electrodes, and of other oxyfluoride semiconductors, in fluoride-containing solvents is currently in progress.

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Intramolecular Hydrosilation of α-Hydroxy Enol Ethers: A New Highly Stereoselective Route to Polyhydroxylated Molecules[1]

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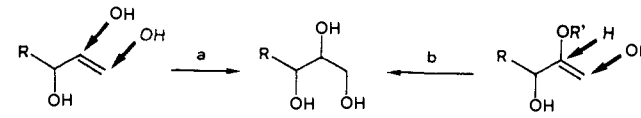
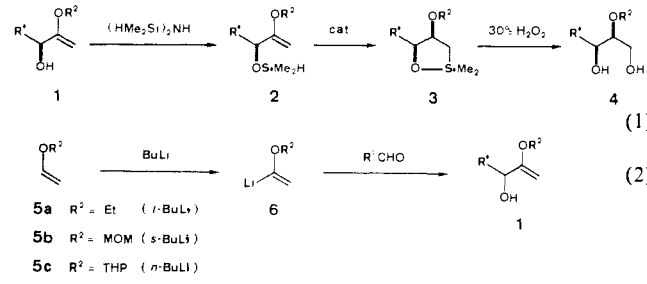
Stereoselective chemical synthesis of carbohydrates constitutes a large and challenging field in modern synthetic organic chemistry.[2] Among a wide variety of methodologies for stereoselective construction of polyoxygenated skeletons,[3] that being the most straightforward is the stereoselective introduction of two oxygen functionalities to the carbon–carbon double bonds (Scheme I, route a), as represented by the Sharpless epoxidation[4] or osmium tetroxide oxidation of allyl alcohols.[3h,5] An alternative route may be achieved by anti-Markownikoff hydration of enol ether counterparts (Scheme I, route b), but such an approach has so far been rarely studied.[6]

Scheme I



We report herein our initial results of stereoselective polyol synthesis via the latter process. Thus, a new route to 2,3-*threo*-1,2,3-triols **4** can be realized by intramolecular hydrosilation[7] of 2-alkoxy-1-alken-3-ols **1**, followed by oxidative cleavage of the carbon–silicon bond,[8] as shown in eq 1. Since the starting materials **1** are readily available from aldehydes and vinyl ethers **5a–c** (eq 2),[9] the new method should find a wide application.



Representative results are listed in Table I. A typical experimental procedure is given for the preparation of **4b** from **1b**. A mixture of **1b** (465 mg, 2.4 mmol), $(HMe_2Si)_2NH$ (2.4 mmol), and ammonium chloride (ca. 3 mg) was allowed to stand at room temperature overnight to ensure silylation of the hydroxy group in **1b**. The excess disilazane was removed in vacuo. To the remaining oil was added a toluene solution of $[Pt\{[(CH_2{=}CH)Me_2Si]_2O\}_2]$[10] (0.25 M, 48 μL; 0.5 mol%), and the mixture was stirred at room temperature for 0.5 h. GLC analysis showed the completion of hydrosilation. The platinum species were removed by stirring the mixture with EDTA·2Na (480 mg) and hexane (10 mL) overnight and subsequent filtration. The filtrate was stripped off the solvent and treated with 15% KOH (1.0 mL) and 30% H_2O_2 (1.62 mL, 14.4 mmol) in a 1:1 mixed solvent of MeOH/THF (ca. 14 mL) at room temperature. The oxidative cleavage was completed in 2 h, as monitored by TLC. The usual anhydrous workup[8c] followed by column chromatography gave 360 mg (71% yield) of **4b** (silica gel; hexane/EtOAc, 1:1, R_f 0.23). The acetonide of **4b** (2,2-dimethoxypropane, CSA catalyst, room temperature, 1 h; 93%) was isomerically pure by GLC and 400 MHz NMR analysis.[11]

Since the most commonly used catalyst, $H_2PtCl_6{\cdot}6H_2O$ in *i*-PrOH or in THF, was not suitable for the hydrosilation of acid-sensitive enol ethers,[12] we examined several neutral catalysts and found the platinum(0)/vinylsiloxane[10] to be most effective.

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(5) Solladie, G.; Hutt, J.; Frechou, C. *Tetrahedron Lett.* **1987**, *28*, 61.

(6) Hydroboration seems to be the only method (McGarvey, G. J.; Bajwa, J. S. *Tetrahedron Lett.* **1985**, *26*, 6297 and references cited therein). They obtained syn/anti ratios in the range of 83/17 to 3/97 in essentially the same systems as those examined in the present study. For applications to cyclic systems in the carbohydrate chemistry, see ref 2f, pp 32, 33.

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(9) While lithiation of **5a** required *t*-BuLi,[9a] **5b**[9b] and **5c**[9c] were lithiated with *sec*-BuLi[9b] or even with *n*-BuLi (our work) in THF at −78 °C, suggesting the chelating stabilization by the MOM and THP oxygens. (a) Baldwin, J. E.; Höfle, G. A.; Lever, O. W., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 7125. (b) McDougal, P. G.; Rico, J. G.; VanDerveer, D. *J. Org. Chem.* **1986**, *51*, 4492. (c) D'Angelo, J. *Bull. Soc. Chem. Fr.* **1969**, 181: We found KOH pelets to be more convenient than *t*-BuOK originally used for dehydrobromination of $THPOCH_2CH_2Br$.

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(11) All products showed consistent spectral and analytical data, some of which are included in the Supplementary Material.

(12) There have been only several papers concerning hydrosilation of vinyl ethers. E.g.: Voronkov, M. G.; Keiko, N. A.; Kuznetsova, T. A.; Pestunovich, V. A.; Tsetlina, E. O.; Bystritskii, A. A. *Bull. Akad. Sci. USSR, Chem. Sci.* **1975**, *23*, 2645. Tsykhanskaya, I. I.; Vlasova, N. N.; Keiko, V. V.; Sakhorovskii, V. G.; Balashenko, L. V. *Bull. Akad. Sci. USSR, Chem. Sci.* **1970**, *19*, 2596. Atavin, A. S.; Shostakovskii, M. F.; Vyalykh, E. P.; Trofimov, B. A.; Kalabin, G. A. *J. Gen. Chem. USSR* **1969**, *39*, 2230.

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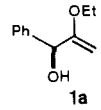
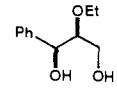
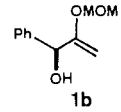
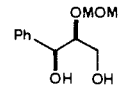
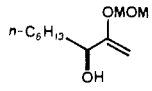
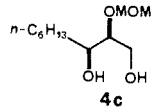
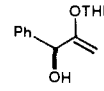
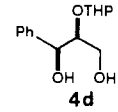
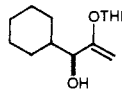
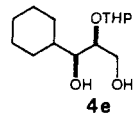
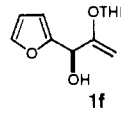
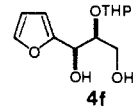
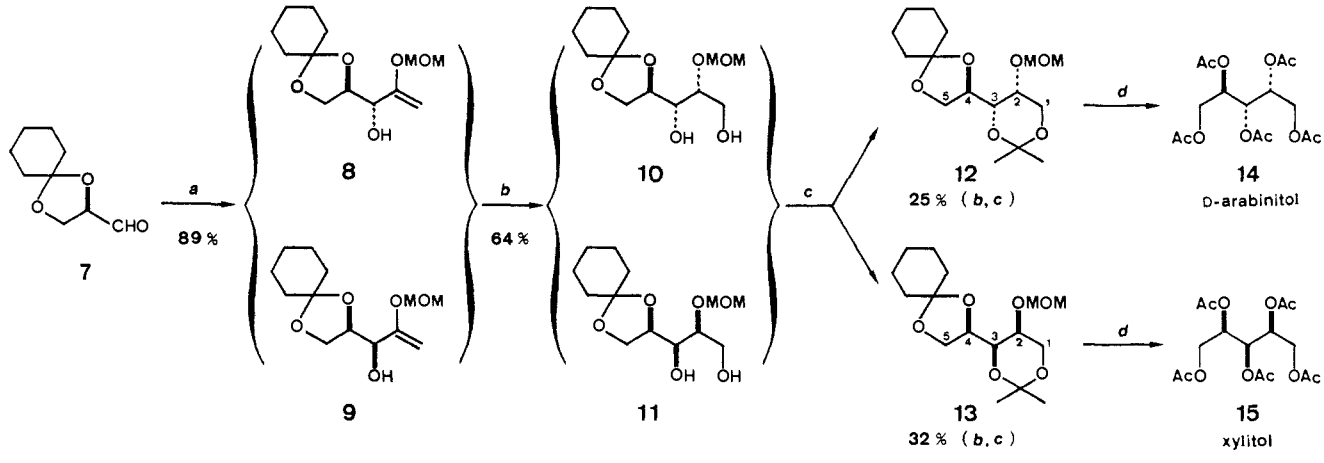
Table I. Transformation of **1** into **4** by the Intramolecular Hydrosilation–Oxidation Sequence[a]

entry	alcohol[b] **1**	hydrosilation conditions[c,d]	product[b] **4**	yield[e] (%)	isomer ratio[f] (syn/anti)
1	 **1a**	B C	 **4a**	64 67	94/1[g] 42/1
2	 **1b**	A[h]	 **4b**	71	>99/1
3	 **1c**	A[h]	 **4c**	71	14/1
4	 **1d**	A B	 **4d**	80 60	>99/1[i] >99/1[i]
5	 **1e**	A	 **4e**	84	>99/1[i]
6	 **1f**	A	 **4f**	90	>99/1[i]

[a] Carried out on 2–3 mmol scales by essentially the same procedure as that described for typical experimental procedure in text, unless otherwise stated. [b] Compounds are racemic. [c] Condition A, $[Pt\{[(CH_2{=}CH)Me_2Si]_2O\}_2]$ (0.5 mol%), 60 °C, 2 h; condition B, $[Pt(PPh_3)_2(CH_2{=}CH_2)]$ (0.3 mol%), 50–60 °C, 4–20 h; condition C, [Rh(acac)(cod)] (0.4 mol%), room temperature, 2.5 h. [d] Conditions for oxidation: 30% H_2O_2, 15% KOH, MeOH, THF, room temperature, 2.5 h. [e] Isolated, overall yield based on **1**. [f] Determined by GLC analysis and/or 400 MHz ^1H NMR of the acetonides. [g] Compared with authentic samples of erythro and threo isomers prepared by hydroboration of **1a** (ref 6). [h] Carried out at room temperature for 0.5–2 h. [i] Determined after deprotonation of the THP group and protection of the primary alcohol by the *t*-BuMe_2Si group followed by acetonide formation.

Scheme II[a]

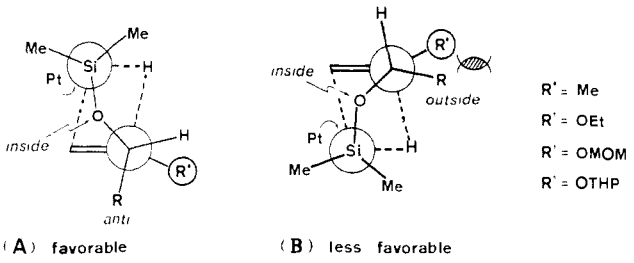


[a] (a) $MOMOCH{=}CH_2$/*sec*-BuLi (1/1), THF, −78 °C ~ room temperature, overnight; (b) (1) $(HMe_2Si)_2NH$, NH_4Cl (catalyst), room temperature, overnight; (2) $[Pt\{[CH_2{=}CH)Me_2Si]_2O\}_2]$ (0.5 mol%), room temperature, 0.5 h; (3) EDTA·2Na, hexane, overnight; (4) 30% H_2O_2, 15% KOH, MeOH, THF, room temperature, 2.5 h; (c) (1) $Me_2C(OMe)_2$, CSA (catalyst), room temperature, 4 h; (2) separation: silica gel, hexane/EtOAc (2.5/1); (d) (1) concentrated HCl, Et_2O, room temperature, 5 h; (2) Ac_2O, pyridine, DMAP, room temperature, 1 day.

A rhodium complex [Rh(acac)(cod)] also exhibited a similar activity but showed somewhat lower stereoselectivity (entry 1).

The most significant feature is the almost complete threo (syn) stereoselection in all cases, with a few exceptions. The stereoselectivity was not largely influenced by the nature of the alkoxy group on the double bond, although the MOMO and the THPO groups appeared to induce higher selectivity than the ethoxy group (entries 1, 2, and 4). Noteworthy is that the chiral carbon in the THP group showed no effect on the stereoselection. Thus, the origin of the stereoselectivity may be attributable primarily to the steric repulsion between the R and R′ groups in the cyclic transition structures (A versus B). It should be noted that the stereoselectivities attained with R′ = OEt, OMOM, and OTHP are much higher than those observed with R′ = Me (R = Ph; syn/anti = 6.7/1),[7a] suggesting also an importance of electronic effects which should be elucidated by further studies.

The synthetic utility may be exemplified by the synthesis of optically pure pentitols, as shown in Scheme II. Thus, protected



glyceraldehyde 7[13] was converted into a mixture of stereoisomers **8** and **9** (1/1.4).[14] The isomeric mixture was subjected to the intramolecular hydrosilation–oxidation sequence to form **10** and **11** in 64% combined yield. The acetonides were, fortunately, readily separated into two optically pure stereoisomers, **12** (R_f 0.5) and **13** (R_f 0.29), by simple column chromatography (silica gel, hexane/EtOAc, 2.5/1).[11] No 2,3-erythro isomers were obtained, if any only trace, indicative of the perfect syn stereoselective hydrosilation.[15] These products, **12** and **13**, were deprotected to free pentitols which were converted into, respectively, optically pure D-arabinitol pentaacetate (**14**) and xylitol pentaacetate (**15**).[16,17] It may be mentioned that the present pentitol synthesis is among the shortest pathways together with the highest stereoselection ever reported,[4a,d,g] starting with optically active glyceraldehyde derivatives.[2a] Refinement and further applications as well as development of the procedure for the opposite stereoselection, 2,3-erythro (anti), are now under investigation.

Acknowledgment. We thank the Ministry of Education, Japan, for a Grant-in-Aid for Scientific Research (no. 60550605) and H. Fujita for measurements of 400 MHz ^{1}H NMR spectra.

Supplementary Material Available: Data and/or copies of 400-MHz ^{1}H NMR spectra of acetonides **4a** and **4b** and **8**, **9**, **12**, and **1** (7 pages). Ordering information is given on any current masthead page.

(13) Sugiyama, T.; Sugawara, H.; Watanabe, M.; Yamashita, K. *Agric. Biol. Chem.* **1984**, *48*, 1841.
(14) We have examined several reagents, such as copper, magnesium, or zinc reagents, derived from the lithiated species **6** to improve both the selectivity and the yield, but have not gotten any satisfactory results yet. The two stereoisomers, **8** and **9**, were separated only with difficulty by medium pressure liquid chromatography.
(15) This point has also been confirmed by similar transformations starting with each isomer, **8** and **9**, separated as above.[14]
(16) *Rodd's Chemistry of Carbon Compounds*; Coffey, S., Ed.; Elsevier: New York, 1976; Vol. 1F, pp 18 19. For ^{1}H and ^{13}C NMR data, see the following literatures: Moore, R. E.; Barchi, J. J., Jr.; Bartolini, G. *J. Org. Chem.* **1985**, *50*, 374. Angyal, S. J.; Le Fur, R. *Carbohydr. Res.* **1980**, *84*, 201.
(17) Optical rotations, $[\alpha]_D^{20}$, of compounds prepared in this study are as follows: **8**, +1.82° (*c* 1.10, benzene); **9**, −2.97° (*c* 1.01, benzene); **12**, −10.0° (*c* 1.56, EtOH); **13**, +21.1° (*c* 1.28, EtOH); **14**, +37.25° (*c* 1.02, $CHCl_3$); **15**, ±0.00° (*c* 1.07, $CHCl_3$).

Biosynthesis of Ephedrine

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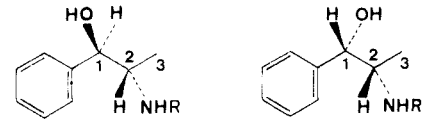
It is remarkable that the biosynthetic origin of the simple phenylpropanoid skeleton of the Ephedra alkaloids (e.g., (−)-ephedrine (**1**) and (+)-pseudoephedrine (**3**)) is still not established.

Label from [3-^{14}C]phenylalanine was shown,[1] 30 years ago, to be specifically incorporated into C-1 of (+)-norpseudoephedrine (**4**) in *Catha edulis* and, 10 years later, into C-1 of (−)-ephedrine



1 R = CH_3 **3** R = CH_3
2 R = H **4** R = H

(**1**) in *Ephedra distachya*.[2,3] Tritium from [ring-^{3}H]phenylalanine also entered the alkaloids.[2,3] It was originally thought[4-6] that the aminophenylpropanoid system of the alkaloids was derived either directly from the aminophenylpropanoid system of phenylalanine[4] or by reaction of a phenylalanine-derived phenylethylamine moiety with a one-carbon unit.[5-7] These views had to be abandoned when it was found[2,3] that label from [2-^{14}C]phenylalanine did not enter (−)-ephedrine (**1**) and that label from [2,3-^{14}C]phenylalanine was found solely at C-1 of ephedrine (from 3-^{14}C) but not at C-2, the site predicted for entry of label from [2-^{14}C]phenylalanine. It thus became evident that phenylalanine supplies neither the intact C_6–C_3 skeleton of the alkaloids nor a C_6–C_2 moiety but merely a C_6–C_1 unit. Benzoic acid and benzaldehyde, whose sidechain carbon atom enters C-1 of (−)-ephedrine,[2,3] are presumably intermediates on the route from phenylalanine into the C_6–C_1 unit of the alkaloids.

The origin of the C_2 unit, C-2,-3, of the alkaloids remained unknown. None of a wide range of ^{14}C-labeled substrates ([2-^{14}C]glycine,[3] [U-^{14}C]alanine,[3] [U-^{14}C]serine,[3] [U-^{14}C]aspartic acid,[3] [2-^{14}C]propionic acid,[3] [^{14}C]formic acid,[3,7] [6-^{14}C]glucose[3]) delivered radioactivity preferentially into this unit.

We now report that this C_2 unit is derived from the intact CH_3CO– group of pyruvic acid.

A freshly prepared solution of sodium [2,3-$^{13}C_2$]pyruvate (99.0 atom % ^{13}C, 100 mg, MSD Isotopes, Montreal, Canada) in demineralized water (1 mL) containing Tween 80 (0.01 mL) was applied with a fine paint brush to the growing stems of mature plants of *Ephedra gerardiana*, on each of 5 successive days (September 1987). Thus, a total of 500 mg of labeled pyruvate was administered. The plants were allowed to grow for 2 more days and were then harvested. The aerial parts (66 g fresh weight) were macerated in methanol (100 mL), hydrochloric acid (4 M, 3 mL) was added, methanol was removed, the residue was suspended in dilute hydrochloric acid (0.1 M, 50 mL), and the aqueous suspension was washed with ether (4 × 50 mL) and was then basified with K_2CO_3. The alkaloids were extracted into ether (4 × 50 mL) and reextracted into hydrochloric acid (1 M, 2 × 5 mL). Evaporation of the acid extracts gave a residue containing base hydrochlorides. The 75.47 MHz proton noise decoupled ^{13}C NMR spectrum of this sample (57 mg in 0.6 mL of D_2O) is presented in Figure 1.

The spectrum shows that the sample consists of the hydrochlorides of pseudoephedrine[8] (**3**), ephedrine[8,9] (**1**), norpseudoephedrine (**4**), and norephedrine[8-10] (**2**) in the ratio 52:35:10:3

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