		Soln. of NaOH		Reaction time/min			Yield/%	
MeOH	: H_2O	MeOH	: H_2O	dropwise addition	+	stirring	4	5
2(dry)	: 0	1(dry)	: 0	60	+	10	15.2	29.3
2(dry)	: 0	1(dry)	: 0	45	+	10	30.0	23.1
12	: 1	6	: 1	10	+	2	58.6	trace
2	: 0	0	: 1	4	+	4	89.2	trace

pressure, residual oil was extracted with ethyl ether to give 4 in 89.2% yield. Further purification of 4 could be achieved by TLC on silica gel or distillation under reduced pressure(0.3 mmHg, at 120-130 °C).

As for the base catalyst, DBU, triethylamine, and 4-(dimethylamino)pyridine were also acceptable. But sodium methoxide gave 5 and 6 as major products and was not suitable for preparation of 4.

Further, conversion of 4 to 6 was tried by using an acidic catalyst, ion exchange resin (DOWEX 50W-X2), in methanol. 6 was obtained in 90.5% yield after refluxing for 2 h.

Based on this result, it was assumed that if this reaction was possible in water, preparation of a valuable synthetic intermediate, 1,3-cyclopentanedione (9),[8] would be possible by combination with decarboxylation as shown below.



4 5' 6' 8 9

Conversion of 4 to 9 proceeded smoothly in the presence of acid in water. Results were as shown in Table 3.

Table 3. Degradation of Cyclopentenone(4) to 1,3-Cyclopentanedione(9) in Water-Acid

Catalyst	Reaction temp /°C	Reaction time/ h	Yield of 9/%
HCl	100	5	55.6
F_3CCOOH	100	2	76.3
DOWEX 50W-X2	52	14	67.5
"	100	6	83.7

A typical example of this reaction was as follows. A solution of 0.196 g (1.26 mmol) of 4 in 4 ml water was stirred at 100 °C for 6.5 h in the presence of a cation exchange resin (DOWEX 50W-X2). After the reaction, the cation exchange resin was filtered off and methanol was evaporated under reduced pressure. The crude 9 was obtained in 87.0% yield. The further purification of 9 could be achieved by sublimation; mp 149-151 °C.$^{9)}$

Although a variety of synthetic methods has been developed for synthesis of 9,$^{9)}$ the present method is good for practical use, because the process is simple and the starting material is easily available.

The results obtained by this investigation demonstrated the possibility of preparation of synthetic intermediates by using degradation products of carbohydrates.

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References

1) For example, T. Popoff and O. Theander, Acta Chem. Scand., Ser. B, 30, 397 (1976).

2) For example, T. Popoff and O. Theander, Carbohydr. Res., 22, 135(1972); K. Olsson, P. Pernemalm, T. Popoff, and O. Theander, Acta Chem. Scand., Ser. B, 31, 469(1977); I. Forsskahl, T. Popoff, and O. Theander, Carbohydr. Res., 48, 13(1976).

3) C. R. Nelson and J. S. Gratzl, Carbohydr. Res., 60, 267(1978).

4) IR(NaCl) 3350, 1720, 1700, 1650, 1585, 1530, 1520, 1420, 1365, 1325, 1305, 1245, 1220, 1190, 1140, 1070, 1030, 980, 840, 802, 798, 760, 730 cm^{-1}; NMR ($CDCl_3$) δ 3.90(s, 5H, $COOCH_3$ and CH_2), 6.04(d, 1H, J=7.0 Hz), 6.37(d, 1H, J=3.5 Hz), 6.65(d, 1H, J=7.0 Hz), 7.14(d, 1H, J=3.5 Hz); m/e 250[M$^+$].

5) IR(NaCl) 3450, 1720, 1595, 1435, 1270, 1200, 1170, 1090, 1060, 1030, 815 cm^{-1}; NMR($CDCl_3$) δ 2.47(d, 1H, H-5, J=18.0 Hz), 2.59(d, 1H, H-5, J=18.0 Hz), 3.79 (s, 3H, $COOCH_3$), 5.50(s, 1H, OH), 6.28(d, 1H, H-2, J=5.2 Hz), 7.32(d, 1H, H-3, J=5.2 Hz); m/e 156[M$^+$].

6) IR(NaCl) 3450, 1750, 1730(shoulder), 1435, 1160, 1120, 1100, 1030 cm^{-1}; NMR ($CDCl_3$) δ 2.46-2.87(m, 4H, $2CH_2$), 3.43(s, 3H, OCH_3), 3.86(s, 3H, $COOCH_3$), 4.30(t, 1H, H-3, J=8.5 and 8.5 Hz); m/e 188[M$^+$].

7) IR(NaCl) 3070, 1720, 1615, 1430, 1200, 1165, 1100 cm^{-1}; NMR($CDCl_3$) δ 2.53-2.70(m, 2H, H-5), 3.46(s, 3H, OCH_3), 3.86(s, 3H, $COOCH_3$), 4.70-5.00(m, 1H, H-4), 6.70(s, 1H, H-2); m/e 170[M$^+$].

8) Aldrichimica, 10, 19(1977).

9) For example, M. Nilsson, Acta Chem. Scand., Ser. B, 35, 667(1981); I. Nishiguchi, T. Hirashima, T. Shono, and M. Sasaki, Chem. Lett., 1981, 551; Y. D. Vankar, N. C. Chaudhuri and C. T. Rao, Tetrahedron Lett., 28, 551(1987).

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