Acknowledgment. We thank the National Science Foundation (CHE 81-03037) for support of this research.

Registry No. 1, 91083-39-5; **2**, 91083-40-8; **3**, 91083-41-9; **4**, 91083-42-0; **5**, 91083-43-1; LiC_6H_5, 591-51-5.

Highly Diastereocontrolled Reduction of Ketones by means of Hydrosilanes. Practical Synthesis of Optically Active 1,2-Diols and 2-Amino Alcohols of Threo or Erythro Configuration

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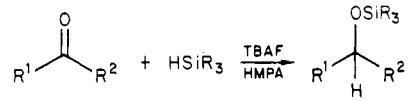
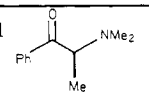
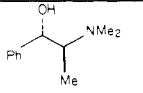
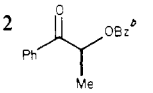
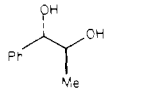
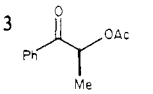
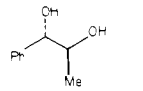
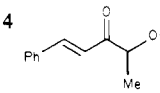
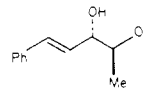
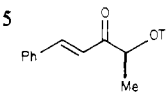
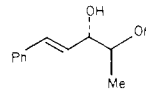
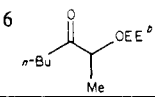
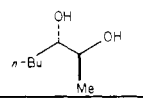
In spite of numerous studies on the stereoselective transformations carried out during last two decades,[1,2] the reduction of 2-amino or 2-hydroxy ketones remains unexplored in a practical point of view.[3,4] Since the resulting 2-amino alcohols and 1,2-diols constitute important structural moieties of pharmacologically useful substances, research on this subject seems to be warranted. In this communication we report a new convenient method for such transformation, wherein diastereometric threo or erythro alcohols can be selectively produced by merely changing the catalyst with almost complete stereochemical control.

Of many hydride reagents, hydrosilanes are outstanding in regard to easy handling. We have found that hydrolsilanes reduce aldehydes and ketones in the presence of a catalytic amount[5] of tetrabutylammonium fluoride (TBAF) in hexamethylphosphoric triamide (HMPA).[6] A solution of an aldehyde or a ketone (1



mmol) and phenyldimethylsilane (1.2 mmol) in HMPA (1–2 mL) was treated with TBAF (0.5 M tetrahydrofuran (THF) solution, 2–5 mol %). After the reaction at 0 °C or at room temperature for 0.5–12 h and subsequent workup, the yield of the resulting silyl ether was estimated by GLC assay. The results are given in the order of substrate and yield (%): *n*-$C_{10}H_{21}CHO$, 91; PhCHO, 91; PhCH=CHCHO, 100;[8] *n*-$C_6H_{13}COMe$, 87; CH_2=$CHCH_2CH_2COMe$, 57. In addition to the regio- and chemoselectivity,[5,7,8] the reaction shows remarkably high stereoselectivity. 2-Methylcyclohexanone was reduced to give *cis*-2-methylcyclohexanol with 94% selectivity. The cis selectivity was found to depend on the bulkiness of the silicon ligands (hydrosilane and % cis): $PhMe_2SiH$, 76; Ph_2SiH_2, 86; Ph_2MeSiH, 94; Ph_3SiH, 95 (yields 40–99%). The results are consistent with the fact that the cis selectivity becomes higher with the increasing steric bulk of the hydride reagent.[9]

Table I. TBAF-Catalyzed Threo-Selected Ketone Reduction with Hydrosilane[a]

run	ketone	hydrosilane and conditions	product (% yield)[c]	threo:erythro
1		$PhMe_2SiH$, room temp, 12 h	 (83)	>99:1[d]
2		$PhMe_2SiH$, 0 °C, 6 h	 (82)	96:4[d]
3		$PhMe_2SiH$, 0 °C, 20 h	 (95)	95:5[d]
4		$PhMe_2SiH$, 0 °C, 20 h	 (90)	93:7[e]
5		Ph_2MeSiH, 0 °C, 16 h	 (77)	87:13[e]
6		$PhMe_2SiH$, 0 °C, 12 h	 (86)[f]	84:16[f]

[a] Generally, 1.1–1.2 mol of hydrosilane and 5–10 mol % of TBAF in HMPA were employed. [b] Bz = benzoyl, EE = 1-ethoxyethyl, THP = tetrahydropyran-2-yl. [c] The *O*-silyl group and the protecting group were removed under acidic (1 M HCl, room temperature) or basic (1 M KOH/MeOH, room temperature) conditions, and the total yield is given. The isolated major product is shown. [d] Estimated by ^1H NMR analysis. The *threo*-amino alcohol showed a peak at δ 4.15 (d, J = 10 Hz, C*H*–OH) and the *threo*-glycol at δ 4.28 (d, J = 7 Hz), whereas each erythro isomer gave a peak at δ 4.88 (d, J = 4 Hz) and δ 4.57 (d, J = 4 Hz), respectively. [e] Determined by HPLC assay. [f] Determined by GLC analysis.

The stereoselective reduction finds further applications in acyclic system. When 2-(dimethylamino)-1-phenyl-1-propanone was treated with dimethylphenylsilane (1.2 mol) in HMPA in the presence of TBAF (5 mol %) (room temperature, 12 h), *N*-methylpseudoephedrine with exclusively threo configuration[10] was produced after desilylation. The similar threo-selective reduction was found applicable to 2-hydroxy ketone derivatives (Table I). It should be emphasized that racemization of the starting ketone does not take place to any measurable extent. For example, (*S*)-2-acetoxy-1-phenyl-1-propanone of 88% ee was reduced to give (1*S*,2*S*)-1-phenyl-1,2-propanediol of 88% ee (Table I, run 3). The stereochemical outcome[11] is attributed to the bulky

(1) (a) Morrison, J. D.; Mosher, H. S. "Asymmetric Organic Reactions"; Prentice-Hall: Englewood Cliffs, NJ, 1971; Chapter 3. (b) Tramomtini, M. *Synthesis* **1982**, 605.

(2) (a) Yamada, S.; Koga, K. *Tetrahedron Lett.* **1967**, 1711. (b) Katzenellenbogen, J. A.; Bowlus, S. B. *J. Org. Chem.* **1973**, *38*, 627. (c) Bowlus, S. B.; Katzenellenbogen, J. A. *Ibid.* **1974**, *39*, 3309. See also (3): Keck, G. E.; Boden, E. P. *Tetrahedron Lett.* **1984**, *25*, 265 and references cited therein.

(3) Threo-selective reduction of 2-hydroxy ketones having a sophisticatedly bulky hydroxyl protecting group: (a) Nakata, T.; Tanaka, T.; Oishi, T. *Tetrahedron Lett.* **1983**, *24*, 2653. (b) Nakata, T.; Fukui, M.; Oishi, T. *Ibid.* **1983**, *24*, 2657. (c) Nakata, T.; Fukui, M.; Ohtsuka, H.; Oishi, T. *Ibid.* **1983**, *24*, 2661. (d) Overman, L. E.; McCready, R. J. *Ibid.* **1982**, *23*, 2355.

(4) Buckley, T. F., III; Rapoport, H. *J. Am. Chem. Soc.* **1981**, *103*, 6157.

(5) Use of fluoride salts such as KF and CsF effects the hydrosilylation of aldehydes, ketones, and esters as shown by Corriu and his co-workers. For efficient reduction they had to employ appropriately activated hydrosilanes such as di- or trihydrosilanes and alkoxysilanes. Boyer, J.; Corriu, R. J. P.; Perz, R.; Reye, C. *J. Organomet. Chem.* **1979**, *172*, 143. Corriu, R. J. P.; Perz, R.; Reye, C. *Tetrahedron* **1983**, *39*, 999.

(6) Other aprotic polar solvents such as 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU) and *N*,*N*-dimethylformamide were also applicable, whereas less polar ones, e.g., tetrahydrofuran (THF) and dichloromethane, were inefficient.

(7) Nitriles and esters were not reduced.

(8) A parallel reaction with $RhCl(PPh_3)_3$ as the catalyst afforded a mixture of 1,2- and 1,4-hydrosilylated products in a ratio of 47:53. Regioselectivity in the $RhCl(PPh_3)_3$ catalyzed hydrosilylation of α,β-unsaturated compounds is discussed in detail: Ojima, I.; Kogure, T. *Organometallics* **1982**, *1*, 1390.

(9) Wigfield, D. C. *Tetrahedron* **1979**, *35*, 449 and references cited therein.

(10) The relative stereochemical nomenclature proposed by Noyori (Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1983**, *105*, 1598, footnote 32) is particularly pertinent. This notation applies not only to recently studied aldols and β-hydroxy esters but also to classical 1,2-diols, 2-amino alcohols, and sugars (Streitwieser, A., Jr.; Heathcock, C. H. "Introduction to Organic Chemistry"; Macmillan: New York, 1976; Chapters 24 and 25), and we need not change the conventional notation. Compare other notations: (a) Masamune, S.; Ali, S. A.; Snitman, D. L.; Garvey, D. S. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 557. (b) Seebach, D.; Prelog, V. *Ibid.* **1982**, *21*, 654. (c) Carey, F. A.; Kuehne, M. E. *J. Org. Chem.* **1982**, *47*, 3811.

(11) The configuration of the products was determined by comparison of their NMR spectra with those of an authentic sample (run 1) or with the reported values (runs 2 and 3: Zioudrou, C.; Chrysochou, P. *Tetrahedron* **1977**, *33*, 2103). Other products were transformed into known compounds or judged as such on the basis of the empirical rule of J(threo) > J(erythro) (see footnote *d* of Table I).

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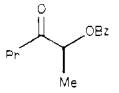
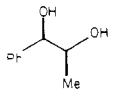
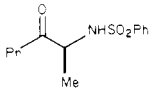
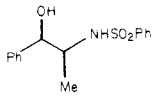
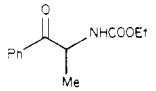
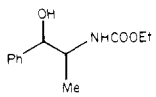
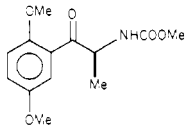
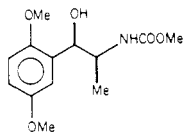
Table II. TFA-Catalyzed Erythro-Selective Ketone Reduction with $PhMe_2SiH$[a]

run	ketone	time, h	product (% yield)[b]	threo:erythro[c]
1		6	 (72)	7:93
2		20	 (66)[d]	2:98
3	 **1**	2.5	 (87) **2**	<1:99
4	 **3**	0.25	 (84) **4**	<1:99

[a] Typically 1.1-1.2 mmol of $PhMe_2SiH$ and 1 mmol of a ketone were allowed to react in 1-2 mL of TFA at 0 °C. [b] The benzoyl protecting group was removed under basic (1 M KOH/MeOH, r.t.) condition, and the total yield is given. The isolated major product is illustrated. [c] Determined by ^1H NMR analysis. The amino alcohol **2** gave a peak at δ 4.83 (d, J = 3 Hz, C*H*-OH) and **4** at δ 5.03 (d, J = 4 Hz). [d] This amino alcohol gave a peak at δ 4.78 (d, J = 3 Hz, C*H*-OH).

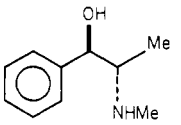
$[R_3SiHF]^-[n\text{-}Bu_4N]^+$ species which attacks the ketone carbonyl carbon according to the Felkin transition-state model.[12] Particularly noteworthy is that no metal cations are involved in the reaction. Thus, coordination effects by a metal cation are completely eliminated, and only the bulkiness of the reagent accounts for the stereoselectivity. In this sense, the reagent is characterized as a "bulky naked hydride".[13]

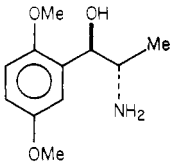
In striking contrast to the TBAF-catalyzed threo-directed reduction, erythro-selective reduction was achieved by using the same hydrosilanes under acidic conditions.[14] For example, dimethylphenylsilane (1.2 mmol) was added to a trifluoroacetic acid (TFA) (1 mL) solution of 2-(benzoyloxy)-1-phenyl-1-propanone at 0 °C. After being stirred for 6 h, the solution was neutralized with aqueous $NaHCO_3$ solution and worked up. Alkaline hydrolysis followed by silica gel filtration gave a 7:93 mixture of *threo*- and *erythro*-1-phenyl-1,2-propanediol in 72% yield. The reduction of N-protected α-amino ketones showed remarkable erythro selectivity as shown in Table II.

The contrastive selectivity under TBAF vs. TFA catalysis is noticeable. Whereas the TBAF-catalyzed reduction is explained by the Felkin model, the TFA catalysis may be rationalized by the proton-bridged Cram's cyclic model.[15]

The usefulness of the stereocontrolled reduction is demonstrated by the chiral syntheses of useful drugs. Reduction of **1**[4,16] ($[\alpha]^{23}_D$ -5.12° (*c* 5, CH_2Cl_2)) and **3**[17] ($[\alpha]^{20}_D$ -33.1° (*c* 1, $CHCl_3$)) with dimethylphenylsilane in TFA gave **2** ($[\alpha]^{20}_D$ -41° (*c* 0.2, $CHCl_3$)) and **4** ($[\alpha]^{20}_D$ -31.7° (*c* 1, $CHCl_3$)), respectively (Table II).

Lithium aluminum hydride reduction (THF, 60 °C) of **2** gave *l*-ephedrine[18] in 80% yield, while alkaline hydrolysis (KOH, MeOH-H_2O (3:1), reflux) of **4** gave *l*-methoxamine,[20] an adrenergic vasopressor, in 83% yield.


l-ephedrine


l-methoxamine

(12) (a) Chêrest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199. (b) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61.

(13) Metal hydrides with tetrabutylammonium gegen cations, Bu_4NBH_3CN: Hutchins, R. O.; Kandasamy, D. *J. Am. Chem. Soc.* **1973**, *95*, 6131. Bu_4NBH_4: Brändström, A.; Junggren, U.; Lamm, B. *Tetrahedron Lett.* **1972**, 3173. Raber, D. J.; Guida, W. C. *J. Org. Chem.* **1976**, *41*, 690. Sorrell, T. N.; Pearlman, P. S. *Tetrahedron Lett.* **1980**, *21*, 3963.

(14) So-called "Ionic Hydrogenation" conditions. Kursanov, D. N.; Parnes, Z. N.; Loim, N. M. *Synthesis* **1974**, 633.

(15) Cram, D. J.; Wilson, D. R. *J. Am. Chem. Soc.* **1963**, *85*, 1245.

(16) Although the reported value for **1** is $[\alpha]^{23}_D$-5.9° (*c* 5, CH_2Cl_2) (ref 4), our sample was found to be optically pure, as repeated recrystallization did not change the $[\alpha]_D$ value.

(17) Prepared from (*S*)-alanine by (i) methoxycarbonylation (MeOCOCl, OH^-), (ii) acid chloride formation ($SOCl_2$), (iii) *N*,*N*-dimethylamide formation ($HNMe_2$), and (iv) ketone synthesis (2,5-$(MeO)_2C_6H_3Li$) in 66% overall yield in optically pure form.

(18) The sample was converted to the hydrochloride, $[\alpha]^{25}_D$-33.5° (*c* 1, H_2O); lit.[19] $[\alpha]^{25}_D$-33 to -35.5° (*c* 5, H_2O).

(19) "The Merck Index", 10th ed.; Merck & Co.: Rahway, NJ, 1983; No. 3558, p 520.

(20) The sample was converted to the hydrochloride, $[\alpha]^{25}_D$-27.9° (*c* 3, H_2O); lit.[21] $[\alpha]^{25}_D$-28.5° (*c* 4, H_2O).

(21) Baltzly, R.; Mehta, N. B. *J. Med. Chem.* **1968**, *11*, 833.

Palladium-Catalyzed Coupling of Vinyl Triflates with Organostannanes. A Short Synthesis of Pleraplysillin-1

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Although a variety of allylic compounds are capable of acting as electrophiles in palladium-catalyzed coupling reactions,[1] vinylic compounds that act as electrophiles are limited almost solely to vinyl halides.[1-3] Allylic sulfonates, for example, readily undergo palladium-catalyzed coupling reactions,[4] but there is no documented example for the insertion of a transition metal into the carbon-oxygen bond of a vinyl sulfonate. This is somewhat surprising since bromide, iodide, and tosylate all show similar leaving group tendencies[5] and similar allylic reactivities in palladium-catalyzed transformations.[4] In an effort to understand this apparent anomaly and to add to the functional groups on vinyl carbons that will undergo catalytic and stoichiometric insertion reactions with the group VIII transition metals, the palladium-catalyzed reactions of vinyl sulfonates were explored. In particular, the reaction of vinyl triflates[6] with organostannanes[7] was undertaken.

Upon addition of 4-*tert*-butylcyclohexenyl triflate (**1**) to a 2 mol% solution of tetrakis(triphenylphosphine)palladium(0) in tetrahydrofuran (THF) at room temperature, a reaction occurred immediately as observed by ^{31}P NMR.[8] However, addition of

(1) For a general review, see: Tsuji, J. "Organic Synthesis with Palladium Compounds"; Springer-Verlag: Berlin, 1980. Trost, B. M.; Verhoeven, T. R. In "Comprehensive Organometallic Chemistry"; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 8, Chapter 57.

(2) (a) For the palladium-catalyzed coupling of alanes with enol phosphates, see: Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1980**, *21*, 2531-2534. (b) For some examples of the palladium-catalyzed coupling of vinyl halides, see: Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146-151. Negishi, E. *ibid.* **1982**, *15*, 340-345.

(3) (a) For the nickel-catalyzed coupling of Grignard reagents with methyl vinyl ethers, see: Wenkert, E.; Michelotti, E. L.; Swindell, C. S. *J. Am. Chem. Soc.* **1979**, *101*, 2246-2247. (b) For the nickel-catalyzed coupling of Grignard reagents with silyl enol ethers, see: Hayashi, T.; Katsura, Y.; Kamuda, M. *Tetrahedron Lett.* **1980**, *21*, 3915-3918.

(4) For example, see: Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315-2325. Matsushita, H.; Negishi, E. *J. Org. Chem.* **1982**, *47*, 4161-4165. Semmelhack, M. F.; Brickner, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3945-3947.

(5) McMurry, J. "Organic Chemistry"; Brooks/Cole: Monterey, CA, 1984; p 301-302.

(6) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1980**, *21*, 4313-4316.

(7) For an example of the palladium-catalyzed reaction of vinyl halides with organostannanes, see: Kosugi, M.; Hagiwara, I.; Migita, T. *Chem. Lett.* **1983**, 839-840.

0002-7863/84/1506-4630$01.50/0