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Selective Methanolysis of Lactone Rings in Some Acyl Carbohydrates

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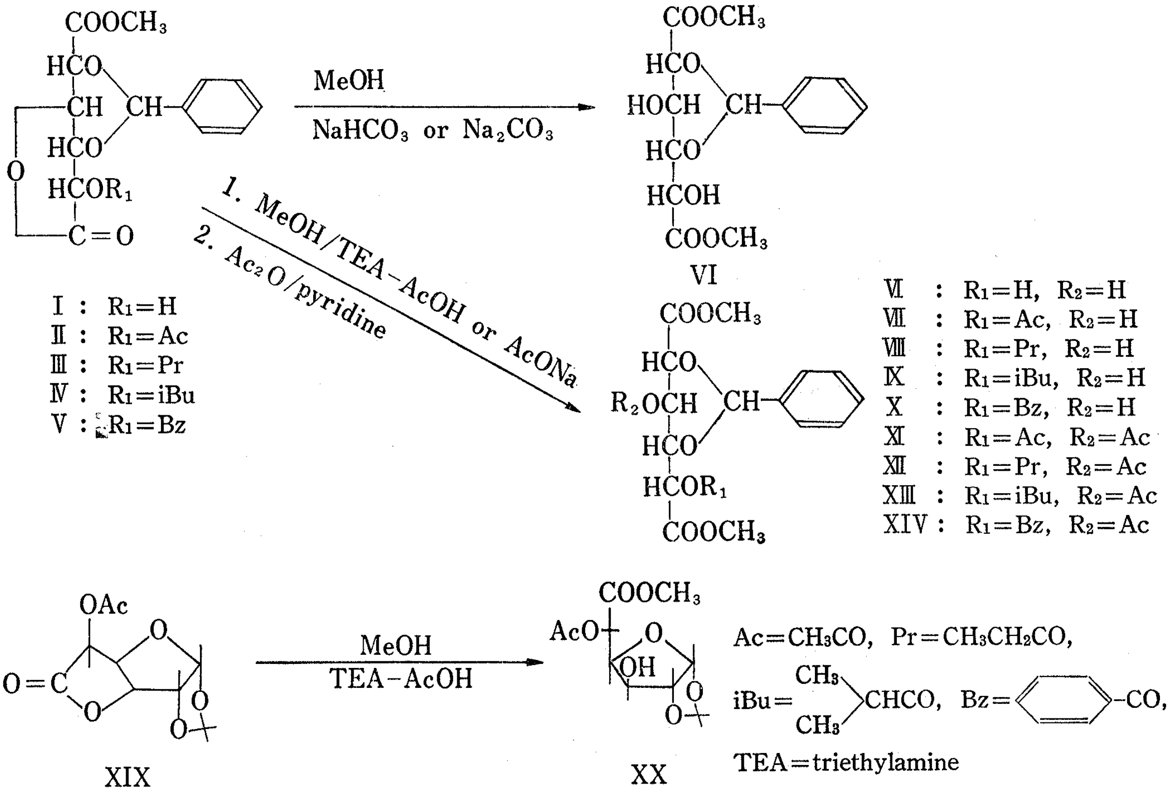
It was found that a lactone ring was esterified to a methyl ester group in the bufferized methanol containing triethylamine–acetic acid or sodium acetate without simultaneous cleavage of the acyl groups and the methyl ester groups and this methanolysis mainly proceeded without acyl migration.

Using this method, 2,4-O-benzylidene-5-O-acyl-D-glucaro-6,3-lactone 1-methyl esters (II, III, IV and V) were esterified in excellent yields to dimethyl 2,4-O-benzylidene-5-O-acyl-D-glucarates (VII, VIII, IX and X respectively), and from the latters, dimethyl 2,4-O-benzylidene-3-O-acetyl-5-O-acyl-D-glucarates (XI, XII, XIII and XIV respectively) were synthesized by the usual acetylation.

Moreover, 1,2-O-isopropylidene-5-O-acetyl-D-glucofuranurono-6,3-lactone (XIX) could be also esterified to methyl 1,2-O-isopropylidene-5-O-acetyl-D-glucofuranuronate (XX) by the same method.

Although lactone rings in some carbohydrates have been esterified by refluxing with methanol,[2] by refluxing with alcohol in the presence of sodium alcoholate,[3–5] or by reacting with methanol in the presence of anion exchange resin,[6,7] it has been difficult to esterify the



I : $R_1=H$
II : $R_1=Ac$
III : $R_1=Pr$
IV : $R_1=iBu$
V : $R_1=Bz$

VI : $R_1=H$, $R_2=H$
VII : $R_1=Ac$, $R_2=H$
VIII : $R_1=Pr$, $R_2=H$
IX : $R_1=iBu$, $R_2=H$
X : $R_1=Bz$, $R_2=H$
XI : $R_1=Ac$, $R_2=Ac$
XII : $R_1=Pr$, $R_2=Ac$
XIII : $R_1=iBu$, $R_2=Ac$
XIV : $R_1=Bz$, $R_2=Ac$

Ac=CH_3CO, Pr=CH_3CH_2CO,
iBu=$(CH_3)_2CHCO$, Bz=C_6H_5-CO,
TEA=triethylamine

Chart 1

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[1] Location: *Hongo-7-chome, Bunkyo-ku, Tokyo.*
[2] W.F. Goebel and F.H. Babers, *J. Biol. Chem.*, **111**, 347 (1935).
[3] T.O. Touster and V.H. Reynolds, *J. Biol. Chem.*, **197**, 863 (1964).
[4] G.N. Bollenback, J.W. Long, D.G. Benjamin and J.A. Lindquist, *J. Am. Chem. Soc.*, **77**, 3310 (1955).
[5] H. Tsukamoto, M. Hamana, K. Kato and T. Kuroda, *Yakugaku Zasshi*, **76**, 1282 (1956).

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lactone rings in acyl carbohydrates without simultaneous cleavage of the acyl groups in the molecules. Recently, Kinoshita, *et al.*[8] reported that methyl 1,2-O-isopropylidene-5-O-acetyl-D-glucofuranuronate (XX) was obtained in 45% yield by the methanolysis of 1,2-O-isopropylidene-5-O-acetyl-D-glucofuranurono-6,3-lactone (XIX) in the presence of Amberlite IR–45 in OH form.

We found that as shown in Chart 1, acetyl (II),[9,10] propionyl (III), isobutyryl (IV) and benzoyl (V) derivatives of 2,4-O-benzylidene-D-glucaro-6,3-lactone 1-methyl ester (I),[9–11] which were synthesized from I and did not react with methanol in the presence of Amberlite IR–45 in OH form, were converted in excellent yields to dimethyl ester derivatives (VII, VIII, IX and X respectively) of 2,4-O-benzylidene-5-O-acyl-D-glucaric acids by the treatment with methanol containing triethylamine–acetic acid or sodium acetate, and from the latters, 3-O-acetyl derivatives (XI, XII, XIII and XIV respectively) of dimethyl 2,4-O-benzylidene-5-O-acyl-D-glucarates were easily obtained by the usual acetylation. On the contrary, by the treatment with methanol containing sodium bicarbonate or sodium carbonate, I and its acyl derivatives (II—V) were converted to dimethyl 2,4-O-benzylidene-D-glucarate (VI) as shown in Fig. 1.

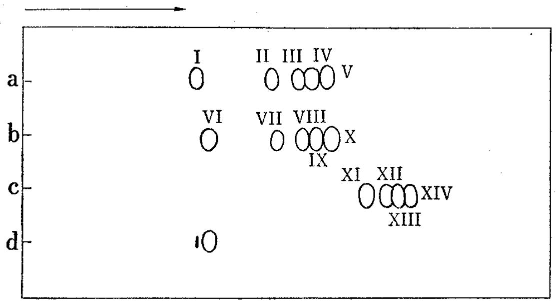
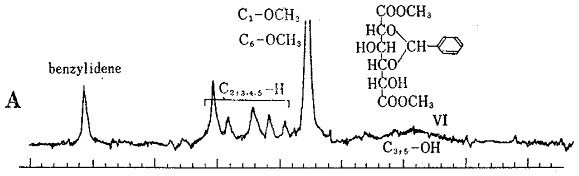
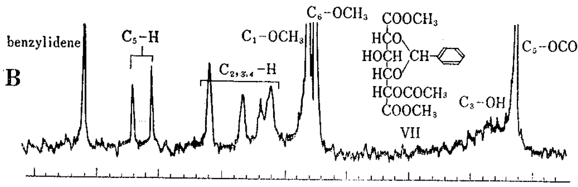


Fig. 1. Thin–Layer Chromatogram of the Reaction Products (MeOH–$NaHCO_3$)

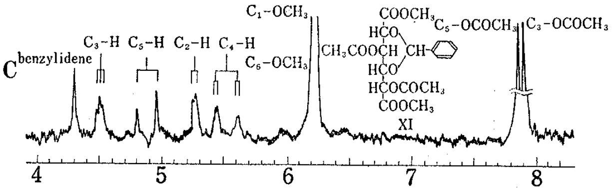
solvent: toluene–acetone–EtOH (6:1:1)
adsorvent: Silica Gel G (Merck)
a, b, c: authentic standards
d: the reaction products by the methanolysis of I—V with $NaHCO_3$



Dimethyl 2,4-O-Benzylidene-D-glucarate (VI),



Dimethyl 2,4-O-Benzylidene-5-acetyl-D-glu carate (VII),



Dimethyl 2,4-O-Benzylidene-3,5-di-O-acetyl-D-glucarate (XI),

Fig. 2. NMR Spectra of VI, VII and XI in $CDCl_3$ at 60 Mc

Moreover, XX[8] was obtained in 52% yield by the treatment of XIX with methanol containing triethylamine and acetic acid for 1 hour.

Differently from the nuclear magnetic resonance (NMR) spectrum of VI, that of VII showed a doublet ($J=9$ cps, one proton) at a lower magnetic field (τ 4.86), and the signal was

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6) Y. Imai and Y. Hirasaka, Abstracts of Papers, the 77th Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April 1957, p. 97; Japan. Patent 3015 (1960) [*C.A.*, **54**, 24431 (1960)].
7) Y. Hirasaka and K. Umemoto, *Yakugaku Zasshi*, **82**, 1676 (1962).
8) T. Kinoshita, M. Ishidate and Z. Tamura, *Chem. Pharm. Bull.* (Tokyo), **14**, 986 (1966).
9) T.P. Bird, W.A.P. Black, E.T. Dewar and H.W.T. Rintoul, *J. Chem. Soc.*, **1964**, 4512.
10) J. Ide, H. Takahashi, A. Tanoura and Y. Nitta, *Yakugaku Zasshi*, **86**, 1057 (1966).
11) R.E. Reeves, *J. Am. Chem. Soc.*, **61**, 664 (1939).

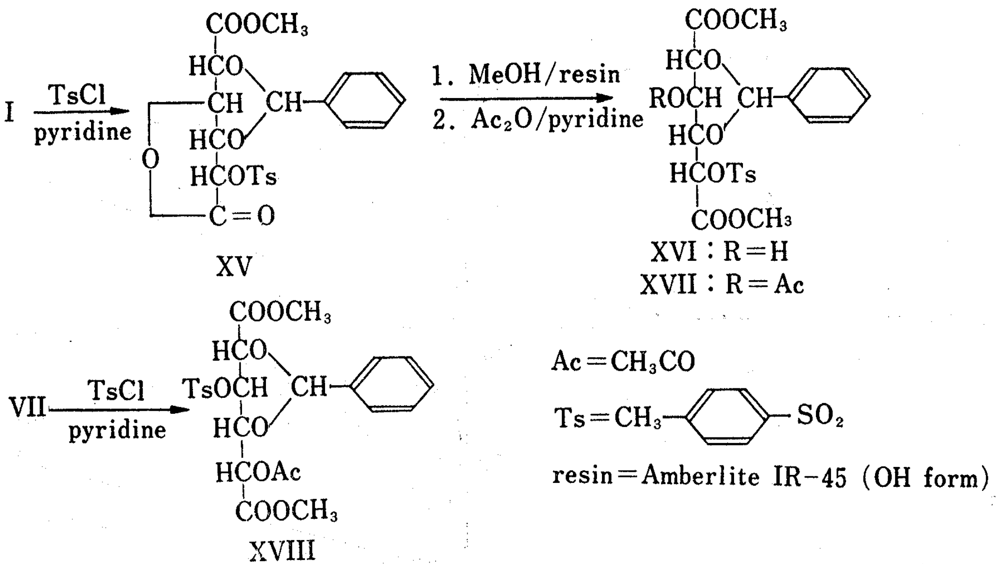
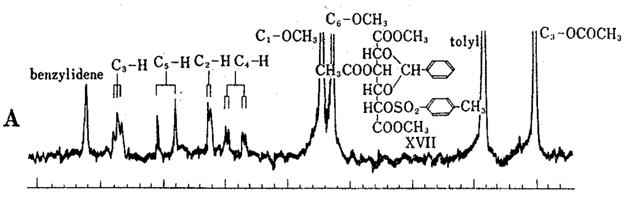
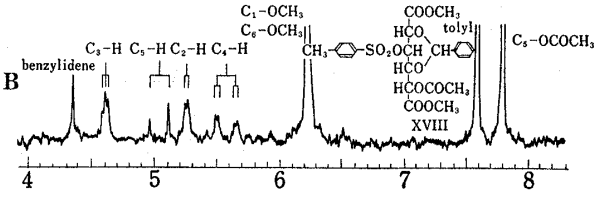


Chart 2

probably assigned to the proton attached to C_5 whose hydroxyl group was acetylated (Fig. 2A and 2B). This was confirmed from the fact that the NMR spectrum of XI, acetyl derivative of VII, showed a triplet (J=1.5 cps, one proton) at τ 4.52 corresponding to C_3 proton (Fig. 2C). Moreover the compound (XVIII) synthesized by the tosylation of VII was obviously different in melting points, specific optical rotations, infrared (IR) spectra and NMR spectra (Fig. 3) from dimethyl 2,4-O-benzylidene-3-O-acetyl-5-O-*p*-tolylsulfonyl-D-glucarate (XVII) synthesized by the methanolysis of 2,4-O-benzylidene-5-O-*p*-tolylsulfonyl-D-glucaro-6,3-lactone 1-methyl ester (XV),[12] followed by the usual acetylation (Chart 2). Accordingly, VII was confirmed to have a free hydroxyl group at C_3, and the fact indicates that the methanolysis mainly proceeds without acyl migration.



Dimethyl 2,4-O-Benzylidene-3-O-acetyl-5-O-*p*-tolylsulfonyl-D-glucarate (XVII)



Dimethyl 2,4-O-Benzylidene-3-O-*p*-tolylsulfonyl-5-O-acetyl-D-glucarate (XVIII)

Fig. 3. NMR Spectra of XVII and XVIII in $CDCl_3$ at 60 Mc

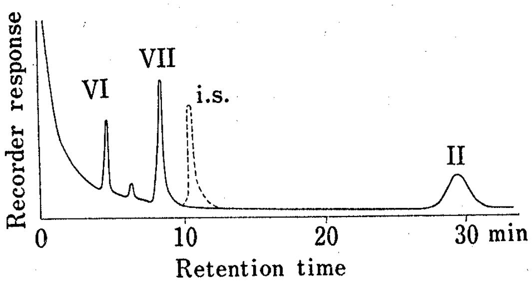


Fig. 4. Gas Chromatogram of the Reaction Mixtures

column: 2% QF-1 on Gas-Chrom P (glass tube 180 cm × 4 mm *i.d.*)
temperature: column 220°, detector 225°
carrier gas: N_2 65 ml/min, sens. 100, range 0.4 V
XI was used as an internal standard (i.s.).

Methanolysis of lactone ring in II by triethylamine–acetic acid, sodium acetate, zinc acetate, mercuric acetate, sodium bicarbonate or sodium methylate was examined by gas chro-

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[12] J. Ide, H. Takahashi, *et al.*, unpublished observations.

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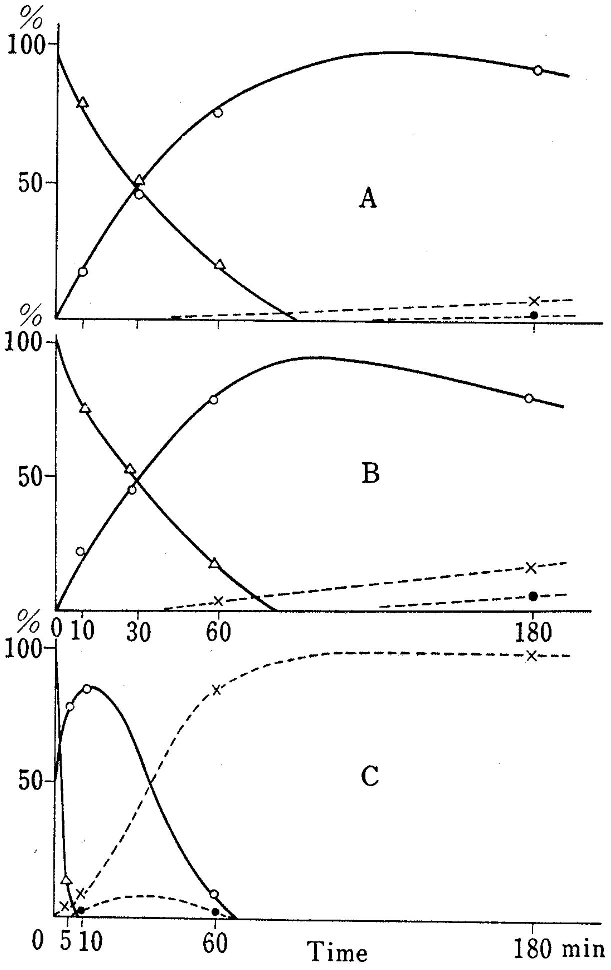


Fig. 5. Methanolysis of 2,4-O-Benzylidene-5-O-acetyl-D-glucaro-6,3-lactone 1-Methyl Ester (II) by 29.8 mM Triethylamine-22.3 mM AcOH (A), 14.9 mM AcONa (B) and 29.8 mM $NaHCO_3$ (C)

—△—: II ---×---: VI
—○—: VII ---●---: unknown substance

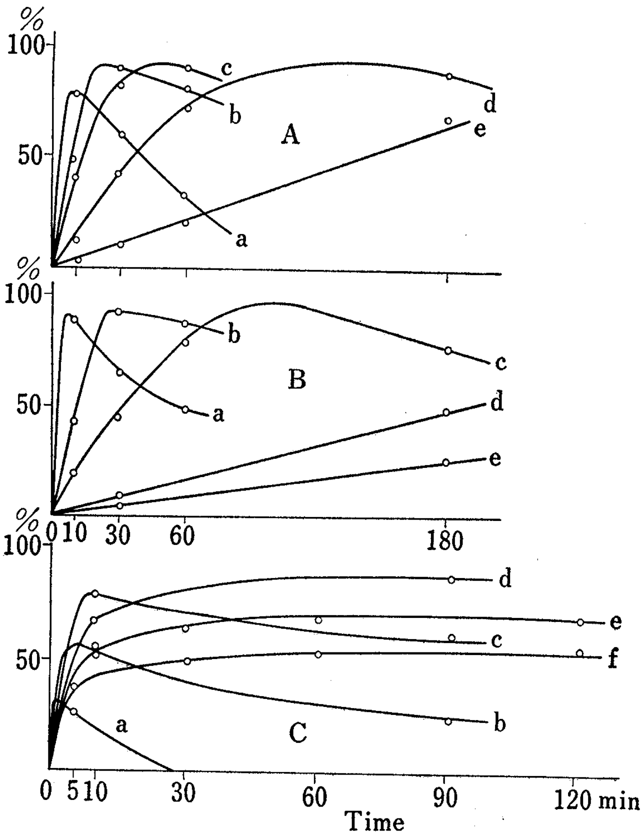


Fig. 6. Yields of Dimethyl 2,4-O-Benzylidene-5-O-acetyl-D-glucarate (VII)

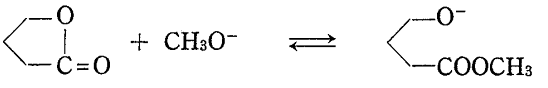
A—a: triethylamine (TEA) 29.8 mM; b: TEA 29.8 mM, AcOH 7.45 mM; c: TEA 29.8 mM, AcOH 14.9 mM; d: TEA 29.8 mM, AcOH 22.3 mM; e: TEA 29.8 mM, AcOH 29.8 mM
B—a: AcONa 74.5 mM; b: AcONa 29.8 mM; c: AcONa 14.9 mM; d: $(AcO)_2Zn$ 74.5 mM; e: $(AcO)_2Hg$ 74.5 mM
C—a: CH_3ONa 1.49 mM; b: CH_3ONa 1.19 mM; CH_3ONa 0.894 mM; d: CH_3ONa 0.596 mM; e: CH_3ONa 0.298 mM; f: CH_3ONa 0.149 mM

matographic analysis (Fig. 4). The minor peak detected between the two peaks of VI and VII may be an acetyl–migrated compound of VII (Fig. 5C). In the case of triethylamine (29.8 mM)-acetic acid (22.3 mM) or sodium acetate (14.9 mM), II was converted in a maximum yield of 95% to VII, but with sodium bicarbonate, to VI by following deacetylation. The use of zinc acetate or mercuric acetate in place of sodium acetate did not give a good result because of a little dissociation of them. In the case of sodium methylate, the reactions proceeded rapidly at the initial stage though went into decay in 30 minutes as shown in Fig. 6C. It is thought that the reactivity against base is in following order: lactone ring>acyl group>methyl ester group, and the reaction mechanism could be elucidated as follows:

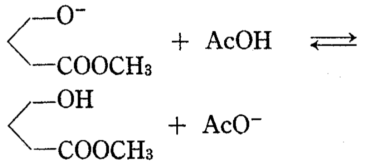
TEA–AcOH : $TEA + AcOH \rightleftarrows TEA\text{-}H^+ + AcO^-$ (1)

AcONa : $AcONa \rightleftarrows AcO^- + Na^+$ (2)

$AcO^- + CH_3OH \rightleftarrows CH_3O^- + AcOH$ (3)



(4)



(5)

Apparent pH in the reaction mixture was measured from an absorbance ratio of a pH indicator (phenol red)[13] and the results are summerized in Fig. 7. The figure indicates that a CH_3O^- concentration in methanol containing sodium methylate decreases repidly with progress of the reaction, because CH_3O^- is consumped by the side reactions such as deacetylation or de-esterification; and that the methanolysis of lactone ring is smoothly performed in methanol containing triethylamine–acetic acid or sodium acetate, as a suitable CH_3O^- concentration in the reaction medium is kept throughout the reaction period.

Thus the bufferized methanol was proved as the suitable medium for selective methanolysis.

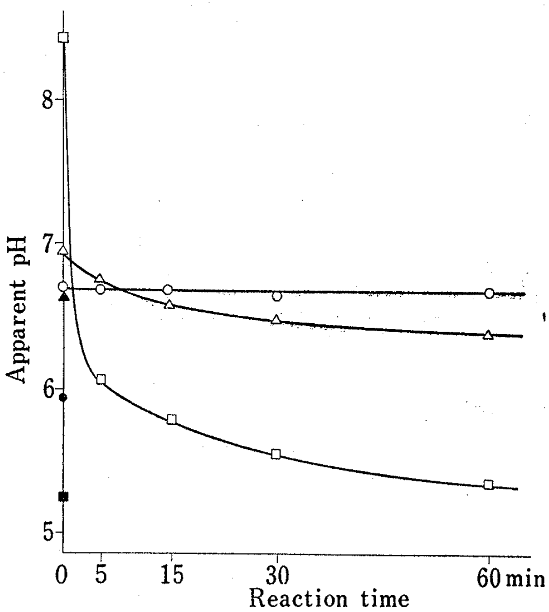


Fig. 7. Change of Apparent pH in the Reaction Mixtures

—○—: TEA 29.8 mM, AcOH 7.45 mM
—△—: AcONa 29.8 mM
—□—: CH_3ONa 0.596 mM
● : TEA 29.8 mM, AcOH 22.3 mM
▲ : AcONa 14.9 mM
■ : CH_3OH only

Experimental

All melting points are uncorrected. All evaporations were carried out under reduced pressure, keeping the bath temperature below 40°.

2,4-O-Benzylidene-D-glucaro-6,3-lactone 1-Methyl Ester (I)——This was prepared by Bird's method[9] and Ide's method.[10]

2,4-O-Benzylidene-5-O-acetyl-D-glucaro-6,3-lactone 1-Methyl Ester (II)——This was prepared from I by Ide's procedure[10] using pyridine and Ac_2O.

2,4-O-Benzylidene-5-O-propionyl-D-glucaro-6,3-lactone 1-Methyl Ester (III)——I (500 mg) was dissolved in pyridine (0.5 ml) and propionic anhydride (2.5 ml) under stirring without cooling, and after standing overnight at room temperature the solution was poured into ice–H_2O (20 ml) and the precipitate was collected. III: Yield, 500 mg (84%). Recrystallization from EtOH. mp 151.5—152.5°. $[\alpha]_D^{27}$ +164 (c=0.915, pyridine). *Anal.* Calcd. for $C_{17}H_{18}O_8$: C, 58.29; H, 5.18. Found: C, 58.33; H, 5.12. IR ν_{max}^{KBr} cm^{-1}: 1805, 1765—1775 (C=O).

2,4-O-Benzylidene-5-O-isobutyryl-D-glucaro-6,3-lactone 1-Methyl Ester (IV)——I (500 mg) was dissolved in pyridine (0.5 ml) and isobutyric anhydride (2.5 ml) under stirring without cooling, and treated with the similar procedure of III. IV: Yield. 500 mg (81%). Recrystallization from EtOH. mp 183—184°. $[\alpha]_D^{27}$ +163 (c=1.08, pyridine). *Anal.* Calcd. for $C_{18}H_{20}O_8$: C, 59.34; H, 5.53. Found: C, 59.41; H, 5.75. IR ν_{max}^{KBr} cm^{-1}: 1800, 1765 (C=O).

2,4-O-Benzylidene-5-O-benzoyl-D-glucaro-6,3-lactone 1-Methyl Ester (V)——I (500 mg) was suspended in pyridine (0.5 ml) and then benzoyl chloride (5 ml) was dropped under cooling. After 1 hr, the solution was poured into ice–H_2O (20 ml) and a few drops of $CHCl_3$ were added. The precipitate was collected. V: Yield, 500 mg (74%). Recrystallization from MeOH. mp 134—135°. $[\alpha]_D^{27}$ +180.4 (c=0.965, pyridine). *Anal.* Calcd. for $C_{21}H_{18}O_8$: C, 63.32; H, 4.55. Found: C, 63.22; H, 4.63. IR ν_{max}^{KBr} cm^{-1}: 1803, 1775, 1753 (C=O).

When the above crystals were recystallized from $CHCl_3$, needles of mp 109—110° and $[\alpha]_D^{27}$ +144 (c=1.02, pyridine) were obtained. *Anal.* Calcd. for $C_{21}H_{18}O_8 \cdot CHCl_3$: C, 51.01; H, 3.70. Found: C, 50.85; H, 3.64. IR ν_{max}^{KBr} cm^{-1}: 1800, 1770, 1740 (C=O).

Dimethyl 2,4-O-Benzylidene-D-glucarate (VI)——a) A suspension of I (500 mg) in dry MeOH (100 ml), dry triethylamine (0.42 ml) and AcOH (0.13 ml) was stirred at room temperature. After 30 to 60 min, the

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13) B. Tamura, *Bunseki Kagaku*, **16**, 193 (1967).

reaction mixture became clear and after 2 to 4 hr, the solution was deionized with dry Amberlite IR–120 (H form) and dry Amberlite IR–45 (OH form), concentrated to a syrup and poured into ice–H_2O. The precipitate was collected. VI: Yield, 400 mg (72%). Recrystallization from EtOH. mp 143—144°. $[\alpha]_D^{27}$ +72.6 (c=0.95, pyridine). *Anal.* Calcd. for $C_{15}H_{18}O_8$: C, 55.21; H, 5.56. Found: C, 55.40; H, 5.51. IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1760, 1740 (C=O). NMR ($CDCl_3$): τ 6.16 (6H, $COOCH_3$).

b) Using AcONa (122 mg) in place of triethylamine and AcOH, I (500 mg) was treated with the similar procedure of a) and VI (400 mg) was obtained. mp 143—144°.

c) II (500 mg) and $NaHCO_3$ or Na_2CO_3 (500 mg) were suspended in dry MeOH (20 ml) and stirred for 3 hr at room temperature. The clear solution was neutralized by addition of dry Amberlite IR–120 (H form) under stirring, concentrated to dryness, and extracted with $CHCl_3$. The $CHCl_3$ layer was concentrated and crystallized by addition of EtOH. Yield, 300 mg (62%). mp 143—144°.

I, II, III, IV or V (50 mg) and $NaHCO_3$ (50 mg) were suspended in dry MeOH (2 ml) and stirred for 3 hr at room temperature. The clear solution gave a large spot of *Rf* 0.35 indicating VI and a small spot of *Rf* 0.32 on a thin–layer chromatogram developed with toluene–acetone–EtOH (6:1:1) and sprayed with hydroxylamine–$FeCl_3$.

Dimethyl 2,4-O-Benzylidene-5-O-acetyl-D-glucarate (VII)——II (500 mg) was treated with the similar procedure of VI a) or b). VII: Yield, 400 mg (73%). Recrystallization from EtOH. mp 184.5—185.5°. $[\alpha]_D^{27}$ +34.3 (c=1.05, $CHCl_3$). *Anal.* Calcd. for $C_{17}H_{20}O_9$: C, 55.43; H, 5.47. Found: C, 55.30; H, 5.56. IR ν_{max}^{KBr} cm^{-1}: 3480 (OH), 1740—1750 (three peaks, C=O). NMR ($CDCl_3$): τ 7.86 (3H, $COCH_3$), 6.24, 6.18 (6H, $COOCH_3$), 4.86 (1H, doublet, $J_{4,5}$=9 cps, C_5–H).

Dimethyl 2,4-O-Benzylidene-5-O-propionyl-D-glucarate (VIII)——III (500 mg) was treated with the similar procedure of VI a) or b). VIII: Yield, 400 mg (73%). Recrystallization from EtOH. mp 147.5—148.5°. $[\alpha]_D^{27}$ +25.4 (c=0.907, $CHCl_3$). *Anal.* Calcd. for $C_{18}H_{22}O_9$: C, 56.54; H, 5.80. Found: C, 56.75; H, 5.64. IR ν_{max}^{KBr} cm^{-1}: 3480 (OH), 1735—1760 (three peaks. C=O).

Dimethyl 2,4-O-Benzylidene-5-O-isobutyryl-D-glucarate (IX)——IV (500 mg) was treated with the similar procedure of VI a) or b). IX: Yield, 400 mg (74%). Recrystallization from EtOH. mp 141.5—143°. $[\alpha]_D^{27}$ +52.2 (c=1.015, $CHCl_3$). *Anal.* Calcd. for $C_{19}H_{24}O_9$: C, 57.57; H, 6.10. Found: C, 57.21; H, 6.10. IR ν_{max}^{KBr} cm^{-1}: 3490 (OH), 1740—1760 (three peaks, C=O).

Dimethyl 2,4-O-Benzylidene-5-O-benzoyl-D-glucarate (X)——V (500 mg) was treated with the similar procedure of VI a) or b). X: Yield, 400 mg (74%). Recrystallization from EtOH. mp 180—181°. $[\alpha]_D^{27}$ 0 (c=0.975, $CHCl_3$). *Anal.* Calcd. for $C_{22}H_{22}O_9$: C, 61.39; H, 5.15. Found: C, 61.34; H, 5.07. IR ν_{max}^{KBr} cm^{-1}: 3470 (OH), 1750—1760 (two peaks, C=O), 1740 (C=O).

Dimethyl 2,4-O-Benzylidene-3,5-di-O-acetyl-D-glucarate (XI)——VI or VII (200 mg) was dissolved in pyridine (0.5 ml) and Ac_2O (2 ml) under stirring, and after standing overnight at room temperature, the solution was poured into ice–H_2O (20 ml) and the precipitate was collected. XI: Yield, 200 mg (90%). Recrystallization from EtOH. mp 150—151°. $[\alpha]_D^{27}$ +19.6 (c=1.02, $CHCl_3$). *Anal.* Calcd. for $C_{19}H_{22}O_{10}$: C, 55.61; H, 5.40. Found: C, 55.47; H, 5.56. IR ν_{max}^{KBr} cm^{-1}: 1755 (C=O). NMR ($CDCl_3$): τ 7.91, 7.87 (6H, $COCH_3$), 6.23 (6H, $COOCH_3$), 5.53 (1H, quartet, $J_{3,4}$=1.5 cps, $J_{4,5}$=9 cps, C_4–H), 5.27 (1H, doublet, $J_{2,3}$=1.5 cps, C_2–H), 4.88 (1H, doublet, $J_{4,5}$=9 cps, C_5–H), 4.52 (1H, triplet, $J_{2,3}$=$J_{3,4}$=1.5 cps, C_3–H).

Dimethyl 2,4-O-Benzylidene-3-O-acetyl-5-O-propionyl-D-glucarate (XII)——VIII (200 mg) was treated with the similar procedure of XI. XII: Yield, 200 mg (90%). Recrystallization from EtOH. mp 101.5—102.5°. $[\alpha]_D^{27}$ +12.1 (c=1.075, $CHCl_3$). *Anal.* Calcd. for $C_{20}H_{24}O_{10}$: C, 56.60; H, 5.70. Found: C, 56.82; H, 5.61. IR ν_{max}^{KBr} cm^{-1}: 1750—1770 (three peaks, C=O).

Dimethyl 2,4-O-Benzylidene-3-O-acetyl-5-O-isobutyryl-D-glucarate (XIII)——IX (200 mg) was treated with the similar procedure of XI. XIII: Yield, 200 mg (90%). Recrystallization from EtOH. mp 102—103°. $[\alpha]_D^{27}$ +11.3 (c=0.354, $CHCl_3$). *Anal.* Cacld. for $C_{21}H_{26}O_{10}$: C, 57.53; H, 5.98. Found: C, 57.60; H, 5.89. IR ν_{max}^{KBr} cm^{-1}: 1760—1780 (three peaks, C=O).

Dimethyl 2,4-O-Benzylidene-3-O-acetyl-5-O-benzoyl-D-glucarate (XIV)——X (200 mg) was treated with the similar procedure of XI. XIV: Yield, 200 mg (91%). Recrystallization from EtOH–H_2O. mp 75—78°. $[\alpha]_D^{27}$ −27.7 (c=1.01, $CHCl_3$). *Anal.* Calcd. for $C_{24}H_{24}O_{10}$: C, 61.02; H, 5.12. Found: C, 60.73; H, 5.13. IR ν_{max}^{KBr} cm^{-1}: 1740—1770 (C=O).

2,4-O-Benzylidene-5-O-*p*-tolylsulfonyl-D-glucaro-6,3-lactone 1 Methyl Ester (XV)[12]——I (500 mg) was suspended in pyridine (2 ml) and *p*-tolylsulfonyl chloride (500 mg) was added under stirring. After standing overnight at room temperature, the solution was poured into ice–H_2O and the precipitate was collected. XV: Yield, 600 mg (79%). Recrystallization from MeOH. mp 190—191°. $[\alpha]_D^{27}$ +119.6 (c=1.02, pyridine). *Anal.* Calcd. for $C_{21}H_{20}O_9S$: C, 56.25; H, 4.50. Found: C, 56 38; H, 4.65. IR ν_{max}^{KBr} cm^{-1}: 1808, 1770 (C=O).

Dimethyl 2,4-O-Benzylidene-5-O-*p*-tolylsulfonyl-D-glucarate (XVI)——a)[12] A suspension of XV (500 mg) are dry Amberlite IR–45 (OH form, 1 g) in dry MeOH (10 ml) was refluxed for a few hours. After the resin was removed, the solution was concentrated to a syrup and crystallized by addition of EtOH. XVI: Yield, 200 mg (37%). Recrystallization from EtOH. mp 166—168°. $[\alpha]_D^{27}$ +15.0 (c=0.267, $CHCl_3$). *Anal.* Calcd. for $C_{22}H_{24}O_{10}S$: C, 54.99; H, 5.03. Found: C, 55.27; H, 5.01. IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1755, 1740 (C=O).

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b) XV (500 mg) was treated with the similar procedure of VI a) or b). XVI: Yield, 500 mg (93%). mp 166—168°.

Dimethyl 2,4-O-Benzylidene-3-O-acetyl-5-O-*p*-tolylsulfonyl-D-glucarate (XVII)——XVI (200 mg) was dissolved in pyridine (1 ml) and Ac_2O (3 ml) under stirring and treated with the similar procedure of XI. XVII: Yield, 200 mg (92%). Recrystallization from MeOH. mp 171—172°. $[\alpha]_D^{27}$ -5.15 ($c=0.97$, $CHCl_3$). *Anal.* Calcd. for $C_{24}H_{26}O_{11}S$: C, 55.17; H, 5.02. Found: C, 55.32; H, 5.00. IR ν_{max}^{KBr} cm^{-1}: 1765 (C=O). NMR ($CDCl_3$): τ 7.98 (3H, $COCH_3$), 7.57 (3H, tolyl), 6.35, 6.27 (6H, $COOCH_3$), 5.58 (1H, quartet, $J_{3,4}=1.5$ cps, $J_{4,5}=9$ cps, C_4–H), 5.37 (1H, doublet, $J_{2,3}=1.5$ cps, C_2–H), 5.02 (1H, doublet, $J_{4,5}=9$ cps, C_5–H), 4.63 (1H, triplet, $J_{2,3}=J_{3,4}=1.5$ cps, C_3–H).

Dimethyl 2,4-O-Benzylidene-3-O-*p*-tolylsulfonyl-5-O-acetyl-D-glucarate (XVIII)——VII (500 mg) was treated with the similar procedure of XV. The crude product: 800 mg. Recrystallization from MeOH. XVIII: Yield, 600 mg (85%). mp 163.5—164.5°. $[\alpha]_D^{27}$ $+17.0$ ($c=1.18$, $CHCl_3$). *Anal.* Calcd. for $C_{24}H_{26}O_{11}S$: C, 55.17; H, 5.02. Found: C, 55.29; H, 4.96. IR ν_{max}^{KBr} cm^{-1}: 1765—1775 (three peaks, C=O). NMR ($CDCl_3$): τ 7.79 (3H, $COCH_3$), 7.59 (3H, tolyl), 6.25 (6H, $COOCH_3$), 5.58 (1H, quartet, $J_{3,4}=1.5$ cps, $J_{4,5}=9$ cps, C_4–H), 5.26 (1H, doublet, $J_{2,3}=1.5$ cps, C_2–H), 5.05 (1H, doublet, $J_{4,5}=9$ cps, C_5–H), 4.61 (1H, triplet, $J_{2,3}=J_{3,4}=1.5$ cps, C_3–H).

Methanolysis of 1,2-O-Isopropylidene-5-O-acetyl-D-glucofuranurono-6,3-lactone (XIX)——XIX (5 g) was dissolved in dry MeOH (100 ml), dry triethylamine (0.42 ml) and AcOH (0.13 ml) under stirring. After standing for 1 hr at room temperature, the solution was deionized by addition of dry Amberlite IR–120 (H form) and dry Amberlite IR–45 (OH form) and concentrated to a syrup. The obtained syrup was dissolved in benzene (10 ml), decolorized with Florizil and concentrated to a syrup. The crystals were obtained by addition of a small amount of toluene. Yield, 3 g (52%). Recrystallization from ether. mp 105—106°. IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1760 (C=O). The mixed melting point and the IR spectrum of the crystals were identical with those of XX, which was obtained by the treatment with methanol and Amberlite IR–45 (OH form).[8]

Methanolysis of II with Anion Exchange Resin——II (500 mg) and dry Amberlite IR–45 (OH form, 1 g) were suspended in dry MeOH (20 ml) and stirred for 24 hr at room temperature. No product was obtained and II (400 mg) was recovered.

Gas Chromatography——A suspension of II (5 mg) and a basic catalyst (a suitable amount) in dry MeOH (1 ml) was shaken at room temperature. XI (5 mg) as an internal standard, $CHCl_3$ and H_2O were added to the reaction mixture, extracted with $CHCl_3$ (a few times), dried over Na_2SO_4 and evaporated to dryness. The residue was dissolved in dry pyridine (0.5 ml) and then hexamethyldisilazane (0.2 ml) and trimethylchlorosilane (0.1 ml) were added to the solution. The mixed solution was warmed for 10 min at 60° and 1—2 μl of the solution was injected directly into the gas chromatograph. A Shimadzu GC–1C gas chromatograph equipped with a hydrogen flame ionization detector was used.

Measurement of Apparent pH——A 0.002% phenol red solution in methanol (1 ml) was diluted with phosphate buffer solution (pH 5—10) and filled up to 10 ml. The absorbance of the solutions was measured at 430 mμ and 560 mμ (A_{430} and A_{560} respectively). The absorbance ratio, $r=A_{560}/(A_{430}+A_{560})$, was calculated and was protted against pH. Using this working curve, apparent pH in the reaction mixture was measured.

Bromothymol blue (0.01%) was also used in place of phenol red, and the same results were obtained.

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