Photooxidation of a Mixture of 4b and 4b-d_8. An oxygen-saturated MeCN-PhH (4:1) solution of **4b** (4.3 mM), **4b**-d_8 (4.3 mM), and TPP (0.1 mM) was irradiated similarly, and the isotope ratios of the resulting acetophenone (**5b**) and methyl benzoate (**6b**) were determined by mass spectrometry. For the ketone **5b**: M(m/e 120):(M + 6):(M + 7):(M + 8) = 100:(3.9 ± 0.4):(20.6 ± 1.2):(81.5 ± 6.8); i.e., **5b**-d_0:**5b**-d_6,d_7,d_8 = 1:(1.06 ± 0.08). On the other hand, for the ester **6b**, M(m/e 136):(M + 1):(M + 2):(M + 3):(M + 4):(M + 5):(M + 6):(M + 7):(M + 8) = 100:(12.1 ± 0.5):(17.5 ± 0.7):(83.9 ± 3.8):(10.7 ± 1.1):(92.5 ± 7.2):(11.6 ± 0.9):(21.5 ± 2.0):(84.1 ± 7.4). After a correction of ^{13}C (8.7%) contained in **6b**, deuterium contents in **6b** are d_0:d_1:d_2:d_3:d_4:d_5:d_6:d_7:d_8 = 100:3.4:17.2:82.4:3.5:92.2:3.6:21.2:82.3; i.e., **6b**-d_0:**6b**-d_1,d_2,d_3:**6b**-d_4,d_5:**6b**-d_6,d_7,d_8 = 1:(1.03 ± 0.05):(0.96 ± 0.08):(1.07 ± 0.10). Therefore, methyl and phenyl groups in **6b** were completely scrambled each other.

Quantum Yields. The quantum yields for the decrease of **4a** on the photooxidation were determined as described previously[62] by using a 150-W Xenon lamp and a monochrometer. The incident photoflux was 6.1×10^{-7} E/min at 405 ± 5 nm, and the decrease of **4a** was monitored by absorption spectroscopy (**4a**, λ_{max} 515 nm, ϵ 38).

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Fluoride Ion Catalyzed Reduction of Aldehydes and Ketones with Hydrosilanes. Synthetic and Mechanistic Aspects and an Application to the Threo-Directed Reduction of α-Substituted Alkanones

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Reduction of aldehydes and ketones with hydrosilanes proceeded in the presence of a catalytic amount of tetrabutylammonium fluoride or tris(diethylamino)sulfonium difluorotrimethylsilicate in aprotic polar solvents under mild conditions. A significant isotope effect (k_H/k_D = 1.50) was observed in competitive reduction of acetophenone with $HSiMe_2Ph$ and $DSiMe_2Ph$. The reaction was of first order in the concentration of an aprotic polar solvent HMPA. Reduction of 2-methylcyclohexanone gave *cis*-2-methylcyclohexanol with selectivities up to 95%. The kinetic and stereochemical results suggest that a hexavalent fluorosilicate $[HSiR_3F(HMPA)]^-$ is involved. α-Alkoxy (acyloxy or dimethylamino) ketones were transformed to threo alcohols in high diastereoselectivities. The reduction was also applied to α-methyl-β-keto amides, $RCOCH(MeCONR)_2$, to afford the corresponding threo alcohols in >98% selectivity. The threo selectivity is explained in terms of the Felkin-Anh model in which interaction of carbonyl oxygen with a countercation is ideally suppressed. The threo-directed reduction was applied to (*R*)-1-phenyl-4-(2-tetrahydropyranyloxy)-1-penten-3-one and *N*-(2-benzoylpropanoyl)piperidine. The resulting threo alcohols were respectively converted into (2*R*,3*S*)-2,3-(cyclohexylidenedioxy)butanal, a key intermediate of daunosamine synthesis, and into a pharmacologically useful compound *threo*-*N*-(3-hydroxy-2-methyl-3-phenylpropyl)piperidine.

Stereochemistry in substitution reactions at silicon has been extensively studied recently, and these reactions were proved to proceed via penta- or hexacoordinated silicate intermediates (eq 1).[1] Fluoride ion as the nucleophile (Nu), in particular, forms a strong Si-F bond (595 kJ/mol)[2] upon the reaction with R_3Si-Nu and thus readily generates nucleophilic species fluorosilicate 1 (Nu = F) and/or Nu'^-. This reaction was first applied to organic synthesis by Corey, who succeeded in selective deprotection of silyl ethers under mild conditions by means of fluoride ion.[3] Kuwajima and Noyori extended the concept independently to the generation of naked enolates.[4] Later, the organosilane/F^- system was demonstrated to be effective as well for the formation of various carbon nucleophiles including acetylides[5] and allyl anions[6] and has been frequently employed in current organic synthesis.[7]

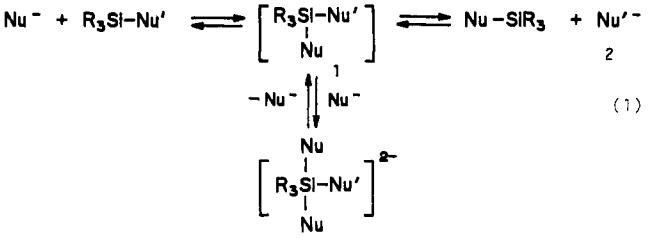

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Table I. Fluoride Ion Catalyzed Hydrosilylation of Aldehydes and Ketones

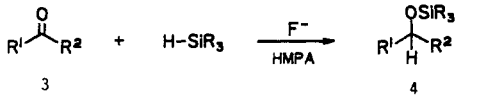
run	aldehyde	hydrosilane[a]	cat.[b]	solvent[c]	condtns: temp (°C), time (h)	prod	% yield[d]
1	**3a**	$PhMe_2SiH$ (1.1)	TBAF (5)	HMPA	25, 1	**4a**	91
2	**3a**	$PhMe_2SiH$ (1.1)	TBAF (5)	DMPU	25, 1	**4a**	89
3	**3a**	$PhMe_2SiH$ (1.1)	TBAF (5)	DMF	25, 1	**4a**	56
4	**3a**	$PhMe_2SiH$ (1.1)	TBAF (5)	THF	25, 1	**4a**	9 (85)[e]
5	**3a**	$PhMe_2SiH$ (1.1)	TBAF (5)	CH_2Cl_2	25, 1	**4a**	1 (75)[e]
6	**3a**	$PhMe_2SiH$ (1.1)	CsF (5)	HMPA	25, 1	**4a**	43 (16)[e]
7	**3a**	$PhMe_2SiH$ (1.1)	KF[f] (5)	HMPA	25, 1	**4a**	14 (68)[e]
8	**3a**	$PhMe_2SiH$ (1.1)	KF (17)	DMF	80, 16	**4a**	56
9	**3b**	$PhMe_2SiH$ (1.2)	TBAF (2)	HMPA	rt,[i] 1.5	**4b**	91
10	**3b**	Et_3SiH (1.2)	TBAF (5)	HMPA	rt, 1	**4b′**	92
11	**3c**	$PhMe_2SiH$ (1.2)	TBAF (2)	HMPA	rt, 0.5	**4c**	100
12	**3d**	Ph_2SiH_2 (1.1)	TBAF (5)	HMPA	rt, 2.5	**4d″**	62
13	**3e**	$PhMe_2SiH$ (1.1)	TBAF (5)	HMPA	rt, 12	**4e**	81
14	**3f**	$PhMe_2SiH$ (1.2)	TBAF (2)	HMPA	rt, 0.5	**4f**	36
						4f*	40
15	**3g**	$PhMe_2SiH$ (1.1)	TBAF (5)	HMPA	rt, 12	**4g**	57
16	**3h**	$PhMe_2SiH$ (1.2)	TBAF (5)	HMPA	0, 24	**4h***	99 [76:24][g,h]
17	**3h**	Ph_2SiH_2 (1.0)	TBAF (5)	HMPA	0, 5	**4h***	74 [86:14][g,h]
18	**3h**	Ph_2MeSiH (1.2)	TBAF (5)	HMPA	0, 24	**4h***	81 [94:6][g,h]
19	**3h**	Ph_3SiH (1.2)	TBAF (5)	HMPA	rt, 12	**4h***	40 [95:5][g,h]

[a] Values in the parentheses are molar equivalents to the aldehydes. [b] Values in the parentheses are mole % to the aldehydes. [c] Usually, 1–2 mL/mmol of the solvent was employed. [d] GLC yields. [e] The value in the parentheses is the yield of recovered **3a**. [f] Spray dry KF was employed. [g] The ratio in the brackets is the ratio of cis and trans isomers. [h] The product was analyzed after acid treatment (1 M HCl–MeOH, room temperature) to remove the silyl group. [i] Room temperature.

The reaction of hydrosilane with fluoride ion according to eq 1 is expected to generate a hydride ion (Nu = F, Nu′ = H). However, at the outset of our study, little attention has been paid to the hydrosilane/F^- system. Corriu et al. reported[8] reductions of carbonyl compounds with hydrosilanes in the presence of an activator KF, CsF, KSCN, or KOCOR. Its synthetic utility was scarcely recognized, unfortunately, due possibly to heterogeneous and drastic conditions including a large excess of the salts. This article details[9] studies on the synthetic and mechanistic aspects of the fluoride ion catalyzed reduction of aldehydes and ketones with the emphasis on the stereoselectivity.

Results and Discussion

General Aspects of the Fluoride Ion Catalyzed Reduction of Carbonyl Groups with Hydrosilanes. We have found that aldehydes and ketones are reduced by hydrosilanes in the presence of fluoride ion catalyst in an aprotic polar solvent. For the elucidation of general aspects of this reaction, effects of the catalyst and solvent were studied at first. Of many fluoride ion sources, tetrabutylammonium fluoride (TBAF) and tris(diethylamino)sulfonium difluorotrimethylsilicate (TASF)[10] were chosen to make the reaction system homogeneous. In contrast to Corriu's salt-promoted reaction, it was found that the employment of such aprotic polar solvents as hexamethylphosphoric triamide (HMPA) markedly accelerated the reaction and that the aldehydes and ketones were reduced at room temperature (eq 2). As shown in



3 4 (2)

a: $R^1 = n\text{-}C_{10}H_{21}$, R^2 = H
b: R^1 = Ph, R^2 = H
c: R^1 = PhCH=CH, R^2 = H
d: $R^1 = n\text{-}C_5H_{11}$, R^2 = H
e: $R^1 = n\text{-}C_6H_{13}$, R^2 = Me
f: R^1 = Ph, R^2 = Me
g: $R^1 = CH_2{=}CHCH_2CH_2$, R^2 = Me
h: R^1,$R^2 = (CH_2)_4CH(Me)$
no superscription: $SiR_3 = SiMe_2Ph$
(′): $SiR_3 = SiEt_3$
(″): $SiR_3 = SiPh_2(OCHR^1R^2)$
(*): SiR_3 = H

Table I, the reaction of dimethylphenylsilane and undecanal (**3a**) was complete within an hour by the use of HMPA or 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU). *N*,*N*-Dimethylformamide (DMF) solvent was less effective to give **4a** in 56% yield; much less polar solvents such as tetrahydrofuran (THF) and dichloromethane reduced the yields drastically (runs 4 and 5).

The reactivity is markedly influenced by the steric bulk of hydrosilanes. For example, the reactivity decreased in the order of $Ph_2SiH_2 \gg PhMe_2SiH > Ph_2MeSiH > Ph_3SiH$ (see the reaction time required for the reduction of 2-methylcyclohexanone (**3h**): runs 16–19). The reactivity of hydrosilanes depends also on the electronic nature of the substituents. The reaction of diphenylsilane with hexanal (1:1.1 ratio) afforded $(n\text{-}C_6H_{13}O)_2SiPh_2$ (**4d″**) only (run 15), and an expected intermediate $(n\text{-}C_6H_{13}O)SiHPh$ could not be detected. The sole formation of **4d″** clearly indicates that the alkoxy-substituted hydrosilane inter-

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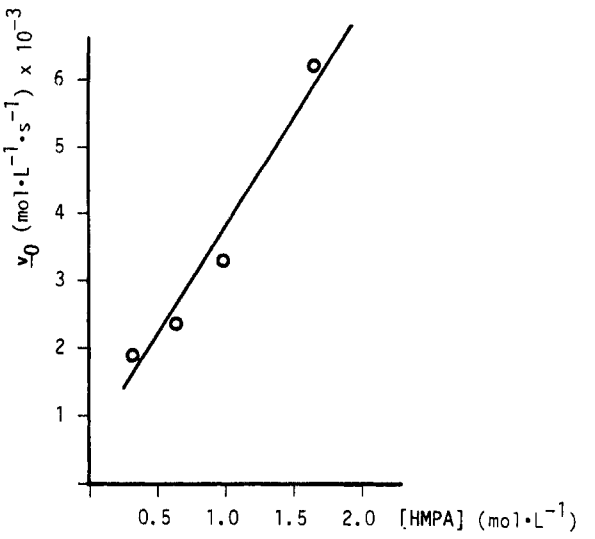
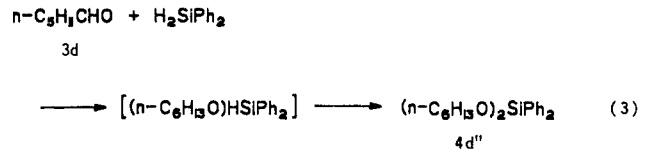
(10) U.S. Patent 3940402; *Chem. Abstr.* **1976**, *85*, 6388*j*.



Initial concentrations: $[PhCOMe]_0$ = 0.33 M, $[HSiMe_2Ph]_0$ = 0.66 M, $[Bu_4NF]_0$ = 6.6 x 10^{-3} M

Figure 1. v_0 vs [HMPA].

mediate is more reactive than diphenylsilane in spite of the increase of steric bulk around silicon (eq 3). Though

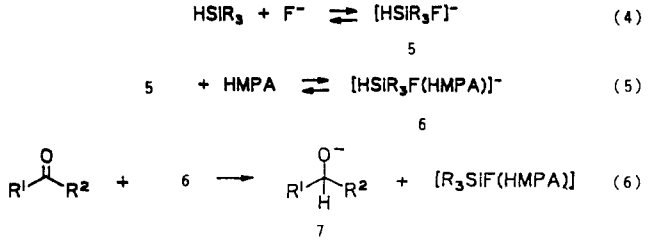


(3)

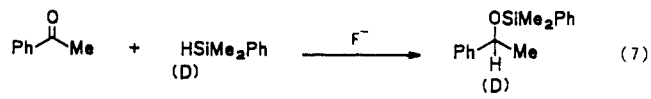
CsF and KF also catalyzed the hydrosilylation of **3a**, these fluorides were far less effective than TBAF or TASF: the yields of **4a** were 43% and 14%, respectively, after 1 h of reaction at 25 °C (runs 6 and 7). Other aldehydes and ketones were hydrosilylated in satisfactory yields (runs 9–13). Chemoselectivity of the carbonyl reduction should be noted: cyano and ester carbonyl groups as well as C=C bonds conjugated with esters remained intact.

In the TBAF catalyzed hydrosilylation of 2-methylcyclohexanone (**3h**), high selectivity for the formation of *cis*-2-methylcyclohexanol (**4h***) was observed (runs 16–19).[11] The cis selectivity grew higher from 76% to 95% as the steric bulkiness of the hydrosilane increased from dimethylphenyl to triphenyl. Accordingly, a hypervalent silicate species generated by the reaction of hydrosilane and fluoride ion is apparently involved as the reactive species rather than a "naked hydride".

Mechanistic Aspects. The reduction is markedly accelerated on the employment of aprotic polar solvents like HMPA.



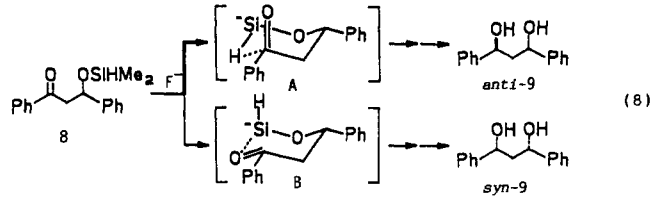
In order to gain insight into the mechanism of the present hydrosilane-based reduction, we measured the reaction rate of the reduction of acetophenone with dimethylphenylsilane by using TASF catalyst and various amounts of HMPA, and the initial reaction rate v_0 was found to be of first order in the concentration of HMPA (Figure 1).[12] In addition, a significant isotope effect (k_H/k_D = 1.50) was observed for the reaction in eq 7.



(7)

k_H/k_D = 1.50

Thus, the rate-determining step should be that of the hydride transfer[13,14] from a hexavalent silicate $[HSiR_3F(HMPA)]^-$ (**6**) (eq 6) which was generated by eq 4 and 5. A similar rate-enhancement effect by HMPA is observed in the racemization and nucleophilic substitution at silicon,[1] for which involvement of hexacoordinated silicon intermedaites is proposed on the basis of kinetic data. Since the hexavalent silicate is a fully coordinated silicon species, additional coordination by ketone carbonyl is apparently improbable. These results contrast sharply to the cyclic transition state proposed for fluoride ion catalyzed conjugate addition of enol ethers.[15] No evidence for the O–Si interaction could be obtained in the reduction of β-dimethylsiloxy ketone 8: treatment of 8 with TASF followed by acid hydrolysis afforded the *anti*-diol **9** preferentially (anti/syn = 75/25)[16] (eq 8). The anti selection may be explained in terms of the transition state A wherein the O–Si interaction is absent by analogy to the anti-selective reduction of β-hydroxy ketones.[17] The cyclic transition state like B applies to the syn-selective reduction.[18]



(8)

Since halosilane behaves as a weak Lewis acid,[19] fluorosilane may interact with the carbonyl oxygen of the substrate. This possibility is, however, excluded by an

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(12) Determination of the reaction rate: Livingston, R. *Technique of Organic Chemistry*, 2nd ed.; Weissberg, A., Ed.; Interscience: NY, 1961; Vol. VIII, Part 1, p 122.

(13) The hydrosilane/F^- reduction is shown to proceed by direct hydride transfer rather than electron transfer: Yang, D.; Tanner, D. D. *J. Org. Chem.* **1986**, *51*, 2267.

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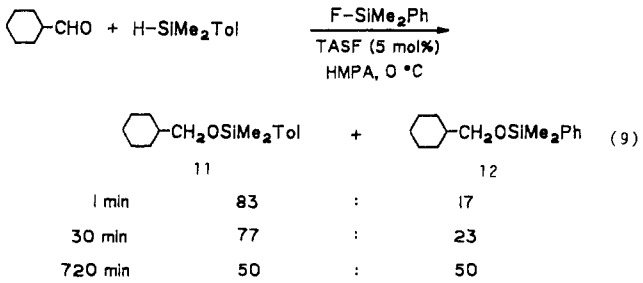
(19) Chlorotrimethylsilane activates enones for conjugate addition of organocopper reagents: Nakamura, E.; Matsuzawa, S.; Horiguchi, Y.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4029. See also: Nakamura, E.; Matsuzawa, S.; Horiguchi, Y.; Kuwajima, I. *Ibid.* **1986**, *27*, 4025.

Table II. Hydrosilane/F⁻ Reduction of α-Oxy and α-Amino Ketones[a]

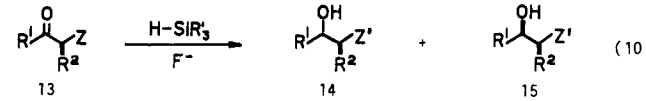
run	ketone[b]	hydrosilane	condtns: temp (°C), time (h)	prod[c,d]	% yield[e]	14:15
1	**13a**	$PhMe_2SiH$	0, 20	**14a**	95	95:5[f]
2	**13a**	$PhMe_2SiH$	0, 4	**14a**	93	93.3:6.7[f]
3	**13a**	$(p\text{-}CF_3C_6H_4)Me_2SiH$	0, 4	**14a**	72	93.1:6.9[f]
4	**13a**	$(p\text{-}MeC_6H_4)Me_2SiH$	0, 4	**14a**	83	93.1:6.9[f]
5	**13a**	$(p\text{-}MeOC_6H_4)Me_2SiH$	0, 4	**14a**	88	93.0:7.0[f]
6	**13a**	$PhMe_2SiH$	rt,[i] 14	**14a**	99	93:7[f]
7	**13a**	Ph_2MeSiH	rt, 14	**14a**	89	92:8[f]
8	**13a**	$(i\text{-}PrO)Ph_2SiH$	rt, 3	**14a**	91	86:14[f]
9	**13a**	$(i\text{-}PrO)_3SiH$	−50, 12	**14a**	71	78:22[f]
10	**13a′**	$PhMe_2SiH$	0, 6	**14a**	82	96:4[f]
11	**13a″**	$PhMe_2SiH$	0, 18	**14a**	55	90:10[f]
12	**13b**	$PhMe_2SiH$	0, 12	**14b**	95	84:16[g]
13	**13b′**	$PhMe_2SiH$	0, 10	**14b′**	86	91:9[f]
14	**13b″**	$PhMe_2SiH$	0, 18	**14b**	77	87:13[g]
15	**13c**	$PhMe_2SiH$	0, 12	**14c**	86	84:16[h]
16	**13d**	$PhMe_2SiH$	0, 4	**14d**	76	33:67[f]
17	**13e**	Ph_2SiH_2	rt, 12	**14e**	97	98:2[f]
18	**13e**	$PhMe_2SiH$	rt, 10	**14e**	83	>99:1[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 protecting group were removed under acidic (1 M HCl, room temperature) or basic (1 M KOH–MeOH, room temperature) conditions. [d] The isolated major product is shown. [e] The total yield is given. [f] Determined by ^1H NMR analysis. [g] Determined by HPLC assay. [h] Determined by GLC analysis. [i] Room temperature.

experiment shown in eq 9. When cyclohexanecarboxaldehyde and dimethyl-*p*-tolylsilane were treated with TASF in the presence of an equimolar amount of fluorodimethylphenylsilane (**10**), the initial products consisted mainly of the dimethyl-*p*-tolylsilyl ether **11**. After prolonged reaction time, **10** and **11** became in equilibrium between the dimethylphenylsilyl ether **12** and fluorodimethyl-*p*-tolylsilane. If activation of the carbonyl group by the fluorosilane initiates the reaction, **12** should have been produced first. The predominant formation of **11** explicitly indicates no participation of fluorosilane as the Lewis acid. The alkoxide **7** (R^1 = c-C_6H_{11}, R^2 = H) is immediately trapped by fluorosilane ($FSiMe_2Tol$) present nearby.[20]



Threo-Selective Reduction of α-Oxy and α-Amino Ketones with Hydrosilane/F⁻ Reagent. It has been commonly recognized that reduction of α-hydroxy and α-amino ketones with hydride reagents is generally erythro selective.[21,22] The stereochemical course of the reduction is explained in terms of the Cram's cyclic model,[23] which involves the assistance of a metal counterion to form a rigid cyclic transition state. In contrast, little attention has been paid to the carbonyl reduction with hydrides having such an onium ion as ammonium or sulfonium.[24] These cations cannot form the chelate discussed above and are thus expected to invert the stereoselection of the hydride reduction. Accordingly, we studied the stereoselectivity in the reduction of α-oxy and α-amino ketones **13** with the hydrosilane/F⁻ reagent (eq 10). The reactions were carried out in HMPA in the presence of fluoride ion catalyst (5–10%). Results are summarized in Table II.



13a: R^1 = Ph, R^2 = Me, Z = OAc
13a′: R^1 = Ph, R^2 = Me, Z = OBz
13a″: R^1 = Ph, R^2 = Me, Z = OEE
13b: R^1 = PhCH=CH, R^2 = Me, Z = OAc
13b′: R^1 = PhCH=CH, R^2 = Me, Z = OBu^t
13b″: R^1 = PhCH=CH, R^2 = Me, Z = OTHP
13c: R^1 = Bu, R^2 = Me, Z = OEE
13d: R^1,R^2 = $(CH_2)_4$, Z = OBz
14a, 15a: R^1 = Ph, R^2 = Me, Z′ = OH
14b, 15b: R^1 = PhCH=CH, R^2 = Me, Z′ = OH
14b′, 15b′: R^1 = PhCH=CH, R^2 = Me, Z′ = OBu^t
14c, 15c: R^1 = Bu, R^2 = Me, Z′ = OH
14d, 15d: R^1,R^2 = $(CH_2)_4$, Z′ = OH
14e, 15e: R^1 = Ph, R^2 = Me, Z′ = NMe_2

In all cases except for a cyclohexanone derivative **13d**, high threo selectivity[25] was recognized for aryl, alkenyl, or alkyl ketones which have various O-protecting groups. Hydrosilanes with alkyl, aryl, and/or alkoxy substituents were all applicable. The stereoselectivity is independent of electronic effects of the hydrosilane substituents: 93.3–93.0% threo for $HSiMe_2Ar$ (Ar = p-XC_6H_4, X = H, CF_3, Me, MeO) (runs 2–5). The lower selectivities observed with alkoxysilanes may be attributed to the lack of steric bulkiness of an alkoxy group compared to an alkyl group.[26] Exceptionally high threo selectivity (>99%) was observed in the reduction of 2-(dimethylamino)-1-phenyl-1-propanone in sharp contrast to the reduction by means of conventional hydride reagents.[27] It is noteworthy that no

(20) A referee suggested the possibility that an aldehyde might play the role of the catalyst. However, the immediate trap of **7** and relatively slow scrambling of the silyl group between **10** and **11** suggest that the concentration of **7** is extremely low under the reaction conditions, and thus, the possibility of **7** as the catalytic species may be precluded.

(21) Tramontini, M. *Synthesis* **1982**, 605.

(22) (a) Yamada, S.; Koga, K. *Tetrahedron Lett.* **1967**, 1711. (b) Katzenellenbogen, J. A.; Bawlus, S. B. *J. Org. Chem.* **1973**, *38*, 627. Bawlus, S. B.; Katzenellenbogen, J. A. *Ibid.* **1974**, *39*, 3309. (c) $Zn(BH_4)_2$ reduction: Oishi, T.; Nakata, T. *Acc. Chem. Res.* **1984**, *17*, 338 and references cited therein.

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

(24) Stereoselective reduction of methyl 2-benzoylpropionate with Me_4NBH_4 is reported,[28] though the selectivity is moderate (threo:erythro = 7:3): Nakata, T.; Oishi, T. *Tetrahedron Lett.* **1980**, *21*, 1641.

(25) The relative stereochemical nomenclature proposed by Noyori is pertinent throughout this work: see ref 3d, footnote 32.

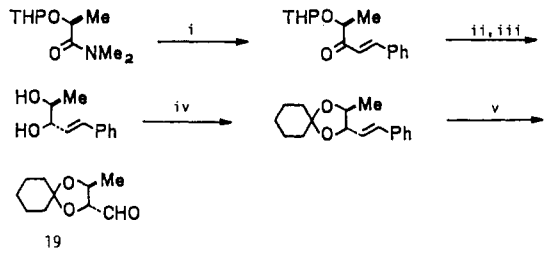
(26) The conformational *A* values of Me and OMe are 1.70 kcal/mol and 0.60 kcal/mol, respectively: Hirsch, J. A. *Top. Stereochem.* **1967**, *1*, 199.

Table III. Stereoselective Reduction of 2,3-Epoxy Ketones

run	2,3-epoxy ketone	hydride	condtns: temp (°C), time (h)	prod, total yield (%)	17:18[a]
1	**16a**	$PhMe_2SiH$–TBAF[b]	0, 12	**17a** + **18a**, 100	65:35
2	**16a**	$NaBH_4$[c]	0, 0.5	**17a** + **18a**, 79[d]	19:81
3	**16b**	$PhMe_2SiH$–TBAF	−20, 24	**17b** + **18b**, 95	71:29
4	**16b**	$NaBH_4$	0, 1	**17b** + **18b**, 98	29:71

[a] Determined by GLC unless otherwise noted. [b] $PhMe_2SiH$ (1.2 mol) and TBAF (5 mol %) in HMPA were employed. [c] $NaBH_4$ (1 mol) in MeOH was employed. [d] Isolated yield.

Scheme I[a]

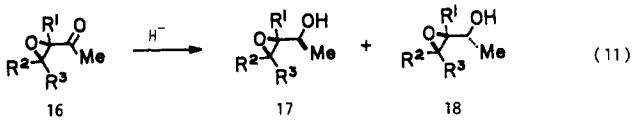


[a] i, PhCH=CHMgBr; ii, $HSiMePh_2$, TBAF; iii, H_3O^+; iv, $(MeO)_2C(CH_2)_5$; v, $NaIO_4$, OsO_4.

racemization of the starting ketones took place during the reaction. For example, the reduction of (*S*)-2-acetoxy-1-phenyl-1-propanone (**13a**) of 88% ee gave (1*S*,2*S*)-1-phenyl-1,2-propanediol (**14a**) of 88% ee.

The opposite stereochemical outcome for **13d** is ascribed simply to the favored equatorial attack[28] of the hydride to **13d** like the reduction of 2-methylcyclohexanone (vide supra), because the benzyloxy group prefers the equatorial position and, therefore, the Felkin–Anh model cannot be applied hereon.

Application of hydrosilane/F^- reduction to α,β-epoxy ketones (**16**) (eq 11) resulted again in predominant formation of the threo alcohols (**17**) as shown in Table III. Though moderate, the threo-selective reduction compensates for erythro-directed reduction of the same ketones with hydride reagents[22d,29] (see runs 2 and 4 in Table III) or the Sharpless epoxidation of secondary allylic alcohols.[30] We attributed the observed threo selectivity again to the Felkin–Anh model,[31] as the absence of metal cation completely rejects the possibility of any cyclic transition state.



16 17 18 (11)

a, R^1 = H, R^2 = R^3 = Me; **b**, R^1 = Me, R^2 = R^3 = H

The threo-selective reduction was applied to the chiral synthesis of (2*R*,3*S*)-2,3-(cyclohexylidenedioxy)butanal (**19**),[32] which is a key synthetic intermediate of L-daunosamine, an amino sugar moiety of natural anthracyclcine antibiotics[33] (Scheme I). Treatment of (*S*)-*N*,*N*-diethyl-2-(2-tetrahydropyranyl)propanamide with phenylmagnesium bromide yielded (*S*)-**13b**″ in 88% yield. The TBAF catalyzed hydrosilylation of (*S*)-**13b**″ with methyldiphenylsilane followed by deprotection in acidic media gave (3*S*,4*S*)-**14b** in 77% yield [(3*S*,4*S*):(3*R*,4*S*) = 87:13] (Table II, run 13). Protection of the *vic*-diol function by the cyclohexylidene group followed by oxidation with OsO_4–$NaIO_4$ gave the aldehyde **19** in 71% yield. The optical purity of **19** was estimated to be >95% by derivation to (2*S*,3*S*)-(2,3-cyclohexylidenedioxy)butanenitrile[32d,34] and comparison of its $[\alpha]_D$ value with that of an authentic sample.

Table IV. Stereoselective Reduction of 20 with $PhMe_2SiH/F^-$ Reagent[a]

substrate[b]	condtns: temp (°C), time (h)	prod[d]	% yield[e]	21:22[f,g]
20a	rt,[c] 12	–	no rctn	–
20b	0, 12	**21b** + **22b**	98	>99:1
20c	0, 22	**21c** + **22c**	91	98:2
20d	0, 19	**21d** + **22d**	90	99:1
20e	0, 16	**21e** + **22e**	86	99:1
20f	0, 16	**21f** + **22f**	92	99:1
20g	0, 22	**21g** + **22g**	93	23:77[h]
20h	0, 24–rt, 72	**21h** + **22h**	27 (84)[i]	25:75
20i	0, 14–rt, 24[j]	**21i** + **22i**	90	91:9

[a] $PhMe_2SiH$ (1.2 molar equiv), TASF (10 mol %), and DMPU (1–2 mL) were employed. [b] See footnote 9. [c] Room temperature. [d] Major stereoisomers are shown. [e] Total yields of **20** and **21** are given. [f] Relative stereochemistry of the products was determined by ^1H and ^{13}C NMR spectrometric analysis.[24] [g] Analysis with 90- or 400-MHz ^1H NMR instrument unless otherwise noted. [h] GLC analysis. [i] A yield based on the consumed **19f**. [j] Ph_2SiH_2 was employed.

Threo-Selective Reduction of α-Substituted β-Keto Amides with Hydrosilane/F^- Reagent. Stereoselective reduction of α-substituted β-keto acid derivatives **20** has been recognized to be an alternative approach to aldols.[35] Though erythro aldols are readily accessible by this approach,[36] the threo-selective reduction still remained to be problematic at the starting point of our study. After we disclosed our own results, Ito, Katsuki, and Yamaguchi disclosed that potassium triethylborohydride accomplishes the threo-directed reduction.[37] However, to achieve high

(27) The stereochemical outcome in the reduction of **13a** (R = Ac) with other hydrides is as follows (the ratio of threo to erythro is given in the brackets): $LiAlH_4$ [55:45]; $HB(i\text{-}Bu)_2$ [58:42]; $PhMe_2SiH$/cat. $RhCl(PPh_3)_3$ [39:61]; $NaBH_4$ [1.1–1.3:1 (ref 22a)].

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

(29) Chautemps, P.; Pierre, J. L. *Tetrahedron* **1976**, *32*, 549.

(30) (a) Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63. Sharpless, K. B.; Behrens, C. H.; Katsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Viti, S. M.; Walker, F. J.; Woodard, S. S. *Pure Appl. Chem.* **1983**, *55*, 589. (b) Mihelich, E. D. *Tetrahedron Lett.* **1979**, 4729. Takai, K.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1980**, *21*, 1657. Tomioka, H.; Suzuki, T.; Oshima, K.; Nozaki, H. *Ibid.* **1982**, *21*, 3387. Hiyama, T.; Obayashi, M. *Tetrahedron Lett.* **1983**, *24*, 395. (c) In the case of allylic alcohols having a cis-β-substituent, the Sharpless epoxidation is threo selective: Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Tetrahedron Lett.* **1980**, *21*, 4733.

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

(32) (a) Furonza, G.; Fuganti, C.; Grasselli, P.; Marinoni, G. *Tetrahedron Lett.* **1979**, 3883. (b) Fuganti, C.; Grasselli, P.; Fantoni, G. P. *Ibid.* **1982**, 23, 4369. (c) Mukaiyama, T.; Goto, Y.; Shoda, S. *Chem. Lett.* **1983**, 671. (d) Hiyama, T.; Kobayashi, K.; Nishide, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2127.

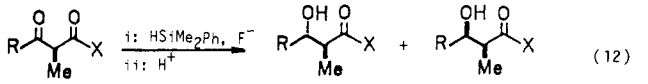
(33) Arcamone, F. *Daunomycin and Related Antibiotics*, in *Topics on Antibiotic Chemistry*; Sammes, P. G., Ed.; Ellis Horwood: Chichester, England, 1978: Vol. 2.

(34) Hiyama, T.; Nishide, K.; Kobayashi, K. *Chem. Lett.* **1984**, 361.

(35) Canceill, J.; Jacques, J. *Bull. Soc. Chim. Fr.* **1970**, 2180.

(36) $Zn(BH_4)_2$ reduction: (a) Nakata, T.; Oishi, T. *Tetrahedron Lett.* **1980**, *21*, 1641. (b) Nakata, T.; Kuwabara, T.; Tani, Y.; Oishi, T. *Ibid.* **1982**, *23*, 1015. (c) Ito, Y.; Yamaguchi, M. *Ibid.* **1983**, *24*, 5385. (d) Dipardo, R. M.; Bock, M. G. *Ibid.* **1983**, *24*, 4805. (e) Evans, D. A.; Ennis, M. D.; Le, T. *J. Am. Chem. Soc.* **1984**, *106*, 1154.

stereoselective, carrying out of the reaction at −78 °C is required. By applying the fluoride ion catalyzed hydrosilylation, we achieved the equally selective reduction of **20** (eq 12). TASF catalyst was employed instead of TBAF,



(12)

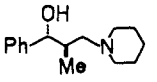
20 21 22

a: R = Ph, X = OMe
b: R = Ph, X = NEt_2
c: R = Ph, X = pyrrolidino
d: R = Ph, X = piperidino
e: R = 4-ClC_6H_4, X = pyrrolidino
f: R = 4-$MeOC_6H_4$, X = pyrrolidino
g: R = Et, X = NEt_2
h: R = *i*-Pr, X = NEt_2
i: R = *t*-Bu, X = pyrrolidino

which turned out to be less active due probably to the contaminative moisture.[38] Results are summarized in Table IV. We first studied the reduction of methyl 2-benzoylpropanoate (**20a**) or ethyl acetate with hydrosilane/F^- under various conditions by using various hydrosilanes. Disappointingly, these β-keto esters were not reduced under the reaction conditions and mostly recovered unchanged. We ascribed this failure to the abstraction of an active methine proton by the fluoride ion catalyst[39] and soon switched to α-substituted β-keto amides whose methine proton was assumed less acidic.[36e] When β-keto amide **20b** was treated with $PhMe_2SiH$ in the presence of TASF (10 mol %), the reduction did proceed smoothly at 0 °C. After acid treatment and usual workup, the crude mixture was assayed by 400-MHz ^1H NMR and was shown to involve the threo isomer **21b** exclusively (>99% selectivity). Isolation of the pure material (98% yield) was carried out by preparative TLC. High threo selectivities (>98%) were again observed for **20c–f,i** (R = aryl or *tert*-butyl). The primary products *O*-silyl ethers are isolable if desired. For example, reduction followed by workup without acid treatment afforded the silyl ether of **21c** in 90% isolated yield. To our surprise, **20g** and **20h** (R = alkyl) gave erythro alcohols (**22g** and **22h**) predominantly. In these substrates the HMPA molecule in the hexavalent silicate species **6** might have been replaced by the carbamoyl group to invoke an intramolecular reduction through a transition state like A in eq 8, and thus the opposite selectivity resulted.

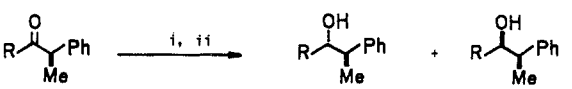
Stereochemical assignment of the products is based mainly on ^1H NMR and/or ^{13}C NMR spectrometric assay. An empirical rule[40] J_{ab} (threo) > J_{ab} (erythro) in ^1H NMR holds for all cases except for **20i**, which has a *tert*-butyl group as R.[41] Carbon chemical shift values for α-carbons of both threo and erythro isomers [δ CH_3(threo) 12–18; δ CH_3(erythro) 9–13] are more reliable criteria.[42]

The threo-selective reduction of α-methyl-β-keto amides is applicable to the stereocontrolled synthesis of *threo*-α-aryl-β-methyl-γ-aminopropyl alcohols of pharmacological interest: reduction of **21d** with lithium aluminum hydride afforded *threo*-*N*-(3-hydroxy-2-methyl-3-phenylpropyl)-piperidine[43] (**23**).



23

The Hydrosilane/F^- Reduction of α-Aryl (-Alkenyl, or -Alkyl) Ketones. The threo-selective reduction was found to be applicable to 1-phenylethyl ketones **24** (eq 13).

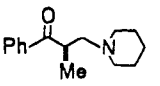


(13)

24 25 26

i, $HSiMe_2Ph$, TASF; ii, H^+; **a**, R = Ph; **b**, R = Et

Irrespective of the kind of R, threo alcohols **25** predominated to a remarkable extent (**24a**, R = Ph, **25a:26a** = 99:1, 89% yield; **24b**, R = Et, **25b:26b** = 93:7, 90% yield). Reduction of 2-methyl-1-phenyl-3-buten-1-one induced unfavorable double-bond isomerization by the fluoride ion catalyst to give 2-methyl-1-phenyl-2-buten-1-one, which underwent the carbonyl reduction. The nonselective reduction observed for *N*-(2-benzoylpropyl)piperidine (**27**) is attributable to the small steric difference between methyl and piperidinomethyl groups.[44]



27

Conclusion. The fluoride ion catalyzed hydrosilylation of carbonyl compounds is remarkable in light of practicability: extremely mild conditions (0 °C to room temperature) and easy handling of commercially available and stable hydrosilanes. By this synthetic technology threo 1,2-diols, threo 2-amino alcohols, and threo aldols of remarkably high stereochemical purity are now readily accessible from the corresponding ketones having an α-oxy, α-amino, or α-amido carbonyl group.

Experimental Section

Instrumentation and Methods. Melting points and boiling points are uncorrected. Bulb-to-bulb distillation was carried out by use of Büchi Kugelrohr or Shibata glass tube oven GTO 250R. ^1H NMR spectra (tetramethylsilane as an internal standard) were obtained with a Varian EM-390, Varian XL-100A, Hitachi R-90H, or Bruker AM-400 spectrometer, chemical shifts being given in ppm units, and ^{13}C NMR spectra with a Bruker AM-400 instrument. IR data of neat liquid film samples (unless otherwise noted) were recorded with a JASCO A-202 instrument. Specific rotation was measured with a Horiba SEPA-200 or Union PM-201 instrument. Mass spectra were recorded with a RMU-6MG instrument and high mass with a Hitachi M-80A spectrometer. GLC analyses were performed with a Shimadzu GC-7A chromatograph using an FID apparatus, and preparative GLC analyses were performed with a Shimadzu GC-3BT chromatograph using a TCD apparatus. HPLC analyses were performed with a Waters Model 440 using an UV detector. Retention times (t_R) are given in minutes. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck silica gel 60 F254. Preparative

(37) $KHBEt_3$ reduction: Ito, Y.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1985**, *26*, 4643. Also see $KHB(i\text{-}Bu)_3$ reduction: Takahashi, T.; Miyazawa, M.; Tsuji, J. *Tetrahedron Lett.* **1985**, *26*, 5139.

(38) Drying commercially available TBAF turns out sometimes to be troublesome: Sharma, R. K.; Fly, J. L. *J. Org. Chem.* **1983**, *48*, 2112.

(39) Fluoride ion is weakly basic in aprotic polar solvents: Parker, A. J. *Adv. Org. Chem.* **1965**, *5*, 1; Yakobson, G. G.; Akhmetova, N. E. *Synthesis* **1983**, 169.

(40) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Porrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

(41) The threo isomer of the corresponding carboxylic acid **20** (R = *t*-Bu, X = OH) also has a lower *J* value (2.0 Hz) than the erythro isomer (3.0 Hz): Heathcock, C. H.; Pirrung, M. C.; Montgomery, S. H.; Lampe, J. *Tetrahedron* **1981**, *37*, 4087. Heathcock, C. H.; Pirrung, M. C.; Lampe, J.; Buse, C. T.; Young, S. D. *J. Org. Chem.* **1981**, *46*, 2290.

(42) Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. *Ibid.* **1979**, *44*, 4294.

(43) (a) Ilarionov, I.; Avramova, P.; Palamareva, M.; Dryanovska, L. *Probl. Farm.* **1982**, *10*, 9. (b) Ilarionov, I.; Avramova, P.; Dryanovska, L. *Farmatsiya (Sofia)* **1983**, *33*, 9. (c) Yoshida, A.; Morita, M.; Ogawa, S. *Yakugaku Zasshi* **1973**, *93*, 1138.

(44) The reduction of α-substituted β-amino ketones with $NaBH_4$ or $LiAlH_4$ gives poor stereoselectivities in general: see ref 21.

TLC plates were prepared with Merck Kiesel-gel PF_{254}. Column chromatography was carried out with silica gel (Wakogel C-200) at atmospheric pressure. Hydrosilanes were purchased from Shin-etsu kagaku Co. Ltd. or Chisso Co. Ltd. and distilled before use. TBAF was prepared by neutralizing tetrabutylammonium hydroxide with hydrofluoric acid followed by azeotropic removal of water[3] and dissolved in dry THF in the presence of activated molecular sieves, 4A. TASF was prepared according to Middleton's procedure.[10]

Fluoride Ion Catalyzed Reduction of Carbonyl Compounds with Hydrosilanes. A Typical Procedure. TBAF (0.5 M THF solution) (0.05 mL, 0.025 mmol) was added to a solution of undecanal (**3a**) (85.5 mg, 0.503 mmol) and dimethylphenylsilane (73.9 mg, 0.542 mmol) in HMPA (2 mL) at 25 °C. After 1 h, the mixture was diluted with diethyl ether (20 mL) and washed with water (20 mL × 3). The ethereal extract was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The yield of dimethylphenyl(undecyloxy)silane (**4a**) was estimated to be 91% by GLC analysis (column, 5% silicon SE-30 on Uniport HP, 2 m; carrier gas, N_2, 50 mL/min; temperature, 240 °C) using pentadecane as an internal standard: t_R of **4a**, 5.9 min; t_R of pentadecane, 2.1 min. The resulting mixture was subjected to preparative GLC to give pure **4a** as a colorless oil: ^1H NMR ($CDCl_3$) δ 0.37 (s, 6 H), 0.88 (br t, J = 6 Hz, 3 H), 1.26 (br s, 18 H), 3.56 (t, J = 6 Hz, 2 H), 7.2–7.45 (m, 3 H), 7.45–7.6 (m, 2 H); IR (neat) 2930, 2860, 1470, 1428, 1252, 1118, 1094, 828, 729, 700 cm^{-1}; MS (70 eV), m/z (relative intensity) 292 (26), 291 (M^+ – Me, 100), 228 (31), 137 (78), 135 (41), 43 (20), 41 (20). Anal. Calcd for $C_{19}H_{34}OSi$: C, 74.44; H, 11.18. Found: C, 74.11; H, 11.15.

Experiments in other solvents and with other fluoride catalysts (Table I, runs 2–8) were carried out under the same conditions.

(Benzyloxy)dimethylphenylsilane (4b): a colorless oil; t_R 7.1 min (200 °C); bp 110–120 °C (bath temperature) (1 mm); ^1H NMR ($CDCl_3$) δ 0.40 (s, 6 H), 4.66 (s, 2 H), 7.26 (s, 5 H), 7.2–7.5 (m, 3 H), 7.5–7.7 (m, 2 H); IR (neat) 1252, 1118, 1092, 1068, 851, 830, 788, 728, 696 cm^{-1}; MS (70 eV), m/e (relative intensity) 227 (M^+ – Me, 8), 137 (100), 108 (20), 91 (27), 79 (27), 77 (22), 28 (24), 18 (79); exact mass calcd for $C_{15}H_{18}OSi$, M^+, 242.1125, found m/z 242.1097.

Dimethylphenyl[(3-phenyl-2-propenyl)oxy]silane (4c): a colorless oil; t_R 5.6 min; bp 140–150 °C (bath temperature) (1 mm); ^1H NMR ($CDCl_3$) δ 0.43 (s, 6 H), 4.28 (d, J = 5.1 Hz, 2 H), 6.19 (dt, J = 16.5, 5.1 Hz, 1 H), 6.55 (d, J = 16.5 Hz, 1 H), 7.1–7.5 (m, 8 H), 7.5–7.7 (m, 2 H); IR (neat) 1253, 1118, 1072, 1054, 966, 828, 790, 730, 699 cm^{-1}; MS (70 eV), m/z (relative intensity) 269 (M^+ + 1, 5), 268 (M^+, 20), 190 (84), 177 (30), 175 (58), 137 (25), 135 (100), 117 (88), 116 (20), 115 (52), 91 (32), 75 (82); exact mass calcd for $C_{17}H_{20}OSi$, M^+, 268.1282, found m/z 268.1262.

Bis(hexyloxy)diphenylsilane (4d″): a colorless oil; t_R 5.8 min (250 °C); ^1H NMR ($CDCl_3$) δ 0.7–1.0 (m, 6 H), 1.0–1.7 (m, 16 H), 3.65–3.85 (m, 4 H), 7.3–7.45 (m, 6 H), 7.55–7.75 (m, 4 H); IR (neat) 1130, 1120, 1092, 740, 720, 700, 528 cm^{-1}; MS (70 eV), m/z (relative intensity) 339 (12), 283 (69), 228 (47), 223 (59), 200 (22), 199 (100), 183 (54), 181 (22), 139 (61), 123 (34), 77 (24), 43 (25), 41 (20). Anal. Calcd for $C_{24}H_{36}O_2Si$: C, 74.94; H, 9.43. Found: C, 74.57; H, 9.28.

Dimethyl(2-octyloxy)phenylsilane (4e): a colorless oil; t_R 7.1 min (200 °C); ^1H NMR ($CDCl_3$) δ 0.38 (s, 6 H), 0.87 (br t, J = 6 Hz, 3 H), 1.10 (d, J = 6.0 Hz, 3 H), 1.1–1.5 (m, 10 H), 3.6–3.9 (m, 1 H), 7.25–7.4 (m, 3 H), 7.4–7.55 (m, 2 H); IR (neat) 2970, 2935, 1250, 1114, 1076, 1046, 828, 784, 696 cm^{-1}; MS (70 eV), m/z (relative intensity) 249 (M^+ – Me, 19), 179 (65), 137 (100), 135 (91), 75 (74), 18 (22). Anal. Calcd for $C_{16}H_{28}OSi$: C, 72.08; H, 10.67. Found: C, 72.38; H, 10.64.

Dimethylphenyl(1-phenylethoxy)silane (4f): a colorless oil; t_R 4.0 min; bp 120–130 °C (bath temperature) (1 mm); ^1H NMR ($CDCl_3$) δ 0.29 (s, 3 H), 0.33 (s, 3 H), 1.41 (d, J = 6.3 Hz, 3 H), 4.82 (q, J = 6.3 Hz, 1 H), 7.25 (s, 5 H), 7.2–7.4 (m, 3 H), 7.4–7.6 (m, 2 H); IR (neat) 1252, 1118, 1090, 960, 840, 829, 790, 700 cm^{-1}; MS (70 eV), m/z (relative intensity) 241 (M^+ – Me, 7), 137 (40), 18 (100), 17 (22); exact mass calcd for $C_{16}H_{20}OSi$, M^+, 256.1281, found m/z 256.1281.

Dimethylphenyl[(1-methyl-4-pentenyl)oxy]silane (4g): a colorless oil; t_R 3.4 min (220 °C); ^1H NMR ($CDCl_3$) δ 3.83 (s, 6 H), 1.10 (d, J = 6 Hz, 3 H), 1.3–1.65 (m, 2 H), 1.8–2.2 (m, 2 H), 3.78 (q, J = 6 Hz, 1 H), 4.87 (d, J = 11 Hz, 1 H), 4.90 (d, J = 17 Hz, 1 H), 5.73 (ddt, J = 11, 17, 6 Hz, 1 H), 7.25–7.4 (m, 3 H), 7.4–7.65 (m, 2 H); IR (neat) 1252, 1117, 1091, 1050, 992, 910, 829, 788, 700 cm^{-1}; MS (70 eV), m/z (relative intensity) 234 (M^+, 2.2), 219 (31), 156 (20), 137 (98), 135 (100), 75 (72). Anal. Calcd for $C_{14}H_{22}OSi$: C, 71.73; H, 9.46. Found: C, 71.68; H, 9.50.

[(2-Methylcyclohexyl)oxy]dimethylphenylsilane (4h): a colorless oil; t_R 6.5 min (220 °C); bp 120–130 °C (bath temperature) (1 mm); ^1H NMR ($CDCl_3$) (cis:trans = 4:6) the cis isomer δ 0.35 (s, 6 H), 0.85 (d, J = 5.7 Hz, 3 H), 1.0–1.8 (m, 9 H), 3.67–3.83 (m, 1 H), 7.2–7.4 (m, 3 H), 7.45–7.65 (m, 2 H), the trans isomer δ 0.37 (s, 6 H), 0.90 (d, J = 5.7 Hz, 3 H), 1.0–1.8 (m, 9 H), 2.9–3.25 (m, 1 H), 7.2–7.4 (m, 3 H), 7.45–7.65 (m, 2 H); IR (neat) 2945, 1042, 1028, 830, 788, 702 cm^{-1}; MS (70 eV), m/z (relative intensity) 248 (M^+, 6), 233 (45), 191 (22), 170 (21), 137 (100), 135 (70), 75 (25), 44 (23); exact mass calcd for $C_{15}H_{24}OSi$, M^+, 248.1594, found m/z 248.1578.

(Benzyloxy)triethylsilane (4b′). To a solution of benzaldehyde (**3b**) (106 mg, 1.00 mmol) and triethylsilane (0.19 mL, 1.2 mmol) in HMPA (1 mL) was added TASF (1.0 M THF solution) (0.05 mL, 0.050 mmol) at room temperature. After 2.5 h, the mixture was quenched with water (2 mL) and extracted with diethyl ether (3 mL × 3). The ethereal extract was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting mixture was subjected to preparative TLC (silica gel, hexane–CH_2Cl_2, 10:1) to give **4b′** (157 mg, 71% yield) as a colorless oil: bp 130 °C (bath temperature) (1 mm); ^1H NMR ($CDCl_3$) δ 0.5–0.8 (m, 6 H), 0.8–1.2 (m, 9 H), 4.70 (s, 2 H), 7.2–7.4 (m, 5 H); IR (neat) 2975, 2895, 1111, 1100, 1072, 732 cm^{-1}; MS (70 eV), m/z (relative intensity) 195 (5), 194 (18), 193 (M^+ – Et, 100), 165 (10), 164 (5), 163 (33), 135 (19), 92 (7), 91 (84), 87 (5), 65 (11), 59 (7).

Measurement of Isotope Effect. TASF (1.0 M, 0.05 mL, 0.05 mmol) was added to a HMPA (0.5 mL) solution of acetophenone (60 mg, 0.50 mmol), dimethylphenylsilane (341 mg, 2.50 mmol), and deuteriodimethylphenylsilane (343 mg, 2.50 mmol) at –23 °C, and the mixture was stirred overnight at –23 °C. Quenching of the reaction with 1 M hydrochloric acid in methanol (room temperature, 15 min) and workup, followed by purification by preparative TLC (CH_2Cl_2), gave a mixture of 1-phenylethanol and 1-deuterio-1-phenylethanol (total 55 mg, 90%). The ratio was estimated to be 60.0:40.0 by comparison of a 400-MHz ^1H NMR spectrum of the mixture with that of an authentic 1:1 mixture of these two alcohols. The isotope effect (k_H/k_D) was thus calculated to be 1.50.

The Effect of HMPA. A dichloromethane (10.0 mL) solution of acetophenone (0.50 M), dimethylphenylsilane (1.0 M), TBAF (0.02 M), and dodecane (0.50 mL) (internal standard) was prepared at –78 °C and was divided into five parts (A–E) of equal amount. To A, B, C, and D was added a dichloromethane (1 mL) solution of HMPA (5.0 M, 3.0 M, 2.0 M, and 1.0 M, respectively), and only dichloromethane (1 mL) was added to E. Each reaction was monitored by GLC analysis. the initial rates v_0 were estimated by a third-order approximation of the relationship of reaction time vs conversion and by extrapolation to time zero (see Figure 1).

Preparation of 3-(Dimethylsiloxy)-1,3-diphenyl-1-propanone (8). In bis(dimethylsilyl)amine (0.5 mL) was dissolved 1,3-diphenyl-3-hydroxypropan-1-one (113 mg, 0.5 mmol), and the mixture was allowed to stand for 3 h. Removal of volatile materials under reduced pressure gave 3-(dimethylsiloxy)-1,3-diphenylpropan-1-one (**8**), 142 mg (100%), as a colorless oil: ^1H NMR ($CDCl_3$) δ 0.05 (d, J = 2.9 Hz, 3 H), 0.08 (d, J = 2.9 Hz, 3 H), 2.99 (dd, J = 3.8, 15.5 Hz, 1 H), 3.56 (dd, J = 8.4, 15.5 Hz, 1 H), 4.58 (septet, J = 2.9 Hz, 1 H), 5.40 (dd, J = 3.8, 8.4 Hz, 1 H), 7.2–7.5 (m, 3 H), 7.8–8.0 (m, 2 H). This sample was used for the following reduction without further purification.

Intramolecular Hydrosilylation of 8. TASF (1 M THF solution, 0.05 mL, 0.05 mmol) was added to **8** dissolved in THF (2 mL) at room temperature, and the mixture was stirred for 0.5 h at room temperature. Acid quenching and workup, followed by purification by preparative TLC (CH_2Cl_2), gave 1,3-diphenylpropane-1,3-diol (**9**), 96 mg, as a colorless solid. The syn:anti ratio was estimated to be 25:75 by 400-MHz ^1H NMR analysis: ^1H NMR ($CDCl_3$) *syn*-**9** δ 1.97 (d of t, J = 14.6, 2.8 Hz, 1 H), 2.20 (d of t, J = 14.6, 10.2 Hz, 1 H), 2.9 (br s, 2 H), 5.03 (dd, J = 2.8, 10.2 Hz, 2 H), 7.2–7.4 (m, 5 H), *anti*-**9** δ 1.6 (br s, 2 H), 2.18 (AA′, 2 H), 4.98 (XX′, 2 H), 7.2–7.4 (m, 5 H).

Reduction of Cyclohexanecarboxaldehyde with $HSiMe_2Tol/F^-$ in the Presence of Fluorodimethylphenylsilane. TASF (0.8 M THF solution, 0.03 mL, 0.024 mmol) was added to a HMPA (0.5 mL) solution of dimethyl-*p*-tolylsilane (75 mg, 0.50 mmol), fluorodimethylphenylsilane (76 mg, 0.49 mmol), and cyclohexanecarboxaldehyde (56 mg, 0.5 mmol) at 0 °C, and the mixture was allowed to react for 3 h at 0 °C and for 9 h at room temperature. During the reaction period, the ratio of (cyclohexylmethoxy)dimethyl-*p*-tolylsilane (**11**) to (cyclohexylmethoxy)dimethylphenylsilane (**12**) monitored by GLC analysis was as follows: 83:17 (1 min); 82:18 (3 min); 78:22 (5 min); 77:23 (30 min); 57:43 (3 h); 50:50 (12 h). Acid treatment of the reaction mixture and workup, followed by purification by preparative TLC (silica gel, CH_2Cl_2–hexane, 1:1), gave cyclohexylmethanol, 50 mg, (88%), as a colorless oil. Pure **11** was prepared by $RhCl(PPh_3)_3$ promoted reaction of cyclohexanecarboxaldehyde with $HSiMe_2Tol$: ^1H NMR ($CDCl_3$) δ 0.36 (s, 6 H), 0.6–1.8 (m, 11 H), 3.36 (d, J = 6 Hz, 2 H), 7.2–7.4 (m, 3 H), 7.4–7.6 (m, 2 H); IR (neat) 2940, 1252, 1118, 1068, 827, 786, 698 cm^{-1}; MS (50 eV), m/z (relative intensity) 224 (14), 233 (M^+ – Me, 64), 193 (139), 170 (47), 165 (11), 151 (15), 138 (14), 137 (100), 135 (57), 105 (10), 95 (21), 91 (13), 75 (23), 55 (23), 45 (10), 43 (11), 41 (17). **12**: ^1H NMR ($CDCl_3$) δ 0.34 (s, 6 H), 0.7–2.0 (m, 11 H), 2.34 (s, 3 H), 3.35 (d, J = 6 Hz, 2 H), 7.20 (d, J = 8 Hz, 2 H), 7.48 (d, J = 8 Hz, 2 H); IR (neat) 2940, 1252, 1113, 1070, 850, 832, 801, 783, 496 cm^{-1}; MS (50 eV), m/z (relative intensity) 248 (11), 247 (M^+ – Me, 50), 170 (53), 152 (15), 151 (100), 149 (47), 105 (16), 95 (12), 91 (10), 75 (29), 55 (15), 41 (10).

Fluorodimethylphenylsilane. Chlorodimethylphenylsilane (1.70, 10 mmol) was added to anhydrous ammonium fluoride (dried with P_2O_5) (3.7 g, 0.1 mol) at 0 °C. The mixture was allowed to stand for 2 h at room temperature and directly distilled to give the title compound, 1.46 g (95%), as a colorless oil: ^1H NMR ($CDCl_3$) δ 0.48 (d, J = 7 Hz, 6 H), 7.25–7.5 (m, 3 H), 7.5–7.65 (m, 2 H); ^{19}F NMR ($CDCl_3$–$CFCl_3$) δ –161.9 (septet, J = 7 Hz); IR (neat) 1428, 1256, 1123, 868, 832, 793, 766, 738, 694, 640, 466 cm^{-1}.

(*p*-Methoxyphenyl)dimethylsilane. To a THF (10 mL) solution of (4-methoxyphenyl)magnesium bromide [10 mmol, prepared in situ from 4-bromoanisole (1.25 mL, 10 mmol) and magnesium turnings (285 mg, 12 mmol)] was added chlorodimethylsilane (1.67 mL, 15 mmol) at 0 °C. After being stirred for 0.5 h at room temperature, the mixture was diluted with hexane (50 mL), washed with water (10 mL), and filtered through silica gel column chromatography (Wako gel C-100, eluted with hexane). The eluate was concentrated and distilled to give the title compound, 1.30 g (78%), as a colorless oil: bp 120 °C (bath temperature) (20 mm); ^1H NMR ($CDCl_3$) δ 0.32 (d, J = 3.5 Hz, 6 H), 3.79 (s, 3 H), 4.38 (septet, J = 3.5 Hz, 1 H), 6.88 (d, J = 8.4 Hz, 2 H), 7.43 (d, J = 8.4 Hz, 2 H); IR (neat) 2120, 1595, 1502, 1280, 1248, 1181, 1113, 878 cm^{-1}. The following three hydrosilanes were prepared similarly.

(*p*-Methylphenyl)dimethylsilane: ^1H NMR ($CDCl_3$) δ 0.32 (d, J = 3.8 Hz, 6 H), 2.33 (s, 3 H), 4.42 (septet, J = 3.8 Hz, 1 H), 7.15 (d, J = 7.8 Hz, 2 H), 7.49 (d, J = 7.8 Hz, 2 H); IR (neat) 2125, 1250, 1110, 874, 761 cm^{-1}.

[*p*-(Trifluoromethyl)phenyl]dimethylsilane: ^1H NMR ($CDCl_3$) δ 0.37 (d, J = 3.6 Hz, 6 H), 4.50 (septet, J = 3.6 Hz, 1 H), 7.5–7.7 (m, 4 H); ^{19}F NMR ($CDCl_3$–$CFCl_3$) δ –63.25 (s); IR (neat) 2140, 1328, 1166, 1128, 1060, 878 cm^{-1}.

(*S*)-2-Acetoxypropionyl Chloride. This compound was prepared according to the procedure described in ref[45]: bp 58 °C (15 Torr) [lit.[45] bp 69–70 °C (18 Torr)]; α^{20}_D –36.1° (neat, l = 1) (89% optical purity); ^1H NMR ($CDCl_3$) δ 1.58 (d, J = 7 Hz, 3 H), 2.17 (s, 3 H), 5.20 (q, J = 7 Hz, 1 H); IR (neat) 1792, 1752, 1373, 1226, 1050, 910, 748 cm^{-1}.

(*S*)-2-Acetoxy-1-phenyl-1-propanone (13a). The acid chloride prepared above (3.01 g, 20 mmol) was dissolved in CH_2Cl_2 (30 mL) and benzene (200 mL), and to the solution was added powdered aluminum chloride (5.61 g, 42 mmol) in one portion. After the mixture was stirred for 18 h at –15 °C, workup and purification by column chromatography (CH_2Cl_2–AcOEt, 1:0 to 2:1) gave (*S*)-**13a** (R = Ac), 3.13 g (82%), as a colorless oil: bp 130–140 °C (bath temperature) (18 Torr) [lit.[46] bp 118–120 °C (5 Torr) for racemic **13a**]; $[\alpha]^{20}_D$ –41.50° (*c* 1.04, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.48 (d, J = 7.0 Hz, 3 H), 2.10 (s, 3 H), 5.93 (q, J = 7.0 Hz, 1 H), 7.3–7.7 (m, 3 H), 7.8–8.1 (m, 2 H); IR (neat) 1744, 1700, 1449, 1373, 1234, 1091, 1040, 973, 703 cm^{-1}. The enantiomeric excess of (*S*)-**13a** (R = Ac) was estimated to be 88% by ^1H NMR analysis using $Eu(tfc)_3$ (0.3 molar equiv, CCl_4) as a chiral shift reagent.

2-(Benzoyloxy)-1-phenyl-1-propanone (13a′). To a DMF (10 mL) solution of 2-bromo-1-phenyl-1-propanone (2.35 g, 11.1 mmol) were added benzoic acid (1.89 g, 15.5 mmol) and K_2CO_3 (1.09 g, 7.85 mmol), and the whole was stirred for 1 h at 50 °C. Workup and recrystallization from diethyl ether–hexane afforded **13a′** as colorless crystals: mp 109 °C (lit.[47] mp 108 °C); ^1H NMR ($CDCl_3$) δ 1.67 (d, J = 7.2 Hz, 3 H), 6.20 (q, J = 7.2 Hz, 1 H), 7.2–7.7 (m, 6 H), 7.8–8.2 (m, 4 H); IR (KBr) 1728, 1696, 1452, 1304, 1276, 1127, 971, 716, 706 cm^{-1}.

2-(Benzoyloxy)cyclohexanone (13d). This compound was prepared in a similar manner as described for **13a′**: mp 86–87 °C (lit.[48] mp 85–86 °C).

(*S*)-*N*,*N*-Dimethyl-2-(1-ethoxyethoxy)propanamide. This was prepared by treating (*S*)-*N*,*N*-dimethyl-2-hydroxypropanamide[47] with ethyl vinyl ether and pyridinium *p*-toluenesulfonate (PPTS): bp 72–78 °C (0.1–0.2 mm); ^1H NMR ($CDCl_3$) δ 1.0–1.5 (m, 9 H), 2.94 (s, 3 H), 3.09 (s, 3 H), 3.12 (s, 3 H), 3.3–3.8 (m, 2 H), 3.3–4.9 (m, 2 H); IR (neat) 1665, 1405, 1130, 1080, 1060, 1035, 970 cm^{-1}. Anal. Calcd for $C_9H_{19}NO_2$: C, 57.12; H, 10.12; N, 7.40. Found: C, 57.10; H, 10.24; N, 7.07.

(*S*)-*N*,*N*-Dimethyl-2-*tert*-butoxypropanamide: bp 81–82 °C (10 mm); $[\alpha]^{21}_D$ –20.6° (*c* 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.20 (s, 9 H), 1.33 (d, J = 7 Hz, 3 H), 2.90 (s, 3 H), 3.18 (s, 3 H, 4.31 (q, J = 7.0 Hz, 1 H); IR (neat) 1642, 1198, 1094 cm^{-1}.

(*S*)-*N*,*N*-Dimethyl-2-(2-tetrahydropyranyloxy)propanamide. This was prepared by treating (*S*)-*N*,*N*-dimethyl-2-hydroxypropanamide with 2,3-dihydropyran and PPTS and used for the synthesis of **13b″** without purification: ^1H NMR ($CDCl_3$) (a mixture of two isomers) major isomer δ 1.41 (d, J = 7 Hz, 3 H), 1.3–2.2 (m, 6 H), 2.93 (s, 3 H), 3.04 (s, 3 H), 3.3–3.7 (m, 1 H), 3.7–4.1 (m, 1 H), 4.62 (dd, J = 6, 14 Hz, 1 H), minor isomer δ 1.35 (d, J = 7 Hz, 3 H), 1.3–2.2 (m, 6 H), 2.95 (s, 3 H), 3.11 (s, 3 H), 3.3–3.7 (m, 1 H), 3.7–4.1 (m, 1 H), 4.4–4.8 (m, 1 H).

(*S*)-2-(1-Ethoxyethoxy)-1-phenyl-1-propanone (13a″). Phenylmagnesium bromide (0.6 M THF solution, 20 mL, 12.0 mmol) was added to a THF (10 mL) solution of (*S*)-*N*,*N*-dimethyl-2-(1-ethoxyethoxy)propanamide prepared as above (1.89 g, 10.0 mmol) at 0 °C over a period of 5 min. The mixture was stirred for 0.5 h at 0 °C. Workup and purification by column chromatography (CH_2Cl_2–hexane, 1:1 to 1:0) gave **13a″**, 1.62 g (73%), as a colorless oil: ^1H NMR ($CDCl_3$) (a mixture of two isomers) δ 0.95–1.55 (m, 9 H), 3.30–3.7 (m, 2 H), 4.60–5.20 (m, 2 H), 7.3–7.7 (m, 3 H), 7.85–8.20 (m, 2 H); IR (neat) 1690, 1450, 1271, 1131, 1028, 972, 703 cm^{-1}; exact mass calcd for $C_9H_{10}O_2$, M^+ – CH_2=CHOEt, 149.0602, found m/z 149.0609.

(*S*)-4-Acetoxy-1-phenyl-1-penten-3-one (13b): mp 73–75 °C; $[\alpha]^{25}_D$ –29° (*c* 1.04, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.47 (d, J = 7.0 Hz, 3 H), 2.14 (s, 3 H), 5.34 (q, J = 7.0 Hz, 1 H), 6.83 (d, J = 16.2 Hz, 1 H), 7.2–7.6 (m, 5 H), 7.7 (d, J = 16.2 Hz, 1 H); IR (KBr) 1735, 1705, 1615, 1450, 1375, 1240, 1055, 1040, 1000, 990, 765, 695 cm^{-1}; MS (70 eV), m/z (relative intensity) 218 (M^+, 2), 176 (9), 158 (6), 132 (10), 131 (100), 103 (27), 77 (13), 51 (5), 43 (38); exact mass calcd for $C_{13}H_{14}O_3$, M^+, 218.0943, found m/z 218.0947.

(*S*)-4-*tert*-Butoxy-1-phenyl-1-penten-3-one (13b′). To a THF (5 mL) solution of (*S*)-*N*,*N*-dimethyl-2-*tert*-butoxypropanamide prepared as above (1.02 g, 5.91 mmol) was slowly added (*E*)-(2-phenylethenyl)magnesium bromide (1 M THF solution, 12.0 mL, 12.0 mmol) at 0 °C, and the mixture was stirred for 1 h at 0 °C. Workup and purification by column chromatography (silica gel, CH_2Cl_2) gave **13b′**, 1.06 g (78%), as colorless crystals: ^1H NMR ($CDCl_3$) δ 1.22 (s, 9 H), 1.30 (d, J = 7.1 Hz, 3 H), 4.14 (q, J = 7.1 Hz, 1 H), 7.23 (d, J = 16.2 Hz, 1 H), 7.2–7.5 (m, 5 H), 7.73 (d, J = 16.2 Hz, 1 H); IR (KBr) 2900, 1694, 1612, 1371, 1338, 1085, 770 cm^{-1}; MS (70 eV), m/z (relative intensity) 176 (5), 132 (11), 131 (100), 103 (21), 101 (44), 77 (12), 58 (5), 57

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(92), 51 (5), 41 (15), 29 (10). Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.73; H, 8.67.

1-Phenyl-4-(tetrahydropyran-2-yloxy)-1-penten-3-one (13b″). This compound was prepared from (2-phenylethenyl)-magnesium bromide and (*S*)-*N*,*N*-dimethyl-2-(2-tetrahydropyranyloxy)propanamide in a similar manner: 88% yield; an oil; ^{1}H NMR ($CDCl_3$) (a mixture of two isomers) δ 1.37, 1.43 (d, *J* = 7 Hz, 3 H), 1.3–1.9 (m, 6 H), 3.3–3.6 (m, 1 H), 3.6–4.0 (m, 1 H), 4.08, 4.30 (q, *J* = 7 Hz, 1 H), 4.5–4.75 (m, 1 H), 7.03 (d, *J* = 16 Hz, 1 H), 7.3–7.7 (m, 5 H), 7.68 (d, *J* = 16 Hz, 1 H); IR (neat) 2900, 1695, 1375, 1338, 1087, 772 cm^{-1}.

Reduction of 13a with $PhMe_2SiH/F^-$. To a HMPA (1 mL) solution of **13a** (59 mg, 0.31 mmol) and $PhMe_2SiH$ (52 mg, 0.38 mmol) was added a THF solution of TBAF (0.5 M, 0.03 mL, 0.015 mmol) at 0 °C, and the mixture was stirred for 20 h at 0 °C. Sodium hydroxide (1 M methanol solution, 2 mL) was added, and the stirring was continued for an additional 2 h. After treatment with water (2 mL), the solution was extracted with diethyl ether (10 mL × 3). The extract was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The resulting mixture was purified by preparative TLC (AcOEt–hexane, 1:1) to give 1-phenyl-1,2-propanediol (**14a**), 45 mg (95%), as an oily mixture of threo and erythro isomers in a ratio of 95:5, which was determined by ^{1}H NMR analysis. A parallel experiment with (*S*)-**13a** (88% ee) afforded (1*S*,2*R*)-**14a** whose enantiomeric excess value was estimated to be 88% by 90-MHz ^{1}H NMR analysis using $Eu(tfc)_3$ (0.3 molar equiv, CCl_4) as a chiral shift reagent. **14a**: ^{1}H NMR ($CDCl_3$) δ 1.00 (d, *J* = 6.5 Hz, 3 H), 3.55 (br s, 2 H), 3.79 (dq, *J* = 7.2, 6.5 Hz, 1 H), 4.28 (d, *J* = 7.2 Hz, 1 H), 7.29 (s, 5 H) [lit.[44] **14a** (threo) δ 4.26 (d, *J* = 7.6 Hz); **15a** (erythro) δ 4.75 (d, *J* = 3.4 Hz)].

The alcohols **14a** and **15a** were alternatively prepared by reduction of **13a** (34 mg) with $LiAlH_4$ (8 mg) in diethyl ether at room temperature for 2 h. Workup gave a mixture of **14a** and **15a**, 33 mg (total 99%), in a ratio of 48:52.

5-Phenyl-4-pentene-2,3-diol (14b and 15b). The ratio threo:erythro was estimated to be 87:13 by an HPLC analysis [column: μBondapak C-18 (i.d. 5 mm × 100 mm); eluent, acetonitrile–water, 1:10, 1.0 mL/min; t_R, **14b**, 50 min; **15b**, 38 min. An authentic mixture of **14b** and **15b** was afforded by $LiAlH_4$ reduction (threo:erythro = 64:36): ^{1}H NMR ($CDCl_3$) (**14b**:**15b** = 64:36) **14b** δ 1.17 (d, *J* = 6.2 Hz, 3 H), 2.40 (br s, 2 H), 3.68 (dq, *J* = 7.0, 6.2 Hz, 1 H), 3.96 (dd, *J* = 7.0, 6.6 Hz, 1 H), 6.13 (dd, *J* = 6.6, 16.2 Hz, 1 H), 6.55 (d, *J* = 16.2 Hz, 1 H), 7.1–7.4 (m, 5 H), **15b** δ 1.14 (d, *J* = 6.2 Hz, 3 H), 2.40 (br s, 2 H), 3.89 (dd, *J* = 6.2, 3.1 Hz, 1 H), 4.19 (dd, *J* = 3.1, 6.6 Hz, 1 H), 6.20 (dd, 6.6, 16.2 Hz, 1 H), 6.55 (d, *J* = 16.2 Hz, 1 H), 7.1–7.4 (m, 5 H). Anal. Calcd for $C_{11}H_{14}O_2 \cdot 0.2H_2O$: C, 72.66; H, 7.98. Found: C, 72.86; H, 7.88.

2-(Benzoyloxy)cyclohexanol: ^{1}H NMR ($CDCl_3$) (33:67 mixture of trans and cis isomers) trans isomer (**14d**) δ 1.1–2.3 (m, 8 H), 3.05 (br s, 1 H), 3.5–3.8 (m, 1 H), 4.7–5.0 (m, 1 H), 7.2–7.6 (m, 3 H), 7.9–8.2 (m, 2 H), cis isomer (**15d**) δ 1.1–2.3 (m, 8 H), 2.90 (br s, 1 H), 3.8–4.0 (m, 1 H), 5.05–5.25 (m, 1 H), 7.2–7.6 (m, 3 H), 7.9–8.2 (m, 2 H).

These were hydrogenolyzed to give cyclohexane-1,2-diol (**14d** and **15d**).

4-*tert*-Butoxy-1-phenyl-1-penten-3-ol (14b′ and 15b′): ^{1}H NMR ($CDCl_3$) (threo and erythro isomers in a ratio of 91: 9) threo isomer δ 1.13 (d, *J* = 6 Hz, 3 H), 1.20 (s, 9 H), 2.90 (d, *J* = 2 Hz, 1 H), 3.47 (dq, *J* = 7, 6 Hz, 1 H), 3.86 (ddd, *J* = 6, 7, 7 Hz, 1 H), 6.03 (dd, *J* = 7, 16 Hz, 1 H), 6.50 (d, *J* = 16 Hz, 1 H), 7.0–7.4 (m, 5 H). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.80; H, 9.24.

***threo*-1-Phenyl-2-(dimethylamino)-1-propanol (14e)**: ^{1}H NMR ($CDCl_3$) δ 0.70 (d, *J* = 6.7 Hz, 3 H), 2.29 (s, 6 H), 2.53 (dq, *J* = 9.9, 6.7 Hz, 1 H), 4.15 (d, *J* = 9.9 Hz, 1 H), 4.85 (br s, 1 H), 7.1–7.4 (m, 5 H).

***erythro*-1-Phenyl-2-(dimethylamino)-1-propanol (15e)**: ^{1}H NMR ($CDCl_3$) δ 0.83 (d, *J* = 6.8 Hz, 3 H), 2.31 (s, 6 H), 2.48 (dq, *J* = 3.9, 6.8 Hz, 1 H), 3.50 (br s, 1 H), 4.88 (d, *J* = 3.9 Hz, 1 H), 7.1–7.4 (m, 5 H).

3,4-Epoxy-3-methyl-2-butanol (17b and 18b): ^{1}H NMR ($CDCl_3$) (threo and erythro isomers) threo isomer δ 1.24 (d, *J* = 6 Hz, 3 H), 1.35 (s, 3 H), 1.95 (br s, 1 H), 2.59 (d, *J* = 4.8 Hz, 1 H), 2.77 (d, *J* = 4.8 Hz, 1 H), 3.50 (q, *J* = 6.0 Hz, 3 H), erythro isomer δ 1.24 (d, *J* = 6 Hz, 3 H), 1.35 (s, 3 H), 2.27 (br s, 1 H), 2.58 (d, *J* = 4.8 Hz, 1 H), 2.87 (d, *J* = 4.8 Hz, 1 H), 3.77 (q, *J* = 6.0 Hz, 1 H).

(3*S*,4*S*,1*E*)-3,4-(Cyclohexylidenedioxy)-1-phenyl-1-pentene. To a dichloromethane (5 mL) solution of (2*S*,3*S*)-**14b** (2*S*,3*S*:2*S*,3*R* = 87:13) (0.30 g, 1.67 mmol) and 1,1-dimethoxycyclohexane (0.29 g, 2.0 mmol) were added powdered 4A molecular sieves (1.5 g) and bis(trimethylsilyl) sulfate (1 M CH_2Cl_2 solution, 0.075 mL, 0.075 mmol), and the solution was stirred for 4 h at room temperature. After addition of triethylamine (0.1 mL), the precipitates were filtered off through a Celite column and the filtrate was concentrated under reduced pressure. The resulting oil was subjected to column chromatography (CH_2Cl_2) to give the desired acetal (3*S*,4*S*:3*R*,4*S* = 9:1), 0.39 g (91%), as colorless crystals: mp 54–55 °C; ^{1}H NMR ($CDCl_3$) (a mixture of 2*S*,3*S* and 2*S*,3*R* isomers in a 9:1 ratio) 2*S*,3*S* isomer δ 1.27 (d, *J* = 5.7 Hz, 3 H), 1.2–1.8 (m, 10 H), 3.82 (dq, *J* = 7.8, 5.7 Hz, 1 H), 4.03 (dd, *J* = 6.9, 7.8 Hz, 1 H), 6.08 (dd, *J* = 6.9, 16.2 Hz, 1 H), 6.58 (d, *J* = 16.2 Hz, 1 H), 7.1–7.4 (m, 5 H); IR (KBr) 2955, 1152, 1143, 1114, 1038, 1028, 974, 949, 753, 699 cm^{-1}; MS (70 eV), *m*/*z* (relative intensity) 259 (M^+ + 1, 1), 258 (M^+, 6), 215 (28), 214 (100), 185 (29), 144 (47), 143 (41), 131 (22), 129 (50), 128 (23), 117 (64), 115 (39), 55 (44), 43 (37), 41 (24). Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.05; H, 8.37.

(2*R*,3*S*)-2,3-(Cyclohexylidenedioxy)butanal (19).[32] To a dioxane (5 mL) solution of the above acetal (3*S*,4*S*:3*R*,4*S* = 9:1) (185 mg, 0.72 mmol) were added water (2 mL), sodium metaperiodate (0.31 g, 1.44 mmol), and osmium tetraoxide (0.5 M THF solution, 0.07 mL, 0.035 mmol), and the resulting solution was stirred for 2.5 h at room temperature. After extraction with diethyl ether (5 mL × 3), the organic layer was dried over anhydrous $MgSO_4$. Filtration followed by concentration gave a crude mixture, which was subjected to preparative TLC (CH_2Cl_2–hexane, 1:3) to afford **19**, 103 mg (2*R*,3*S*:2*S*,3*S* = 9:1, 78%), as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.2–1.8 (m, 13 H), 3.4–4.2 (m, 2 H), 9.71 (d, *J* = 2 Hz, 1 H).

(2*S*,3*S*)-2,3-(Cyclohexylidenedioxy)butanenitrile. To an ethanol (5 mL) solution of **19** (132 mg, 0.72 mmol) (2*R*,3*S*:2*S*,3*S* = ca. 9:1) were added pyridine (2 mL) and hydroxylamine hydrochloride (500 mg, 7.30 mmol), and the resulting mixture was stirred for 12 h at 80 °C. The precipitates were filtered off through a silica gel short-path column, and the filtrate was concentrated under reduced pressure. Column chromatography (AcOEt–hexane, 1:3) gave the corresponding oxime, 140 mg (98%), as a colorless oil.

To a 1,2-dichloroethane (10 mL) solution of the oxime (140 mg, 0.70 mmol) were added triphenylphosphine (800 mg, 3.01 mmol), triethylamine (0.42 mL), and CCl_4 (0.29 mL), and the solution was stirred for 3 h at 80 °C. The precipitates were filtered off through a silica gel short-path column, and the filtrate was concentrated. Column chromatography (silica gel, AcOEt–hexane, 1:7) gave (2*S*,3*S*)-2,3-(cyclohexylidenedioxy)butanenitrile ($[\alpha]^{20}_D$ 14.60° (*c* 0.452, $CHCl_3$); 95% optical purity based on the literature value:[32d] $[\alpha]_D$ 15.5°), 90 mg, and its 2*R*,3*S* isomer, 13 mg (total 81%), as colorless oils.

***threo*-2-Methyl-3-piperidino-1-phenylpropanol (23).** Lithium aluminum hydride (40 mg, 1.05 mmol) was added to a THF (2 mL) solution of **21d** (55 mg, 0.22 mmol), and the mixture was heated to reflux for 5 h. The reaction mixture was quenched with a small amount of saturated Na_2SO_4 aqueous solution (ca. 0.5 mL), dried over anhydrous Na_2SO_4, filtrated, and concentrated in vacuo. Purification by preparative TLC (silica gel, AcOEt) gave **23**, 39 mg (75%), as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.54 (d, *J* = 6.5 Hz, 3 H), 1.3–2.2 (m, 7 H), 2.2–2.9 (m, 6 H), 4.37 (d, *J* = 9.0 Hz, 1 H), 7.2–7.4 (m, 5 H).

Preparation of α-Substituted β-Keto Amides. A Typical Procedure. Lithium diisopropylamide (LDA) (0.5 M THF solution, 6.2 mL, 3.1 mmol) was added to a THF (30 mL) solution of *N*,*N*-diethylpropanamide (0.37 g, 2.9 mmol) at −80 °C, and the solution was stirred for 40 min at −80 °C. The lithium enolate thus prepared was kept at −80 °C and added to a THF (30 mL) solution of propanoyl chloride (0.52 mL, 6.0 mmol) at −80 °C with the aid of a syringe. After being stirred for 1 min at −80 °C, the reaction mixture was worked up and subjected to column chromatography (CH_2Cl_2–diethyl ether) to give *N*,*N*-diethyl-3-oxo-2-methylpentanamide (**20g**), 0.50 g (94%), as a colorless oil: ^{1}H

NMR ($CDCl_3$) δ 1.03 (t, J = 7 Hz, 3 H), 1.11 (t, J = 7 Hz, 3 H), 1.19 (t, J = 7 Hz, 3 H), 2.3–2.7 (m, 2 H), 3.2–3.5 (m, 4 H), 3.58 (q, J = 7 Hz, 1 H); IR (neat) 3000, 2955, 1730, 1633, 1460, 1430 cm^{-1}; MS (70 eV), m/z (relative intensity) 185 (M^+, 7), 129 (30), 128 (31), 114 (27), 101 (14), 100 (63), 86 (16), 73 (12), 72 (64), 58 (100), 57 (78), 56 (11), 55 (12), 44 (39), 42 (12), 29 (70), 28 (15), 27 (23). Anal. Calcd for $C_{10}H_{19}NO_2$: C, 64.38; H, 10.34; N, 7.56. Found: C, 64.30; H, 10.34; N, 7.44.

The following compounds (**20b–i**) were prepared in a similar manner.

***N,N*-Diethyl-2-benzoylpropanamide (20b)**: ^1H NMR ($CDCl_3$) δ 1.09 (t, J = 7 Hz, 3 H), 1.18 (t, J = 7 Hz, 3 H), 1.50 (d, J = 7 Hz, 3 H), 3.1–3.6 (m, 4 H), 4.35 (q, J = 7 Hz, 1 H), 7.2–7.7 (m, 3 H), 7.9–8.1 (m, 2 H); IR (neat) 2992, 1698, 1632, 1463, 1448, 1432, 1224, 693 cm^{-1}; MS (70 eV), m/z (relative intensity) 233 (M^+, 6), 134 (11), 128 (15), 105 (100), 100 (20), 77 (40), 72 (57), 58 (23), 51 (11), 29 (17). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 71.77; H, 8.33; N, 5.89.

***N*-(2-Benzoylpropanoyl)pyrrolidine (20c)**: mp 96–97 °C; ^1H NMR ($CDCl_3$) δ 1.48 (d, J = 7 Hz, 3 H), 1.7–2.0 (m, 4 H), 3.2–3.6 (m, 4 H), 4.31 (q, J = 7 Hz, 1 H), 7.3–7.6 (m, 3 H), 7.85–8.05 (m, 2 H); IR (KBr) 1694, 1627, 1453, 1426, 1225, 689 cm^{-1}; MS (70 eV), m/z (relative intensity) 231 (M^+, 1), 126 (24), 105 (100), 77 (45), 70 (75). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.40; H, 7.39; N, 5.89.

***N*-[2-(*p*-Chlorobenzoyl)propanoyl]pyrrolidine (20e)**: mp 108 °C; ^1H NMR ($CDCl_3$) δ 1.48 (d, J = 7 Hz, 3 H), 1.7–2.1 (m, 4 H), 3.2–3.6 (m, 4 H), 4.20 (q, J = 7 Hz, 1 H), 7.40 (d, J = 9 Hz, 2 H), 7.89 (d, J = 9 Hz, 2 H); IR (KBr) 1711, 1630, 1593, 1451, 1428, 1225, 1090, 799 cm^{-1}; MS (70 eV), m/z (relative intensity) 267 (M^+ + 2, 4), 265 (M^+, 13), 168 (12), 141 (34), 139 (99), 126 (48), 113 (12), 111 (34), 98 (24), 75 (14), 70 (100), 56 (13), 55 (23). Anal. Calcd for $C_{14}H_{16}ClNO_2$: C, 63.28; H, 6.07; N, 5.27. Found: C, 63.29; H, 6.18; N, 5.30.

***N*-[2-(*p*-Methoxybenzoyl)propanoyl]pyrrolidine (20f)**: mp 106–108 °C; ^1H NMR ($CDCl_3$) δ 1.48 (d, J = 7 Hz, 3 H), 1.7–2.0 (m, 4 H), 3.2–3.6 (m, 4 H), 3.83 (s, 3 H), 4.21 (q, J = 7 Hz, 1 H), 6.88 (d, J = 9 Hz, 2 H), 7.91 (d, J = 9 Hz, 2 H); IR (KBr) 1688, 1624, 1596, 1447, 1428, 1256, 1227, 1168, 1026 cm^{-1}; MS (70 eV), m/z (relative intensity) 262 (M^+ + 1, 2), 261 (M^+, 9), 164 (12), 151 (11), 136 (9), 135 (100), 126 (20), 107 (10), 92 (11), 77 (18), 70 (32). Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 69.21; H, 7.48; N, 5.37.

***N,N*-Diethyl-3-oxo-2,4-dimethylpentanamide (20h)**: ^1H NMR ($CDCl_3$) δ 1.05 (d, J = 6.8 Hz, 3 H), 1.09 (d, J = 6.8 Hz, 3 H), 1.13 (d, J = 7.2 Hz, 3 H), 1.21 (t, J = 7.2 Hz, 3 H), 1.35 (d, J = 6.8 Hz, 3 H), 2.87 (septet, J = 6.8 Hz, 1 H), 3.2–3.6 (m, 4 H), 3.70 (q, J = 6.8 Hz, 1 H); IR (neat) 2980, 1728, 1644, 1633, 1464, 1454, 1428 cm^{-1}; MS (70 eV), m/z (relative intensity) 199 (M^+, 7), 129 (56), 128 (24), 114 (33), 105 (15), 101 (17), 100 (100), 72 (68), 71 (27), 58 (80), 56 (11), 55 (12), 44 (43), 43 (75), 42 (15), 41 (20), 29 (46), 28 (24), 27 (27), 18 (40), 17 (10). Anal. Calcd for $C_{11}H_{21}NO_2$: C, 66.29; H, 10.62; N, 7.03. Found: C, 66.38; H, 10.63; N, 6.87.

***N*-[2-(2,2-Dimethylpropanoyl)propanoyl]pyrrolidine (20i)**: mp 88 °C; ^1H NMR ($CDCl_3$) δ 1.15 (s, 9 H), 1.29 (d, J = 7 Hz, 3 H), 1.75–2.15 (m, 4 H), 3.35–3.60 (m, 4 H), 3.90 (q, J = 7 Hz, 1 H); IR (KBr) 2980, 2875, 1713, 1602, 1476, 1448, 1420, 1362, 1111, 1048, 983, 969 cm^{-1}; MS (70 eV), m/z (relative intensity) 211 (M^+, 15), 154 (14), 127 (40), 126 (14), 99 (18), 98 (100), 71 (11), 70 (20), 57 (37), 56 (13), 55 (28), 43 (12), 41 (18), 29 (13). Anal. Calcd for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63. Found: C, 68.43; H, 9.86; N, 6.63.

Hydrosilane/F^- Reduction of β-Keto Amides. A Typical Procedure. To a DMPU (1 mL) solution of **20b** (117 mg, 0.50 mmol) and dimethylphenylsilane (0.092 mL, 0.60 mmol) was added TASF (1 M THF solution, 0.050 mL, 0.050 mmol) at 0 °C, and the mixture was stirred for 12 h at 0 °C. Then, hydrochloric methanol solution (1 M, 0.5 mL) was added to the solution, and the stirring was continued for an additional 15 min. The bulk of DMPU was removed by rapid filtration through a short silica gel column (elution with diethyl ether–hexane, 1:1), and the eluent was concentrated under reduced pressure. The resulting mixture was subjected to preparative TLC (AcOEt–hexane, 1:1) to afford *threo-N,N*-diethyl-3-hydroxy-2-methyl-3-phenylpropanamide (**21b**), 115 mg (98%), as colorless crystals. The ratio **21b**:**22b** was >99:1 (400-MHz ^1H NMR analysis). The threo isomer **21b** had mp 56 °C: ^1H NMR ($CDCl_3$) δ 0.92 (t, J = 7.2 Hz, 3 H), 1.00 (t, J = 7.1 Hz, 3 H), 1.29 (d, J = 7.0 Hz, 3 H), 2.92 (dq, J = 4.7, 7.0 Hz, 1 H), 2.95–3.1 (m, 2 H), 3.15–3.3 (m, 2 H), 4.77 (dd, 4.7–7.5 Hz, 1 H), 5.07 (d, J = 7.5 Hz, 1 H), 7.25–7.35 (m, 5 H); IR (KBr) 1610, 1453, 1433, 1148, 765, 709 cm^{-1}; MS (70 eV), m/z (relative intensity) 235 (M^+, 5), 220 (12), 129 (100), 114 (27), 107 (25), 101 (14), 100 (49), 79 (24), 77 (23), 74 (10), 72 (28), 58 (74), 57 (19), 44 (43), 30 (10), 29 (36), 27 (12). Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.76; H, 9.11; N, 5.87.

***threo*-*N*-(3-Hydroxy-2-methyl-3-phenylpropanoyl)-pyrrolidine (21c).** A mixture of **21c** and **22c** (91% yield, 98:2 by HPLC analysis) was obtained as colorless crystals along with recovered **1b** (7%). Recrystallization from diethyl ether–hexane gave pure **21c**: mp 115 °C; ^1H NMR ($CDCl_3$) δ 1.07 (d, J = 7 Hz, 3 H), 1.7–2.0 (m, 4 H), 2.88 (quintet, J = 7 Hz, 1 H), 3.2–3.5 (m, 4 H), 3.94 (s, 1 H), 4.69 (d, J = 7 Hz, 1 H), 7.3 (s, 5 H); IR (KBr) 3370, 1614, 1472, 1447, 1048, 755, 704 cm^{-1}; MS (70 eV), m/z (relative intensity) 234 (M^+, 2), 218 (13), 127 (100), 126 (11), 107 (10), 99 (21), 98 (26), 79 (12), 77 (13), 72 (11), 71 (19), 70 (25), 55 (13), 43 (19). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 71.85; H, 8.28; N, 5.79.

***threo*-*N*-(3-Hydroxy-3-phenyl-2-methylpropanoyl)-piperidine (21d).** The ratio **21d**:**22d** was 99:1 (400-MHz ^1H NMR analysis). Recrystallization from diethyl ether–hexane gave pure **21d**: mp 79–80 °C; ^1H NMR ($CDCl_3$) δ 1.22 (d, J = 7 Hz, 3 H), 1.1–1.7 (m, 6 H), 2.8–3.8 (m, 5 H), 4.7–4.8 (m, 2 H), 7.31 (s, 5 H); IR (KBr) 3380, 1606 cm^{-1}; MS (70 eV), m/z (relative intensity) 247 (M^+, 6), 232 (16), 141 (100), 112 (23), 84 (39), 79 (15). Anal. Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.70; H, 8.63; N, 5.65.

***threo*-*N*-[3-(*p*-Chlorophenyl)-3-hydroxy-2-methylpropanoyl]pyrrolidine (21e).** The total yield of **21e** and **22e** was 86%. The ratio **21e**:**22e** was 99:1 (90-MHz ^1H NMR analysis). Recrystallization from diethyl ether–hexane gave pure **21e**: mp 118–119 °C; ^1H NMR ($CDCl_3$) δ 1.23 (d, J = 7 Hz, 3 H), 1.6–1.9 (m, 4 H), 2.6–2.9 (m, 1 H), 3.0–3.5 (m, 4 H), 4.73 (s, 1 H), 7.27 (s, 5 H); ^1H NMR ($CDCl_3$–CD_3OD) δ 2.79 (dq, J = 6, 7 Hz, 1 H), 4.68 (d, J = 7 Hz, 1 H), no peak around 4.73; IR (KBr) 3290, 1620, 1472, 1444, 1084, 827, 564 cm^{-1}; MS (70 eV), m/z (relative intensity) 269 (M^+ + 2, 3), 267 (M^+, 6), 252 (14), 141 (14), 127 (100), 126 (13), 99 (25), 98 (32), 77 (24), 72 (12), 71 (21), 70 (29), 56 (12), 55 (18), 43 (25), 28 (10). Anal. Calcd for $C_{14}H_{18}ClNO_2$: C, 62.80; H, 6.78; N, 5.23. Found: C, 62.96; H, 6.91; N, 5.11.

***threo*-*N*-[3-Hydroxy-3-(*p*-methoxyphenyl)-2-methylpropanoyl]pyrrolidine (21f).** A mixture of **21f** and its erythro isomer **22f** (99:1) was produced in 92% total yield as colorless crystals. Recrystallization from diethyl ether–hexane gave pure **21f**: mp 134–136 °C; ^1H NMR ($CDCl_3$) δ 1.18 (d, J = 7 Hz, 3 H), 1.6–2.0 (m, 4 H), 2.79 (dq, J = 6, 7 Hz, 1 H), 3.0–3.6 (m, 4 H)e, 3.78 (s, 3 H), 4.30 (br s, 1 H), 4.68 (d, J = 6 Hz, 1 H), 6.81 (d, J = 9 Hz, 2 H), 7.18 (d, J = 9 Hz, 2 H); IR (KBr) 3390, 1618, 1461, 1440, 1246, 1020, 829 cm^{-1}; MS (70 eV), m/z (relative intensity) 263 (M^+, 6), 137 (21), 135 (14), 127 (100), 99 (23), 98 (24), 77 (14), 72 (14), 71 (17), 70 (20), 55 (13), 43 (20). Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04; N, 5.32. Found: C, 68.26; H, 7.78; N, 5.16.

Reduction of 20g. Reduction of **20g** was alternatively carried out with $NaBH_4$ to give a mixture of ratio **21g**:**22g** = 67:33. ^1H NMR spectral data ($CDCl_3$) attributable to **21g** are as follows: δ 1.05 (t, J = 7 Hz, 3 H), 1.22 (t, J = 7 Hz, 6 H), 1.16 (d, J = 7 Hz, 3 H), 1.3–1.65 (m, 2 H), 2.63 (dq, J = 6.6, 7.2 Hz, 1 H).

Reduction of 20h. TASF (1 M THF solution, 0.02 mL, 0.02 mmol) was added to a DMPU (0.2 mL) solution of **20h** (40 mg, 0.20 mmol) and dimethylphenylsilane (0.037 mL, 0.24 mmol) at 0 °C, and the mixture was stirred for 19 h at that temperature. As most of **20h** remained unchanged (TLC), TASF (1 M THF solution, 0.02 mL) was added, and stirring was continued for 72 h at room temperature. Acid treatment and workup followed by purification by preparative TLC (CH_2Cl_2–diethyl ether, 9:1) gave recovered **20h**, 27 mg (68% yield), along with a mixture of threo and erythro alcohols, **21h** and **22h**, 11 mg (27% yield; 83% yield based on the consumed **20h**). The ratio **21h**:**22h** was 25:75.

Alternative reduction of **20h** with $NaBH_4$ afforded a mixture of **21h** and **22h** (73:27) in 96% yield. ^1H NMR spectral data ($CDCl_3$) attributable to **21h** are as follows: δ 0.92 (d, J = 6.8 Hz,

3 H), 0.96 (d, J = 6.7 Hz, 3 H), 1.12 (t, J = 7.2 Hz, 3 H), 1.22 (t, J = 7.2 Hz, 3 H), 1.26 (d, J = 7.1 Hz, 3 H), 1.70 (d, of septet, J = 6.8, 6.7 Hz, 1 H), 2.80 (dq, J = 4.2, 7.1 Hz, 1 H), 3.28 (ddd, J = 4.2, 6.8, 8.3 Hz, 1 H), 3.36 (q, J = 7.2 Hz, 2 H), 3.37 (q, J = 7.1 Hz, 2 H), 4.38 (d, J = 8.3 Hz, 1 H).

***N*-(3-Hydroxy-2,4,4-trimethylpentanoyl)pyrrolidine (21i and 22i).** TASF (1 M THF solution, 0.05 mL, 0.05 mmol) was added to a DMPU (1 mL) solution of **20i** (106 mg, 0.51 mmol) and diphenylsilane (0.110 mL, 0.60 mmol) at 0 °C, and the mixture was stirred for 14 h at 0 °C. Diphenylsilane (0.050 mL, 0.27 mmol) was added, and stirring was continued for 24 h at room temperature. Acid treatment and workup followed by purification by preparative TLC (CH_2Cl_2–ethyl ether, 9:1) gave *N*-(3-hydroxy-2,4,4-trimethylpentanoyl)pyrrolidine, 96 mg (90% yield), as a colorless oil. The threo:erythro ratio was 91:9 (90-MHz ^1H NMR analysis). Repeated recrystallization from diethyl ether–hexane afforded pure threo isomer **21i** as colorless crystals: mp 60 °C; ^1H NMR ($CDCl_3$) δ 0.89 (s, 9 H), 1.34 (d, J = 7 Hz, 3 H), 1.8–2.1 (m, 4 H), 2.69 (dq, J = 2, 6 Hz, 1 H), 3.17 (br s, 1 H), 3.3–3.6 (m, 4 H), 5.73 (br s, 1 H); IR (KBr) 3360, 2990, 2890, 1069, 1473, 1431, 1254, 1131, 985, 610 cm^{-1}; MS (70 eV), m/z (relative intensity) 198 (M^+ – Me, 5), 156 (80), 127 (13), 99 (12), 98 (100), 72 (16), 71 (10), 70 (22), 56 (10), 55 (31), 43 (16), 41 (16), 29 (14). Anal. Calcd for $C_{12}H_{23}NO_2$: C, 67.56; H, 10.87; N, 6.57. Found: C, 67.45; H, 10.67; N, 6.48.

Chemical shifts of α-methyl groups of **21** and **22** in ^{13}C NMR are as follows: **21b**, 17.4; **22b**, 10.4; **21g**, 16.0; **22g**, 10.3; **21h**, 16.0; **22h**, 10.1; **21i**, 18.0; **22i**, 11.8.

***threo*-*N*-[2-Methyl-3-(dimethylphenylsiloxy)-3-phenylpropanoyl]piperidine**: ^1H NMR ($CDCl_3$) δ 0.13 (s, 3 H), 0.22 (d, J = 6.4 Hz, 3 H), 1.3–1.8 (m, 6 H), 3.07 (dq, J = 9.6, 6.4 Hz, 1 H), 3.3–3.7 (m, 4 H), 4.81 (d, J = 9.6 Hz, 1 H), 7.1–7.5 (m, 10 H).

Registry No. **3a**, 112-44-7; **3b**, 100-52-7; **3c**, 104-55-2; **3d**, 66-25-1; **3e**, 111-13-7; **3f**, 98-86-2; **3g**, 13891-87-7; **3h**, 583-60-8; **4a**, 91110-95-1; **4b**, 17908-86-0; **4b′**, 13959-92-7; **4c**, 91110-96-2; **4d″**, 18754-85-3; **4e**, 91110-97-3; **4f**, 34074-18-5; **4f***, 98-85-1; **4g**, 91110-98-4; *cis*-**4h***, 7443-70-1; *trans*-**4h***, 7443-52-9; *cis*-**4h**, 116596-11-3; *trans*-**4h**, 116596-12-4; **8**, 116596-13-5; *syn*-**9**, 5381-86-2; *anti*-**9**, 59825-14-8; **11**, 114660-36-5; **12**, 98264-23-4; **13a**, 91111-01-2; **13a′**, 1030-23-5; **13a″** (isomer 1), 116595-99-4; **13a″** (isomer 2), 116596-18-0; **13b**, 116696-50-5; **13b′**, 91111-02-3; **13b″** (isomer 1), 116696-51-6; **13b″** (isomer 2), 116696-52-7; **13c**, 116596-00-0; **13d**, 7472-23-3; **13e**, 15351-09-4; **14a**, 88196-06-9; **14b**, 91177-70-7; **14b′**, 91111-06-7; **14c**, 38217-37-7; **14d**, 1460-57-7; **14e**, 62560-55-8; **15a**, 40421-52-1; **15b**, 67470-74-0; **15b′**, 91111-07-8; **15c**, 38196-27-9; **15d**, 1792-81-0; **15e**, 39263-91-7; **16a**, 4478-63-1; **16b**, 4587-00-2; **17a**, 6464-55-7; **17b**, 22520-27-0; **18a**, 6464-37-5; **18b**, 22520-26-9; **19** (isomer 1), 80952-63-2; **19** (isomer 2), 80928-01-4; **20a**, 29540-54-3; **20b**, 51975-15-6; **20c**, 106181-33-3; **20d**, 24956-53-4; **20e**, 106181-34-4; **20f**, 106181-35-5; **20g**, 116596-01-1; **20h**, 116596-02-2; **20i**, 116596-03-3; **21b**, 106181-39-9; **21c**, 76943-97-0; **21d**, 116596-04-4; **21e**, 106181-40-2; **21f**, 106181-41-3; **21g**, 116596-05-5; **21h**, 116596-06-6; **21i**, 116596-07-7; **22g**, 116596-08-8; **22h**, 116596-09-9; **22i**, 116596-10-2; **23**, 32213-47-1; **24a**, 2042-85-5; **24b**, 16819-77-5; **25a**, 7693-84-7; **25b**, 1502-78-9; **26b**, 1502-77-8; TASF, 59201-86-4; TBAF, 429-41-4; $RhCl(PPh_3)_3$, 14694-95-2; CsF, 13400-13-0; KF, 7789-23-3; $PhMe_2SiH$, 766-77-8; (p-$F_3CC_6H_4$)Me_2SiH, 19254-78-5; (p-$MeOC_6H_4$)Me_2SiH, 1432-38-8; (p-MeC_6H_4)Me_2SiH, 1432-39-9; Ph_2MeSiH, 776-76-1; (i-PrO)Ph_2SiH, 40391-86-4; (i-PrO)$_3SiH$, 6675-79-2; Ph_2SiH_2, 775-12-2; $HSiMe_2Tol$, 1432-39-9; $FSiMe_2Ph$, 454-57-9; Et_3SiH, 617-86-7; Ph_3SiH, 789-25-3; deuteriodimethylphenylsilane, 22034-19-1; 1-phenylethanol, 98-85-1; 1-deuterio-1-phenylethanol, 3101-96-0; bis(dimethylsilyl)amine, 15933-59-2; 1,3-diphenyl-3-hydroxypropan-1-one, 42052-51-7; cyclohexanecarboxaldehyde, 2043-61-0; cyclohexylmethanol, 100-49-2; chlorodimethylphenylsilane, 768-33-2; 4-bromoanisole, 104-92-7; chlorodimethylsilane, 1066-35-9; (*p*-chlorophenyl)dimethylsilane, 1432-31-1; (*S*)-2-acetoxypropionyl chloride, 36394-75-9; 2-bromo-1-phenyl-1-propanone, 2114-00-3; *cis*-2-(benzoyloxy)cyclohexanol, 37854-36-7; *trans*-2-(benzoyloxy)-cyclohexanol, 59694-07-4; (*S*)-*N*,*N*-dimethyl-2-(1-ethoxyethoxy)propanamide, 116596-14-6; (*S*)-*N*,*N*-dimethyl-2-hydroxypropanamide, 53636-17-2; ethyl vinyl ether, 109-92-2; (*S*)-*N*,*N*-dimethyl-2-*tert*-butoxypropanamide, 116596-15-7; (*S*)-*N*,*N*-dimethyl-2-(2-tetrahydropyranyloxy)propanamide (isomer 1), 116596-16-8; (*S*)-*N*,*N*-dimethyl-2-(2-tetrahydropyranyloxy)-propanamide (isomer 2), 116596-17-9; (*E*)-(2-phenylethenyl)-magnesium bromide, 35672-47-0; 2-(benzyloxy)propanoic acid, 6625-78-1; 1,1-dimethoxycyclohexane, 933-40-4; (3*S*,4*S*,1*E*)-3,4-(cyclohexylidenedioxy)-1-phenyl-1-pentene, 116696-53-8; (3*R*,4*S*,1*E*)-3,4-(cyclohexylidenedioxy)-1-phenyl-1-pentene, 116696-54-9; bis(trimethylsilyl)sulfate, 18306-29-1; (2*S*,3*S*)-2,3-(cyclohexylidenedioxy)butanenitrile, 90458-03-0; (2*R*,3*S*)-2,3-(cyclohexylidenedioxy)butanenitrile, 90458-04-1; (2*S*,3*S*)-2,3-(cyclohexylidenedioxy)butanenitrile oxime, 91517-10-1; (2*R*,3*S*)-2,3-(cyclohexylidenedioxy)butanenitrile oxime, 116696-55-0; *N*,*N*-diethylpropanamide, 1114-51-8; propanoyl chloride, 79-03-8; *threo*-*N*-[2-methyl-3-(dimethylphenylsiloxy)-3-phenylpropanoyl]piperidine, 116596-19-1.

Erythro-Directive Reduction of α-Substituted Alkanones by Means of Hydrosilanes in Acidic Media

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Hydrosilane reduced α-oxy and α-amino ketones and β-keto acid derivatives in trifluoroacetic acid to afford the corresponding erythro alcohols with high diastereoselectivity. The reaction proceeded without racemization at the carbon α to the carbonyl group. The erythro-directive reduction was explained in terms of the proton-bridged Cram cyclic model and successfully applied to the synthesis of physiologically important amino alcohols such as *l*-ephedrine, *l*-methoxamine, and *erythro*-2-methyl-3-piperidino-1-phenylpropanol.

Reduction of carbonyl compounds with chemoselective reagents is a prevailing synthetic strategy for alcohols but still remains problematic with respect to the selectivity.[1] For this purpose, hydrosilane-based reduction is of considerable interest, since the organosilanes are fairly stable under ordinary conditions and become reactive only in the presence of such a promoter as a transition-metal complex,[2]

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