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Saponin and Sapogenol. XXIII.[1] Degradation of Methyl Glucuronide and Methyl Galacturonide by Lead Tetraacetate Oxidation followed by Alkali Treatment

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In a continuing study on the selective cleavage method for the β-D-glucuronide linkage contained in oligoglycoside, the behavior of methyl β-D- and α-D-glucuronides and methyl β-D- and α-D-galacturonides has been examined towards lead tetraacetate oxidation followed by alkali treatment. It has been found that the lead tetraacetate degradation method is a useful tool for cleavage of the α-D-glucuronide and β-D-galacturonide linkages as well as the β-D-glucuronide linkage. The α-D-galacturonide has been found to show considerable resistance for lead tetraacetate oxidation. In addition, the dialdehyde intermediate (**23**) in the reaction sequence has been shown to be a promissing species which is readily convertible to nitrocyclitols.

Keywords——methyl glucuronide; methyl galacturonide; lead tetraacetate oxidation; cleavage of uronide linkage; nitrocyclitol

During the course of studies on the selective cleavage method for a certain glycoside linkage contained in oligoglycoside, the following three methods have been found to be useful for selective cleavage of the β-D-glucuronide linkage which is directly attached to the aglycone in saponin. They are photolysis,[3] lead tetraacetate oxidation followed by alkali treatment,[4] and treatment with acetic anhydride and pyridine.[5]

Among these cleavage methods, the lead tetraacetate degradation[4] is effected for the methylated derivative of glucuronide-saponin[6] which preserves the free carboxyl function in the glucuronide moiety. It has been suggested to be useful for structure studies of not only glucuronide-saponins but also other types of glucuronides and polysaccharides containing the β-D-glucuronide linkage in their molecules. Futhermore, since several kinds of uronide linkages other than β-D-glucuronide are known to occur in nature, the application of the lead tetraacetate method to those uronide linkages seems to be of interest.

Prior to the application of the method to other uronide linkages which are contained in the carbohydrate chain, we have recently examined the behavior of methyl β-D- and α-D-glucuronides and methyl β-D- and α-D-galacturonides towards lead tetraacetate oxidation followed by alkali treatment. As described in the present paper, it has become clear that the lead tetraacetate method is conveniently applicable for cleavage of the α-D-glucuronide and β-D-galacturonide linkages as well as the β-D-glucuronide linkage.[7] On the other hand, methyl

1) Part XXII: I. Kitagawa, H. Yamanaka, T. Nakanishi, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **25**, 2430 (1977).
2) Location: *133–1, Yamada-kami, Suita, Osaka 565, Japan.*
3) *a*) I. Kitagawa, M. Yoshikawa, Y. Imakura, and I. Yosioka, *Chem. and Ind.*, **1973**, 276; *b*) I. Kitagawa, M. Yoshikawa, and I. Yosioka, *Tetrahedron Lett.*, **1973**, 3997; *c*) I. Kitagawa, M. Yoshikawa, Y. Imakura, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **22**, 1339 (1974).
4) *a*) I. Kitagawa, M. Yoshikawa, Y. Ikenishi, K.S. Im, and I. Yosioka, *Tetrahedron Lett*, **1976**, 549; *b*) I. Kitagawa, M. Yoshikawa, K.S. Im, and Y. Ikenishi, *Chem. Pharm. Bull.* (Tokyo), **25**, 657 (1977).
5) I. Kitagawa, Y. Ikenishi, M. Yoshikawa, and K.S. Im, *Chem. Pharm. Bull.* (Tokyo), **25**, 1408 (1977).
6) The abbreviation for a saponin which contains a β-D-glucuronide moiety directly attached to the sapogenol.
7) Presented at the 96th Annual Meeting of Pharmaceutical Society of Japan, Nagoya, April 1976. Abstract Paper II-275.

α-D-galacturonide has been found to show considerable resistance for lead tetraacetate oxidation presumably due to the steric congestion at C-5. In addition, it has been shown that a provisional dialdehyde intermediate (*e.g.* **23**) in the reaction sequence of the lead tetraacetate degradation[4] is a promissing species readily convertible to the cyclitol derivatives.

Degradation of Methyl β-D-Glucuronide Derivative (4)

Treatment of D-glucuronic acid (**1**) with methyl iodide (CH_3I)–dimethyl sulfoxide (DMSO)–sodium hydride (NaH)[8] furnished two isomers: methyl (methyl 2,3,4-tri-O-methyl-β-D-glucopyranosid)uronate (**2**)[9] and methyl (methyl 2,3,4-tri-O-methyl-α-D-glucopyranosid)uronate (**3**).[10] Potassium carbonate hydrolysis of the β-isomer (**2**) yielded methyl 2,3,4-tri-O-methyl-β-D-glucopyranosiduronic acid (**4**)[11] which was the starting substance for the degradation. Treatment of **4** with lead tetraacetate in benzene under reflux furnished four reaction products: **5** (42%), **6** (30%), **7** (5%), and **8** (3%).

The major product (**5**) possesses one acetoxyl and four methoxyls as shown by its infrared (IR) (1770, 1223 cm^{-1}) and proton magnetic resonance (PMR) spectra (both taken in carbon tetrachloride (CCl_4)). The PMR spectrum also shows the signals due to the anomeric proton (δ 4.27, m) and 5-H (δ 5.42, m) which attaches to a carbon bearing an acetoxyl. Since the signal patterns of 1-H and 5-H were rather complicated probably due to the virtual long-range coupling,[4,12] the PMR pectrum of **5** was taken in hexadeutero (d_6-) acetone. The signals due to 1-H and 5-H are then observed at δ 4.44 and δ 5.57 as a doublet respectively (J=7 Hz), which indicate the axial character of both protons. In the mass spectrum (MS) of **5**, the characteristic fragment ion peaks are observed at *m/e* 233 (**i**), 205 (**ii**), 101 (**iii**), and 88 (**iv**, base peak). Based on these findings, the major product has been assigned **5** having an equatorial acetoxyl at C-5 (in the $^4C_1$ conformation[13]).

The second major product (**6**) is an isomer of **5**. It possesses one acetoxyl and four methoxyls as **5** (IR and PMR). Although the signal due to the anomeric proton of **6** is observed at δ 4.40 as a doublet of J=7 Hz, the signal due to 5-H (geminal to the acetoxyl function) is observed at δ 6.17 as a doublet of smaller J value (4 Hz). Based on these physical properties, together with the mass spectrum of **6** which shows the similar fragment ion peaks as that of **5**, the structure of the second major product has been clarified as **6** which carries an axial 5α-acetoxyl (in the $^4C_1$ conformation).

One of the minor product (**7**), $C_{19}H_{34}O_{12}$ (M^+: *m/e* 454), is a dimeric ester (IR: 1772 cm^{-1} in CCl_4). The PMR spectrum of **7** lacks the acetoxyl signal but shows the signals due to eight methoxyls and two anomeric protons at δ 4.11 (d, J=7 Hz) and δ 4.33 (d, J=6 Hz). It also shows a doublet (J=7 Hz) at δ 5.54 which is ascribable to an axial proton attached to a carbon (C-5) carrying an oxygen function in the ester group. Based on these findings, the structure (**7**) has been assigned to the product which is formed probably *via* a β-side attack of **4** to the carbonium cation (**v**) derived from **4** during the lead tetraacetate treatment.[14] In contrast, it is noted here that for the formation of **5** or **6**, the acetoxyl anion is considered to attack at C-5 of **v** either from the β-side or the α-side. A fragment ion of *m/e* 353 observed

8) S. Hakomori, *J. Biochem.* (Tokyo), **55**, 205 (1964).

9) G.O. Aspinall and P.E. Barron, *Can. J. Chem.*, **50**, 2203 (1972).

10) F. Smith, *J. Chem. Soc.*, **1951**, 2646.

11) *a*) F. Smith, M. Stacey, and P.I. Wilson, *J. Chem. Soc.*, **1944**, 131; *b*) S.W. Challinor, W.N. Haworth, and E.L. Hirst, *J. Chem. Soc.*, **1931**, 258.

12) *a*) J.I. Musher and E.J. Corey, *Tetrahedron*, **18**, 791 (1962); *b*) I. Yosioka, K. Imai, Y. Morii, and I. Kitagawa, *ibid.*, **30**, 2283 (1974).

13) Rules for Conformation Nomenclature for Five- and Six-membered Rings in Monosaccharides and their Derivatives. *J. Chem. Soc. Chem. Comm.*, **1973**, 505.

14) For the carbonium cation formation, *cf.* A.L.J. Beckwith, R.T. Cross, and G.E. Gream, *Aust. J. Chem.*, **27**, 1673 (1974).

in the mass spectrum of **7** constitutes an additional evidence for the structure and may be expressed as **vi** (Chart 2).[15]

The fourth minor product (**8**) is also a dimeric ester (IR and M^+) and is isomeric to **7**. The PMR spectrum of **8** shows the signals due to eight methoxyls and two anomeric protons (δ 4.14, d, J=7 Hz, and δ 4.46, d, J=8 Hz). However, the signal due to 5-H in **8** is observed at δ 6.24 as a narrower doublet (J=3 Hz) as compared with that of 5-H in **7**. Based on these findings together with the mass fragmentation pattern (giving **ii, iii, iv,** and **vi**), the structure (**8**) has become reasonable for the product which may be formed *via* the α-side attack of **4** to **v**.

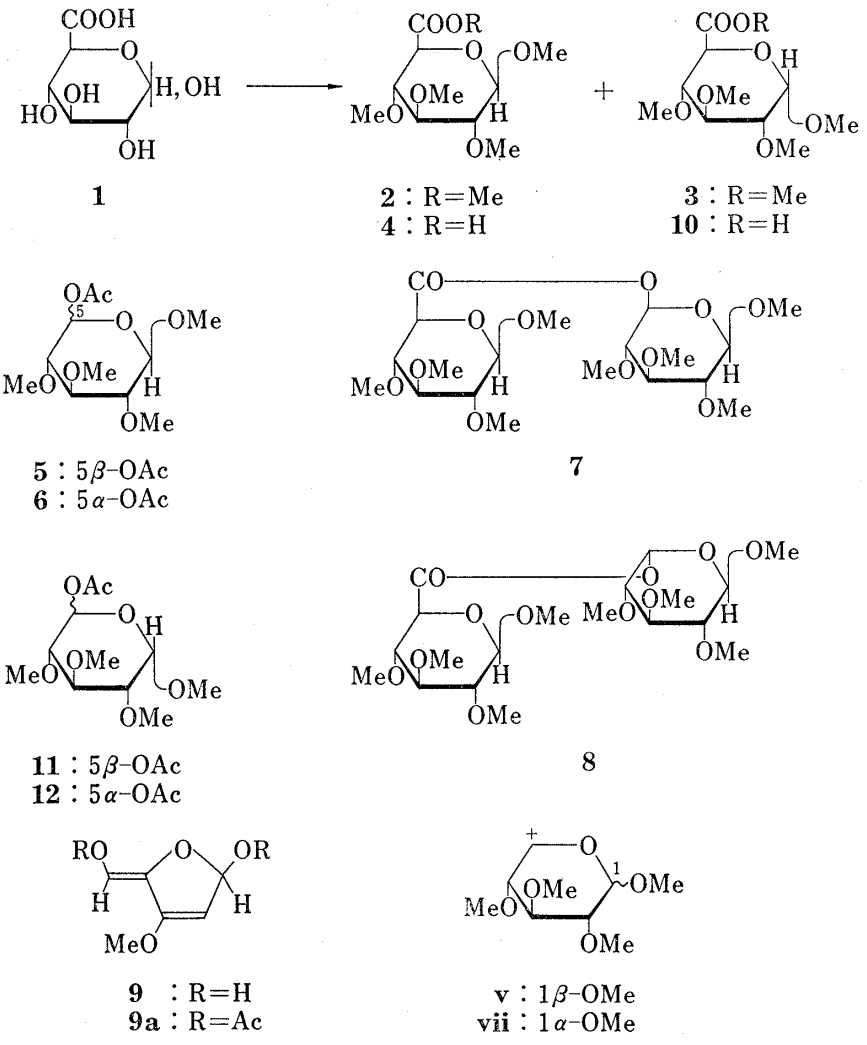

Chart 1

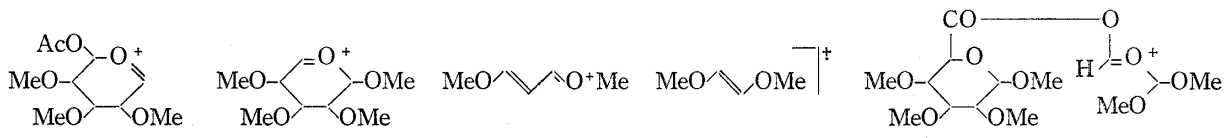

Chart 2. The Elemental Compositions of **i, ii,** and **vi** were confirmed by High Resolution Mass Spectrometry

15) For the analogous formulation, *cf.* J. Lönngren and S. Svensson, *Advan. Carbohyd. Chem. and Biochem.*, **29**, 41 (1974).

Next, the alkali degradation of these four products was carried out. Treatment of **5** and **6**, respectively, with 0.2 N sodium methoxide in methanol at room temperature for 10 minutes afforded a dienic product (**9**). In order to facilitate the purification, it was acetylated. The diacetate commonly obtained (69% from **5** and 73% from **6**) has been found to be identical to **9a** which was previously obtained in the lead tetraacetate degradation of glucuronide-saponin.[4] In the case of **7** and **8**, the similar methanolic alkaline treatment followed by acetylation furnished **2** and **9a**, respectively, thus the structures (**7** and **8**) being further substantiated.

As is apparent from the above-mentioned evidence, on the alkaline treatment of **5** and **6**, the methoxyls at C-2 and C-4 are readily eliminated during the reaction pathway to furnish the diene (**9**) (*cf.* Chart 4). It should be pointed out here that any dimeric ester like **7** or **8** was not obtained in the lead tetraacetate oxidation of glucuronide-saponin,[4] probably due to the steric congestion.

Degradation of Methyl α-D-Glucuronide Derivative (10)

The behavior of methyl α-D-glucuronide derivative (**10**) towards the lead tetraacetate degradation has been examined. The α-D-glucuronide (**3**), which was obtained above from **1**, was hydrolyzed with aqueous potassium carbonate to afford methyl 2,3,4-tri-O-methyl-α-D-glucopyranosiduronic acid (**10**). Treatment of **10** with lead tetraacetate as for **4** furnished two products: **11** (36%) and **12** (24%). No dimeric ester was obtained in this case presumably due to the more steric congestion at C-5 in **vii** than in **v**.[14]

The major product (**11**) possesses one acetoxyl (IR and PMR) and four methoxyls (PMR). The PMR spectrum of **11** shows the signals assignable to the β-equatorial anomeric proton (δ 4.61, d, J=4 Hz) and 5α-axial proton (δ 5.55, d, J=8 Hz). The mass spectrum of **11** shows the fragment ion peaks which are respectively assignable to **i**, **ii**, **iii**, and **iv**, thus the structure (**11**) being substantiated for the product (in the $^4C_1$ conformation).

The minor product has been assigned as **12**, which corresponds to the C-5 epimer of **11**, on the similar physicochemical basis as for **11**. However, in the PMR spectrum of **12**, the anomeric proton signal is observed as a singlet at δ 4.69, while the 5β-H signal is found at δ 5.65 as a doublet of J=6 Hz. These signal features suggest that **12** may be in the twisted $^4C_1$ conformation which is presumably brought about by the 1,3-diaxial interaction of 1α-methoxyl and 5α-acetoxyl in **12**.

Alkali treatment followed by acetylation of **11** and **12** respectively furnished the dienic diacetate (**9**) in a good yield. Consequently, it is favorably reasoned that the α-D-glucuronide linkage in the carbohydrate chain may be also cleaved by the lead tetraacetate degradation method similarly as in the case of the β-D-glucuronide linkage. In the other words, it has become clear that there is no distinct difference in the behavior of **5**, **6** (1β-methoxyl derivatives) and **11**, **12** (1α-methoxyl derivatives) towards the alkali treatment.

Degradation of Methyl β-D-Galacturonide Derivative (18)

Methylation of D-galacturonic acid (**13**) as for **1**[8] furnished four products: methyl (methyl 2,3,5-tri-O-methyl-β- and -α-D-galactofuranosid)uronate (**14**,[16] **15**) and methyl (methyl 2,3,4-tri-O-methyl-β- and -α-D-galactopyranosid)uronate (**16**,[17] **17**[18]). The structures of these products have been assured on the basis of their physical properties (IR, PMR, and specific rotations) (see Experimental). In addition, **16** and **17** were respectively converted to methyl 2,3,4-tri-O-methyl-β- and -α-D-galactopyranoside by lithium aluminum hydride ($LiAlH_4$) reduction. Aqueous potassium carbonate hydrolysis of **16** gave methyl 2,3,4-tri-O-methyl-β-

16) S. Luckett and F. Smith, *J. Chem. Soc.*, **1940**, 1106.
17) S. Luckett and F. Smith, *J. Chem. Soc.*, **1940**, 1506.
18) P.A. Levene and L.C. Kreider, *J. Biol. Chem.*, **120**, 597 (1937).

D-galactopyranosiduronic acid (**18**). Treatment of **18** with lead tetraacetate as for **4** and **10** yielded an acetate (**19**) as a single product in a 73% yield.

The IR and PMR spectra of **19** show the presence of one acetoxyl and four methoxyls. The signals due to the anomeric proton and 5-H in the PMR spectrum (in CCl_4) are observed at δ 4.35 (m) and δ 5.98 (d, J=3 Hz), respectively, while those in the PMR spectrum taken in d_6-acetone are observed at δ 4.49 (d, J=7 Hz) and δ 6.05 (d, J=3 Hz). It follows therefore that the complicated signal pattern of the anomeric proton (in CCl_4) is attributable to the virtual long-range coupling.[4,12] These physical properties along with the mass spectrum of **19**, which gives the fragment ion peaks (**i**, **ii**, **iii**, and **iv**), have led to the structure assignment (**19**) (taking the $^4C_1$ conformation) for the product. The selective formation of the 5α-acetoxyl derivative (**19**) is probably due to the selective α-side attack of the acetoxyl anion at C-5 presumably due to the presence of 4β-methoxyl. On treatment with alkali followed by acetylation, **19** was converted to the dienic diacetate (**9a**) as expected, thus it has been demonstrated that the β-D-galacturonide linkage in the carbohydrate chain may be cleaved by the lead tetraacetate degradation method.

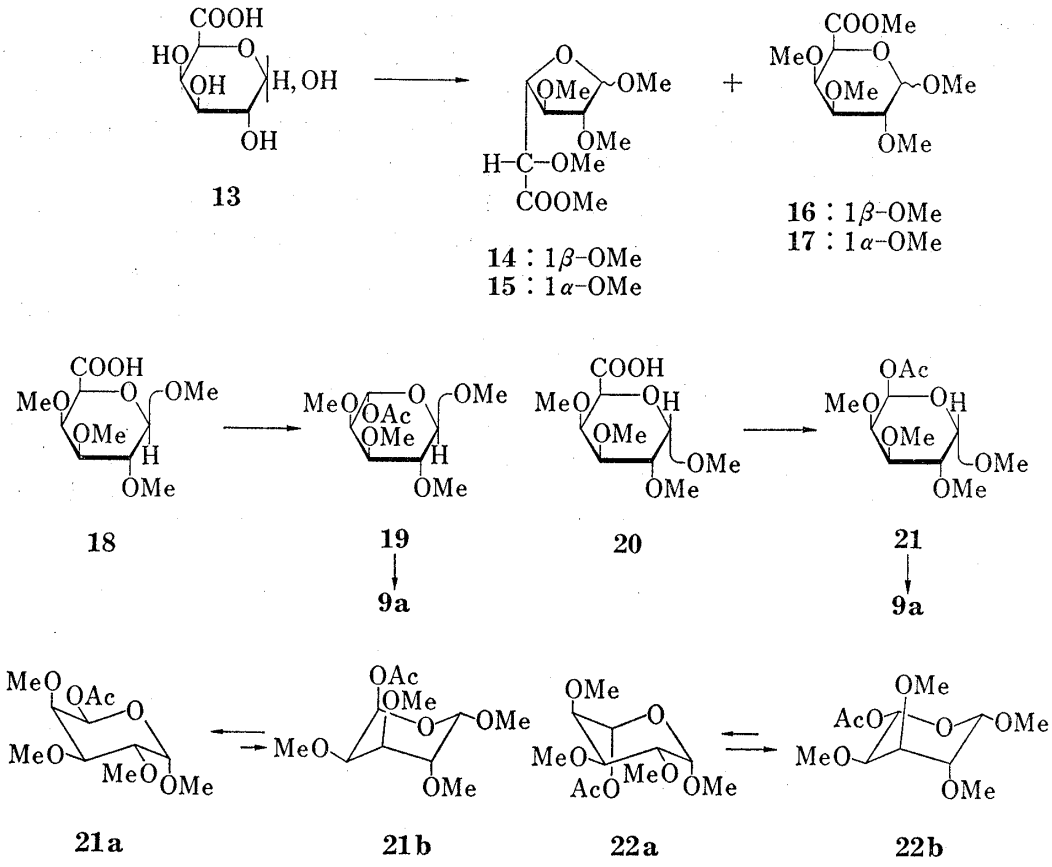

Chart 3

Degradation of Methyl α-D-Galacturonide Derivative (20)

Alkaline treatment of the α-D-galacturonide (**17**) gave methyl 2,3,4-tri-O-methyl-α-D-galactopyranosiduronic acid (**20**) which was subjected to lead tetraacetate oxidation. However, **20** showed considerable resistance for the oxidation. Finally, it has been found that treatment of **20** with large excess of lead tetraacetate and with prolonged heating under reflux results in the formation of a small amount of an acetate (**21**) (7.1%) with a recovery of most of the starting acid (**20**) (81.9%). Therefore, it has been inferred that the steric hindrance caused by both 1α- and 4β-methoxyls may be responsible for such less reactivity of 5β-carboxyl in **20** for lead tetraacetate.

The acetate (**21**) thus obtained possesses one acetoxyl and four methoxyls as shown by the IR and PMR spectra. The mass spectrum of **21** shows the same fragment ion peaks (**i, ii, iii,** and **iv**) as were observed in the mass spectra of **5, 6, 11, 12,** and **19,** although the molecular ion was not detected. In the PMR spectrum of **21**, the signals due to the anomeric proton and 5-H (geminal to an acetoxyl) are respectively observed at δ 4.68 (d, J=3 Hz) and δ 5.79 (d, J=4 Hz) with small coupling constants. If the 5α-acetoxyl structure has been presumed for the acetate (**21**), the Dreiding model examinations suggest that the $^1C_4$ conformer (**22b**) is more favored than the $^4C_1$ conformer (**22a**). However, **22b** would not be consistent with the PMR data of **21** mentioned above. On the other hand, if the 5β-acetoxyl structure has been assigned to the acetate (**21**), both $^4C_1$ and $^1C_4$ conformers (**21a, 21b**) would satisfy the PMR data of **21** although **21a** seems to be more favored than **21b** on the basis of the Dreiding model inspections. Consequently, the structure **21** has become reasonable for the acetate.

Treatment of **21** with sodium methoxide in methanol followed by acetylation furnished the dienic diacetate (**9a**) in a good yield. It has become clear therefore that, for cleavage of the α-D-galacturonide linkage by the lead tetraacetate method, the substitution of 5-carboxyl with an acetoxyl is a critical step. We are currently searching for the other degradation method which is suitable for cleavage of the α-D-galacturonide linkage.

As the conclusion so far, both methyl D-glucuronide and methyl D-galacturonide have been found to be readily decomposed by the present lead tetraacetate method and to afford the diene (**9**) although the reactivity and the reaction products are somewhat diverse. The reaction pathway have been presumed to proceed as shown in Chart 4, which are analogous to those presented for the degradation of glucuronide-saponins.[4]

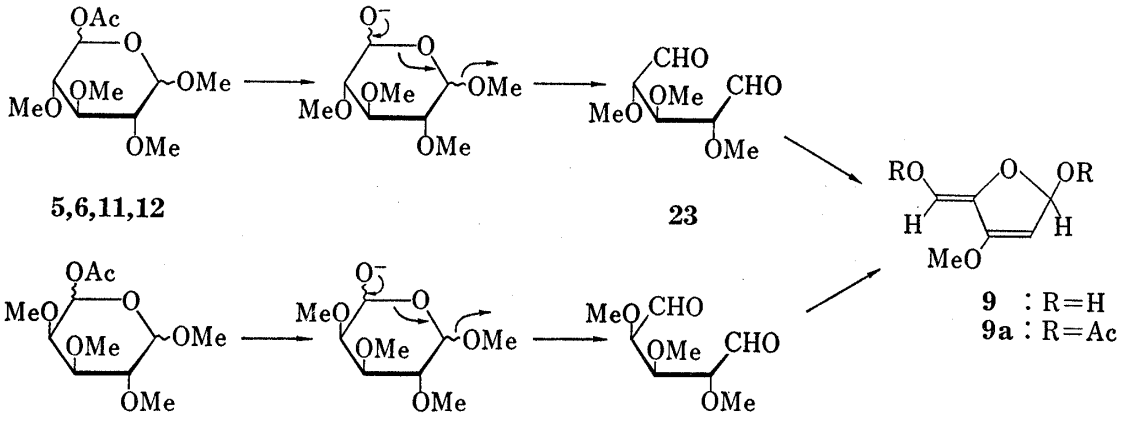

Chart 4

Conversion of D-Glucuronic Acid to Nitrocyclitols

In order to define the reaction pathway mentioned above (Chart 4), the isolation of the dialdehyde intermediate (**23** or **24**) has been attempted. However, because of instability of these dialdehydes in the alkaline medium and also the ready conversion to the diene (**9**), all the attempts for the isolation of the dialdehydes (**23, 24**) were without success. Next, our attention has been focused on trapping the dialdehyde through conversion to any isolable derivative, and nitromethane has been chosen as the trapping reagent.[19]

When the methanolic solution of **5** was treated with sodium methoxide and nitromethane, three cyclization products (**25, 27, 29**) were formed together with the diene (**9**). After examina-

19) *a*) H.H. Baer, *Advan. Carbohyd. Chem.*, **24**, 67 (1969); *b*) F.W. Lichtenthaler, "Methods in Carbohydrate Chemistry," Vol. VI, ed. by R.L. Whistler and J.N. BeMiller, Academic Press, New York and London, 1972, p. 250.

tions of various alkaline conditions (see Experimental), the addition order of sodium methoxide and nitromethane has been found to be important especially for avoiding the formation of the diene (**9**). Thus, the acetate (**5**) was dissolved in nitromethane first and the solution was treated with 1N sodium methoxide in methanol at 4° for 12 hours to furnish three crystalline products: **25** (25%), **27** (30%), and **29** (12%).

The IR spectrum of the second major product (**25**) shows the presence of hydroxyl (3430 cm^{-1}) and nitro group (1560, 1345 cm^{-1}). The PMR spectrum shows the signals due to three methoxyls and a triplet (J=10 Hz) at δ 4.43 which is attributable to a proton attached to a carbon bearing a nitro group. The coupling pattern of the latter proton suggests the equatorial character of the nitro group. Acetylation of **25** with acetic anhydride and concentrated sulfuric acid[20] furnished the diacetate (**26**). The IR spectrum of **26** lacks the hydroxyl absorption band, but shows the absorption bands of acetoxyl and nitro group. The PMR spectrum of

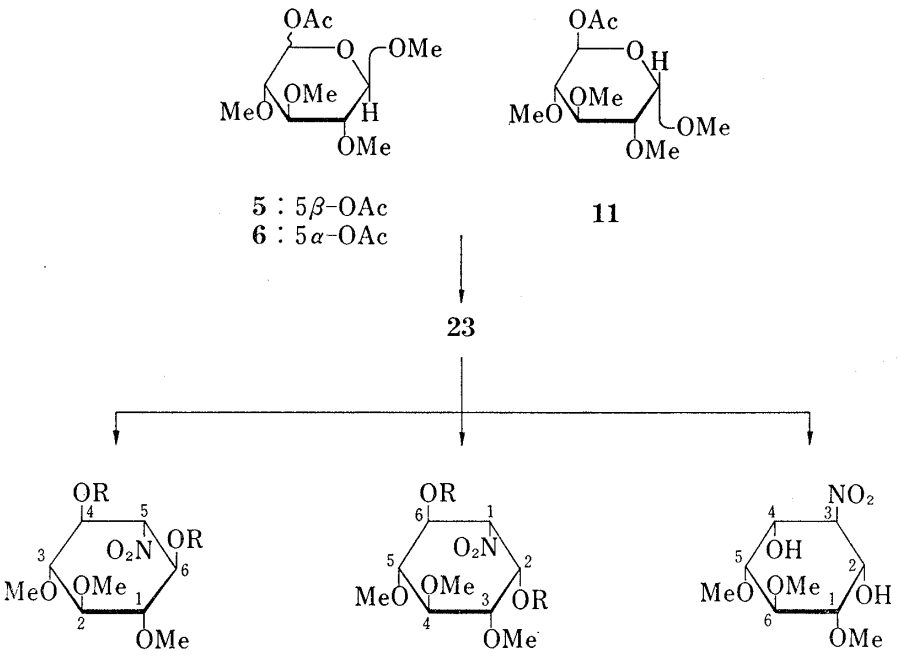

Chart 5

Table I. Spin-Decoupling Experiments of **26**[a]

Decoupled proton (δ)	Irradiated at δ		
	3.25 (1-H, 3-H)	4.60 (5-H)	5.45 (4-H, 6-H)
1-H, 3-H (3.25, 2H, m)	—		Deformed[b]
5-H (4.60, 1H, t, J=10 Hz)		—	Singlet
4-H, 6-H (5.45, 2H, br.t, J=*ca.* 10 Hz)	Doublet (J=10 Hz)	Broad doublet (J=*ca.* 10 Hz)	—

a) Abbreviations: br.t=broad triplet, d.d=doublet of doublet, m=multiplet, t=triplet.
b) The coupling pattern is unclear due to the overlapping with the signal of 2-H.

20) F.W. Lichtenthaler and H.O.L. Fisher, *J. Am. Chem. Soc.*, **83**, 2005 (1961). Acetylation in the basic medium (*e.g.* in pyridine, *etc.*) results in the concomitant dehydration and the elimination of the nitro group.

26 shows the signals due to three methoxyls and two acetoxyls at δ 2.09 (6H, s), the chemical shift of the latter suggests the equatorial character of the acetoxyls.[21] The PMR spectrum also shows a triplet (J=10 Hz) at δ 4.60 due to a proton which attaches to the same carbon as the nitro group and a two-proton broad triplet (J=*ca.* 10 Hz) due to two protons which are respectively geminal to an acetoxyl. The disposition of the substituents in **26** has been elucidated by the spin-decoupling experiments as shown in Table I. Based on the accumulated evidence mentioned above, the second major product has been clarified to be 5-deoxy-1,2,3-tri-O-methyl-5-nitro-*scyllo*-inositol (**25**)[22] whose substituents are all equatorial.

The major product (**27**) also possesses hydroxyls, nitro groups, and three methoxyls (IR, PMR) as **25**. Acetylation of **27** gave the diacetate (**28**), which lacks the hydroxyl absorption band but shows the acetoxyl and the nitro group absorption bands in the IR spectrum. The PMR spectrum shows the signals due to an equatorial acetoxyl (δ 2.07) and an axial acetoxyl (δ 2.11)[21] together with the signals of three methoxyls. It also shows a one-proton doublet of doublet (δ 4.64, J=2 and 10 Hz) which is ascribable to a proton on a carbon bearing a nitro group, a one-proton doublet of doublet (δ 5.83, J=9 and 10 Hz) due to a proton which is geminal to an equatorial acetoxyl, and a one-proton doublet of doublet (δ 6.01, J=2 and 2 Hz) due to a proton which is geminal to an axial acetoxyl. The assignments of these protons have been assured by the spin-decoupling experiments as given in Table II. Based on these findings and optical inactivity of **27**, the major product has been elucidated to be DL-1-deoxy-3,4,5-tri-O-methyl-1-nitro-*myo*-inositol (**27** and the antipode).[22]

Table II. Spin-Decoupling Experiments of **28**

Decoupled proton (δ)	Irradiated at δ			
	4.64 (1-H)	6.01 (2-H)	3.32 (3-H, 5-H)	5.83 (6-H)
1-H (4.64, 1H, d.d, J=2, 10 Hz)	—	Doublet (J=10 Hz)		Doublet (J=2 Hz)
2-H (6.01, 1H, d.d, J=2, 2 Hz)	Doublet (J=2 Hz)	—	Doublet (J=2 Hz)	
3-H, 5-H (3.32, 2H, m)		Deformed[a]	—	Deformed[a]
6-H (5.83, 1H, d.d, J=9, 10 Hz)	Doublet (J=9 Hz)		Doublet (J=10 Hz)	—

a) The coupling pattern is unclear due to the overlapping with the signal of 4-H.

The IR spectrum of the minor product (**29**) shows the presence of hydroxyl and nitro group as in **25** and **27**. In the PMR spectrum of **29**, in addition to the signals of three methoxyls, are observed a two-proton doublet of doublet (J=3 and 3 Hz) at δ 3.64 and a one-proton triplet (J=3 Hz) at δ 3.84, which are respectively assignable to a proton attached to a carbon bearing a methoxyl. The PMR spectrum also shows a two-proton doublet of doublet (J=3 and 10 Hz) at δ 4.06 due to the carbinyl protons and a one-proton triplet at δ 4.70 (J=10 Hz) due to a proton attached to a carbon bearing a nitro group. Based on these physical properties, **29** has been revealed to possess two equatorial hydroxyls, one equatorial nitro group, and three axial methoxyls. The structure of the minor product has now been elucidated to be 3-deoxy-1,5,6-tri-O-methyl-3-nitro-*muco*-inositol (**29**).[22]

Based on these nitrocyclitol formations, the presence of the dialdehyde intermediate (*e.g.* **23**) in the reaction pathway from **5** to **9** (Chart 4) has been defined. Since the conversion of the dialdehyde intermediate to nitrocyclitols mentioned above seems to be a potential process

21) *a*) F.W. Lichtenthaler and P. Emig, *Tetrahedron Lett.*, **1967**, 577; *b*) *Idem*, *Carbohyd. Res.*, **7**, 121 (1968).

22) IUPAC Commission on the Nomenclature of Organic Chemistry and IUPAC-IUB Commission of Biochemical Nomenclature. *European J. Biochem.*, **5**, 1 (1968).

for general transformation from uronic acids leading to nitrocyclitols which could be readily convertible to aminocyclitols, the similar conversions of **6** and **11** using nitromethane as the trapping reagent were carried out.

Table III. Comparison of the Reaction Products obtained from **5**, **6**, and **11** (monitored by GLC)[a]

Starting compounds	Products (%)		
	25	**27**	**29**
5	32(25)[b]	35(30)	20(12)
6	29(23)	36(31)	21(13)
11	32(29)	38(33)	20(16)

a) The percentages are based on the GLC analyses of the trimethylsilyl derivatives of **25**, **27**, and **29**.
b) The percentage yields given in the parentheses are based on the isolated products.

It has been found that, under the similar reaction conditions as for **5**, **6** gave **25** (23%), **27** (31%), and **29** (13%), and **11** gave **25** (29%), **27** (33%), and **29** (16%), respectively. The yields of reaction products obtained from **5**, **6**, and **11** were compared by monitoring with gas–liquid chromatography (GLC). As shown in Table III, the conversions have been revealed to proceed regardless of the configurations of 5-acetoxyl and 1-methoxyl in the starting compounds (**5**, **6**, **11**) and to furnish the dialdehyde as the common intermediate which is readily transformed to nitrocyclitols by nitromethane. Conversions of uronic acid derivatives to the other types of cyclitols are currently under investigation in our laboratory.

Experimental[23]

Methylation of D-Glucuronic Acid (1) giving 2 and 3——To a solution of **1** (2 g) in DMSO (10 ml) was added dimsyl carbanion (20 ml) (prepared from 1 g of NaH and 20 ml of DMSO)[4b] under a nitrogen atmosphere. After stirring at room temperature for one hour, the mixture was treated with CH_3I (15 ml) and kept stirring overnight in the dark. The reaction mixture was poured into ice-water, and extracted with ether. The ether extract was then decolorized with aq. 10% $Na_2S_2O_3$, washed with water, and dried over $MgSO_4$. The syrupy residue, obtained by evaporation of ether, was dissolved in benzene and chromatographed on silica gel (100 g). Elution with a benzene–acetone mixture (increasing order of the polarity) gave **2** (600 mg, 22%) and **3** (400 mg, 15%). **2**, colorless needles of mp 51° (recryst. from ether), $[\alpha]_D^{21}$ −34.0° (c=1.5, MeOH). IR ν_{max}^{Nujol} cm^{-1}: no OH, 1759 (COOMe), 1097 (C–O–C). PMR (90 MHz, $CDCl_3$, δ): 3.46, 3.50, 3.52, 3.58 (3H each, all s, $OCH_3\times4$), 3.78 (3H, s, $COOCH_3$), 4.23 (1H, d, J=7 Hz, 1-H). lit.[10] mp 52—53° (light petroleum), $[\alpha]_D$ −36.4°. IR ν_{max}^{Nujol} cm^{-1}: 1750, PMR ($CDCl_3$, δ): 3.43, 3.47, 3.50, 3.55 (3H, each, all s), 3.75 (3H, s), 4.12 (1H, d, J=7 Hz). **3**, colorless oil, $[\alpha]_D^{21}$ +149.0° (c=1.0, MeOH) (lit.[11] $[\alpha]_D^{26}$ +156° (c=2.0, MeOH)). IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1759 (COOMe), 1102 (C–O–C). PMR (CCl_4, δ): 3.38, 3.40, 3.41, 3.52 (3H each, all s, $OCH_3\times4$), 3.72 (3H, s, $COOCH_3$), 4.67 (1H, d, J=3 Hz, 1-H).

Alkaline Hydrolysis of 2 giving 4——A solution of **2** (370 mg) in MeOH (20 ml) was treated with aq. 10% K_2CO_3 (10 ml) and heated under reflux for 2 hr. After removing MeOH under reduced pressure, the reaction mixture was made weakly acidic with aq. 1 N HCl and extracted with ether. The ether extract was dried over $MgSO_4$ and evaporated to dryness to give **4** (340 mg, 97%). Crystallization from ether–CCl_4 furnished the analytical sample of **4** as colorless needles (250 mg) of mp 138—139° (lit.[12a] 137° (ether–light petroleum)), $[\alpha]_D^{20}$ −58.0° (c=1.8, $CHCl_3$) (lit.[12b] $[\alpha]_D^{21}$ −63° (c=0.6, $CHCl_3$)). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1767, 1735 (COOH). PMR ($CDCl_3$, δ): 3.51 (9H, s), 3.58 (3H, s) ($OCH_3\times4$), 4.21 (1H, d, J=7 Hz, 1-H), 8.88 (1H, br.s, $W_{h/2}$=9 Hz, exchangeable with D_2O, COOH).

Lead Tetraacetate Oxidation of 4 giving 5, 6, 7, and 8——To a solution of **4** (250 mg, 1 mmol) in benzene (20 ml) was added $Pb(OAc)_4$ (1.6 g, 3.6 mmol), and the total mixture was heated under reflux for 5 hr. After cooling, the mixture was diluted with a large quantity of ether and washed with water. The organic layer

23) The instruments used for obtaining the physical data and the experimental conditions for chromatography were same as in our previous paper[1] unless specified otherwise. The specific rotations were taken with JASCO DIP-181 Digital Polarimeter. The pH was determined by using Toyo Universal pH Test-paper.

was concentrated and the residue was purified by preparative thin-layer chromatography (TLC) (hexane–ether=1:5) to furnish **5** (110 mg, 42%), **6** (78 mg, 30%), **7** (25 mg, 5%), and **8** (13 mg, 3%). **5**, colorless needles of mp 50—50.5° (recryst. from ether–CCl_4), $[\alpha]_D^{21}$ −12.0° (c=1.2, $CHCl_3$). High resolution MS: Calcd. for $C_{11}H_{20}O_7$ (M^+), 264.121; Found: 264.120. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770, 1223 (OAc). PMR (CCl_4, δ): 2.07 (3H, s, $OCOCH_3$), 3.41 (3H, s), 3.46 (6H, s), 3.51 (3H, s) ($OCH_3\times4$), 4.27 (1H, m, signal width=7 Hz, 1-H), 5.42 (1H, m, signal width=7 Hz, 5-H). PMR (d_6-acetone, δ): 2.08 (3H, s, $OCOCH_3$), 3.39, 3.45, 3.47, 3.52 (3H each, all s, $OCH_3\times4$), 4.44 (1H, d, J=7 Hz, 1-H), 5.57 (1H, d, J=7 Hz, 5-H). MS m/e (%): 264 (M^+, 0.3), 233 (**i**, 1), 205 (**ii**, 5), 101 (**iii**, 19), 88 (**iv**, 100). **6**, colorless oil, $[\alpha]_D^{21}$ −127.9° (c=1.1, $CHCl_3$). High resolution MS: Calcd. for $C_{11}H_{20}O_7$ (M^+), 264.121; Found: 264.120. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1764, 1228 (OAc). PMR (CCl_4, δ): 2.09 (3H, s, $OCOCH_3$), 3.41 (6H, s), 3.48, 3.52 (3H each, both s) ($OCH_3\times4$), 4.40 (1H, d, J=7 Hz, 1-H), 6.17 (1H, d, J=4 Hz, 5-H). MS m/e (%): 264 (M^+, 0.2), 233 (**i**, 1), 205 (**ii**, 6), 101 (**iii**, 18), 88 (**iv**, 100). **7**, colorless needles of mp 83—85° (recryst. from ether–CCl_4), $[\alpha]_D^{21}$ −45.0° (c=1.3, $CHCl_3$). High resolution MS: Calcd. for $C_{19}H_{34}O_{12}$ (M^+) 454.205; Found: 454.205, Calcd. for $C_{14}H_{25}O_{10}$ (**vi**) 353.145; Found: 353.145. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1772 (–COO–), 1098 (C–O–C). PMR (CCl_4, δ): 3.41 (3H, s), 3.46 (6H, s), 3.48 (9H, s), 3.52, 3.55 (3H each, both s) ($OCH_3\times8$), 4.11 (1H, d, J=7 Hz), 4.33 (1H, d, J=6 Hz) (1-H, 1′-H), 5.54 (1H, d, J=7 Hz, 5-H). MS m/e (%): 454 (M^+, 0.1), 353 (**vi**, 2), 205 (**ii**, 11), 101 (**iii**, 60), 88 (**iv**, 100). **8**, colorless oil, $[\alpha]_D^{21}$ −85.7° (c=1.0, $CHCl_3$). High resolution MS: Calcd. for $C_{19}H_{34}O_{12}$ (M^+) 454.205; Found: 454.205, Calcd. for $C_{14}H_{25}O_{10}$ (**vi**) 353.145; Found: 353.146. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770 (–COO–), 1105 (C–O–C). PMR (CCl_4, δ): 3.40, 3.44, 3.48 (3H each, all s), 3.49 (9H, s), 3.54, 3.55 (3H each, both s) ($OCH_3\times8$), 4.14 (1H, d, J=7 Hz), 4.46 (1H, d, J=8 Hz) (1-H, 1′-H), 6.24 (1H, d, J=3 Hz, 5-H). MS m/e (%): 454 (M^+, 0.4), 353 (**vi**, 7), 205 (**ii**, 13), 101 (**iii**, 75), 88 (**iv**, 100).

Alkaline Treatment followed by Acetylation of 5 and 6 giving 9a——A solution of **5** (30 mg) in dry MeOH (1 ml) was added with 0.2 N MeONa–MeOH (1 ml) and kept stirring at room temperature for 10 min. The reaction mixture was then neutralized with 10% HCl–dry MeOH and concentrated under reduced pressure. The residue was acetylated overnight with acetic anhydride (1 ml) and pyridine (1 ml), poured into ice-water, and extracted with ether. Working-up of the ether extract in the usual manner gave a syrupy product, which was crystallized from ether–CCl_4 to furnish **9a** (16 mg) as colorless prisms of mp 129—130°. Purification of the mother layer by preparative TLC (hexane–ether=1:10) gave an additional crop of **9a** (2 mg) (total yield: 69%), being identical to the authentic sample[4] by mixed mp, IR (CCl_4), and TLC (hexane–ether=1:5; hexane–AcOEt=1:3).

Similar treatment of **6** (30 mg) in dry MeOH (1 ml) with 0.2 N MeONa–MeOH (1 ml) and acetylation gave **9a** (19 mg, 73%), which was identified as above by mixed mp, IR (CCl_4), and TLC.

Alkaline Treatment followed by Acetylation of 7 and 8 giving 2 and 9a——To a solution of **7** (119 mg) in dry MeOH (1 ml) was added 1 N MeONa–MeOH (1 ml) and the total solution was kept stirring at room temperature for 10 min. After neutralization with 10% HCl–dry MeOH, the solvent was evaporated under reduced pressure to give a residue. The dried residue was then acetylated with acetic anhydride (0.5 ml) and pyridine (0.5 ml) overnight, poured into cold water, and extracted with AcOEt. The product, obtained by the usual work-up, was purified by preparative TLC (hexane–ether=1:7) to afford **9a** (23 mg, 33.2%) and **2** (46 mg, 66.5%) which was identified by TLC (hexane–AcOEt=1:2, benzene–AcOEt=30:1, benzene–acetone=10:1), GLC (column: 15% ethylene glycol succinate polyester on uniport B (80—100 mesh), 2 m×3 mm, carrier gas N_2 flow rate 30 ml/min, column temp. 165°, t_R (min): 15′11″), and IR (CCl_4). Similar treatment of **8** (112 mg) as above furnished **9a** (16 mg, 28.4%) and **2** (35 mg, 53.7%).

Alkaline Hydrolysis of 3 giving 10——A solution of **3** (210 mg) in MeOH (15 ml) was treated with aq. 10% K_2CO_3 (5 ml) and heated under reflux for 2 hr. After removing MeOH under reduced pressure, the reaction mixture was poured into cold water, made weakly acidic with aq. 1 N HCl, and extracted with ether. After the usual work-up, the ether extract furnished **10** (190 mg, 96%), colorless oil, $[\alpha]_D^{20}$ +58.5° (c=1.0, $CHCl_3$). High resolution MS: Calcd. for $C_{10}H_{18}O_7$ (M^+) 250.094; Found: 250.097. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1734 (COOH), 1102 (C–O–C). PMR (CCl_4, δ): 3.40, 3.45, 3.48, 3.57 (3H each, all s, $OCH_3\times4$), 4.76 (1H, d, J=3 Hz, 1-H).

Lead Tetraacetate Oxidation of 10 giving 11 and 12——To a solution of **10** (110 mg, 0.45 mmol) in benzene (20 ml) was added $Pb(OAc)_4$ (1 g, 2.25 mmol). The total mixture was heated under reflux for 4 hr and treated as for **4**. Purification of the product by preparative TLC (hexane–ether=1:4) furnished **11** (42 mg, 36%) and **12** (28 mg, 24%). **11**, colorless oil, $[\alpha]_D^{21}$ +79.4° (c=1.0, $CHCl_3$). High resolution MS: Calcd. for $C_{11}H_{20}O_7$ (M^+) 264.121; Found: 264.120. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1768, 1223 (OAc). PMR (CCl_4, δ): 2.05 (3H, s, $OCOCH_3$), 3.39 (3H, s), 3.46 (6H, s), 3.52 (3H, s) ($OCH_3\times4$), 4.61 (1H, d, J=4 Hz, 1-H), 5.55 (1H, d, J=8 Hz, 5-H). MS m/e (%): 264 (M^+, <0.1), 233 (**i**, 4), 205 (**ii**, 11), 101 (**iii**, 33), 88 (**iv**, 35), 43 (100). **12**, colorless oil, $[\alpha]_D^{21}$ −50.2° (c=1.3, $CHCl_3$). High resolution MS: Calcd. for $C_{11}H_{20}O_7$ (M^+) 264.121; Found: 264.119. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1754, 1240 (OAc). PMR (CCl_4, δ): 2.00 (3H, s, $OCOCH_3$), 3.29, 3.32, 3.35, 3.43 (3H each, all s, $OCH_3\times4$), 4.69 (1H, s, 1-H), 5.65 (1H, d, J=6 Hz, 5-H). MS m/e (%): 264 (M^+, <0.1), 233 (**i**, 3), 205 (**ii**, 7), 101 (**iii**, 100), 88 (**iv**, 26), 43 (68).

Alkaline Treatment followed by Acetylation of 11 and 12 giving 9a——A stirred solution of **11** (20 mg) in dry MeOH (0.5 ml) was treated with 1 N MeONa–MeOH (1 ml) for 10 min at room temperature. Treatment of the reaction product as for **5** gave **9a** (10 mg, 58%) as colorless prisms (identified as above). From

12 (20 mg), after similar treatment in dry MeOH (0.5 ml) with 2 N MeONa–MeOH (1 ml) and acetylation, **9a** (12 mg, 69%) was obtained.

Methylation of D-Galacturonic Acid (13) giving 14, 15, 16, and 17——To a solution of **13** (3 g) in DMSO (5 ml) was added dimsyl carbanion (30 ml)[4b] under a nitrogen atmosphere. After stirring at room temperature for one hour, the stirred reaction mixture was treated with CH_3I (15 ml) overnight in the dark. Working-up of the reaction mixture as for **1** gave a syrupy product, which was purified by preparative TLC (benzene–MeOH=15:1) to furnish **14** (223 mg, 5%), **15** (410 mg, 10%), **16** (300 mg, 7%), and **17** (76 mg, 2%). **14**, colorless oil, $[\alpha]_D^{21}$ −115.0° (c=2.0, MeOH) (lit.[16] $[\alpha]_D^{12}$ −123° (c=1.0, MeOH)). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1765, 1745 ($COOCH_3$), 1110 (C–O–C). PMR (CCl_4, δ): 3.27, 3.30, 3.34, 3.40 (3H each, all s, $OCH_3\times4$), 3.71 (3H, s, $COOCH_3$), 4.72 (1H, s, 1-H). **15**, colorless oil, $[\alpha]_D^{21}$ +69.8° (c=1.1, MeOH). High resolution MS: Calcd. for $C_{11}H_{20}O_7$ (M^+) 264.121; Found: 264.120. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1765, 1749 (COOMe), 1126 (C–O–C). PMR (CCl_4, δ): 3.31, 3.32, 3.35, 3.38 (3H each, all s, $OCH_3\times4$), 3.72 (3H, s, $COOCH_3$), 4.74 (1H, d, J=4 Hz, 1-H). **16**, colorless needles of mp 101.5—102° (recryst. from ether–light petroleum), $[\alpha]_D^{21}$ −20.0° (c=1.2, MeOH) (lit.[17] mp 102° (from ether–light petroleum), $[\alpha]_D^{18}$ −21° (c=1.2, MeOH)). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1778, 1741 ($COOCH_3$), 1092 (C–O–C). PMR (CCl_4, δ): 3.43 (3H, s), 3.48 (6H, s), 3.49 (3H, s) ($OCH_3\times4$), 3.74 (3H, s, $COOCH_3$), 3.98 (1H, d, J=7 Hz, 1-H). **17**, colorless plates of mp 70—71° (recryst. from ether), $[\alpha]_D^{21}$ +140.5° (c=1.2, $CHCl_3$) (lit.[18] mp 70° (from ether), $[\alpha]_D$ +142.1° ($CHCl_3$)). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1775, 1740 (COOMe), 1098 (C–O–C). PMR (CCl_4, δ): 3.35 (3H, s), 3.41 (6H, s), 3.45 (3H, s) ($OCH_3\times4$), 3.71 (3H, s, $COOCH_3$), 4.73 (1H, d, J=2 Hz, 1-H).

$LiAlH_4$ Reduction of 16 and 17——A solution of **16** (4 mg) in dry ether (0.5 ml) was added with $LiAlH_4$ (15 mg) and kept stirring at room temperature for 30 min. The reaction mixture was treated with aqueous ether, aq. 5% HCl, and water, successively. The ether layer was taken, dried over $MgSO_4$, and evaporated to dryness. The crystalline residue was recrystallized from ether to give colorless needles of mp 70—72°, which was identified with methyl 2,3,4-tri-O-methyl-β-D-galactopyranoside[17] by mixed mp, TLC (benzene–acetone=1:1, ether–iso-PrOH–H_2O=25:4:1), and GLC (column: 15% polyneopentylglycol succinate on chromosorb WAW (80—100 mesh), 2 m×3 mm, carrier gas N_2 flow rate 30 ml/min, column temp. 200°, t_R (min): 8′33″). Similar reduction of **17** (5 mg) gave methyl 2,3,4,-tri-O-methyl-α-D-galactopyranoside (syrup)[24] which was identified by TLC and GLC (t_R (min): 9′55″) as above.

Alkaline Hydrolysis of 16 giving 18——A solution of **16** (200 mg) in MeOH (20 ml) was treated with aq. 10% K_2CO_3 (10 ml) and heated under reflux for 3 hr. After removing MeOH under reduced pressure, the reaction mixture was made weakly acidic with aq. 1 N HCl and extracted with ether. The usual work-up of the ether extract gave colorless needles of **18** (160 mg, 84.5%). Recrystallization from ether gave the analytical sample of **18** of mp 71°, $[\alpha]_D^{21}$ +10.0° (c=1.0, H_2O). *Anal.* Calcd. for $C_{10}H_{18}O_7$: C, 47.99; H, 7.25. Found: C, 47.82; H, 7.20. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1775, 1740 (COOH). PMR (CCl_4, δ): 3.54, 3.58 (6H each, both s, $OCH_3\times4$), 4.23 (1H, d, J=7 Hz, 1-H), 6.38 (1H, br.s, $W_{h/2}$=8 Hz, COOH).

Lead Tetraacetate Oxidation of 18 giving 19——A solution of **18** (150 mg, 0.6 mmol) in benzene (20 ml) was treated with $Pb(OAc)_4$ (1 g, 2.25 mmol) and heated under reflux for 3 hr. After dilution with ether, the reaction mixture was washed with water. Concentration of the organic layer gave a product which was purified by preparative TLC (hexane–ether=1:5) to furnish **19** (115 mg, 73%), colorless oil, $[\alpha]_D^{21}$ −65.0° (c=1.2, $CHCl_3$). High resolution MS: Calcd. for $C_{10}H_{17}O_6$ (**i**) 233.102; Found: 233.101, Calcd. for $C_9H_{17}O_5$ (**ii**) 205.107; Found: 205.108. The molecular ion was not detected. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770, 1225 (OAc). PMR (CCl_4, δ): 2.05 (3H, s, $OCOCH_3$), 3.42, 3.43 (3H each, both s), 3.47 (6H, s) ($OCH_3\times4$), 4.35 (1H, m, signal width=7 Hz, 1-H), 5.98 (1H, d, J=3 Hz, 5-H). PMR (d_6-acetone, δ): 2.08 (3H, s, $OCOCH_3$), 3.41, 3.45 (3H each, both s), 3.48 (6H, s) ($OCH_3\times4$), 4.49 (1H, d, J=7 Hz, 1-H), 6.05 (1H, d, J=3 Hz, 5-H). MS m/e (%): 233 (**i**, 1), 205 (**ii**, 1), 101 (**iii**, 59), 88 (**iv**, 100).

Alkaline Treatment followed by Acetylation of 19 giving 9a——To a stirred solution of **19** (90 mg) in MeOH (1 ml) was added 2 N MeONa–MeOH (1 ml), and the solution was kept stirring at room temperature for 10 min. Treatment of the reaction mixture as for **5** and acetylation with acetic anhydride (0.5 ml) and pyridine (0.5 ml), gave a product which was crystallized from ether–CCl_4 to furnish **9a** as colorless prisms (30 mg, 38.6%) (identified as above).

Alkaline Hydrolysis of 17 giving 20——A solution of **17** (43 mg) in MeOH (2 ml) was treated with aq. 10% K_2CO_3 (2 ml) and heated under reflux for one hour. After making weakly acidic with aq. 1 N HCl, the mixture was extracted with AcOEt. The usual work-up of the AcOEt extract gave **20** (38 mg, 93%) as colorless oil, $[\alpha]_D^{22}$ +84.9° (c=1.1, $CHCl_3$). High resolution MS: Calcd. for $C_9H_{17}O_5$ (**ii**) 205.107; Found: 205.109. The molecular ion was not detected. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1779, 1741 (COOH). PMR ($CDCl_3$, δ): 3.45 (3H, s), 3.53 (6H, s), 3.55 (3H, s) ($OCH_3\times4$), 4.98 (1H, d, J=3 Hz, 1-H), 6.75 (1H, br.s, $W_{h/2}$=14 Hz, exchangeable with D_2O, COOH).

Lead Tetraacetate Oxidation of 20 giving 21——To a solution of **20** (160 mg, 0.64 mmol) in benzene (10 ml) was added $Pb(OAc)_4$ (4 g, 9 mmol) and the total mixture was heated under reflux for 30 hr. The reaction mixture was filtered and the residue, obtained by evaporation of the filtrate under reduced pressure, was

24) F. Smith, *J. Chem. Soc.*, **1939**, 1724.

treated with hexane. The hexane soluble portion was purified by preparative TLC (hexane–ether=1:30) to furnish **21** (12 mg, 7.1%). The hexane insoluble portion was next extracted with AcOEt and the AcOEt extractive gave recovered **20** (131 mg, 81.9%). **21**, colorless oil, $[\alpha]_D^{19}$ +123.7° (c=1.2, $CHCl_3$). High resolution MS: Calcd. for $C_{10}H_{17}O_6$ (**i**) 233.102; Found: 233.100, Calcd. for $C_9H_{17}O_5$ (**ii**) 205.107; Found: 205.106. The molecular ion was not detected. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1770, 1757 (OAc). PMR (CCl_4, δ): 2.04 (3H, s, $OCOCH_3$), 3.34, 3.43 (3H each, both s), 3.46 (6H, s) ($OCH_3\times4$), 4.68 (1H, d, J=3 Hz, 1-H), 5.79 (1H, d, J=4 Hz, 5-H). MS *m/e* (%): 233 (**i**, 2), 205 (**ii**, 5.9), 101 (**iii**, 61.8), 88 (**iv**, 100), 43 (42.6).

Alkaline Treatment followed by Acetylation of 21 giving 9a——Treatment of a solution of **21** (12 mg) in dry MeOH (1 ml) with 2 N MeONa–MeOH (0.5 ml) at room temperature and following acetylation as for **5** furnished **9a** (6 mg, 58%) as colorless prisms (identified as above).

Examinations of Reaction Conditions for Nitromethane Cyclization——The nitromethane cyclization of **5** under the following reaction conditions was carried out and the products were examined by TLC (hexane–ether=1:5, $CHCl_3$–MeOH=5:1). a) To a solution of **5** (5 mg) in dry MeOH (0.15 ml) was added 1 N MeONa–MeOH (0.15 ml). The reaction mixture was then treated with nitromethane (0.25 ml) and kept stirring at room temperature. b) To a solution of **5** (5 mg) in dry MeOH (0.15 ml) was added nitromethane (0.25 ml). The total solution was then added with 1 N MeONa–MeOH (0.15 ml) and kept stirring at room temperature. c) To a solution of **5** (5 mg) in MeOH (0.25 ml) was added nitromethane (0.25 ml). The total solution was then added with aq. 2 N K_2CO_3 (0.15 ml) and kept stirring at room temperature. d) To a solution of **5** (5 mg) in MeOH (0.25 ml) was added nitromethane (0.25 ml). The total solution was then treated with aq. 3 N NaOH (0.15 ml) and kept stirring at room temperature. e) To a solution of **5** (5 mg) in dry MeOH (0.25 ml) was added nitromethane (0.25 ml). The total solution was then treated with 10% *tert.* BuOK–MeOH (0.15 ml) and kept stirring at room temperature. In the case of a), the reaction products were disclosed to comprise **25**, **27**, **29**, and **9**. In the case of b), **25**, **27**, and **29** were produced, but **9** was not formed. In the cases of c), d), and e), the reaction products were almost identical to those obtained in the case of b). For the sake of the ready isolation of the reaction products, the condition b) was chosen and carried out in the larger scale as below.

Nitromethane Cyclization of 5 giving 25, 27, and 29——To a solution of **5** (975 mg) in nitromethane (11 ml) was added 1 N MeONa–MeOH (10 ml) at 4° and the total mixture was kept stirring at 4° for 12 hr. After making weakly acidic (pH 6) with AcOH, the reaction mixture was concentrated under reduced pressure and extracted with AcOEt. The AcOEt extract was washed with water, dried over $MgSO_4$, and evaporated to dryness. The product was then purified by preparative TLC (hexane–AcOEt=1:5) to furnish **25** (232 mg, 25%), **27** (277 mg, 30%), and **29** (111 mg, 12%). **25**, colorless needles of mp 179.5—181.0° (cryst. from ether), $[\alpha]_D^{26}$ 0.0° (c=0.5, acetone). *Anal.* Calcd. for $C_9H_{17}NO_2$: C, 43.02; H, 6.82; N, 5.58. Found: C, 42.92; H, 6.69; N, 5.41. IR ν_{max}^{KBr} cm^{-1}: 3430 (OH), 1560, 1345 (NO_2). PMR (d_6-acetone, δ): 3.57 (9H, s, $OCH_3\times3$), 4.43 (1H, t, J=10 Hz, 5-H), 4.85 (2H, d, J=4 Hz, exchangeable with D_2O, OH×2). **27**, colorless needles of mp 167.0—168.5° (cryst. from ether), $[\alpha]_D^{26}$ 0.0° (c=0.5, acetone). *Anal.* Calcd. for $C_9H_{17}NO_2$: C, 43.02; H, 6.82; N, 5.58. Found: C, 42.82; H, 6.93; N, 5.32. IR ν_{max}^{KBr} cm^{-1}: 3540, 3490 (OH), 1555, 1350 (NO_2). PMR (d_6-acetone, δ): 3.42, 3.51, 3.55 (3H each, all s, $OCH_3\times3$), 4.30—4.70 (4H, m). **29**, colorless needles of mp 139.0—141.0° (cryst. from ether), $[\alpha]_D^{26}$ 0.0° (c=0.5, acetone). High resolution MS: Calcd. for $C_9H_{17}NO_7$ (M^+) 251.101; Found: 251.100. IR ν_{max}^{KBr} cm^{-1}: 3550, 3480, 3410 (OH), 1555, 1360 (NO_2). PMR (d_6-acetone+D_2O, δ): 3.43 (9H, s, $OCH_3\times3$), 3.64 (2H, d.d, J=3 and 3 Hz, 1-H, 5-H), 3.84 (1H, t, J=3 Hz, 6-H), 4.06 (2H, d.d, J=3 and 10 Hz, 2-H, 4-H), 4.70 (1H, t, J=10 Hz, 3-H).

Acetylation of 25 giving 26——A solution of **25** (115 mg) in a mixture of acetic anhydride (0.3 ml) and conc. H_2SO_4 (0.05 ml) was left standing at 25° for 30 min, and poured into ice-water. The precipitated product was collected by filtration and crystallized from ether to furnish **26** (123 mg, 80%) as colorless needles of mp 124.5—126.0°. *Anal.* Calcd. for $C_{13}H_{21}NO_9$: C, 46.56; H, 6.31; N, 4.18. Found: C, 46.67; H, 6.28; N, 4.42. IR ν_{max}^{KBr} cm^{-1}: 1760, 1207 (OAc), 1566, 1380 (NO_2). IR ν_{max}^{Nujol} cm^{-1}: no OH. PMR ($CDCl_3$, δ): 2.09 (6H, s, $OCOCH_3\times2$), 3.21—3.35 (3H, m, 1-H, 2-H, 3-H), 3.50 (6H, s), 3.65 (3H, s) ($OCH_3\times3$), 4.60 (1H, t, J=10 Hz, 5-H), 5.45 (2H, br.t, J=*ca.* 10 Hz, 4-H, 6-H). The chemical shift of 1-H and 3-H was shown to be δ 3.25 by spin-decoupling experiments (Table I).

Acetylation of 27 giving 28——A solution of **27** (82 mg) in a mixture of acetic anhydride (0.3 ml) and conc. H_2SO_4 (0.05 ml) was left standing at 25° for 30 min, and poured into ice-water. The total aqueous mixture was extracted with AcOEt and the AcOEt extract was washed with water, dried over $MgSO_4$, and evaporated to dryness under reduced pressure to give **28** (103 mg, 94%). Crystallization from ether gave the pure sample of **28** as colorless needles of mp 96.0—98.0°. *Anal.* Calcd. for $C_{13}H_{21}NO_9$: C, 46.56; H, 6.31; N, 4.18. Found: C, 46.70; H, 6.34; N, 4.28. IR ν_{max}^{KBr} cm^{-1}: 1770, 1230 (OAc), 1561, 1375 (NO_2). IR ν_{max}^{Nujol} cm^{-1}: no OH. PMR ($CDCl_3$, δ): 2.07, 2.11 (3H each, both s, $OCOCH_3\times2$), 3.05—3.52 (3H, m, 3-H, 4-H, 5-H), 3.44, 3.55, 3.61 (3H each, all s, $OCH_3\times3$), 4.64 (1H, d.d, J=2 and 10 Hz, 1-H), 5.83 (1H, d.d, J=9 and 10 Hz, 6-H), 6.01 (1H, d.d, J=2 and 2 Hz, 2-H). The chemical shift of 3-H and 5-H was shown to be δ 3.32 by spin-decoupling experiments (Table II).

Nitromethane Cyclization of 6 giving 25, 27, and 29——To a solution of **6** (500 mg) in nitromethane (6 ml) was added 1 N MeONa–MeOH (5 ml) at 4°. The total solution was kept stirring at 4° for 7 hr. Working-up of the reaction product as for **5** followed by preparative TLC purification (hexane–AcOEt=1:5) afforded

25 (109 mg, 23%), **27** (147 mg, 31%), and **29** (61 mg, 13%). The products were respectively identified with those obtained above from **5** by mixed mp, IR (KBr), and TLC (benzene–acetone=3:1, hexane–AcOEt=1:5, hexane–ether=1:10).

Nitromethane Cyclization of 11 giving 25, 27, and 29——To a solution of **11** (241 mg) in nitromethane (3 ml) was added 1 N MeONa–MeOH (3 ml) at 4°. The total solution was then kept stirring at 4° for 12 hr and worked up as above. Purification of the product by preparative TLC (hexane–AcOEt=1:5) gave **25** (66 mg, 29%), **27** (75 mg, 33%), and **29** (36 mg, 16%), which were recrystallized from ether respectively and identified with those obtained from **5** as above.

GLC Analyses of Nitromethane Cyclization Products——i) Trimethylsilylation reagent was prepared by addition of hexamethyldisilazane (1.8 ml) to a mixture of dry pyridine (2.0 ml) and trifluoroacetic acid (0.2 ml).

ii) The syrupy product (2 mg each), which was obtained by the nitromethane cyclization of **5**, **6**, or **11** as described above, was treated with the above-prepared trimethylsilylation reagent (0.1 ml). The total mixture was shaken vigorously to yield a clear solution which was subjected to the GLC analysis. The results were as given in Table III. As for the standards, the authentic samples (**25**, **27**, **29**) were also trimethylsilylated in the similar manner and analyzed by GLC. GLC: column: 2% silicone OV-17 on chromosorb WAWDMCS (80—100 mesh), 1 m×3 mm, carrier gas N_2 flow rate 30 ml/min, column temp. 150°, t_R (min): **25** 4′18″; **27** 3′37″; **29** 5′55″.

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