Lewis Acid Induced Homoallylic C-Alkylation. A New Approach to C-Glycosides

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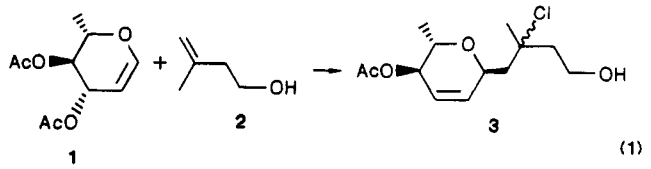
A direct and highly stereoselective route to 1-aldo and 2-keto C-glycosides has been developed by using the first example of Lewis acid induced generation of homoenolate ions from allylic ethers.

As part of our ongoing interest in the development of new procedures for the preparation of C-glycosides[1-3] we have recently explored reaction of olefins with peracetylated glycals.[4] By this methodology 2',3'-unsaturated C-glycosides could be produced in good to excellent yields with an high degree of stereoselectivity, allowing in addition the direct introduction of polyfunctional aglycons. We have now turned out our attention to Lewis acid induced reactions of allylic alcohols[5] in order to investigate a straightforward preparation of 1-aldo and 2-keto C-glycosides.

This idea originates from the reaction of diacetyl L-rhamnal (1) with 3-methyl-3-buten-1-ol (2)[6] (eq 1) in the presence of $SnCl_4$ which shown clearly that activated olefins reacted faster than alcohols with peracetylated glycals. This result prompted us to examine analogous reactions with derivatives of 2-methyl-2-propen-1-ol (4) in order to investigate the possible direct introduction of a propionyl synthon.



1 2 3 (1)

Lewis acid induced addition of enolates to electrophilic carbons occupies an important position in carbon–carbon bonds formation. However despite recent progress in homoenolate chemistry[7-9] the generation of an homoenolate equivalent under Lewis acid catalysis has been to the best of our knowledge never been communicated (Scheme I). In this report we describe the first Lewis acid promoted generation of an homoenolate equivalent from an allylic silyloxy ether and its use for the preparation of higher branched chain carbohydrates.[10]

Scheme I

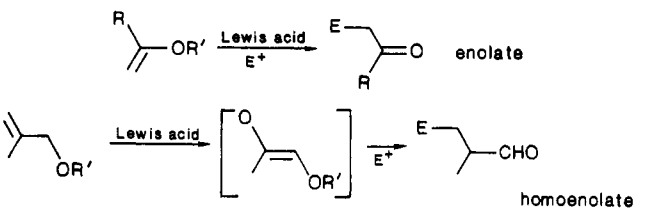
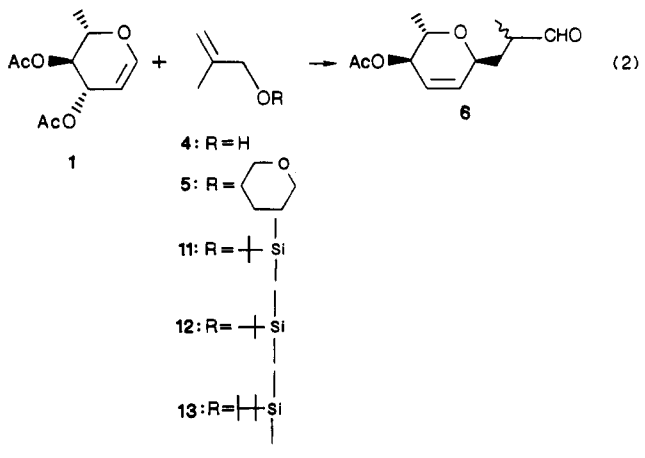


Table I. ^{1}H NMR Chemical Shift and Coupling Constants for the H-3 Protons of 7-*O*-Acetyl-4,8-anhydro-2(*R*,*S*)-*C*-methyl-2,3,5,6,9-pentadeoxy-L-*ribo*-non-5-enose (6)

		J, Hz			
	δ	2,3	3,3	3,3	3,4
H-3a (*R*)	1.80	9.25		14.00	4.40
H-3b (*R*)	1.95	3.80	14.00		8.00
H-3a (*S*)	1.42	7940		14.30	3.35
H-3b (*S*)	2.15	6.02	14.30		10.30

We first examined the condensation of L-rhamnal (1) with 1-[(tetrahydropyranyl)oxy]-2-methyl-2-propene (5) (eq 2). The reaction was carried out at −20 °C in meth-



1 6 (2)

(1) Reviews: (a) Hanessian, S.; Pernet, A. G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111. (b) Daves, G. D.; Cheng, C. C. *Prog. Med. Chem.* **1976**, *13*, 303.

(2) For some recent examples, see: (a) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976. (b) Cupps, T. L.; Wise, D. S.; Towsend, L. B. *J. Org. Chem.* **1982**, *47*, 5115. (c) Kozilowski, A. P.; Sorgi, K. L.; Wang, B. C.; Zu, S. *Tetrahedron Lett.* **1983**, *24*, 1563. (d) Lancellin, J. M.; Amvan Zollo, P. H.; Sinay, P. *Tetrahedron Lett.* **1983**, *24*, 4833. (e) Cupps, T. L.; Wise, D. S.; Townsend, L. B. *Carbohydr. Res.* **1983**, *115*, 59. (f) Hosomi, A.; Sakata, Y.; Sakurai, H. *Tetrahedron Lett.* **1984**, *25*, 2383. (g) Keck, G. E.; Enholm, E. J.; Kachensky, D. F. *Tetrahedron Lett.* **1984**, *25*, 1867.

(3) 2,3-Unsaturated C-glycosides: (a) Grynkiewics, G.; BeMiller, J. N. *J. Carbohydr. Res.* **1982**, *1*, 121. (b) Danishefsky, S. J.; Kerwin, J. F. *J. Org. Chem.* **1982**, *47*, 3803. (c) Yougai, S.; Miwa, T. *J. Chem. Soc., Chem. Commun.* **1983**, 68. (d) Dawe, R. D.; Fraser-Reid, B. *J. Org. Chem.* **1984**, *49*, 522. (e) Rajambabu, T. V. *J. Org. Chem.* **1985**, *50*, 3642. (f) Danishefsky, S. J.; DeNinno, S.; Lartey, P. *J. Am. Chem. Soc.* **1987**, *109*, 2082.

(4) Herscovici, J.; Muleka, K.; Antonakis, K. *Tetrahedron Lett.* **1984**, *25*, 5653.

(5) Reaction of peracetylated glycals with alcohols: (a) Ferrier, R. J. *J. Chem. Soc.* **1964**, 5443. Ferrier, R. J.; Prasad, N. *J. Chem. Soc.* **1969**, 570. (b) With allylic alcohols: Heyns, K.; Hohlweg, R. *Chem. Ber.* **1978**, *111*, 1632.

(6) Muleka, K. Thèse de Doctorat, Université de Paris VII, 1985.

(7) For recent publications on homoenolate, see: (a) Enda, J.; Kuwajima, I. *J. Am. Chem. Soc.* **1985**, *107*, 5495. (b) Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 83 and reference cited therein.

(8) For homoenolate from metalated allylic ether, see: (a) Evans, D. A.; Andrews, G. C.; Buckwalter, B. J. *J. Am. Chem. Soc.* **1974**, *96*, 5560. (b) Still, W. C.; Macdonald, T. L. *J. Am. Chem. Soc.* **1974**, *96*, 5561.

(9) For Pd(0)-assisted aromatic substitution using allylic alcohol, see: (a) Heck, R. F.; Melpolder, J. B. *J. Org. Chem.* **1976**, *41*, 265. (b) Chalk, A. J.; Magennis, S. A. *J. Org. Chem.* **1976**, *41*, 273.

(10) For recent publication on higher carbon sugars, see: Brimacombe, J. S.; Kabir, K. M. S.; Bennett, F. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1677.

0022-3263/87/1952-5691$01.50/0

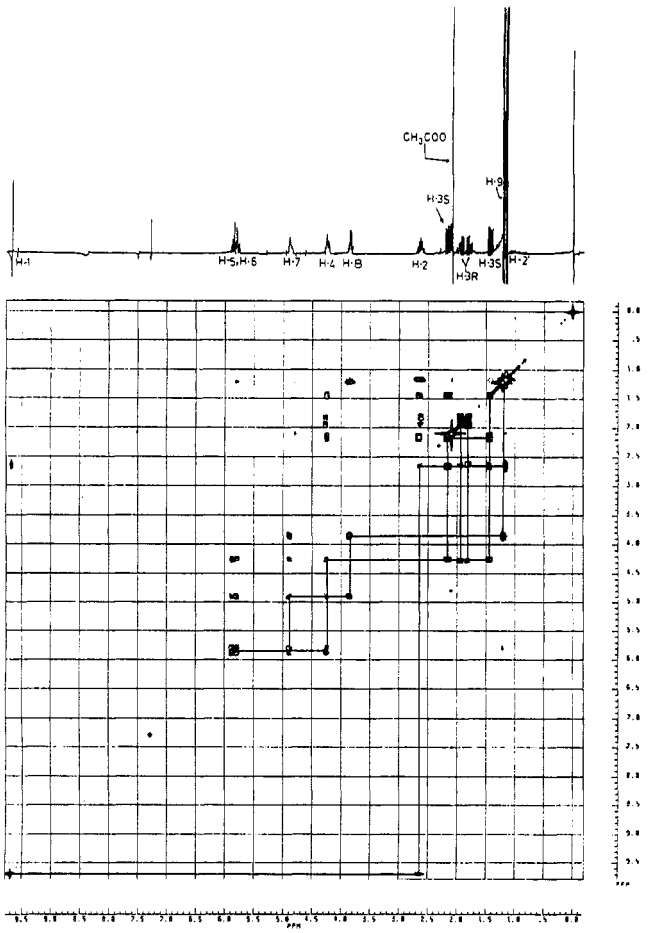


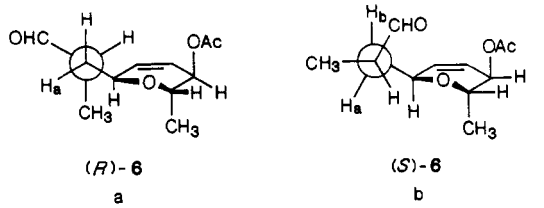
Figure 1. Contour plot of a high-resolution COSY for **6**. The 1D 300-MHz ^1H NMR spectrum is shown above.

ylene chloride using 1 equiv of $SnCl_4$ and 1.2 equiv of **5**. After 5 min the starting material completely disappeared, and a more polar compound reacting positively with 2,4-dinitrophenylhydrazine was identified. The reaction was quenched with aqueous sodium hydrogen phosphate solution then extraction with ether and flash chromatography[11] afforded the C-glycoside **6**.

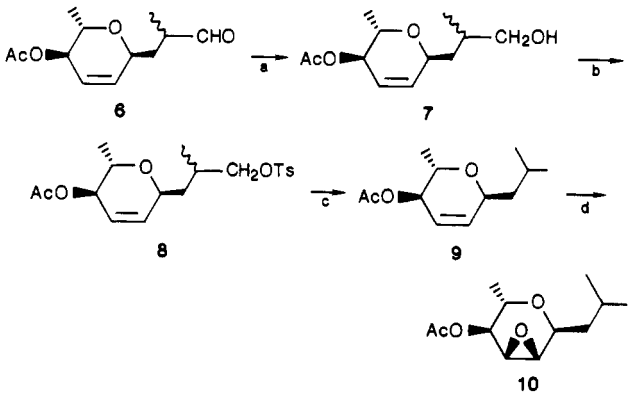
The presence of an aldehyde was dictated by the characteristic 300-MHz ^1H and ^{13}C NMR spectra of **6** consisting of resonances at δ 9.67 (d, 1 H, J = 1.7 Hz) and 194.73 (d). Olefinic signals at δ 5.77–5.85 assigned to H-5 and H-6 indicated the regioselective addition of the homoenolate ion at C1. The two multiplets at δ 3.83 (dq, 0.6 H, J = 5.4 and 7 Hz) and 3.85 (dq, 0.4 H, J = 4.8 and 7 Hz) were assigned to the H-8 proton. The $J_{8,9}$ coupling constants (J = 4.8 and 5.4 Hz) indicated[12] that the alkylation has occurred from the α side. In addition the NMR integration suggests the presence of a 3:2 mixture of 2*R* and 2*S* L-*ribo* enoses. Confirmation of this hypothesis was obtained from the examination of the C-2 methyl signals and by the study of the ^{13}C NMR decoupled spectrum which revealed the presence of twin signals.

The stereochemistry at C-2 was deduced from the ^1H 1D and 2D spectra. Examination of the COSY spectrum (Figure 1) indicates closely that the H-3 methylene signals at δ 1.80 (ddd, 0.4 H) was correlated to the resonance at 1.95 (ddd, 0.4 H) while the protons at δ 1.42 (ddd, 0.6 H) and 2.15 (ddd, 0.6 H) are coupled to each other. Decoupling experiments provide complete coupling informations as summarized in Table I.

Chart I



Scheme II[a]



[a] (a) $NaBH_4$; (b) TsCl/pyridine; (c) $(CH_3CH_2CHCH_3)_3BHLi$; (d) MCPBA.

For the minor isomer the small chemical shift difference between H-3a and H-3b reflects a similar magnetic environment. This small difference would only be anticipated for the 6*R* isomer with a syn relationship between the C2–C3 and the C4–C5 bond. In this configuration, consistent with the $J_{2,3}$ and $J_{3,4}$ coupling constants, the anisotropic effect of both the pyran oxygen and the C1 carbonyl could combine to create the similar environment experienced by H-3 protons (Chart I, a). For the 6*S* isomer the large chemical shift difference between H-3a and H-3b reflects a severe difference in their magnetic environments and suggested an eclipsed conformation, with the carbonyl close to the H-3b proton, confirmed by the value of the $J_{2,3}$ coupling constants (Chart I, b).

The assigned structures were ascertained in the following manner (Scheme II). C-Glycoside **6** was first treated with sodium borohydride (MeOH, 10 equiv, 15 min, 0 °C, 76%). Examination of the 300-MHz NMR spectra indicates the presence of a primary alcohol at C1 (δ 3.35 and 3.45, (d, H-1)) and an acetyl signal at δ 2.1, consistent with the chemoselective reduction of the aldehyde. Tosylation (TsCl, 1.2 equiv, pyridine, room temperature) of alditol **7** for one night afforded the 1-tosyloxy derivative **8** in 80% yield. Reduction of **8** using lithium tri-*sec*-butylborohydride (L-Selectride, Aldrich) produced the isopropyl C-glycoside **9** (3 equiv, room temperature, 1 h, 82%). Examination of the ^1H NMR spectra[13] revealed now only one signal for the H-9 methyl at δ 1.28 (d, 3 H, J = 6.3 Hz, H-9) and two multiplets at δ 1.27 (ddd, 1 H, J = 4.6, 8.3

(11) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(12) Achamanowitz, O.; Bukowski, P. *Rocz. Chem.* **1973**, *47*, 99 and ref 3d.

(13) **4,8-Anhydro-2-*C*-methyl-1,2,3,5,6,9-hexadeoxy-L-*ribo*-non-5-enitol (9)**: ^1H NMR δ 1.04 and 1.06 (2 d, 2 × 3 H, J = 6.7 Hz, H-1 and H-2'), 1.27 (ddd, 1 H, J = 4.6, 8.3, and 15 Hz, H-3), 1.28 (d, 3 H, J = 6.3 Hz, H-9), 1.63 (ddd, J = 5.6, 9.5, and 15 Hz, H-3), 1.68 (br d, 1 H, J = 5.9 Hz, OH), 1.81 (ddq, 1 H, J = 5.6, 6.7, and 8.3 Hz, H-2), 3.67 (dq, 1 H, J = 6.2 and 6.3 Hz, H-8), 3.75 (ddd, 1 H, J = 5.9, 6.2, and 6.3 Hz, H-7), 4.18 (ddd, 1 H, J = 2, 4.6, and 9.5 Hz, H-4), 5.78 (m, 2 H, H-5 and H-6); ^{13}C NMR δ 17.36 (q, C-9), 21.98 and 23.13 (q, C-1 and C-2'), 24.75 (d, C-2), 42.16 (t, C-3), 68.31 (d, C-8), 69.40 (d, C-8), 69.40 (d, C-7), 70.16 (d, C-4), 127.19 (d, C-6), 132.18 (d, C-5).

Table II. Effect of Various Lewis Acids on the Addition of 5 to L-Rhamnal 1

acid	equiv	T,[a] °C	yield, %
$AlCl_2Et$	1	−30	poor
$AlCl_2Me$	1	−30	poor
$SnCl_4$	1	−30	poor
$SnCl_4$	1	0 → RT	trace
BF_3,EtO	1	−30	15
$TiCl_4$	1	−30	very poor
$TiCl_4$	1	0 → RT	
$ZnCl_2$	1	RT	15
$ZnBr_2$	1	0 → RT	38
$FeCl_3/SiO_2$	1	RT	38
ZnI_2	1	RT	O-glycoside
$MgBr_2$	1	RT	O-glycoside
TMSOTf	1	−70	poor

[a] RT = room temperature.

Table III. Condensation of Various 2-Methyl-2-propenyl Ethers with L-Rhamnal 1 in the Presence of Zinc Bromide

compd	R	yield, %
4	H	29
5	tetrahydropyranyl	38
11		66
12		84
13		82

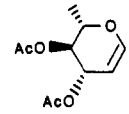
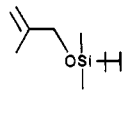
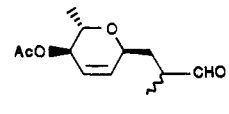
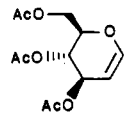
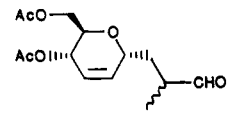
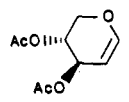
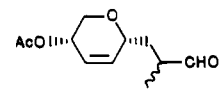
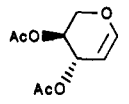
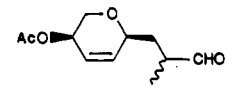
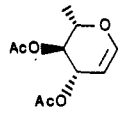
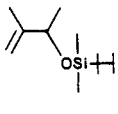
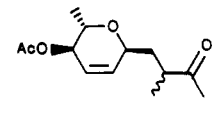
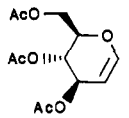
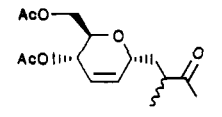
and 15 Hz, H-3) and 1.63 (ddd, J = 5.6, 9.5 and 15 Hz, H-3), indicating the presence of a single product. Homogeneity of **9** was confirmed by the ^{13}C NMR decoupled spectra which showed a single peak for each nucleus.

Epoxidation of the alkyl C-glycoside using MCPBA yielded the 2,3-epoxy C-glycoside **10**. Measurement of the $J_{4,5}$ = 3.2 Hz and $J_{6,7}$ = 2.2 Hz coupling constants[14] demonstrated the syn relationship of the H-4, H-5, H-6, and H-7 protons[15] thus confirming the α configuration for the aldo C-glycoside **6**.

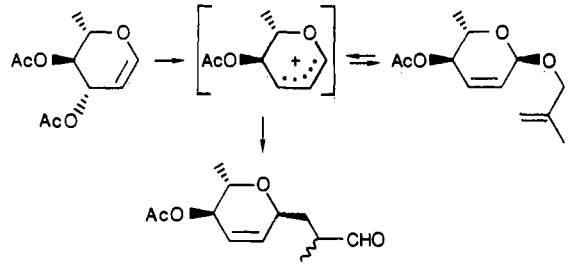
In order to improve the yield various parameters were studied. First the effect of several Lewis acids were examined. From Table II it could be seen that zinc bromide was the most efficient catalyst. Ferric chloride absorbed on silica gel gave also good results but led to side products on larger scale. Variation of the protecting group had a marked effect upon reaction yields. Among various protecting groups *tert*-butyldimethylsiloxane[16] and thexyldimethylsiloxane[17] were found to be the more attractive derivatives affording the aldo C-glycoside **6** in an excellent yield (Table III).

Condensation of 1-[(thexyldimethylsilyl)oxy]-2-methyl-2-propene (**13**) with several glycals was examined. In each case (Table IV) the 4-α-aldo derivative was obtained with yields up to 80%. Furthermore the condensation of **13** with peracetylated glycals induced some selectivity at C2. Thus reaction of di-*O*-acetyl-L-rhamnal **1** and tri-*O*-acetyl-D-glucal **14** with **13** afforded a 3:2 ratio of *S* and *R* derivatives. Addition of **13** with di-*O*-acetyl-D-xylal **16** and di-*O*-acetyl-L-xylal **18** gave a 2:1 mixture of C2 *S* and C2 *R* isomers.

Table IV. Reaction of Peracetylated Glycals with Thexyldimethylsiloxanes 13 and 20

glycals	thexyldimethylsiloxanes	C-glycosides	yield, % (*S*/*R*)
 **1**	 **13**	 **6**	82 (3/2)
 **14**	**13**	 **15**	81 (3/2)
 **16**	**13**	 **17**	96 (2/1)
 **18**	**13**	 **19**	77 (2/1)
 **1**	 **20**	 **21**	61 (1/1)
 **14**	**20**	 **22**	57 (1/1)

Scheme III



Our process was extended to secondary siloxanes. Thus reaction of di-*O*-acetyl-L-rhamnal **1** with 2-[(thexyldimethylsilyl)oxy]-3-methyl-2-propene (**20**) under zinc bromide catalysis gave rise to a 61% yield of 8-*O*-acetyl-5,6-anhydro-3(*R*,*S*)-*C*-methyl-1,3,4,6,7,10-hexadeoxy-L-*ribo*-dec-6-enulose (**21**). The presence of a terminal methyl ketone was indicated by the three-proton signal at δ 2.1 and by the C-2 resonance at δ 207.36. Once again the $J_{8,9}$ = 4.38 and 5.83 Hz coupling constant indicated that the addition has stereoselectively occurred from the α face. In the same fashion condensation of **20** with tri-*O*-acetyl-D-glucal **14** gave rise to a 57% yield of ketose **22**.

(14) **5,6:4,8-Dianhydro-2-*C*-methyl-1,2,3,9-tetradeoxy-L-*allo*-non-5-enitol (10)**: ^1H NMR δ 0.94 and 0.95 (2 d, 2 × 3 H, J = 6.5 Hz, H-1 and H-2'), 1.19 (d, 3 H, J = 6.2 Hz, H-9), 1.41 (ddd, 1 H, J = 5.4, 7.7, and 13.4 Hz, H-3), 1.7 (ddd, 1 H, J = 6, 8.8, and 13.4 Hz, H-3), 1.76 (ddq, 1 H, J = 6, 6.5, and 7.7 Hz, H-2), 3.45 (dd, 1 H, J = 3.2 and 4.4 Hz, H-5), 3.48 (m, 2 H, H-6 and H-8), 3.58 (dd, 1 H, J = 2.2 and 7.7 Hz, H-7), 4.05 (ddd, 1 H, J = 3.2, 5.4, and 8.8 Hz, H-4); ^{13}C NMR δ 17.54 (q, C-9), 22.39 and 23.12 (q, C-1 and C-2'), 24.5 (d, C-2), 38 (t, C-3), 54.4 (d, C-5), 58.44 (d, C-6), 66.90 (d, C-8), 67.69 (d, C-7), 70.72 (d, C-4).

(15) Buss, D. H.; Hough, L.; Hall, L. D.; Manville, J. F. *Tetrahedron* **1965**, *21*, 69.

(16) Corey, E. J.; Venkateswarlu, A. L. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

(17) Wetter, H.; Oertle, K. *Tetrahedron Lett.* **1985**, *26*, 5515.

In each reaction the transitory formation of O-glycosides could be detected. The amount of O-glycoside depends clearly on the stability of the silyloxy ether and suggested the mechanism indicated in Scheme III. The reaction could be depicted in term of an equilibrium between the carbonium ion and the O-glycoside displaced by the irreversible formation of the carbon–carbon bond.

Experimental Section

Melting point are uncorrected. Proton and carbon NMR spectrum were obtained with a Bruker MSL 300 spectrometer with $CDCl_3$ as solvent and Me_4Si as internal standard. Homonuclear chemical shift correlation (COSY) experiments were carried out by using furnished software. Experiments (512) of 16 transients were recorded. The relaxation delay was 1 s, and the digital resolution along both axes was 1.47 Hz/point. Microanalysis were performed by the Laboratoire Central de Microanalyse du CNRS, Vernaison, France. Zinc bromide was purchased from Aldrich Chemical, and transfer was made under nitrogen using a glovebox. Thexyldimethylsilyl chloride and thexyldimethylsilyl ether were prepared according to ref 17. Dichloromethane was distilled from calcium hydride.

General Procedure for 1-Aldo and 2-Keto C-Glycosides. A flame-dried 100-mL round-bottom flask was filled under nitrogen with dry zinc bromide (4.5 g, 40 mmol) and dichloromethane 25 mL. Then a solution of peracetylated glycal (40 mmol) and thexyldimethylsilyl ether (1–1.3 equiv) in dichloromethane (20 mL) was added dropwise (0.5–2 h) at 0 °C. The resulting brown suspension was stirred for 30 min and then poured into a mixture of saturated sodium hydrogen phosphate (25 mL) and diethyl ether (50 mL). The organic phase was separated, and the aqueous layer was extracted with diethyl ether (2 × 25 mL). The combined extracts were washed successively with saturated sodium bicarbonate (25 mL) and brine (25 mL) and then dried ($MgSO_4$). Removal of the solvent under reduced pressure and then flash chromatography in the indicated solvents furnished the C-glycosides.

7-*O*-Acetyl-4,8-anhydro-2(*R*,*S*)-*C*-methyl-2,3,5,6,9-pentadeoxy-L-*ribo*-non-5-enose (6): 82% (pentane–ether, 9:1); $[\alpha]^{20}_D$ −88° (*c* 0.1, $CHCl_3$); ^1H NMR δ 1.15 (d, 1.8 H, *J* = 7 Hz, H-2′ (*S*)), 1.18 (d, 1.2 H, *J* = 7 Hz, H-2′ (*R*)), 1.2 (d, 3 H, *J* = 7 Hz, H-9), 1.42 (ddd, 0.6 H, *J* = 3.35, 7.4, and 14.3 Hz, H-3 (*S*)), 1.8 (ddd, 0.4 H, *J* = 4.4, 9.25, and 14 Hz, H-3 (*R*)), 1.95 (ddd, 0.4 H, *J* = 3.8, 8, and 14 Hz, H-3 (*R*)), 2.08 (s, 3 H, MeCO), 2.15 (ddd, 0.6 H, *J* = 6.02, 10.3, and 14.3 Hz, H-3 (*S*)), 2.6 (m, 1 H, H-2), 3.83 (dq, 0.6 H, *J* = 5.4 and 7 Hz, H-8), 3.85 (dq, 0.4 H, *J* = 4.8 and 7 Hz, H-8), 4.25 (m, 1 H, H-4), 4.85 (m, 0.4 H, H-7), 4.9 (m, 0.6 H, H-7), 5.77–5.87 (m, 2 H, H-5 and H-6), 9.67 (d, 1 H, *J* = 1.7 Hz, H-1); ^{13}C NMR δ 13.7 and 13.78 (q, C-2′), 16.84 and 16.92 (q, C-9), 21.14 and 21.23 (q, *Me*COO), 34.17 and 34.42 (t, C-3), 43.83 (d, C-2), 67.47 and 67.73 (d, C-7), 69.69 (d, C-8), 69.69 (d, C-4), 123.37 and 123.78 (d, C-6), 133.2 and 133.43 (d, C-5), 170.64 (s, MeCOO), 194.73 (d, C-1). The (2,4-dinitrophenyl)hydrazone: mp 138 °C (EtOH). Anal. Calcd for $C_{18}H_{22}N_4O_7$: C, 53.20; H, 5.42; N, 13.79. Found: C, 53.64; H, 5.47; N, 13.78.

7,9-Di-*O*-acetyl-4,8-anhydro-2(*R*,*S*)-*C*-methyl-2,3,5,6-tetradeoxy-D-*ribo*-non-5-enose (15): 81% (hexane–ethyl acetate, 8:2); $[\alpha]^{20}_D$ +85° (*c* 0.1, $CHCl_3$); ^1H NMR δ 1.1 (d, 1.8 H, *J* = 7.1 Hz, H-2′ (*S*)), 1.12 (d, 1.2 H, *J* = 7.3 Hz, H-2′ (*R*)), 1.36 (ddd, 0.6 H, *J* = 3.13, 7.32, and 14.56 Hz, H-3′ (*S*)), 1.75 (ddd, 0.4 H, *J* = 4.5, 9.6, and 14.6 Hz, H-3′ (*R*)), 1.85 (ddd, 0.4 H, *J* = 3.7, 7.75, and 14.6 Hz, H-3′ (*R*)), 2.02 and 2.03 (2 s, 2 × 3 H, MeCOO), 2.12 (ddd, 0.6 H, *J* = 6.2, 10.75, and 14.56 Hz, H-3′ (*S*)), 2.6 (m, 1 H, H-2), 3.85 (ddd, 1 H, *J* = 3.4, 6.45, and 6.45 Hz, H-8), 4.05 (dd, 1 H, *J* = 3.4 and 12 Hz, H-9), 4.15 (dd, 1 H, *J* = 6.45 and 12 Hz, H-9), 4.3 (m, 1 H, H-4), 5.1 (m, 1 H, H-7), 5.75 (ddd, 1 H, *J* = 2.2, 2.2, and 10.3 Hz, H-6), 5.82 (ddd, 1 H, *J* = 1.2, 2.2, and 10.3 Hz, H-5), 9.7 (d, 1 H, *J* = 1.7 Hz, H-1); ^{13}C NMR δ 13.64 (q, C-2′), 20.75 and 21.07 (q, *Me*COO), 33.79 (t, C-3), 42.95 and 43.78 (d, C-2), 62.59 (t, C-9), 64.83 (d, C-7), 69.16 (d, C-8), 69.49 and 69.69 (d, C-4), 123.76 and 123.78 (d, C-6), 132.78 and 132.99 (d, C-5), 170.35 and 170.73 (s, Me*C*O), 204.06 (d, C-1). Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.16; H, 7.04. Found: C, 58.91; H, 7.19.

7-*O*-Acetyl-4,8-anhydro-2(*R*,*S*)-*C*-methyl-2,3,5,6-tetradeoxy-D-*erythro*-oct-5-enose (17): 96% (hexane–ethyl acetate, 8:2); $[\alpha]^{20}_D$ +158.33° (*c* 0.1, $CHCl_3$); ^1H NMR δ 1.10 (d, 2 H, *J* = 7.1 Hz, H-2′ (*S*)), 1.12 (d, 1 H, *J* = 7.25 Hz, H-2′ (*R*)), 1.38 (ddd, 0.66 H, *J* = 3.26, 7.5, and 14.14 Hz, H-3 (*S*)), 1.64 (ddd, 0.33 H, *J* = 3.9, 8.98, and 14.29 Hz, H-3 (*R*)), 1.90 (ddd, 0.33 H, *J* = 3.57, 8.3, and 14.29 Hz, H-3 (*R*)), 1.98 (ddd, 0.66 H, *J* = 5.94, 10, and 14.14 Hz, H-3 (*S*)), 2 (s, 3 H, MeCOO), 2.6 (m, 1 H, H-2), 3.42 (dd, 0.33 H, *J* = 6.7 and 11.6 Hz, H-8 (*R*)), 3.45 (dd, 0.66 H, *J* = 6.4 and 11.7 Hz, H-8 (*S*)), 3.99 (dd, 0.33 H, *J* = 4.9 and 11.6 Hz, H-8 (*R*)), 4 (dd, 0.66 H, *J* = 4.6 and 11.7 Hz, H-8 (*S*)), 4.23 (br, dd, 1 H, *J* = 3.26 and 10 Hz, H-4), 5.2 (m, 1 H, H-7), 5.82 (m, 2 H, H-5 and H-6), 9.51 (d, 1 H, *J* = 1.8 Hz, H-1); ^{13}C NMR δ 13.56 and 13.98 (q, C-2′), 20.92 (q, *Me*COO), 34.55 and 34.94 (t, C-3), 42.44 and 43.17 (d, C-2), 64.56 (t, C-8), 64.75 (d, C-7), 71.21 (d, C-4), 124.56 and 124.86 (d, C-6), 133.51 and 133.76 (d, C-5), 170.31 (s, MeCOO), 195.62 (d, C-1). Anal Calcd for $C_{11}H_{16}O_4 \cdot 0.5H_2O$: C, 59.73; H, 7.69. Found: C, 60.29; H, 7.40.

7-*O*-Acetyl-4,8-anhydro-2(*R*,*S*)-*C*-methyl-2,3,5,6-tetradeoxy-L-*erythro*-oct-5-enose (19): 77% (hexane–ethyl acetate, 8:2); $[\alpha]^{20}_D$ −135° (*c* 0.1, $CHCl_3$); ^1H NMR δ 1.15 (d, 2 H, *J* = 7.1 Hz, H-2′ (*S*)), 1.17 (d, 1 H, *J* = 7.2 Hz, H-2′ (*R*)), 1.45 (ddd, 0.66 H, *J* = 3.30, 7.5, and 14.40 Hz, H-3 (*S*)), 1.65 (ddd, 0.33 H, *J* = 3.9, 8.98, and 14.50 Hz, H-3 (*R*)), 1.95 (ddd, 0.33 H, *J* = 3.60, 8.36, and 14.50 Hz, H-3 (*R*)), 2.04 (overlapped m, 0.66 H, H-3 (*S*)), 2.06 (s, 3 H, MeCOO), 2.6 (m, 1 H, H-2), 3.48 (dd, 0.33 H, *J* = 6.8 and 11.5 Hz, H-8 (*R*)), 3.53 (dd, 0.66 H, *J* = 6.3 and 11.5 Hz, H-8 (*S*)), 4 (dd, 0.33 H, *J* = 4.8 and 11.5 Hz, H-8 (*R*)), 4.01 (dd, 0.66 H, *J* = 4.9 and 11.5 Hz, H-8 (*S*)), 4.23 (m, 1 H, H-4), 5.18 (m, 1 H, H-7), 5.85 (m, 2 H, H-5 and H-6), 9.65 (d, 1 H, *J* = 1.8 Hz, H-1); ^{13}C NMR δ 13.66 and 14.01 (q, C-2′), 21.08 (q, *Me*COO), 34.54 and 34.95 (t, C-3), 42.51 and 43.25 (d, C-2), 64.57 (t, C-8), 64.80 (d, C-7), 71.22 (d, C-4), 124.56 and 124.83 (d, C-6), 133.56 and 133.76 (d, C-5), 170.55 (s, MeCOO), 195.48 (d, C-1). Anal. Calcd for $C_{11}H_{16}O_4 \cdot H_2O$: C, 57.39; H, 7.83. Found: C, 57.70; H, 7.34. The (2,4-dinitrophenyl)hydrazone: mp 111.3 °C.

8-*O*-Acetyl-5,9-anhydro-3(*R*,*S*)-*C*-methyl-1,3,4,6,7,10-hexadeoxy-L-*ribo*-dec-6-enulose (21): 61% (hexane–ethyl acetate, 6:4); $[\alpha]^{20}_D$ −235 (*c* 0.1, $CHCl_3$); ^1H NMR δ 1.12 (d, 1.5 H, *J* = 7.30 Hz, H-3′ (*S*)), 1.16 (d, 1.5 H, *J* = 7.30 Hz, H-3′ (*R*)), 1.15 (d, 1.5 H, *J* = 6.18 Hz, H-10 (*S*)), 1.18 (d, 1.5 H, *J* = 6.61 Hz, H-10 (*R*)), 1.37 (ddd, 0.5 H, *J* = 3.28, 6.12, and 14.21 Hz, H-4 (*S*)), 1.56 (ddd, 0.5 H, *J* = 3.98, 9.49, and 14.03 Hz, H-4 (*R*)), 1.95 (ddd, 0.5 H, *J* = 3.66, 9.28, and 14.03 Hz, H-4 (*R*)), 2.08 (s, 3 H, MeCOO), 2.12 (m, 0.5 H, H-4 (*S*)), 2.18 and 2.19 (2 s, 2 × 1.5 H, H-1), 2.8 (ddq, 0.5 H, *J* = 6.12, 7, and 7.3 Hz, H-3 (*S*)), 2.85 (ddq, 0.5 H, *J* = 3.98, 7.3, and 9.28 Hz, H-3 (*R*)), 3.73 (dd, 0.5 H, *J* = 5.83 and 6.18 Hz, H-9 (*S*)), 3.87 (dd, 0.5 H, *J* = 4.38 and 6.61 Hz, H-9 (*R*)), 4.08 (ddddd, 0.5 H, *J* = 1.09, 1.82, 2.2, 3.66, and 9.49 Hz, H-5 (*R*)), 4.15 (ddddd, 0.5 H, *J* = 1.09, 1.8, 2.2, 3.28, and 10.6 Hz, H-5 (*S*)), 4.83 (dddd, 0.5 H, *J* = 1.82, 2.20, 3.28, and 4.38 Hz, H-8 (*R*)), 4.86 (dddd, 0.5 H, *J* = 1.82, 2.2, 3.28, and 5.83 Hz, H-8 (*S*)), 5.74 and 5.77 (2 ddd, 2 × 0.5 H, *J* = 1.82, 3.28 and 10.23 Hz, H-7), 5.82 and 5.87 (2 ddd, 2 × 0.5 H, *J* = 1.09, 1.82, and 10.23 Hz, H-6); ^{13}C NMR δ 16.89 and 17.59 (q, C-3′ and C-10), 21.18 (q, *Me*COO), 29.09 (q, C-1), 36 and 36.40 (t, C-4), 42.82 and 43.89 (d, C-3), 67.49 and 68.52 (d, C-9), 68.10 and 69.77 (d, C-5), 69.50 and 69.94 (d, C-8), 122.88 and 123.85 (d, C-6), 133.07 and 134.05 (d, C-7), 170.60 (s, MeCOO), 207.36 (s, C-2). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.62; H, 8.44.

8,10-Di-*O*-acetyl-5,9-anhydro-3(*R*,*S*)-*C*-methyl-1,3,4,6,7-pentadeoxy-D-*ribo*-dec-6-enulose (22): 57% (hexane–ethyl acetate, 6:4); $[\alpha]^{20}_D$ +80 (*c* 0.1, $CHCl_3$); ^1H NMR δ 1.1 (d, 1.5 H, *J* = 7.2 Hz, H-3′ (*S*)), 1.12 (d, 1.5 H, *J* = 7.2 Hz, H-3′ (*R*)), 1.37 (ddd, 0.5 H, *J* = 3.10, 6.60, and 14.40 Hz, H-4 (*S*)), 1.60 (ddd, 0.5 H, *J* = 3.1, 10.00, and 14.30 Hz, H-4 (*R*)), 1.93 (ddd, 0.5 H, *J* = 3.60, 9.20, and 14.30 Hz, H-4 (*R*)), 2.06 and 2.08 (2 s, 2 × 3 H, MeCOO), 2.14 (ddd, 0.5 H, *J* = 6.67, 10.89, and 14.4 Hz, H-4 (*S*)), 2.20 (s, 3 H, MeCO), 2.77 (ddq, 0.5 H, *J* = 6.60, 6.67, and 7.2 Hz, H-3 (*S*)), 2.85 (ddq, 0.5 H, *J* = 3.1, 7.2, and 9.2 Hz, H-3 (*R*)), 3.80 (ddd, 0.5 H, *J* = 3.20, 6.00, and 6.70 Hz, H-9 (*S*)), 3.86 (ddd, 0.5 H, *J* = 3.8, 6, and 6.21 Hz, H-9 (*R*)), 4.03 (dd, 0.5 H, *J* = 3.2 and 12 Hz, H-10 (*S*)), 4.08 (dd, 0.5 H, *J* = 3.8 and 12 Hz, H-10 (*R*)), 4.17 (dd, 2 H, *J* = 6 and 12 Hz, H-5 overlapped with H-10), 5.05 (dddd, 0.5 H, *J* = 1.83, 2.19, 2.19, and 6.21, H-8 (*R*)), 5.11 (dddd, 0.5 H, *J* = 2.19, 2.19, 2.19, and 6.70, H-8 (*S*)), 5.77 (ddd, 0.5 H, *J* = 2.19, 2.19, and 10.6 Hz, H-7 (*S*)), 5.78 (ddd, 0.5 H, *J* = 2.19, 2.19, and 10.6 Hz, H-7 (*R*)), 5.84 (ddd, 0.5 H, *J* = 1.83, 1.83, and

10.6 Hz, H-6 (S)), 5.89 (ddd, 0.5 H, J = 1.83, 2.19, and 10.6 Hz, H-6 (R)); ^{13}C NMR δ 17.43 (q, C-3), 20.66 and 20.92 (q, MeCOO), 28.87 (q, C-1), 35.5 and 35.61 (t, C-4), 42.86 and 43.86 (d, C-3), 62.46 (t, C-10), 64.88 (d, H-8), 68.92 (d, C-9), 70.75 (d, C-5), 123.26 and 123.97 (d, C-7), 132.61 and 133.46 (d, C-6), 170.16 and 170.46 (s, MeCO), 207.98 (s, C-2). Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.40; H, 7.38. Found: C, 60.10; H, 7.59.

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Registry No. 1, 34819-86-8; 4, 513-42-8; 5, 53250-10-5; 6 (R diastereomer), 111160-63-5; 6 (R diastereomer, 2,4-dinitrophenylhydrazone), 111160-84-0; 6 (S diastereomer), 111160-64-6; 6 (S diastereomer, 2,4-dinitrophenylhydrazone), 111160-85-1; 7 (R diastereomer), 111160-77-1; 7 (S diastereomer), 111160-78-2; 8 (R diastereomer), 111160-79-3; 8 (S diastereomer), 111160-80-6; 9, 111160-81-7; 10, 111160-82-8; 11, 25195-85-1; 12, 111160-83-9; 13, 111160-62-4; 14, 111160-65-7; 15 (R diastereomer), 111160-66-8; 15 (S diastereomer), 111160-67-9; 16, 3152-43-0; 17 (R diastereomer), 111160-68-0; 17 (S diastereomer), 111160-69-1; 18, 101052-70-4; 19 (R diastereomer), 111160-70-4; 19 (R diastereomer, 2,4-dinitrophenylhydrazone), 111160-86-2; 19 (S diastereomer), 111160-71-5; 19 (S diastereomer, 2,4-dinitrophenylhydrazone), 111160-87-3; 20, 111160-72-6; 21 (R diastereomer), 111160-73-7; 21 (S diastereomer), 111160-74-8; 22 (R diastereomer), 111160-75-9; 22 (S diastereomer), 111160-76-0.

Reduction of Organic Compounds with Rare-Earth Intermetallics Containing Absorbed Hydrogen

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The hydrogenation of organic compounds with rare-earth intermetallic hydrides has been investigated. Alkynes, alkenes, aldehydes, ketones, nitriles, imines, and nitro compounds are hydrogenated in excellent yields with $LaNi_5H_6$ or $LaNi_{4.5}Al_{0.5}H_5$ at 0–60 °C. The present hydrogenation method has the following characteristic features. (1) The intermetallic compounds (alloys) are not poisoned by compounds containing an amino group or a halogen atom. (2) The alloys can be used repeatedly without decrease in activity. (3) The reaction conditions are mild, and selective hydrogenations of some organic functional groups can be achieved. The reaction mechanism of this hydrogenation is briefly discussed in terms of stereochemistry and H/D exchange reactions.

Rare-earth intermetallics (alloy) such as $LaNi_5$, $PrCo_5$, and $SmCo_5$ absorb large quantities of hydrogen rapidly and reversibly under mild conditions, and hence they possess a high potential for uses as hydrogen storage substances. These classes of alloys are currently receiving considerable attention, particularly from the standpoint of energy storage, and their physicochemical characteristics have been extensively studied.[1]

On the other hand, relatively less attention has been paid to the utilization of these alloys in chemical reactions as reagents and catalysts. The works reported hitherto are mostly concerned with the kinetic investigation on the hydrogenation activity of the alloys from a physicochemical point of view.[2] The substrates used in the previous investigations are limited to several selected model compounds such as carbon monoxide, ethylene, butadiene, and acetonitrile.[3] Consequently, there have been little precedent investigations directed toward the practical utilization of these alloys in organic synthesis.

In our continuing study on the utilization of lanthanoid elements in organic synthesis,[4] we have been interested in the characteristic properties of the rare-earth intermetallics and intended to utilize them in the reduction of organic functional groups.[5]

Results and Discussion

Hydrogenation of Organic Functional Groups over $LaNi_5H_6$. Our initial study was undertaken with the use of lanthanum–nickel alloys ($LaNi_5$) which is one of the representative rare-earth alloys. The hydrogen absorption/desorption pressure of this alloy is 1–2 atm at room temperature, and it is capable of absorbing hydrogen up to the composition represented by the formula $LaNi_5H_6$.[1] This intermetallic hydride is known to be pyrophoric and often burns on contact with air. Therefore, we devised an experimental procedure, by which experiments could be carried out safely (see Experimental Section). By employing this procedure, we tried the reduction of many organic functional groups. The results are summarized in Table I.

Mono- and disubstituted olefins were hydrogenated at around room temperature in essentially quantitative yields (entries 1–6). The more highly substituted olefins were virtually inert to these reducing conditions (entries 3 and 5).

Alkynes were also reduced to saturated compounds under the similar conditions (entries 7 and 8). Semihydrogenation of alkynes to (Z)-olefins was attempted at

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