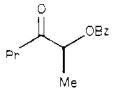
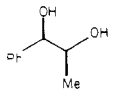
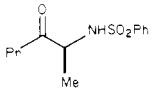
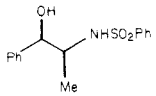
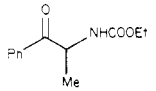
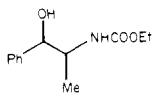
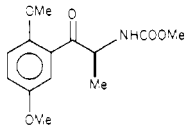
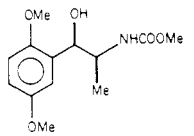
Table II. TFA-Catalyzed Erythro-Selective Ketone Reduction with $PhMe_2SiH$[a]

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).

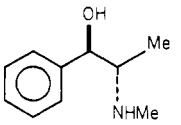
$[R_3SiHF]^-[n\text{-}Bu_4N]^+$ species which attacks the ketone carbonyl carbon according to the Felkin transition-state model.[12] Particularly noteworthy is that no metal cations are involved in the reaction. Thus, coordination effects by a metal cation are completely eliminated, and only the bulkiness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

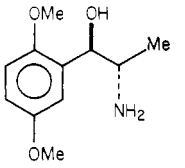
In striking contrast to the TBAF-catalyzed threo-directed reduction, erythro-selective reduction was achieved by using the same hydrosilanes under acidic conditions.[14] For example, dimethylphenylsilane (1.2 mmol) was added to a trifluoroacetic acid (TFA) (1 mL) solution of 2-(benzoyloxy)-1-phenyl-1-propanone 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.

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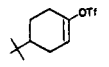
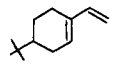
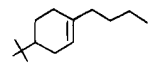
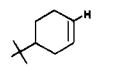
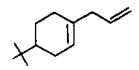
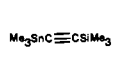
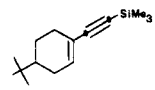
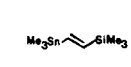
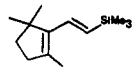
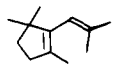
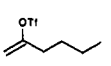
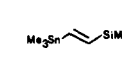
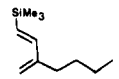
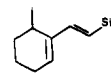
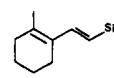
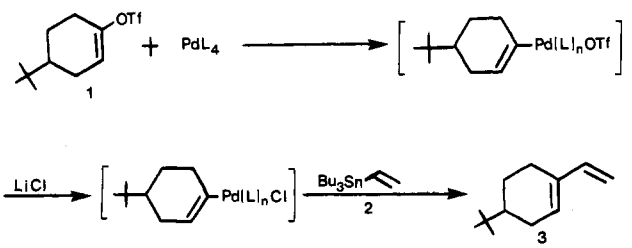
Table I. Palladium-Catalyzed Coupling of Vinyl Triflates with Organotins

EXAMPLE	TRIFLATE	ORGANOTIN	REACTION TIME (h)	PRODUCT	ISOLATED YIELD(%)
1			17		91
2			41		80
3			0.5		78
4			31		96
5			41		90
6			36		100
7			133		80
8			17		90
9			6		100
10			100		90

vinyltributylstannane (**2**) to the resulting dark brown solution did not lead to the coupled product (**3**).

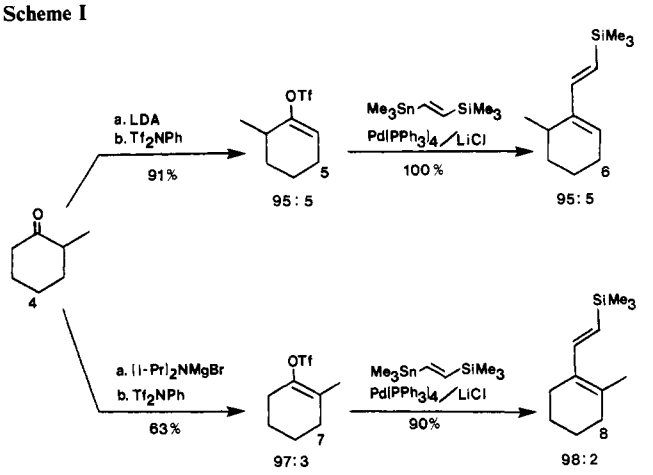
When **1** was added to a mixture of 2 equiv of lithium chloride and 2 mol% of palladium(0) in THF at room temperature, a reaction again occurred immediately, as observed by ^{31}P NMR, and now a colorless solution was generated. Addition of **2** to this mixture (70 °C, 17 h) led to a quantitative conversion of **1** to **3**, as indicated by GC analysis.

Assuming that the oxidative addition of triflate (**1**) to palladium takes place, the resulting vinylpalladium(II) triflate appears incapable of entering a catalytic cycle.[8,9] In the presence of lithium chloride, apparently a vinylpalladium(II) chloride complex was generated, which was then capable of undergoing further reaction with **2** to afford coupled products and generate a palladium(0) species.

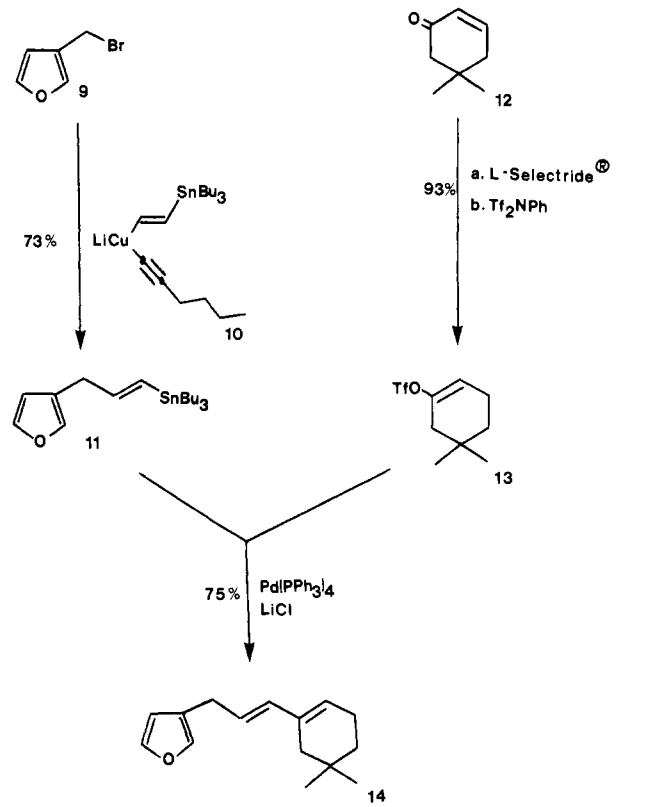


As shown in Table I, the coupling of vinyl triflates with organotin compounds has been found to be general.[10,11] The reduction of **1** proceeded in good yield, as shown by example 3. The coupling reaction seems suited to alkylation at sterically hindered centers, as shown in examples 6 and 7. Finally, the reaction allows the facile stereoselective formation of 1,3-dienes under mild conditions (examples 1 and 6–10).

Scheme I



Scheme II



The ability to regioselectively form vinyl triflates by utilizing well-known enolate chemistry[12,13] and then to convert them into olefins is illustrated in Scheme I. Thus, 2-methylcyclohexanone could be converted into the 6-methyl triflate **5** (**5**:**7** = 95:5) or the 2-methyl triflate **7** (**7**:**5** = 97:3), and these could then be coupled to afford **6** and **8**, respectively.

The following procedure is illustrative. To a mixture of 0.56 g (13 mmol) of lithium chloride and 0.032 g (0.028 mmol, 1.6

(8) The stoichiometric reaction of **1** with palladium(0) complexes both in the presence and in the absence of lithium chloride is currently under investigation.

(9) Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129–6137.

(10) Details of the scope of this reaction will be reported in due course.

(11) Satisfactory IR, ^1H NMR, and ^{13}C NMR spectra and either HRMS or combustion analyses were obtained for all new compounds.

(12) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24*, 979–982.

(13) Kraft, M. E.; Holton, R. A. *Tetrahedron Lett.* **1983**, *24*, 1345–1348.

(14) (a) Cimino, G.; DeStefano, S.; Minale, L. *Tetrahedron* **1972**, *28*, 4761–4767. (b) Cimino, G.; DeStefano, S.; Minale, L. *Experimentia* **1974**, *30*, 864. (c) Thompson, J. E.; Walker, R. P.; Wratten, S. J.; Faulkner, D. J. *Tetrahedron Lett.* **1982**, *23*, 1865–1873.

mol %) of tetrakis(triphenylphosphine)palladium(0) under argon was added 10 mL of dry THF followed by a solution of 0.51 g (1.8 mmol) of vinyl triflate **1** and 0.62 g (1.8 mmol) of tetrabutyltin in 10 mL of THF. This slurry was heated to reflux for 17 h, cooled to room temperature, and diluted with 60 mL of pentane. After washing with a 10% ammonium hydroxide solution (3 × 25 mL) and drying ($MgSO_4$), the resulting solution was filtered through a short pad of silica gel and concentrated under reduced pressure to give 0.28 g (80%) of 1-butyl-4-*tert*-butylcyclohexene[6] (example 2) as a colorless oil.

This methodology was applied to the synthesis of pleraplysillin-1 (**14**),[14] as shown in Scheme II. (*E*)-Vinyltin **11** was formed by addition of the lithium (*E*)-vinyltin cuprate **10**[15] to 3-furfuryl bromide[16] (73% yield). Triflate **13** was prepared as one regioisomer from 5,5-dimethyl-2-cyclohexenone[17] by conjugate reduction[18] followed by enolate trapping with *N*-phenyltriflimide.[12] Palladium-catalyzed coupling of **11** with **13** afforded pleraplysillin-1 (**14**) in 75% yield.[19,20] No other isomers were observed.

Thus, vinyl triflates couple with organostannanes in the presence of lithium chloride and palladium(0) catalysts to give a variety of olefin-substituted products. This reaction represents the first case of a transition-metal-catalyzed reaction of a vinyl sulfonate. In effect, this allows the conversion of the oxygen of regioselectively formed enolates into a leaving group for palladium-catalyzed reactions.

Acknowledgment. We gratefully acknowledge support for this research through Grant CHE-8305468 from the National Science Foundation. Palladium chloride was generously loaned by Johnson-Matthey Inc. through the Johnson-Matthey Metal Loan Program.

(15) Corey, E. J.; Wollenberg, R. H. *Tetrahedron Lett.* **1975**, *16*, 2225-2226.
(16) Parker, K. A.; Johnson, W. S. *Tetrahedron Lett.* **1969**, *10*, 1329-1332.
(17) Hiegel, G. A.; Burk, P. *J. Org. Chem.* **1973**, *38*, 3637-3639.
(18) (a) Ganem, B. *J. Org. Chem.* **1975**, *40*, 146-147. (b) Fortunato, J. M.; Ganem, B. *Ibid.* **1976**, *41*, 2194-2200.
(19) For a prior synthesis of **14**, see: Masaki, Y.; Hashimoto, K.; Serizawa, Y.; Kaji, K. *Chem. Lett.* **1982**, 1879-1880.
(20) NMR and IR spectra of **14** were identical with spectra of authentic material. The authors thank Professors Faulkner, Masaki, and Minale for copies of the spectra of **14**.

Reversible Protonation of the Oxo Bridge in a Hemerythrin Model Compound. Synthesis, Structure, and Properties of (μ-Hydroxo)bis(μ-acetato)-bis[hydrotris(1-pyrazolyl)borato]diiron(III), $[(HB(pz)_3)Fe(OH)(O_2CCH_3)_2Fe(HB(pz)_3)]^+$

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Recently the synthesis and properties of binuclear iron complexes that serve as structural, spectroscopic, and chemical models for the (μ-oxo)bis(μ-carboxylato)diiron(III) core of the met forms of marine invertebrate respiratory proteins hemerythrin (Hr) and myohemerythrin (myoHr)[1,2] were described.[3,4] Oxo-bridged binuclear iron centers are also believed to occur in ribonucleotide reductase from *Escherichia coli*[5] and in some purple acid phosphatases.[6] Here we report that, from the reaction mixture used by us to produce binuclear iron model compounds for metHr and metmyoHr, we have now isolated the novel hydroxo-bridged derivative $[(HB(pz)_3)Fe(OH)(O_2CCH_3)_2Fe(HB(pz)_3)]^+$ (**1**). This complex has properties quite distinct from those of the oxo-bridged model compound $[(HB(pz)_3)FeO(O_2CCH_3)_2Fe(HB(pz)_3)]$ (**2**). Compounds **1** and **2** may be reversibly interconverted by direct protonation–deprotonation reactions which, to our knowledge, are unprecedented in iron chemistry. These discoveries strongly support the current belief, based on physical studies of the proteins, that the two iron atoms in methemerythrins are linked by oxo, rather than hydroxo, bridges and raise the possibility that analogous hydroxo-bridged diiron(III) centers may exist in biology.

The perchlorate salt of **1** was first isolated from the same reaction mixture that produced **2**,[3] but with use of shorter reaction times and a different workup procedure. It was found that using less than 1 equiv of $KHB(pz)_3$ per iron atom decreased the amount of $[Fe(HB(pz)_3)_2]^+$[7] in the crude product. Addition of 0.500 g (1.98 mmol) of potassium hydrotris(1-pyrazolyl)borate ($KHB(pz)_3$) in 20 mL of water to a stirred solution of 2.12 g (3.97 mmol)

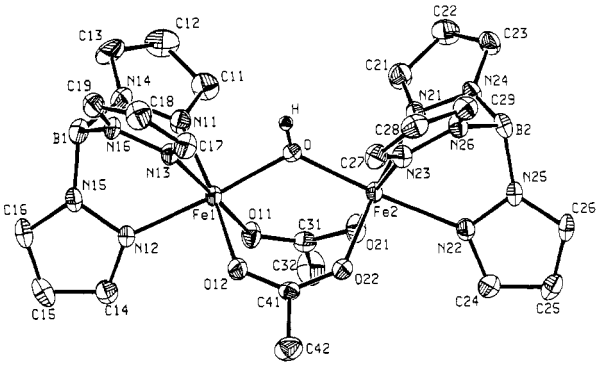

Figure 1. Structure of the (μ-hydroxo)bis(μ-acetato)bis[hydrotris(1-pyrazolyl)borato]diiron(III) cation (**1**) showing the 40% probability thermal ellipsoids and atom labeling scheme. The hydrogen atom bound to atom O is depicted at its refined position with an arbitrary *B* value of 1.0 Å^2. The remaining hydrogen atoms are omitted for clarity.

Table I. Comparison of Structural Features of $[Fe_2(OH)(O_2CCH_3)_2(HB(pz)_3)_2]^+$ (**1**)[a] and $[Fe_2O(O_2CCH_3)_2(HB(pz)_3)_2]$ (**2**)[b]

bond length, Å or angle, deg[c]	**1**[d]	**2**[d]
Fe(1)···Fe(2)	3.439 (1)	3.1457 (6)
$Fe-O_{bridge}$	1.960 (4), 1.952 (4)[e]	1.780 (2), 1.788 (2)
Fe(1)–O–Fe(2)	123.1 (2)	123.6 (1)
Fe–N	2.087 (4)–2.110 (5) mean 2.102	2.148 (3)–2.200 (3) mean 2.165
$Fe-O_{acetate}$	1.994 (4)–2.001 (4) mean 1.999	2.040 (2)–2.050 (3) mean 2.043

[a] This work. [b] Reference 3b. [c] Atoms are labeled for both compounds as shown in Figure 1. [d] Numbers in parentheses are estimated standard deviations in the last digit. [e] The H atom was first located on a difference Fourier map at 0.94 Å from the O atom; the refined O–H distance is 0.70 (6) Å.

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