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Reaction of Enohexopyranoside Acetates with Lithium Dimethylcuprate(I) and Its Application to Synthesis of Prelog-Djerassi Lactone

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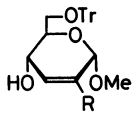
In the reaction of two 2-*O*-acetyl-3-enohexopyranosides and four 4-*O*-acetyl-2-enohexopyranosides including 2-*C*-methyl and 4-*C*-methyl derivatives, respectively, with lithium dimethylcuprate(I), anti S_N2' substitution was proved to be preferential, giving the corresponding *C*-methylated derivatives. On the other hand, S_N2 substitution occurred in the reaction of the 2-enopyranoside without methyl branch and D-glucal triacetate.

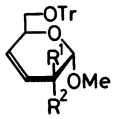
Allylic structure is readily introduced into hexopyranoside ring by elimination of vicinal diol among three consecutive hydroxyl groups.[1] Alkylation of allylic ester with lithium organocuprates[2] have been widely used for synthesis of such natural products as prostaglandin D_2.[3] In this paper, the reaction of unsaturated sugars having allylic acetate structure in the hexopyranoside ring with lithium dimethylcuprate(I) was studied in order to develop a new method for preparation of *C*-methylated chiral synthons, one of which was used for synthesis of Prelog-Djerassi lactone.

Results and Discussion

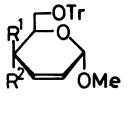
Because preliminary studies on reactions of such allylic alcohols as **1** and **2** with $MeCu \cdot BF_3$[4] or with methylmagnesium bromide in the presence of bis(triphenylphosphine)nickel(II) chloride[5] did not give promising results,[6] the reaction of allylic acetate with lithium dimethylcuprate(I) was examined. Nine pyranosides having allylic acetate structure (**3**, **4**, **6**, **9**, **10**, **12**, and **15**—**17**) and one glycal acetate (**20**) were subjected for this reaction. The syntheses of **3**,[9] **9**,[10] and **16**[11] were reported by Fraser-Reid et al., while that of **15** by Ferrier and Prasad.[12] 2-*C*-Methyl-branched (**4** and **6**) and 4-*C*-methyl-branched (**10** and **12**) allylic acetates were prepared by 1,2-addition reaction of the corresponding enone **21**[9] and **23**,[13] respectively, with methyllithium or methylcerium(III) dichloride,[14] followed by acetylation. It was noteworthy that the reactions with the latter reagent gave almost exclusively axially attacked products **4** and **10**, while those with the former reagent afforded the same epimers a little preferentially, as shown in Table 1. 4-*C*-Methyl allylic acetate **17** was prepared by 1,2-reduction of the 4-*C*-methyl enone **22**[15] with sodium borohydride and cerium(III) chloride,[16] also followed by acetylation. The



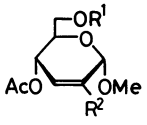
1 R = H
2 R = Me



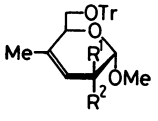
3 R^1 = H, R^2 = OAc
4 R^1 = Me, R^2 = OAc
5 R^1 = Me, R^2 = OH
6 R^1 = OAc, R^2 = Me
7 R^1 = OH, R^2 = Me
8 R^1 = Me, R^2 = H



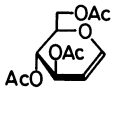
9 R^1 = H, R^2 = OAc
10 R^1 = Me, R^2 = OAc
11 R^1 = Me, R^2 = OH
12 R^1 = OAc, R^2 = Me
13 R^1 = OH, R^2 = Me
14 R^1 = Me, R^2 = H



15 R^1 = Ac, R^2 = H
16 R^1 = Tr, R^2 = Me



17 R^1 = H, R^2 = OAc
18 R^1 = Me, R^2 = H
19 R^1 = H, R^2 = Me



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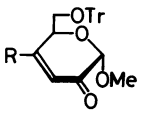

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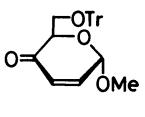
22 R = Me



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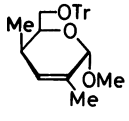

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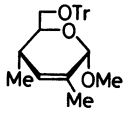

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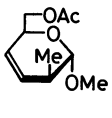

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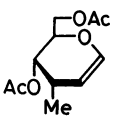

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Table 1. 1,2-Addition Reaction of **21** and **23** with MeLi or $MeCeCl_2$

Enone	Reagent	Product[a]			Yield
		ax-attack	eq-attack	ax/eq	%
21	MeLi	**4**	**6**	5:2	82.8
21	$MeCeCl_2$	**4**	**6**	10:1	85.9
23	MeLi	**10**	**12**	4:3	96.8
23	$MeCeCl_2$	**10**	**12**	1:0	quant.

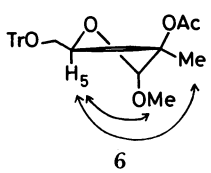
a) Isolated as acetates.

Table 2. Reaction of Enohexopyranoside Acetates with Lithium Dimethylcuprate(I) in Diethyl Ether

Allylic acetate	Condition		Product/%	Recovered Starting Material/% (deacetylated)
	Temperature/°C	Time/h		
3	−30	4	**8** 52.9	38.7(38.7)
3	0	4	**8** 79.2	17.1(17.1)
3[a]	0	4	**8** 52.1	40.8 (6.3)
4	−40	4	**24** 69.2	13.9 (5.9)
6	−40	4	**25** 82.6	10.0(trace)
9	−30	6	**8** 28.6	64.9(10.4)
9	−10	4	**8** 48.9	32.1(17.7)
9	0	4	**8** 50.9	35.2(23.0)
10	−30	6	**18** 80.3	8.5(trace)
12	−30	6	**19** trace	82.7 (4.4)
12	0	4	**19** 15.7	67.3 (7.2)
15	−10	4	**26** 54.6[b]	39.5(39.5)[c]
20	−30	4	**27** 35.0	12.7 (−)

a) THF was used as a solvent. b) Isolated as acetate. c) 4-*O*-Deacetylated (25.8%)+6-*O*-deacetylated (13.7%).

structures of these methyl-branched enopyranosides were ascertained by ^1H NMR data shown in Table 3, while the configurations at the branched carbon were determined by NOE. The *C*-methyl signal of **6** showed clear NOE when H-5 or *O*-methyl protons were irradiated, while that of **4** not. Further, the *C*-methyl signal of **12** was slightly enhanced when H-5 was irradiated. These configurational assignment was supported also by stereochemical course of reactions, i.e., above-mentioned selectivity of 1,2-addition reaction and the anti S_N2' substitution mechanisms which was observed in cyclohexenyl system.[17]



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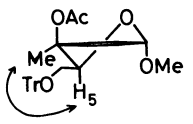

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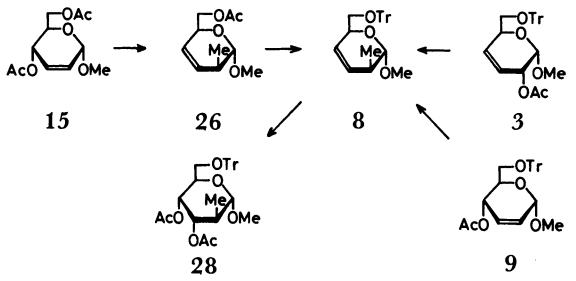
The reaction of the above-described nine allylic acetates with lithium dimethylcuprate(I) were performed in ether and the results were summarized in Table 2. The configurations of methyl-branching carbons in the products were determined by $J_{4,5}$ (the coupling constant between H-4 and H-5 in ^1H NMR) for the 2-enopyranosides such as **24** and **25** and by $J_{1,2}$ and $J_{2,3}$ (allylic geminal coupling)[7] for 3-enopyranosides such as **18**, **19**, and **26** (Table 3). Four enopyranosides having tertiary acetoxyl group at the branching carbon (**4**, **6**, **10**, and **12**) gave stereoselectively *C*-methylated derivatives (**24**, **25**, **18**, and **19**, respectively) in good yields except the last one. The anti S_N2' type reaction may be predominant as reported for cyclohexene derivatives.[18] On the other hand, unbranched 3-eno-**3** and 2-enopyranoside **9** gave the same 2-*C*-methyl derivative **8**, and another unbranched 2-enopyranoside **15** gave, after acetylation, the corresponding 2-*C*-methyl derivative **26**, in each case stereoselectively. The structure of **26** was confirmed by chemical conversion into **8** by deacetylation and tritylation. Because the possibility of 2-enopyranoside **14** could not be excluded completely from the ^1H NMR spectrum, compound **8** was further converted, by oxidation with osmium tetroxide and acetylation, into the corresponding 3,4-diacetoxy derivative **28**. Its ^1H NMR data analyzed by decoupling technique confirm the 2-*C*-methyl structure. This indicates the reaction of **3** proceeded via S_N2 type mechanism. The result may be attributed to the higher reactivity of the 2-acetoxyl group which lies between olefinic and electron-withdrawing anomeric center. However, introduction of methyl group into the acetoxyl group-bearing carbon reduces the reactivity of S_N2 reaction to prefer rather normal S_N2' reaction as shown in the case of **4**. Furthermore, introduction of methyl group into the olefin moiety showed a limitation of this reaction, that is, **16** and **17** did not react at all and the expected *gem*-di-*C*-methyl derivative could not obtained. In the case

Table 3. ^{1}H NMR Data of Starting Allylic Acetates and *C*-Methylated Products

Compound	H-1 ($J_{1,2}$)	H-2 ($J_{2,3}$)	H-3 ($J_{3,4}$)	H-4 ($J_{4,5}$)	H-5 ($J_{5,6}$)	H-6,6′ ($J_{5,6'}$)	($J_{6,6'}$)	OMe	C_2-Me	C_4-Me	Others
4	4.76s	—	6.26d (10.4)	5.88dd (4.8)	4.24m (3.0)	3.18dd, (2.6)	3.42dd (10.0)	3.52s	1.74	—	2.22s(Ac), 7.2—7.6m(Ph)
5	4.48s	—	5.72bs(2H)		4.20t (6.0)	3.18d(2H)		3.44s	1.18s	—	7.2—7.6m(Ph)
6	4.74s	—	5.86bs(2H)		4.20m (3.0)	3.06dd, (2.4)	3.28dd (10.4)	3.40s	1.62s	—	2.06s(Ac), 7.2—7.6m(Ph)
7	4.62s	—	5.64bs(2H)		4.12t (6.4)	3.34d(2H)		3.38s	1.42s	—	7.2—7.6m(Ph)
8	4.56bs	2.14m	5.69s(2H)		4.30m	3.17dd,	3.25dd	3.46s	1.06d ($J_{2,Me}$ 7.1)		7.1—7.6m(Ph)
10	4.90d (1.8)	5.64dd (10.8)	6.38d	—	4.10t (5.6)	3.42d(2H)		3.58s	—	1.40s	1.92s(Ac), 7.2—7.6m(Ph)
11	4.92bs	5.76bs(2H)		—	4.00t (6.2)	3.44d(2H)		3.52s	—	1.00s	7.1—7.6m(Ph)
12	4.76bs (1.0)	5.84dd (11.6)	6.22dd ($J_{3,Me}$ 0.8)	—	4.22t (4.8)	3.26d(2H)		3.46s	—	1.74bs	1.96s(Ac), 7.2—7.6m(Ph)
13	4.78d (1.2)	5.54dd (10.2)	5.76bd	—	4.06dd (5.8)	3.30dd, (10.6)	3.52t (10.6)	3.46s	—	1.00s	7.2—7.6m(Ph)
18	4.62d (0.8)	2.12m (4.6)	5.44m ($J_{3,4\text{-Me}}$ 0.8)	—	4.12m (4.4)	3.10ddd, (3.8)	3.40dd (10.4)	3.44s	1.12d ($J_{2,Me}$ 7.4)	1.40bs ($J_{5,4\text{-Me}}$ 1.0)	7.1—7.6m(Ph)
19	4.70d (3.8)	2.42m (2.8)	5.40m	—	4.06m	3.12—3.36m(2H)		3.38s	1.08d ($J_{2,Me}$ 7.0)	1.50bs ($J_{4,Me}$ 1.0)	7.2—7.6m(Ph)
24	4.76s	—	5.52dd (3.8)	2.14ddq (4.4)	3.7m (7.8)	3.06dd, (4.0)	3.38dd (10.2)	3.60s	1.80bs ($J_{3,Me}$ 0.6)	0.76d ($J_{4,Me}$ 9.6)	7.2—7.6m(Ph)
25	4.58bs	—	5.56dd (6.2)	2.04ddq (8.2)	4.00m (6.6)	3.30dd, (4.0)	3.44dd (8.4)	3.44s	1.70bs ($J_{3,Me}$ 0.6)	0.66d ($J_{4,Me}$ 7.8)	7.2—7.6m(Ph)
26	4.82d (1.0)	2.14m	5.80dd (11.6)	5.60dd (2.2)	3.8—4.1m(3H)			3.44s	1.08d ($J_{2,Me}$ 6.0)	—	2.06s(Ac)
27	6.24dd (6.0) ($J_{1,3}$ 1.8)	4.66dd (4.2)	2.64dddq (5.8)	5.02dd (7.4)	4.0—4.2m(3H)			—	1.08d ($J_{3,Me}$ 7.2)	—	2.06s(Ac)

of a glycal **20** only S_N2 substitution was observed to give a 3-*C*-methyl derivative **27**. These results indicate the predominance of anti S_N2' mechanism except the cases of **3** and **20**. The result of **15** is consistent with that of the corresponding ethyl glycoside, reaction of which with several organolithium derivatives including lithium dimethylcuprate(I) was reported very recently to give 2-*C*-substituted derivatives.[18]



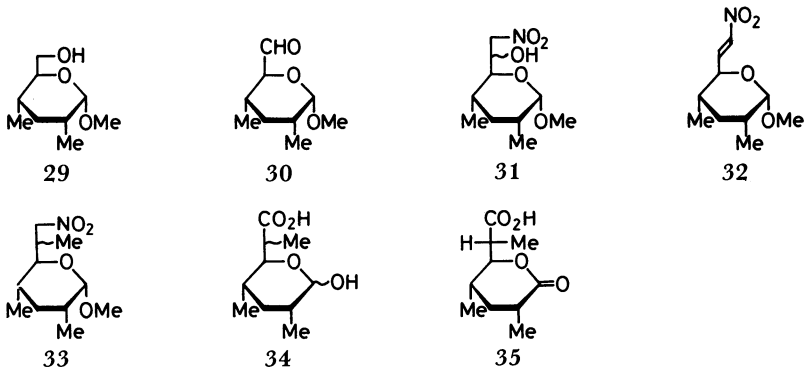
Prelog-Djerassi lactone (**35**) has been one of the key compounds for macrolide construction since synthesis of methymycin[20] and was also synthesized from D-glucose by a few groups.[21] As described above a convenient method for preparation of **25** was developed and then its utilization for synthesis of **35** was undertaken. Hydrogenation of **25** in the presence of palladium(II) hydroxide gave **29** preferentially in 43% yield. This yield seems to be fairly good in comparison with its preparation from the 4-*C*-methyl enone **22** via the corresponding 2-*C*-methylene derivative, where the yield for the latter step were not reported.[21a] Although the synthetic route from **29** to **35** has been already reported,[21a] the following alternative route was also developed.

Swern oxidation of **29** afforded a dialdopyranoside **30** in 75% yield. Treatment of **30** with nitromethane in the presence of sodium methoxide in methanol gave an epimeric mixture of condensation product **31**, which was converted into a nitro olefin **32** with acetic anhydride and pyridine in dichloromethane in 84% yield in two steps. For the last step a conventional treatment with methanesulfonyl chloride and triethylamine gave only poor results. Addition reaction of **32** with $MeCu \cdot BF_3$ in ether gave 6-*C*-methylated product **33** as an epimeric mixture with a ratio of 3 to 2 in 54% yield. On the other hand, the same reactions with lithium dimethylcuprate(I) or $Me_2Cu(CN)Li_2$ proved to give **33** trace and in 26% yield, respectively. Oxidation of **33** with potassium permanganate followed by treatment with acetic acid gave an uronic acid **34**, which was further oxidized with chromium trioxide afforded a mixture of **35** and its 6-epimer. Pure **35** was obtained as crystal from pentane-ether in 7% yield from **33**.

Table 4. ^{13}C NMR Data of *C*-Methylated Products

Compound	C-1	C-2	C-3	C-4	C-5	C-6	O-Me	C-Me
8	102.35d	34.13d	125.43d[a)]	124.18d[a)]	68.22d	66.32t	55.32q	18.58q
18	102.35d	34.49d	124.56d	131.44s	72.44d	64.42t	55.43q	18.91q, 18.46q
19	99.20d	34.60d	129.62d	130.92s	71.95d	64.83t	55.16q	18.95q, 13.06q
24	98.55d	131.55s	129.82d	30.94d	72.71d	64.75t	55.21q	18.75q, 16.80q
25	101.15d	131.29s	129.49d	30.88d	68.48d	64.42t	55.10q	18.85q, 12.57q
26	101.91d	32.31d	125.83d[a)]	123.35d[a)]	70.31d	66.61t	56.97q	19.11q
27	141.46d	104.46d	27.69d	70.98d	68.70d	62.74t	—	16.15q

a) These signals are interchangable.



Experimental

General Methods. Melting points determined with a Yanagimoto micro melting point apparatus, were uncorrected. Optical rotations were measured in chloroform, by using a 0.5-dm tube with a Carl Zeiss LEP-Al polarimeter. Infrared spectra were recorded on a Hitachi EPI-G2 grating spectrometer. ^1H and ^{13}C NMR spectra were recorded at 100 MHz with a JEOL JMN PS-100 spectrometer and at 22.5 MHz with a JEOL FX-90Q spectrometer, respectively, in $CDCl_3$ with tetramethylsilane as internal standard. Column chromatography was performed on silica gel (Wakogel C-300: Wako Pure Chemical Industries, Ltd.).

Reaction of Allylic Alcohols 1 and 2 with MeCu · BF_3. To a suspension of copper(I) iodide (0.22 g, 1.2 mmol) in ether (35 ml) were added 1.2 M (1 M=1 mol dm^{-3}) ethereal solution of methyllithium (1 ml, 1.2 mmol) at −30 °C, and then after 30 min boron trifluoride etherate (0.14 ml, 1.2 mmol) at −78 °C. After 30 min, to this mixture was added a solution of **1** (380 mg, 0.94 mmol) in ether (2 ml) at 0 °C. Being stood at this temperature for 24 h, the reaction mixture was stirred with saturated ammonium chloride solution and extracted with dichloromethane. The extract was washed with water, dried over sodium sulfate, and evaporated to a syrupy mixture of a few components, which was fractionated on a column with hexane-ethyl acetate (50:1). The products, whose yields are give in references,[6)] were characterized only by ^1H NMR.

(*S*)-2-[1-Hydroxy-2-(trityloxy)ethyl]furan (36): Mp 89—91 °C (decomp); ^1H NMR δ=6.32 (2H, bs, H-3 and H-5), 7.10 (1H, bs, H-4), 4.68 (1H, bdd, $J_{1',2'a}$=4.4 Hz, $J_{1',2'b}$=6.8 Hz, H-1'), 3.34 (1H, dd, $J_{2'a,2'b}$=8.0 Hz, H-2'a), 3.58 (1H, dd, H-2'b), and 7.2—7.6 (15H, m, Ph).

Reaction of Allylic Alcohol 2 with Methylcopper(I) Trifluoroborate. The reaction was performed in the same manner as described above using **2** instead of **1**. The products[6)] were characterized only by ^1H NMR.

(*S*)-2-[1-Hydroxy-2-(trityloxy)ethyl]-4-methylfuran (37): ^1H NMR δ=7.66 (1H, m, H-5), 6.24 (1H, m, H-3), 4.72 (1H, bt, H-1'), 3.90 (2H, bd, CH_2OTr), 2.06 (3H, m, C-Me), and 7.2—7.6 (15H, m, Ph).

(*S*)-3,5-Dimethyl-2-trityloxymethyl-2*H*-pyran (38): ^1H NMR δ=7.78 (1H, m, H-6), 6.14 (1H, m, H-4), 3.84 (1H, bt, H-2), 3.66 (2H, bd, CH_2OTr), 2.12 (3H, bs, CMe), 1.98 (3H, m, CMe), and 7.2—7.6 (15H, m, Ph).

Reaction of Allylic Alcohol 1 with Methylmagnesium Bromide in the Presence of Bis(triphenylphosphine)nickel(II) Chloride. To bis(triphenylphosphine)nickel(II) chloride (131 mg, 0.2 mmol) was added under argon a solution of **1** (2 mmol) in THF (8 ml), and the mixture was stirred at room temprature for 5 min. Then, to this solution was added 1 M tetrahydrofuran solution of methylmagnesium bromide (8 ml, 8 mmol). Being kept at room temperature for 24 h, the mixture was quenched with aqueous ammonium chloride, and extracted with dichloromethane. The extract was washed with water, dried over sodium sulfate, and evaporated to give a mixture of **39** and **1**, which was fractionated on a column with hexane-ethyl acetate (50:1). The compound **39** was characterized only by ^1H NMR data.

Methyl 2,3,4-Trideoxy-6-*O*-trityl-2,4-dienopyranoside (39): ^1H NMR δ= 4.84 (1H, d, $J_{1,2}$=1.4 Hz, H-1), 5.08 (2H, bs, H-2 and H-4), 6.22 (1H, bs, H-3), 3.82 and 3.90 (2H, ABq, J=10.4 Hz, H-6 and H-6'), 3.26 (3H, s, OMe), and 7.2—7.6 (15H, m, Ph).

Reaction of Enones 21 and 23 with Methyllithium. To a solution of the enone (582 mg, 1.45 mmol) in ether (60 ml), was added 0.8 M ethereal solution of methyllithium (7.3 ml, 5.8 mmol) at −78 °C. Being kept at the same temperature for 4 h, the reaction mixture was poured into water and extracted with ethyl acetate. The extract was washed with water, dried over magnesium sulfate, and evaporated to give a crude epimeric mixture of 1,2-addition product, whose separation was described in the following paragraph.

Methyl 2-*O*-Acetyl-3,4-dideoxy-2-*C*-methyl-6-*O*-trityl-α-D-*erythro*-hex-3-enopyranoside (4) and Methyl 2-*O*-Acetyl-3,4-

dideoxy-2-*C*-methyl-6-*O*-trityl-α-D-*threo*-hex-3-enopyranoside (6). The reaction of **21** with methyllithium as described above gave a mixture of **5** and **7**, which was separated on a column with hexane-ethyl acetate (12 : 1).

5: Syrup, $[\alpha]_D$ −13.7° (*c* 0.9, $CHCl_3$); IR (NaCl) 3400 (OH) and 1610 cm^{-1} (C=C).

Found: C, 77.52; H, 6.83%. Calcd for $C_{27}H_{28}O_4$: C, 77.86; H, 6.78%.

7: Syrup, $[\alpha]_D$ +173.5° (*c* 1.9, $CHCl_3$); IR (NaCl) 3400 (OH) and 1610 cm^{-1} (C=C).

Found: C, 77.90; H, 6.48%. Calcd for $C_{27}H_{28}O_4$: C, 77.86; H, 6.78%.

Acetylation of **5** and **7** with acetic anhydride and pyridine in the presence of 4-(dimethylamino)pyridine geve **4** and **6**, respectively, which were purified on a column with hexane-ethyl acetate (15 : 1).

4: Syrup $[\alpha]_D$ +44.7° (*c* 0.9, $CHCl_3$); IR (NaCl) 1730 (C=O) and 1600 cm^{-1} (C=C).

Found: C, 75.80; H, 6.33%. Calcd for $C_{29}H_{30}O_5$: C, 75.96; H, 6.59%.

6: Syrup, $[\alpha]_D$ +38.9° (*c* 5.1, $CHCl_3$); IR (NaCl) 1730 (C=O) and 1600 cm^{-1} (C=C).

Found: C, 75.53; H, 6.28%. Calcd for $C_{29}H_{30}O_5$: C, 75.96; H, 6.59%.

The ^1H NMR data for compounds **4—7** are given in Table 3.

Methyl 4-*O*-Acetyl-2,3-dideoxy-4-*C*-methyl-6-*O*-trityl-α-D-*erythro*-hex-2-enopyranoside (10) and Methyl 4-*O*-Acetyl-2,3-dideoxy-4-*C*-methyl-6-*O*-trityl-α-D-*threo*-hex-2-enopyranoside (12). The reaction of **23** with methyllithium as described above gave a mixture of **11** and **13**, which were separated on a column with hexane-ethyl acetate (14 : 1).

11: Syrup, $[\alpha]_D$ −11.8° (*c* 0.6, $CHCl_3$); IR (NaCl) 3400 (OH) and 1600 cm^{-1} (C=C).

Found: C, 77.94; H, 6.58%. Calcd for $C_{27}H_{28}O_4$: C, 77.86; H, 6.78%.

13: Syrup, $[\alpha]_D$ +17.5° (*c* 0.93, $CHCl_3$); IR (NaCl) 3400 (OH) and 1600 cm^{-1} (C=C).

Found: C, 77.95; H, 7.04%. Calcd for $C_{27}H_{28}O_4$: C, 77.86; H, 6.78%.

Acetylation of **11** and **13** with acetic anhydride and pyridine in the presence of 4-(dimethylamino)pyridine gave **10** and **12**, respectively, which were purified on a column with hexane-ethyl acetate (18 : 1).

10: Syrup, $[\alpha]_D$ +56.9° (*c* 2.3, $CHCl_3$); IR (NaCl) 1740 (C=O) and 1610 cm^{-1} (C=C).

Found: C, 76.04; H, 6.74%. Calcd for $C_{29}H_{30}O_5$: C, 75.96; H, 6.59%.

12: Syrup, $[\alpha]_D$ −25.5° (*c* 1.5, $CHCl_3$); IR (NaCl) 1740 (C=O) and 1610 cm^{-1} (C=C).

Found: C, 76.11; H, 6.41%. Calcd for $C_{29}H_{30}O_5$: C, 75.96; H, 6.59%.

The ^1H NMR data for compounds **10—13** are given in Table 3.

Reaction of Enones 21 and 23 with Methylcerium(III) Dichloride. To a suspension of finely powdered and dried cerium(III) chloride (740 mg, 3 mmol) in tetrahydrofuran (15 ml), was added with stirring 1.2 M ethereal solution of methyllithium (2.5 ml, 3 mmol) at 0 °C under argon. To this suspension was added a solution of enone (400 mg, 1 mmol) in tetrahydrofuran (3 ml) at −78 °C. The stirring was continued for 7 h at −78 °C, and the mixture was processed as in the same manner described for **4** and **6** or **10** and **12**. The results are summarized in Table 1.

Methyl 2-*O*-Acetyl-3,4-dideoxy-4-*C*-methyl-6-*O*-trityl-α-D-*erythro*-hex-3-enopyranoside (17). To a solution of **22**[15] (414 mg, 1 mmol) in ethanol (1 ml), was added with stirring cerium(III) chloride (490 mg, 2 mmol) and then sodium borohydride (75 mg, 2 mmol) at 0 °C. The stirring was continued for 3 h until gas evolution ceased. The reaction mixture was then poured into aqueous sodium chloride and extracted with dichloromethane. The extract was washed with aqueous sodium chloride, dried over magnesium sulfate, and evaporated to give a crude allylic alcohol as syrup, which was acetylated with acetic anhydride (3 ml) and pyridine (5 ml). The 2-acetate **17** was purified on a column with hexane-ethyl acetate (15 : 1). Yield, 348 mg (76%).

17: Syrup, $[\alpha]_D$ −24.7° (*c* 0.9, $CHCl_3$); IR (NaCl) 1730 (C=O) and 1600 cm^{-1} (C=C); ^1H NMR δ=5.16 (1H, bd, $J_{1,2}$=4.2 Hz, H-1), 5.54 (1H, m, H-2), 5.88 (1H, m, H-3), 4.32 (1H, bt, H-5), 3.36 (2H, bd, $J_{5,6}$=7.8 Hz, H-6 and H-6′), 1.98 (3H, bs, CMe), 2.00 (3H, s, OAc), 3.42 (3H, s, OMe), and 7.2—7.6 (15H, m, Ph).

Found: C, 75.92; H, 6.41%. Calcd for $C_{29}H_{30}O_5$: C, 75.96; H, 6.59%.

Reaction of Allylic Acetates with Lithium Dimethylcuprate-(I). To a suspension of CuI (3 equiv) in ether were added 1.2 M ethereal solution of methyllithium (6 equiv) at 0 °C, and then, after 5 min, a solution of an allylic acetate (1 equiv) in ether. The reaction mixture was poured into saturated aqueous ammonium chloride, and extracted with dichloromethane. The extract was evaporated to give residue, which was purified on a column with a solvent system given in each case. In the reaction of **15** the product was acetylated in usual manner. The yields, ^1H NMR and ^{13}C NMR data of the products (**8**, **18**, **19**, **24**, **25**, **26**, and **27**) are given in Table 2, 3, and 4, respectively.

Methyl 2,3,4-Trideoxy-2-*C*-methyl-6-*O*-tirtyl-α-D-*threo*-hex-3-enopyranoside (8). (a) From 3 or 9. The reaction of **3** or **9** with lithium dimethylcuprate(I) as described above gave crude **8**, which was purified on a column with hexane-ethyl acetate (15 : 1).

8: $[\alpha]_D$ −19.3° (*c* 2.1, $CHCl_3$); IR (NaCl) 1610 cm^{-1} (C=C).

Found: C, 81.27; H, 6.92%. Calcd for $C_{27}H_{28}O_3$: C, 80.97; H, 7.05%.

(b) From 26. To a solution of **26** (25.6 mg, 0.13 mmol) in methanol (1 ml) was added a drop of 1 M sodium methoxide and after 5 min the mixture was neutralized with IR-120 (H^+). The residue obtained by evaporation of the filtrate was treated with trityl chloride (55.8 mg, 0.2 mmol) in pyridine (0.5 ml) in a conventional manner. The crude product was purified on a column with hexane-ethyl acetate (25 : 1) to give **8** (49.9 mg, 88%), which was identified by ^1H NMR spectrum.

Methyl 2,3,4-Tridexoy-2,4-di-*C*-methyl-6-*O*-trityl-α-D-*threo*-hex-3-enopyranoside (18). The reaction of **10** with lithium dimethylcuprate(I) as described above gave crude **18**, which was purified on a column with hexane-ethyl acetate (20 : 1).

18: Syrup, $[\alpha]_D$ +47.5° (*c* 1.4, $CHCl_3$); IR (NaCl) 1610 cm^{-1} (C=C).

Found: C, 81.23; H, 7.51%. Calcd for $C_{28}H_{30}O_3$: C, 81.13; H, 7.29%.

Methyl 2,3,4-Trideoxy-2,4-di-*C*-methyl-6-*O*-trityl-α-D-*erythro*-hex-3-enopyranoside (19). The reaction of **12** with lithium dimethylcuprate(I) as described above gave crude **19**, which was purified on a column with hexane-ethyl acetate

(20 : 1).

19: Syrup, $[\alpha]_D$ −34.0° (*c* 1.0, $CHCl_3$); IR (NaCl) 1610 cm^{-1} (C=C).

Found: C, 81.12; H, 7.07%. Calcd for $C_{28}H_{30}O_3$: C, 81.13; H, 7.29%.

Methyl 2,3,4-Trideoxy-2,4-di-*C*-methyl-6-*O*-trityl-α-D-*threo*-hex-2-enopyranoside (24). The reaction of **4** with lithium dimethylcuprate(I) as described above gave crude **24**, which was purified on a column with hexane-ethyl acetate (15 : 1).

24: Syrup, $[\alpha]_D$ −18.3° (*c* 0.7, $CHCl_3$); IR (NaCl) 1600 cm^{-1} (C=C).

Found: C, 81.01; H, 7.01%. Calcd for $C_{28}H_{30}O_3$: C, 81.13; H, 7.29%.

Methyl 2,3,4-Trideoxy-2,4-di-*C*-methyl-6-*O*-trityl-α-D-*erythro*-hex-2-enopyranoside (25). The reaction of **6** with lithium dimethylcuprate(I) as described above gave crude **24**, which was purified on a column with hexane-ethyl acetate (20 : 1).

25: Syrup, $[\alpha]_D$ +6.5° (*c* 0.8, $CHCl_3$); IR (NaCl) 1600 cm^{-1} (C=C).

Found: C, 80.95; H, 7.38%. Calcd for $C_{28}H_{30}O_3$: C, 81.13; H, 7.29%.

Methyl 6-*O*-Acetyl-2,3,4-trideoxy-2-*C*-methyl-α-D-*threo*-hex-3-enopyranoside (26). The reaction of **15** with lithium dimethylcuprate(I) as described above, followed by a conventional acetylation with acetic anhydride in pyridine, gave crude **26**, which was purified on a column with hexane-acetone (7 : 1).

26: Syrup, $[\alpha]_D$ −19.3° (*c* 2.1, $CHCl_3$); IR (NaCl) 1730 (C=O) and 1610 cm^{-1} (C=C).

Found: C, 60.02; H, 8.14%. Calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05%.

4.6-Di-*O*-acetyl-1,5-anhydro-2,3-dideoxy-3-*C*-methyl-D-*ribo*-hex-1-enitol (27). The reaction of **20** with lithium dimethylcuprate(I) as described above gave crude **27**, which was purified on a column with hexane-acetone (3 : 1).

27: Syrup, $[\alpha]_D$ +3.7° (*c* 0.8, $CHCl_3$); IR (NaCl) 1740, 1720 (C=O) and 1620 cm^{-1} (C=C).

Found: C, 58.19; H, 6.21%. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24%.

Methyl 3,4-Di-*O*-acetyl-2-deoxy-2-*C*-methyl-6-*O*-trityl-α-D-altropyranoside (28). To a solution of **8** (120 mg, 0.29 mmol) in oxolane (1.5 ml)-acetone (1.5 ml)-water (1.5 ml) was added *N*-methylmorpholine *N*-oxide (50 mg, 0.43 mmol) and osmium tetroxide (3.3 mg). Being stood at room temperature for 2 d, the reaction mixture was poured into water and extracted with chloroform. A conventional processing of the extract gave a syrupy residue, which was acetylated in a conventional manner with acetic anhydride (3 ml) and pyridine (4 ml). A syrup obtained by usual processing was purified on a column with hexane-ethyl acetate (13 : 2) to give **28**, 87.2 mg (58%), mp 136—139.5 °C (white needles), $[\alpha]_D$ +51.5° (*c* 1.0, $CHCl_3$); ^1H NMR δ=4.45 (1H, d, $J_{1,2}$=3.0 Hz, H-1), 2.15 (H-2), 5.00 (1H, dd, $J_{2,3}$=5.6 Hz, $J_{3,4}$=3.6 Hz, H-3), 5.14 (1H, dd, $J_{4,5}$=8.0 Hz, H-4), 4.12 (1H, ddd, $J_{5,6}$=3.0 Hz, $J_{5,6'}$=4.5 Hz, H-5), 3.25 (2H, m, H-6 and H-6'), 1.14 (3H, d, $J_{2,Me}$=7.5 Hz, CMe), 1.81 and 2.02 (each 3H, each s, OAc), 3.40 (3H, s, OMe), and 7.1—7.5 (15H, m, Ph).

Found: C, 71.64; H, 6.55%. Calcd for $C_{31}H_{34}O_7$: C, 71.80; H, 6.61%.

Methyl 2,3,4,6,7-Pentadeoxy-2,4-di-*C*-methyl-7-nitro-α-D-*ribo*-hept-6-enopyranoside (32). Compound **25** (3.7 g, 8.9 mmol) was hydrogenolyzed (1 atm) in ethanol (200 ml) in the presence of $Pd(OH)_2$-carbon (20%, 0.3 g) at room temperature for 1 week. Undissolved materials were filtered off, and the filtrate was evaporated and then distilled (86 °C/20 mmHg (1 mmHg=133.322 Pa)) to give acolorless oil **29**, (667 mg, 43%), whose NMR data was identical with those reported.[21a] Then, **29** (500 mg, 2.9 mmol) was oxidized with DMSO (0.29 ml, 3.4 mmol) and oxalyl dichloride (0.27 ml, 3.4 mmol) in dichloromethane (50 ml) at −78 °C for 1 h. The reaction mixture was quenched with triethylamine, poured into water and extracted with dichloromethane. Evaporation of the extract gave **30** (363 mg, 75%).

To a solution of nitromethane (1.4 ml) in methanol (2.5 ml), were added 2 M sodium methoxide (0.22 ml) and then a solution of **30** (530 mg, 3.0 mmol) in methanol (2 ml) at 0 °C. Being kept at 0 °C for 3 h, the reaction mixture was acidified with 10% acetic acid and extracted with chloroform. The extract was washed with water, dried over magnesium sulfate and evaporated to give a crude **31** as a mixture of 6-epimers.

To a solution of crude **31** in pyridine (6 ml), was added acetic anhydride (3 ml) and the mixture was kept at room temperature overnight. A usual processing gave crude **32**, which was purified on a column with hexane-ethyl acetate (3 : 1). Yield, 611 mg (84%).

32: Syrup, $[\alpha]_D$ +103° (*c* 0.9, $CHCl_3$); IR (NaCl) 1360, 1530 (NO_2) and 1655 cm^{-1} (C=C). ^1H NMR δ=5.22 (1H, d, $J_{1,2}$=3.4 Hz, H-1), 4.24 (1H, bd, $J_{4,5}$=6.6 Hz, H-5), 7.28 (2H, bs, H-6 and H-7), 1.16 and 1.30 (each 3H, d, C-Me), 1.8—2.3 (4H, m, H-2, H-3,3', and H-4), 3.48 (3H, s, OMe).

Found: C, 55.83; H, 7.67: N, 6.84%. Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51%.

Prelog-Djerassi Lactone (35). To a suspension of copper(I) iodide (162 mg, 0.85 mmol) in ether (10 ml), were added methyllithium (1.2 M in ether, 0.71 ml, 0.85 mmol) at −10 °C, and then after cooling to −30 °C a solution of boron trifluoride etherate (0.11 ml, 0.85 mmol) in ether (10 ml). The mixture was stirred for 20 min at −30 °C, then cooled to −78 °C, and to this mixture was added a solution of **32** (60.3 mg, 0.28 mmol) in ether 5 ml. The stirring was continued for 4 h at −30 °C and, the reaction mixture was poured into water, extracted with dichloromethane, dried over magnesium sulfate, and evaporated. Purification of the residue on a column with hexane-ethyl acetate (2 : 1) gave **33** as a mixture of 6-epimers (35 mg, 54%).

To a suspension of **33** (163 mg, 0.71 mmol) in water (5 ml) was added 0.1 M potassium hydroxide (0.76 mmol) and then, after 20 min, 2 M aqueous manganese(II) sulfate (1 ml) and potassium permanganate (266 mg, 1.5 mmol) in two portions. The reaction mixture was stirred for 6 h at room temperature, and to this mixture was added aqueous sodium thiosulfate. After removal of the precipitated manganese dioxide by filtration, the filtrate was adjusted at pH 2—3 with 10% acetic acid, stood at room temperature for 1 h and then extracted with chloroform-1-butanol. The extract was dried over magnesium sulfate, and evaporated to give crude **34**. To a solution of **34** in acetic acid (15 ml) and water (5 ml) was added chromium trioxide (90 mg, 0.9 mmol) at 0 °C. Being kept at 0 °C for 6 h, the reaction mixture was extracted with chloroform-DMF. The extract was washed with saturated aqueous sodium thiosulfate, and evaporated. Crude product was passed through a short column with chloroform-methanol-acetic acid (5 : 1 : 0.1) to give white syrup (32 mg, 22%) which was crystallized from pentane-ether to give pure **35** (10 mg, 7% from **33**). The data of **35** were identical to

the reported ones. Mp 125—126 °C; lit, mp 124—125 °C;[22] mp 126—128 °C,[23] $[\alpha]_D$ +37.2° (*c* 1.0, $CHCl_3$), lit,[23] $[\alpha]_D$ +38.0° (*c* 1.9, $CHCl_3$). ^{13}C NMR ($CDCl_3$) δ=8.5 (α-CH_3), 16.6 and 17.1 (C_3-CH_3 and C_5-CH_3), 30.6 (C_4), 36.2 and 37.0 (C_3 and C_5), 41.2 (C_α), 86.1 (C_2), 174.4 and 174.9 (HO_2C and C_6), lit,[17b] δ=8.4 (α-CH_3), 16.8 and 17.2 (C_3-CH_3 and C_5-CH_3), 30.8 (C_4), 36.2 and 37.1 (C_3 and C_5), 41.0 (C_α), 86.4 (C_2), 174.7 and 177.6 (HO_2C and C_6).

Found: C, 59.76; H, 8.24%. Calcd for $C_{10}H_{16}O_4$; C, 59.98; H, 8.05%.

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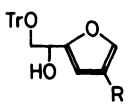
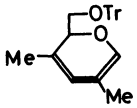
6) The reaction of **1** with methylcopper(I) trifluoroborate in ether at 0 °C for 24 h gave 2-*C*-methyl-substituted derivative **8** and (*S*)-2-[1-hydroxy-2-(trityloxy)ethyl]furan derivative[7] **36** in 19% and 26% yields, respectively (recovered **1**, 49%). At room temperature the yield of **36** increased to 66% (**8**, 14% and **1**, 9%). The same reaction of **2** at 0 °C for 24 h gave the corresponding dimethyl derivative (**24**), 4-methylfuran (**37**) and 3,5-dimethyl-2*H*-pyran (**38**) derivatives, in 15, 7, and 59% yields, respectively. On the other hand, the reaction of **1** with methylmagnesium bromide in the presence of bis(triphenylphosphine)nickel(II) chloride in tetrahydrofuran at room temperature for 24 h gave dienopyranoside[8] (**39**) in only 16% yield (recovered **1**, 79%).



36 R=H
37 R=Me



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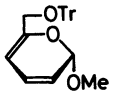

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