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Saponin and Sapogenol. XXI.[1] Photochemical Cleavage of Glycoside Linkage in Triterpenoidal and Steroidal Arabinoside and Galactoside *via* Ultraviolet Irradiation of Their 2′-Keto Derivatives

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In order to explore a new cleavage method for an arabinoside or a galactoside linkage which attaches to a triterpenoidal or a steroidal aglycone, a photochemical method has been investigated. It has been found that glycoside linkages in 2′-keto-arabinoside and 2′-keto-galactoside derivatives of triterpenoids and a steroid are cleaved upon photolysis to furnish their aglycones in their oxidized forms. In addition, it has been shown that, through the present photochemical procedure, an arabinoside linkage in ziyu-glycoside II (**8**), which has been known to give an artifact aglycone upon ordinary acid hydrolysis, is cleaved while its acid-labile moiety in the aglycone part is left unchanged.

Keywords——triterpenoidal arabinoside; steroidal arabinoside; triterpenoidal galactoside; cleavage of glycoside linkage; photochemical Norrish type II reaction; ziyu-glycoside II

Recently, we reported three new selective cleavage methods for the glucuronide linkage directly attached to the aglycone of oligoglycoside such as saponin, *i.e.* photolysis,[3] lead tetraacetate oxidation followed by alkali treatment,[4] and acetic anhydride and pyridine treatment.[1] As a continuing study in search of a new selective cleavage method for another kind of glycoside linkage, we have been exploring a new cleavage method for an arabinoside or a galactoside linkage which is attached to a triterpenoidal or a steroidal aglycone.

In 1972, Collins, *et al.* reported in their photochemical studies on the Norrish type II reaction of carbohydrate derivatives that methyl 3,4-O-isopropylidene-L-*erythro*-pento-pyranosid-2-ulose undergoes degradation upon photolysis to give 1,5-anhydro-3,4-O-isopropylidene-L-*erythro*-pent-2-ulose and formaldehyde.[5] We have considered that this type of reaction would be applicable for photochemical cleavage of a triterpenoidal or a steroidal arabinoside or galactoside linkage through a reaction sequence as schematically shown in Chart 1. As shown in the present paper, we prepared three triterpenoidal and steroidal arabinoside derivatives and one triterpenoidal galactoside derivative, and have examined their photochemical behavior. It has been found that ultraviolet irradiation of 2′-keto derivatives of these arabinosides and galactoside (having a moiety [A]) results in cleavage of

1) Part XX: I. Kitagawa, Y. Ikenishi, M. Yoshikawa, and K.S. Im, *Chem. Pharm. Bull.* (Tokyo), **25** (1977) (in the press).

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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 Letters*, **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 Letters*, **1976**, 549; *b*) I. Kitagawa, M. Yoshikawa, K.S. Im, and Y. Ikenishi, *Chem. Pharm. Bull.* (Tokyo), **25**, 657 (1977).

5) P.M. Collins, P. Gupta, and R. Iyer, *J. Chem. Soc. Perkin I*, **1972**, 1670.

their respective glycoside linkages and liberation of their aglycones in the oxidized forms [B] (Chart 1).[6]

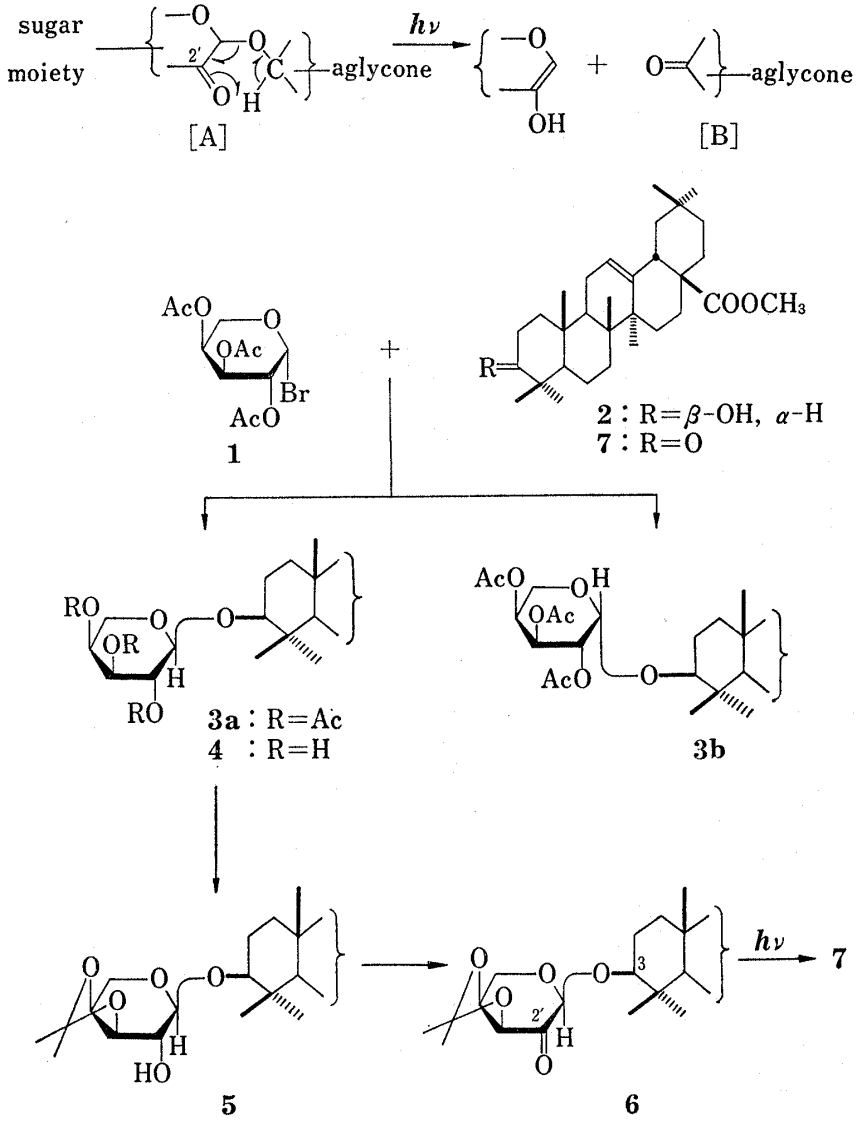

Chart 1

Cleavage of Arabinoside Linkage

In order to examine photochemical cleavage of a glycoside linkage in a triterpenoidal or a steroidal glycoside which possesses a photosensitive carbonyl group at C–2 position of its glycone moiety, at first a 2′-keto-arabinoside derivative of methyl oleanolate (**6**) was synthesized and subjected to photolysis.

Treatment under reflux of a toluene solution of 2,3,4-tri-O-acetyl-β-L-arabinopyranosyl bromide(**1**) and methyl oleanolate (**2**) with cadmium carbonate[7] furnished methyl 3-O-α-L-arabinopyranosyl-oleanolate triacetate (**3a**) and its β-anomer (**3b**) in a 81.8% combined yield (yield ratio=10 : 1). The structures including their anomeric configurations of both arabinosides were supported by their physicochemical properties and by spectral data of **4** which was prepared by alkali treatment of **3a**. The proton magnetic resonance (PMR) spectrum (taken

6) Partly presented at the 95th Annual Assembly of Pharmaceutical Society of Japan held at Nishinomiya (1975, April). I Kitagawa, Y. Fujimoto, and I. Yosioka, Abstract Paper, II-267.
7) R.B. Conrow and S. Bernstein, *J. Org. Chem.*, 36, 863 (1971).

in deuterochloroform ($CDCl_3$)) of **3a** shows signals due to seven tertiary methyls, three acetoxyls, one methoxycarbonyl, and an anomeric proton at δ4.45 (d, J= 7 Hz), and that (in pentadeutero (d_5-)-pyridine and deuterium oxide (D_2O)) of **4** shows an anomeric proton signal at δ4.70 (d, J= 7 Hz), thus the α-orientation of the arabinoside linkage in **3a** being corroborated. An anomeric proton signal in the PMR spectrum of **3b** is observed at δ5.23 as a doublet of J= 3 Hz (indicating the β-orientation of the arabinoside linkage (Cl form)). Methyl 3-O-α-L-arabinopyranosyl-oleanolate (**4**) was then converted to an isopropylidene derivative (**5**) by treatment with 2,2-dimethoxypropane in dry acetone and a cationic resin

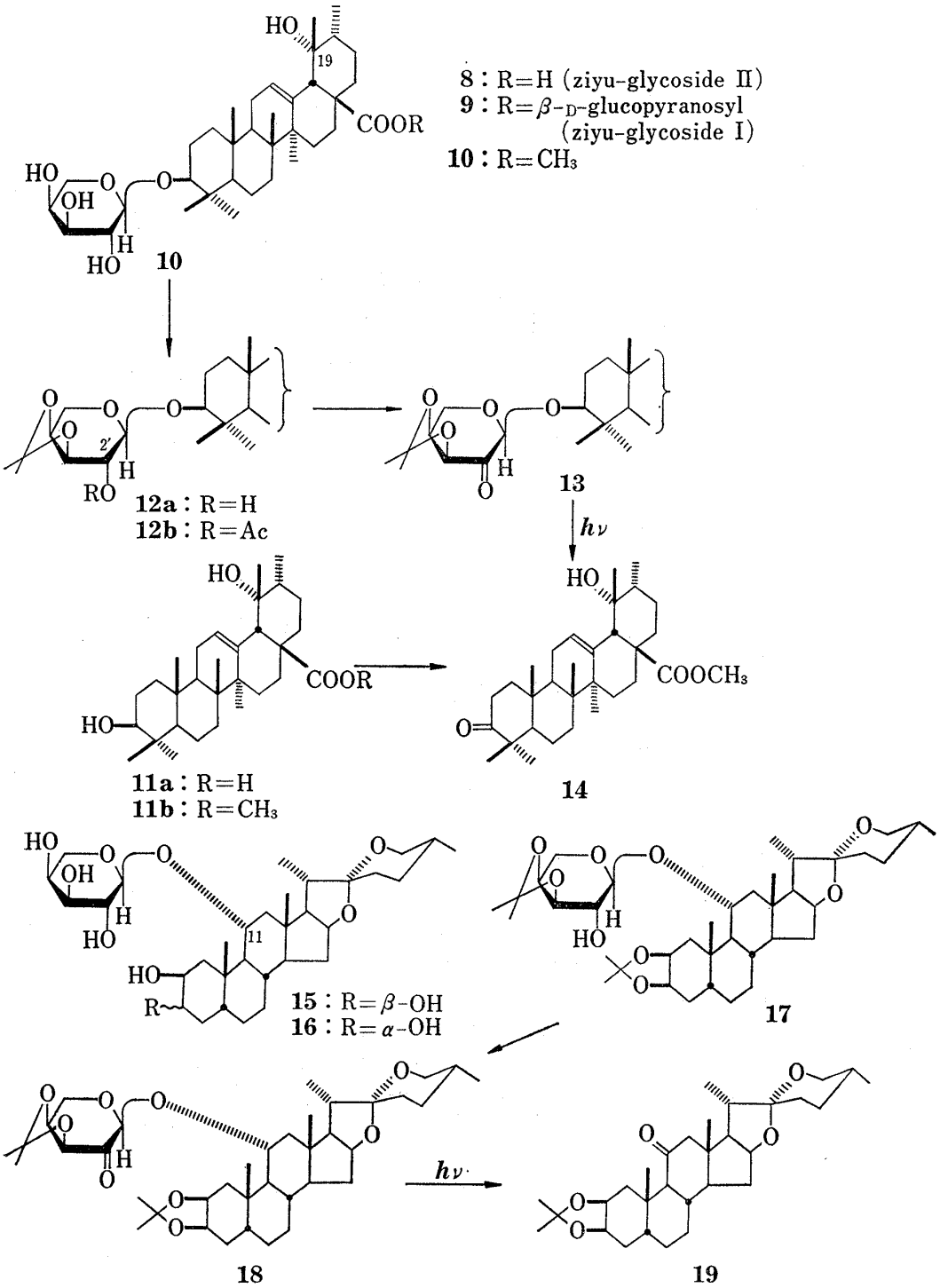

Chart 2

(Dowex) as a catalyst.[8] Oxidation of **5** with dimethyl sulfoxide (DMSO) and acetic anhydride[9] furnished the objective 2′-keto-arabinoside derivative (**6**). The infrared (IR) spectrum (in carbon tetrachloride(CCl_4)) of **6** shows the presence of a 2′-keto function (1768 cm^{-1})[5] and a methoxycarbonyl (1735 cm^{-1}) while the PMR spectrum ($CDCl_3$) shows an anomeric proton signal as a singlet at δ4.86, thus the structure **6** being substantiated. The other signals due to protons on the glycone part are observed at the expected positions[5] (see Experimental).

Irradiation of **6** in tertiary butanol with a 500W high pressure mercury lamp through a Pyrex filter furnished methyl oleanonate (**7**), identified with an authentic sample, in a 44.8% yield. Since **7** thus liberated was also photosensitive, the irradiation was terminated in 40 minutes while leaving a considerable amount of **6** in the reaction mixture and further efforts for improving the yield of **7** was unfruitful. We also attempted the isolation of any product originated from the glycone part. Although a product probably originated in the arabinose moiety was detected on a thin-layer chromatogram (TLC) of the photolysis product, the isolation in a pure form was unsuccessful due to its instability. However, it has been shown that a triterpenoidal arabinoside linkage is photochemically cleaved by irradiation of its 2′-keto derivative and the aglycone part can be obtained in its oxidized form.

Next, a similar 2′-keto-arabinoside derivative of a ursene-type triterpenoid was prepared and subjected to photolysis. For this purpose, ziyu-glycoside II (**8**)[10] was taken as a starting arabinoside. As previously shown by Yosioka, *et al.*[10] ziyu-glycoside II (**8**) is a 3-O-arabinoside of pomolic acid (**11a**)[11] and was isolated from Sanguisorbae Radix along with ziyu-glycoside I (**9**), and the soil bacterial hydrolysis[12] was useful for cleavage of the glycoside linkages to liberate their genuine aglycone pomolic acid (**11a**), since **11a** was readily converted under ordinary acid hydrolysis conditions to artifact sapogenols such as tomentosolic acid and vanguerolic acid. Therefore, application of the present photolysis procedure for cleavage of the arabinoside linkage in **8** seemed of interest whether its genuine aglycone could be isolated.

The methyl ester of ziyu-glycoside II (**10**) was treated with 2,2-dimethoxy-propane and *p*-toluenesulfonic acid in dry acetone to furnish an acetonide (**12a**), the PMR spectrum ($CDCl_3$) of which shows two three-proton singlets at δ1.35 and δ1.52 due to newly induced isopropylidene methyls. A monoacetate (**12b**) prepared from **12a** provided a further support for the structure by its PMR signals observed at δ4.36 (1H, d, J= 7 Hz) due to an anomeric proton and at δ5.03 (1H, t, J= 7 Hz) due to C-2′ proton. Oxidation of **12a** with DMSO-acetic anhydride as for **5** afforded a 2′-keto-arabinoside derivative (**13**), the structure of which received a support from its physical data, *e.g.* IR bands ($CHCl_3$) at 1763 cm^{-1} (carbonyl) and 1721 cm^{-1} (methoxycarbonyl), and a PMR signal at δ4.88 (1H, s, anomeric proton).

Irradiation of a solution of **13** in tertiary butanol for 30 minutes as for **6** furnished in a 25.1% yield a product, which was found to be identical to methyl pomonate (**14**) being prepared from methyl pomolate (**11b**) by chromium trioxide oxidation. Here again, the isolation in a pure form of any product resulting from the glycone part was unsuccessful. It is interestingly pointed out that the photochemical cleavage method left intact the acid-labile 19α-OH group in **14** and seems to be a promissing method useful for liberation of a certain kind of genuine aglycone from an arabinoside derivative.

Thirdly, a steroidal arabinoside possessing its glycone moiety at sterically crowded position was chosen as another subject of the study. Recently, we isolated two steroidal

8) J.G. Moffatt, *J. Am. Chem. Soc.*, **85**, 1118 (1963).
9) J.D. Albright and L. Goldman, *J. Am. Chem. Soc.*, **87**, 4214 (1965).
10) I. Yosioka, T. Sugawara, A. Ohsuka, and I. Kitagawa, *Chem. Pharm. Bull.* (Tokyo), **19**, 1700 (1971).
11) C.H. Brieskorn and H. Wunderer, *Chem. Ber.*, **100**, 1252 (1967).
12) *a*) I. Yosioka, M. Fujio, M. Osamura, and I. Kitagawa, *Tetrahedron Letters*, **1966**, 6303; *b*) I. Yosioka, K. Imai, Y. Morii, and I. Kitagawa, *Tetrahedron*, **30**, 2283 (1974) and the literatures cited therein.

arabinoside derivatives from the epigeous part of *Metanarthecium luteo-viride* and elucidated their structures as 11-O-α-L-arabinopyranosyl-metagenin (**15**) and 11-O-α-L-arabinopyranosyl-3-*epi*-metagenin (**16**) on the basis of chemical and spectral evidence.[13] Both arabinosides were characterized by having an O-arabinoside moiety attached at C-11 of the steroidal aglycone, and **15** was taken as a starting material.

A diacetonide derivative (**17**) prepared similarly as for **5** from **4** using 2,2-dimethoxypropane was oxidized with DMSO-acetic anhydride to give a 2′-keto-arabinoside derivative **18**. The PMR spectrum ($CDCl_3$) of **18** shows an anomeric proton signal as a one-proton singlet at δ4.96 and the IR spectrum (CCl_4) shows a carbonyl absorption band at 1767 cm^{-1}, thus the structure **18** being substantiated. Irradiation of **18** in a Pyrex tube for 40 minutes as for two preceding examples (**6** and **13**) liberated in a 39.0% yield an aglycone, which was identical to metagenone acetonide (**19**) prepared from metagenin acetonide[13] by chromium trioxide oxidation. Therefore, it has become clear that the present photochemical method is applicable for cleavage of a sterically crowded arabinoside linkage.

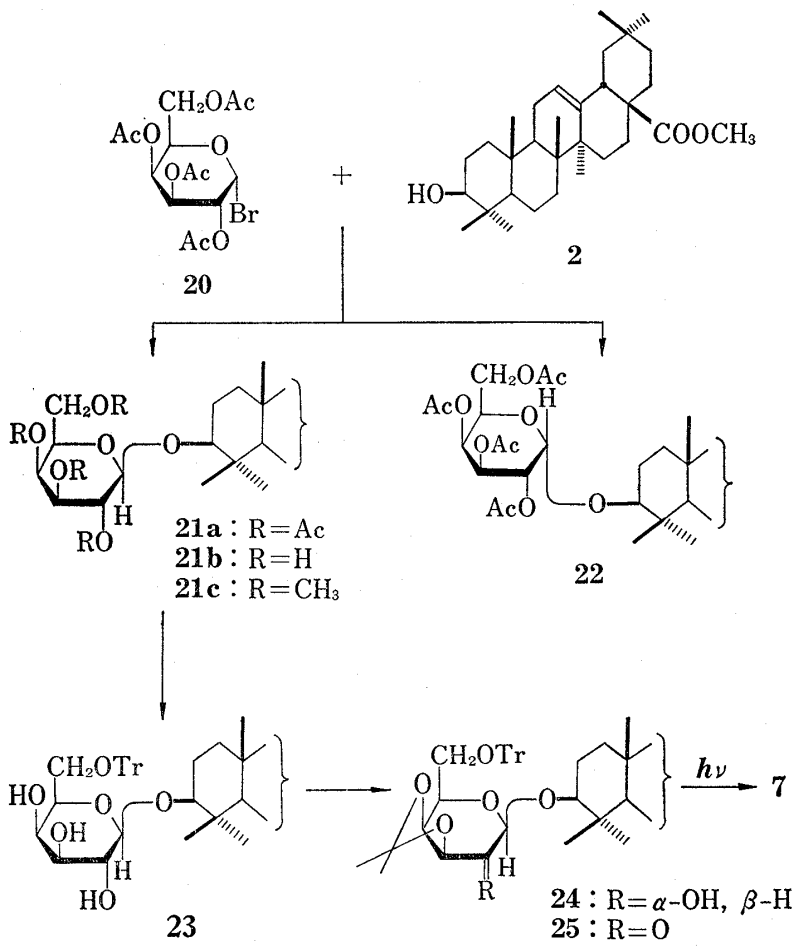

Chart 3

Cleavage of Galactoside Linkage

If a primary alcoholic function in a galactoside moiety can properly be protected, the present photochemical method has been considered to be applicable for cleavage of a galactoside linkage on a similar basis. Methyl 3-O-galactopyranosyl-oleanolate was prepared and taken as a starting material for the examination.

13) I. Kitagawa, K.S. Im, and Y. Morii, *Chem. Pharm. Bull.* (Tokyo), 24, 3114 (1976).

Condensation of 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide (**20**) with methyl oleanolate (**2**) in refluxing dry toluene with cadmium carbonate as a catalyst gave methyl 3-O-β-D-galactopyranosyl-oleanolate (**21a**) and its α-anomer (**22**) in a 10: 1 ratio (in a 55% combined yield). The structures of both galactosides were supported by their spectral properties as in the case of **3a** and **3b**: an anomeric proton of **21a** at δ4.49 (d, J= 7 Hz, in $CDCl_3$) and that of **22** at δ5.24 (d, J= 4 Hz). In order to assure the assignment of anomeric configuration of β-galactoside (**21a**), a penta-O-methyl derivative (**21c**) was prepared from **21a** *via* a desacetyl derivative (**21b**)(anomeric proton at δ4.71, d, J= 7 Hz, in $CDCl_3$). An anomeric proton signal of **21c** is observed at δ4.25 also as a doublet of J=7 Hz (in $CDCl_3$).

The desacetyl derivative (**21b**) was converted by refluxing with trityl chloride in pyridine to a monotrityl derivative (**23**), which was then subjected to acetonidation as for **5** from **4**. The PMR spectrum of **23** shows signals due to a trityl group (15H, at δ7.1—7.6) and isopropylidene methyls (δ1.27 & δ1.46, 3H each). Oxidation of **24** with DMSO-acetic anhydride gave a 2′-keto-galactoside derivative (**25**), whose structure was corroborated by its spectral properties: a carbonyl absorption band at 1768 cm^{-1} (CCl_4) and an anomeric proton singlet at δ4.77 ($CDCl_3$). Finally, irradiation of **25** in tertiary butanol as in the preceding case of 2′-keto-arabinoside derivatives furnished methyl oleanonate (**7**) in a 32.5% yield. Although the isolation in a pure form of any product resulting from galactose part was unsuccessful, it has thus been shown that 2′-keto-galactoside derivative is also favorable for photochemical cleavage of a triterpenoidal galactoside linkage.

In conclusion, it has become clear that a glycoside linkage in an arabinoside or a galactoside derivative of a triterpenoid or a steroid could be cleaved photochemically *via* its 2′-keto derivative. Although this photochemical method has a limit in improving the yield of aglycone, its application for selective splitting of an arabinoside or a galactoside linkage directly attached to an aglycone of oligoglycoside such as saponin seems to be of interest and will be a subject of our future study.

Experimental[14]

Preparation of 3a and 3b——To a solution of methyl oleanolate (**2**, 1.41 g) in dry toluene (80 ml) was added cadmium carbonate (1.04 g) and the mixture was heated with stirring to distill off 20 ml of the solvent. The stirred mixture was then added dropwise with a solution of 2,3,4-tri-O-acetyl-β-L-arabinopyranosyl bromide (**1**) while azeotropically distilling off a mixture of toluene and water to keep total volume of the reaction mixture in 60 ml (40 min). After adding dry toluene dropwise in a similar manner during further 90 min, the reaction mixture was filtered and evaporated under reduced pressure to give a product (3.15 g) which was purified by column chromatography (silica gel 100 g) developing with benzene–ethyl acetate (30: 1) mixture to give **3a** (1.62 g) and **3b** (0.16 g). **3a**, amorphous,[16] $[\alpha]_D^{12}$ +51° (c=1.48, $CHCl_3$). *Anal.* Calcd. for $C_{42}H_{64}O_{10}$: C, 69.20; H, 8.85. Found: C, 69.13; H, 9.01. IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1757, 1222 (OAc), 1736 ($COOCH_3$). PMR ($CDCl_3$) δ: 0.71, 0.76, 0.89, 1.11 (3H each, all s), 0.91 (9H, s) (*tert.* $CH_3\times7$), 2.00, 2.02, 2.11 (3H each, all s, OAc×3), 3.62 (3H, s, $COOCH_3$), 4.45 (1H, d, J=7 Hz, anomeric H). **3b**, amorphous,[16] $[\alpha]_D^{12}$ +121° (c=1.20, $CHCl_3$). *Anal.* Calcd. for $C_{42}H_{64}O_{10}$: C, 69.20; H, 8.85. Found: C, 68.98; H, 8.86. IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1757, 1228 (OAc), 1737 ($COOCH_3$). PMR ($CDCl_3$) δ: 0.72, 0.82, 0.89, 1.01, 1.11 (3H each, all s), 0.92 (6H, s) (*tert.* $CH_3\times7$), 2.00, 2.04, 2.13 (3H each, all s, OAc×3), 3.62 (3H, s, $COOCH_3$), 5.23 (1H, d, J=3 Hz, anomeric H).

Deacetylation of 3a giving 4——A solution of **3a** (572 mg) in 1% methanolic NaOMe–MeOH (2—20 ml) was kept stirring at room temperature for 30 min, treated with Dowex 50W-X8 (H^+) (100 mg), filtered, and evaporated under reduced pressure. The product (485 mg) was crystallized from $CHCl_3$–MeOH to give **4** of mp 222.5—224.5°, $[\alpha]_{15}^{D}$ +48° (c=0.69, $CHCl_3$). *Anal.* Calcd. for $C_{36}H_{58}O_7\cdot2H_2O$: C, 67.68; H, 9.78. Found: C, 67.87; H, 9.57. IR ν_{max}^{KBr} cm^{-1}: 3400 (br, OH), 1730 ($COOCH_3$). PMR (d_5-pyridine) δ: 0.81, 0.89

14) Instruments used in the experimental section and experimental conditions for chromatography were same as in our previous paper[13,15] unless specified otherwise.
15) I. Kitagawa, K.S. Im, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **24**, 1260(1976).
16) The crystallization was failed.

(3H each, both s), 0.93 (9H, s), 1.21, 1.22 (3H each, both s) (*tert.* $CH_3\times7$), 3.68 (3H, s, $COOCH_3$), 5.26 (1H, t-like, 12-H), 4.70 (1H, d, $J=7$ Hz, anomeric H).[17]

Acetonidation of 4 giving 5——To a solution of **4** (300 mg) in dry acetone–2,2-dimethoxypropane (20 ml—8 ml) mixture was added Dowex 50W-X8 (H^+) (120 mg)[18] and the total mixture was kept stirring at room temperature for 40 min, filtered, and the residue was washed with acetone. The combined filtrate and washings were evaporated under reduced pressure and the product (365 mg) was purified by TLC (benzene–acetone=3: 1) to give **5** (312 mg). The analytical sample of **5** was obtained by crystallization from $CHCl_3$–acetone as colorless needles of mp 239—240.5°, $[\alpha]_D^{12}$ +44° ($c=1.06$, $CHCl_3$). *Anal.* Calcd. for $C_{39}H_{62}O_7$: C, 72.86; H, 9.72. Found: C, 72.77; H, 9.70. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3613, 3448 (OH), 1734 ($COOCH_3$), 851 (acetonide). PMR ($CDCl_3$) δ: 0.72, 0.83 (3H each, both s), 0.92 (9H, s), 0.99, 1.13 (3H each, both s) (*tert.* $CH_3\times7$), 1.36, 1.54 (3H each, both s, acetonide $CH_3\times2$), 3.64 (3H, s, $COOCH_3$), 5.28 (1H, m, $W_{h/2}=8$ Hz, 12-H).

Oxidation of 5 giving 6——To a solution of **5** (250 mg) in DMSO (10 ml) was added acetic anhydride (1 ml) and the total mixture was kept stirring at 34° for 17 hr, diluted with $CHCl_3$ (30 ml), poured into ice-water, and extracted with ether. The ether extract was successively washed with water, sat. aq. $NaHCO_3$, and water, and dried over $MgSO_4$. Evaporation of the solvent gave a product which was purified by TLC (benzene–acetone=6: 1) to give **6** (206 mg). The analytical sample of **6** was obtained by crystallization from petr. ether (bp 40—60°) as fine crystals of mp 163—164°, $[\alpha]_D^{12}$ +26° ($c=2.06$, $CHCl_3$). *Anal.* Calcd. for $C_{39}H_{60}O_7$: C, 73.09; H, 9.44. Found: C, 73.03; H, 9.44. IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1768 (CO), 1735 ($COOCH_3$), 852 (acetonide). PMR ($CDCl_3$) δ: 0.71, 0.85, 0.90 (3H each, all s), 0.92 (6H, s), 0.99, 1.10 (3H each, both s) (*tert.* $CH_3\times7$), 1.37, 1.46 (3H each, both s, acetonide $CH_3\times2$), 3.14 (1H, t-like, 3α-H), 3.60 (3H, s, $COOCH_3$), 3.96 (2H, d, $J=7$ Hz, 5′-H_2), 4.50 (1H, d, $J=7$ Hz, 3′-H), 4.73 (1H, d.t, $J=7$ and 7 Hz, 4′-H), 4.86 (1H, s, anomeric H), 5.24 (1H, t-like, $W_{h/2}=8$ Hz, 12-H).

Photolysis of 6 giving 7——A solution of **6** (43 mg) in *tert.* butanol (45 ml) was irradiated externally through a Pyrex filter with a 500 W high pressure mercury lamp (Eikosha PIH-500) for 40 min (temperature of the reaction mixture: 20—30°). Evaporation of the solvent under reduced pressure and TLC separation (*n*-hexane–ether=2: 1) of the product gave methyl oleanonate (**7**) (7 mg, 44.8% based on consumed **6**) and recovered **6** (21 mg). **7** was recrystallized from $CHCl_3$–MeOH (colorless needles) and identified with an authentic sample by mixed mp (185—186°), TLC (benzene–ethyl acetate=4: 1; ether–*n*-hexane=1: 1), IR (CCl_4), and PMR ($CDCl_3$).

Acetonidation of 10 giving 12——A solution of **10** (741 mg)[10] in 2,2-dimethoxypropane (30 ml) was treated with *p*-TsOH·H_2O (catalytic amount), kept stirring at 15° for 1.5 hr, diluted with ether (400 ml), and neutralized with sat. aq. $NaHCO_3$. The ether layer was taken and worked up in the usual manner to give a product (803 mg) which was crystallized from acetone–*n*-hexane and **12a** (427 mg) was obtained as colorless needles. Purification of the mother layer by TLC (benzene–acetone=4: 1) gave an additional crop of **12a** (104 mg), mp 239—240° (from acetone–*n*-hexane), $[\alpha]_D^{12}$ +45° ($c=1.0$, $CHCl_3$). *Anal.* Calcd. for $C_{39}H_{62}O_8$: C, 71.09; H, 9.49. Found: C, 70.95; H, 9.42. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3605, 3500 (OH), 1728 ($COOCH_3$), 849 (acetonide). PMR ($CDCl_3$) δ: 0.68, 0.83, 0.92 (3H each), 0.99, 1.24 (6H each) (*tert.* $CH_3\times6$ and *sec.* $CH_3\times1$), 1.35, 1.52 (3H each, both s, acetonide $CH_3\times2$), 3.10 (1H, t-like, 3α-H), 3.60 (3H, s, $COOCH_3$), 4.24 (1H, d, $J=7$ Hz, anomeric H), 5.33 (1H, m, $W_{h/2}=7$ Hz, 12-H).

Acetylation of 12a giving 12b——Acetylation of **12a** (35 mg) with acetic anhydride–pyridine (2 ml—1 ml) mixture at 34° for 6 hr followed by the usual work-up gave a product which was crystallized from *n*-hexane–acetone to give **12b** as colorless needles of mp 268—269°, $[\alpha]_D^{22}$ +25.2° ($c=1.0$, $CHCl_3$). *Anal.* Calcd. for $C_{41}H_{64}O_9$: C, 70.25; H, 9.20. Found: C, 69.97; H, 9.15. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3609, 3508 (OH), 1746 (OAc), 1722 ($COOCH_3$), 845 (acetonide). PMR ($CDCl_3$) δ: 0.67, 0.74 (3H each), 0.91 (9H), 1.20, 1.23 (3H each) (*tert.* $CH_3\times6$ and *sec.* $CH_3\times1$), 1.34, 1.54 (3H each, both s, acetonide $CH_3\times2$), 2.06 (3H, s, OAc), 3.00 (1H, t-like, 3α-H), 3.58 (3H, s, $COOCH_3$), 4.36 (1H, d, $J=7$ Hz, anomeric H),[19] 5.03 (1H, d.t, $J=7$ and 7 Hz, 2′-H),[19] 5.32 (1H, m, $W_{h/2}=8$ Hz, 12-H).

Oxidation of 12a giving 13——A solution of **12a** (200 mg) in DMSO–acetic anhydride (8 ml—8 ml) mixture was kept stirring at 34° for 16 hr, poured into ice-water, and extracted with ether. The product obtained from the ether extract was crystallized from ether–acetone to give **13** as colorless crystals (110 mg). An additional crop of **13** (61 mg) was obtained from the mother liquor by TLC purification (benzene–acetone=6: 1). **13**, mp 211—212°, $[\alpha]_D^{22}$ +13.4° ($c=1.0$, $CHCl_3$). *Anal.* Calcd. for $C_{39}H_{60}O_8$: C, 71.31; H, 9.19. Found: C, 71.25; H, 9.25. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3614, 3504 (OH), 1763 (CO), 1721 ($COOCH_3$), 848 (acetonide). PMR ($CDCl_3$) δ: 0.67, 0.86, 0.92, 0.99, 1.20 (3H each), 1.23 (6H) (*tert.* $CH_3\times6$ and *sec.* $CH_3\times1$), 1.37, 1.46 (3H each, both s, acetonide $CH_3\times2$), 2.58 (1H, br.s, $W_{h/2}=5$ Hz, 19α-OH), 3.15 (1H, t-like, 3α-H), 3.59 (3H, s, $COOCH_3$), 3.96 (2H, d, $J=7$ Hz, 5′-H_2), 4.52 (1H, d, $J=7$ Hz, 3′-H), 4.74 (1H, d.t, $J=7$ and 7 Hz, 4′-H), 4.88 (1H, s, anomeric H), 5.33 (1H, m, $W_{h/2}=7$ Hz, 12-H).

17) The signal was overlapped with signals of hydroxyls, and it was visualized as a doublet by addition of D_2O.
18) A commercial sample was washed with dry acetone and dried in a vacuum desiccator for a week before use.
19) The assignment was confirmed by decoupling experiments.

Photolysis of 13 giving 14——A solution of **13** (50 mg) in *tert.* butanol (49 ml) was irradiated in a Pyrex tube with a 500 W high pressure mercury lamp as for **6** and evaporated under reduced pressure. The product was separated by TLC (*n*-hexane–ether=5: 3) to give **14** (5 mg) and recovered **13** (23 mg). **14** was identified with methyl pomonate[11] by IR (CCl_4) and TLC (ether–*n*-hexane=1: 1).

Acetonidation of 15 giving 17——A solution of **15** (280 mg, slightly contaminated with **16**)[13] in 2,2-dimethoxypropane (10 ml)– dry acetone (20 ml) was treated with Dowex 50 W-X8 (H^+) (100 mg) and kept stirring at room temperature for 2 hr. After dilution with acetone (50 ml), the reaction mixture was filtered and evaporated under reduced pressure. The product was purified by TLC (ether–*n*-hexane=3: 1) to give **17** (114 mg, amorphous[16]), $[\alpha]_D^{16}$ −48.5° (c=1.0, $CHCl_3$). High resolution mass spectrum: Calcd. for $C_{38}H_{60}O_9$ (M^+): 660.424. Found: 660.426. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3613, 3418 (OH), 984, 923, 901, 865 (intensity at 923<901, 25R-spiroketal), 850 (acetonide). PMR ($CDCl_3$) δ: 0.74 (3H, s, 13-CH_3), 0.77 (3H, d, J=6 Hz, 25-CH_3), 0.97 (3H, d, J=6 Hz, 20-CH_3), 1.09 (3H, s, 10-CH_3), 1.28, 1.36, 1.43, 1.56 (3H each, all s, acetonide $CH_3\times4$).

Oxidation of 17 giving 18——To a solution of **17** (110 mg) in DMSO (8 ml) was added acetic anhydride (0.8 ml) and the total solution was kept stirring at 34° for 14 hr, poured into ice-water, neutralized with sat. aq. $NaHCO_3$, and extracted with ether. An oily product obtained from the ether extract was purified by TLC (benzene–acetone=5: 1) to give **18** (87 mg, amorphous[16]), $[\alpha]_D^{16}$ −43.7° (c=0.75, $CHCl_3$). *Anal.* Calcd. for $C_{33}H_{58}O_9$: C, 69.27; H, 8.87. Found: C, 68.79; H, 8.86. IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1767 (CO), 982, 921, 901, 863 (921<901, 25R-spiroketal), 849 (acetonide). PMR ($CDCl_3$) δ: 0.74 (3H, s, 13-CH_3), 0.77 (3H, d, J=6 Hz, 25-CH_3), 0.94 (3H, d, J=6 Hz, 20-CH_3), 1.09 (3H, s, 10-CH_3), 1.25 (3H, s), 1.46 (6H, s), 1.47 (3H, s) (acetonide $CH_3\times4$), 4.96 (1H, s, anomeric H).

Photolysis of 18 giving 19——A solution of **18** (50 mg) in *tert.* butanol (50 ml) was irradiated for 40 min as for **6** and evaporated under reduced pressure. Separation of the product by TLC (ether–*n*-hexane=2: 1) gave **19** (9 mg) and recovered **18** (20 mg). **19** was recrystallized from $CHCl_3$–MeOH and identified with metagenone acetonide (prepared below) by mixed mp, IR (CCl_4), PMR ($CDCl_3$), and TLC (ether–*n*-hexane=2: 1, benzene–acetone=5: 1).

Oxidation of Metagenin Acetonide giving 19——To a solution of metagenin acetonide (100 mg)[13] in pyridine (5 ml) was added a complex solution (2 ml) of CrO_3-pyridine (prepared from 1 g and 10 ml each) and the total mixture was kept stirring at room temperature for one hour and poured into ice-water. A precipitated product was collected by filtration, washed with water, and crystallized from $CHCl_3$–MeOH to give **19** (87 mg) as colorless crystals of mp 186—188°, $[\alpha]_D^{17}$ −32.7° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{30}H_{46}O_5$: C, 74.03; H, 9.53. Found: C, 73.94; H, 9.52. IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1716 (CO), 984, 923, 901, 865 (923<901, 25R-spiroketal), 849 (acetonide). PMR ($CDCl_3$) δ: 0.69 (3H, s, 13-CH_3), 0.77 (3H, d, J=6 Hz, 25-CH_3), 0.92 (3H, d, J=6 Hz, 20-CH_3), 1.20 (3H, s, 10-CH_3), 1.28, 1.46 (3H each, both s, acetonide $CH_3\times2$), 2.23 (2H, s, 12-H_2).

Preparation of 21a and 22——Methyl oleanolate (**2**, 2.0 g, 0.43 mmole) and cadmium carbonate (1.71 g, 10 mmole) was added in dry toluene (160 ml) and 80 ml of the solvent was azeotropically distilled off. To a stirred mixture thus prepared was added dropwise a solution of 2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl bromide (PMR in $CDCl_3$: anomeric proton at δ 6.72, d, J=4 Hz) (0.37 g, 0.9 mmole) in dry toluene (160 ml) while a mixture of toluene and water was azeotropically distilled off. An additional amount of dry toluene (300 ml) was added similarly while stirring for 5 hr. After dilution with benzene (100 ml), the reaction mixture was filtered and the filtrate was evaporated under reduced pressure. The residue (2.5 g) was purified by column chromatography (silica gel 100 g) developing with ether–*n*-hexane mixture to give **21a** (1.6 g) and **22** (0.1 g). The analytical sample of **21a** was prepared by recrystallization from $CHCl_3$–MeOH as colorless needles of mp 223—224°, $[\alpha]_D^{16}$ +46.4° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{45}H_{68}O_{12}$: C, 67.47; H, 8.56. Found: C, 67.37; H, 8.54. IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1769, 1221 (OAc), 1738 ($COOCH_3$). PMR ($CDCl_3$) δ: 0.72, 0.75, 0.90 (3H each, all s), 0.93 (9H, s), 1.12 (3H, s) (*tert.* $CH_3\times7$), 1.98 (3H, s), 2.03 (6H, s), 2.14 (3H, s) (OAc×4), 3.62 (3H, s, $COOCH_3$), 4.49 (1H, d, J=7 Hz, anomeric H). **22**, mp 273° (colorless needles from $CHCl_3$–MeOH), $[\alpha]_D^{16}$ +134.6° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{45}H_{68}O_{12}$: C, 67.47; H, 8.56. Found: C, 67.63; H, 8.57. IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1759, 1226 (OAc), 1735 ($COOCH_3$). PMR ($CDCl_3$) δ: 0.74, 0.82, 0.90 (3H each, all s), 0.92 (6H, s), 1.01, 1.12 (3H, each, both s) (*tert.* $CH_3\times7$), 1.99, 2.02, 2.05, 2.12 (3H each, all s, OAc×4), 3.62 (3H, s, $COOCH_3$), 5.24 (1H, d, J=4 Hz, anomeric H).

Deacetylation of 21a giving 21b——To a solution of **21a** (1.01 g) in dry MeOH (30 ml) was added 1% NaOMe–MeOH (10 ml) and the solution was kept stirring at room temperature for 30 min, treated with Dowex 50W-X8 (H^+) (150 mg), filtered, and evaporated under reduced pressure. A product (750 mg) thus obtained was crystallized from $CHCl_3$–MeOH to give **21b** as colorless needles of mp 222—224°, $[\alpha]_D^{16}$ +44.2° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{37}H_{60}O_8\cdot2H_2O$: C, 66.43; H, 9.64. Found: C, 66.53; H, 9.41. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: no OAc, 3388 (br, OH), 1720 ($COOCH_3$), PMR (d_5-pyridine) δ: 0.80, 0.87 (3H each, both s), 0.93 (9H, s), 1.23, 1.25 (3H each, both s) (*tert.* $CH_3\times7$), 3.68 (3H, s, $COOCH_3$), 4.71 (1H, d, J=7 Hz, anomeric H), 5.36 (1H, m, $W_{h/2}$=7 Hz, 12-H).

Methylation of 21b giving 21c——To a solution of **21b** (100 mg) in DMSO (6 ml) was added dimsyl carbanion (1.2 ml)[15] and the total mixture was kept stirring under a nitrogen atmosphere at room temperature for 40 min, treated with CH_3I (1.2 ml) in the dark, kept stirring for further 2 hr, poured into ice-water, and extracted with ether. After the usual work-up of the ether extract, the product (148 mg) was purified

by TLC (ether–*n*-hexane=3: 1) to give **21c** (41 mg, amorphous[16]), $[\alpha]_D^{15}$ +40.7° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{41}H_{68}O_8$: C, 71.47; H, 9.95. Found: C, 71.49; H, 9.93. IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1728 ($COOCH_3$). PMR ($CDCl_3$) δ: 0.71, 0.82 (3H each, both s), 0.90 (9H, s), 1.01, 1.12 (3H each, both s) (*tert.* $CH_3\times7$), 3.39, 3.52, 3.55, 3.61, 3.62 (3H each, all s, $OCH_3\times4$ and $COOCH_3$), 4.25 (1H, d, J=7 Hz, anomeric H), 5.27 (1H, m, 12-H).

Tritylation of 21b giving 23——A solution of **21b** (316 mg) in dry pyridine (10 ml) was treated with trityl chloride (420 mg) and Drierite (150 mg), heated under reflux for 1.5 hr, poured into ice-water, and extracted with $CHCl_3$. A product (754 mg) obtained from the $CHCl_3$ extract was purified by TLC (ether–*n*-hexane=30: 1, detection by ultraviolet light) to give **23** (324 mg), mp 178—180° (fine crystals from acetone–*n*-hexane), $[\alpha]_D^{16}$ +28.6° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{56}H_{74}O_8$: C, 76.85; H, 8.52. Found: C, 76.43; H, 8.70. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3416 (br, OH), 1731 ($COOCH_3$), 1451 (aromatic C=C). PMR ($CDCl_3$) δ: 0.78, 0.85 (3H each, both s), 0.91 (9H, s), 1.02, 1.15 (3H each, both s) (*tert.* $CH_3\times7$), 3.63 (3H, s, $COOCH_3$), 4.28 (1H, d, J=7Hz, anomeric H), 5.27 (1H, m, 12-H), 7.1—7.6 (15H, trityl group).

Acetonidation of 23 (giving 24) followed by Oxidation (giving 25) and Photolysis giving 7——A solution of **23** (300 mg) in 2,2-dimethoxypropane (15 ml)–dry acetone (8 ml) mixture was treated with Dowex 50W-X8 (H^+) (80 mg), kept stirring at room temperature for one hour, diluted with acetone (20 ml), and filtered. Evaporation of the solvent from the filtrate under reduced pressure gave a product which was purified by TLC (ether–*n*-hexane=2: 1) to give **24** (287 mg, amorphous[16]), IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3618, 3398 (OH), 1731 ($COOCH_3$), 1451 (aromatic C=C), 871 (acetonide). PMR ($CDCl_3$) δ: 0.73, 0.87 (3H each, both s), 0.93 (9H, s), 1.01, 1.14 (3H each, both s) (*tert.* $CH_3\times7$), 1.27, 1.46 (3H each, both s, acetonide $CH_3\times2$), 3.61 (3H, s, $COOCH_3$), 4.18 (1H, d, J=7 Hz, anomeric H), 5.26 (1H, *m*, $W_{h/2}$=7 Hz, 12-H), 7.1—7.6 (15H, trityl group). Since **24** was fairly unstable and its purity was secured by TLC, it was immediately subjected to oxidation.

A stirred solution of **24** (200 mg) in DMSO (16 ml) was treated with acetic anhydride (1.5 ml) at 33° for 17 hr. After treatment of the reaction mixture as described above, the product was purified by TLC (benzene–acetone=10: 1) to give **25** (162 mg, amorphous[16]), $[\alpha]_D^{17}$ +9.1° (c=0.75, $CHCl_3$), IR $\nu_{max}^{CCl_4}$ cm^{-1}: no OH, 1768 (CO), 1732 ($COOCH_3$), 1451 (aromatic C=C), 867 (acetonide). PMR ($CDCl_3$) δ: 0.71 (3H, s), 0.89 (9H, s), 0.91, 0.96, 1.14 (3H each, all s) (*tert.* $CH_3\times7$), 1.31, 1.37 (3H each, both s, acetonide $CH_3\times2$), 3.61 (3H, s, $COOCH_3$), 4.77 (1H, s, anomeric H), 5.25 (1H, m, $W_{h/2}$=7 Hz, 12-H), 7.1—7.6 (15H, trityl group). Due to a similar reason as for **24**, **25** thus obtained was subjected to photolysis without delay.

A solution of **25** (58 mg) in *tert.* butanol (50 ml) was irradiated in a Pyrex tube with a 500 W high pressure mercury lamp (with a Pyrex filter) for 40 min as above (temp. of the reaction mixture: 28—31°). Evaporation of the solvent under reduced pressure gave a product which was purified by TLC (ether–*n*-hexane=1: 1) to give **7** (8 mg) and recovered **25** (10 mg). **7** was identified with an authentic sample by mixed mp, IR (CCl_4), PMR ($CDCl_3$), and TLC (benzene–acetone=5: 1; ether–*n*-hexane=1: 1).

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