Chelating Diphosphines That Contain a Rhenium Stereocenter in the Backbone: Applications in Rhodium-Catalyzed Enantioselective Ketone Hydrosilylations and Alkene Hydrogenations

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Rhodium chelate complexes of the title diphosphines, [(η^5-C_5H_4PPh$_2$)Re(NO)(PPh$_3$)(μ-(CHR)$_n$PPh$_2$)Rh(NBD)]$^+PF_6^-$ ((*S*)-**5**, *n* = 0; (*S*)-**6**, *n*/R = 1/H; ($S_{Re}S_C$)- and ($S_{Re}R_C$)-**7**, *n*/R = 1/Ph), are catalyst precursors (1.0 mol %, 24−26 °C) for additions of Ph_2SiH_2 to the ketones $PhCOCH_2R$ (R = H, CH_3, CH_2CH_3, CH_2CH_2Cl; 93−77% conversions). Hydrolyses give the alcohols (*R*)-$HOCH(Ph)CH_2R$ in 83−60% isolated yields; configurations correlate with the relative rhenium configurations of the catalysts. The ee values with (*S*)-**6** (63/62/60/92%) exceed those of (*S*)-**5** (44/38/47/48%); ee values of ($S_{Re}R_C$)-**7** (41/46/62/58%) are higher than those of the diastereomer ($S_{Re}S_C$)-**7** (23/11/15/35%). The alkenes (*Z*)-$RCH{=}C(NHCOCH_3)$-CO_2R' (R/R′ = H/H, Ph/H, Ph/CH_3) and H_2 (1 atm) react in the presence of ($S_{Re}S_C$)- and ($S_{Re}R_C$)-**7** (0.5 mol %, 30 °C) to give the protected amino acids $RCH_2CH(NHCOCH_3)CO_2R'$ in 85−92% yields. The ee values with ($S_{Re}S_C$)-**7** (37/62/61%) are lower than those found earlier for (*S*)-**6** (62/72/65%) or (*S*)-**5** (92/93/88%), with *S* enantiomers dominant in all cases. Surprisingly, ($S_{Re}R_C$)-**7** gave much higher ee values (93/94/97%), but with *R* enantiomers dominant. Hence, the carbon stereocenter of **7** controls the product configuration.

Introduction

The enantioselective reduction of ketones to alcohols or their derivatives is one of the most important functional group transformations in contemporary organic chemistry. Hydrosilylations catalyzed by chiral metal complexes constitute one of the most actively investigated approaches.[1−3] Although a variety of successes have been reported, there is a never-ending need for even more active, enantioselective, and/or long-lived catalysts.[4] Toward these ends, many clever new design strategies are being applied. For example, syntheses of chiral ferrocene-based chelating ligands have seen rapidly increasing attention over the past decade, and diverse structural types are now known.[5] Various metal complexes have been applied with considerable success as catalysts for numerous enantioselective organic reactions, including hydrosilylations.[6−9]

Ferrocene is noted for its thermal stability and robustness. We wondered whether a more diverse range of chiral, transition-metal-containing chelating ligands could be successfully applied in catalytic organic syntheses. To date, our efforts have focused on diphosphines of the general formula (η^5-$C_5H_4PPh_2$)Re(NO)(PPh$_3$)-((CHR)$_n$PPh$_2$) (*n* = 0, 1; R = H, Ph), as depicted by **1**−**3**

(1) (a) Nishiyama, H. In *Comprehensive Asymmetric Catalysis I*−*III*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H. Eds.; Springer: Berlin, Germany, 1999; Chapter 6.3. (b) Nishiyama, H.; Itoh, K. In *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I.; Ed.; Wiley-VCH: New York, 2000; Chapter 2.

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(6) (a) Sawamura, M.; Kuwano, R.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 111; *Angew. Chem.* **1994**, *106*, 92. (b) Kuwano, R.; Sawamura, M.; Shirai, J.; Takahashi, M.; Ito, Y. *Tetrahedron Lett.* **1995**, *36*, 5239. (c) Sawamura, M.; Kuwano, R.; Shirai, J.; Ito, Y. *Synlett* **1995**, 347. (d) Kuwano, R.; Uemura, T.; Saitoh, M.; Ito, Y. *Tetrahedron Lett.* **1999**, *40*, 1327. (e) Kuwano, R.; Sawamura, M.; Shirai, J.; Takahashi, M.; Ito, Y. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 485.

(7) (a) Nishibayashi, Y.; Segawa, K.; Takada, H.; Ohe, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1996**, 847. (b) Nishibayashi, Y.; Segawa, K.; Ohe, K.; Uemura, S. *Organometallics* **1995**, *14*, 5486. (c) Nishibayashi, Y.; Segawa, K.; Singh, J. D.; Fukuzawa, S.; Ohe, K.; Uemura, S. *Organometallics* **1996**, *15*, 370. (d) Nishibayashi, Y.; Takei, I.; Uemura, S. Hidai, M. *Organometallics* **1998**, *17*, 3420.

(8) (a) Hayashi, T.; Yamamoto, K.; Kumada, M. *Tetrahedron Lett.* **1974**, *15*, 4405. (b) Hayashi, T.; Hayashi, C.; Uozumi, Y. *Tetrahedron: Asymmetry* **1995**, *6*, 2503. (c) Tsuruta, H.; Imamoto, T. *Tetrahedron: Asymmetry* **1999**, *10*, 877. (d) Zhang, W.; Yoneda, Y.; Kida, T.; Nakatsuji, Y.; Ikeda, I. *J. Organomet. Chem.* **1999**, *574*, 19.

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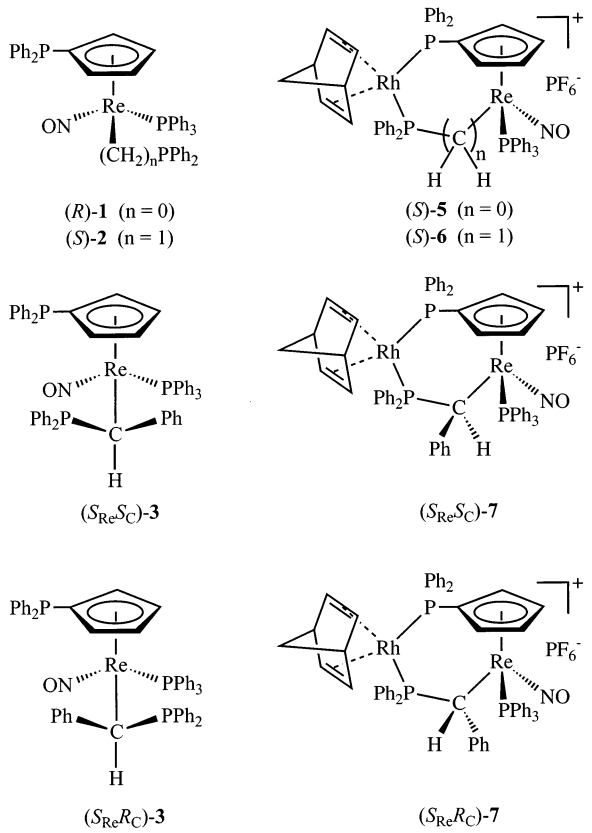
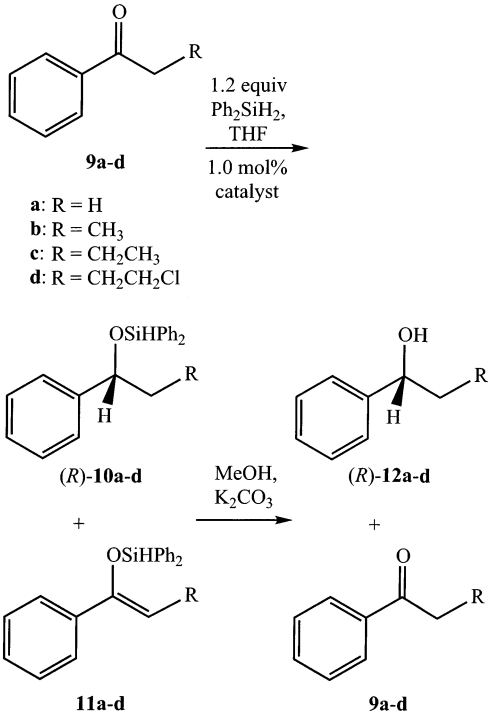


Figure 1. Chiral-at-rhenium diphosphines and related rhodium chelates.

in Figure 1.[10−13] These contain a chiral rhenium moiety in the backbone and, with diastereomers ($S_{Re}S_C$)-**3** and ($S_{Re}R_C$)-**3**, a neighboring carbon stereocenter. All are easily obtained in enantiomerically (and diastereomerically) pure form. They readily afford rhodium[10,12] and palladium[11] chelate complexes, as exemplified by **5**−**7** in Figure 1. The rhodium/rhenium complexes (*S*)-**5** and (*S*)-**6** were found to be excellent catalyst precursors for asymmetric hydrogenations of protected dehydroamino acids.[10] The activities, lifetimes, and (with (*S*)-**5**) enantioselectivities compared well with the best systems of their generation.

Other groups have reported additional types of chiral transition-metal-containing chelate ligands based upon nonferrocenyl templates and applications in enantioselective catalysis.[14,15] In accord with the inherently diverse architectural possibilities, all three types of stereogenic elements (centers, planes, axes) have been employed, often in combination. Selected examples are given in the Discussion. We naturally sought to apply our new families of diphosphines and rhodium complexes to a wider set of catalytic reactions. In this paper, we report the successful utilization of rhodium/rhenium chelates (*S*)-**5**, (*S*)-**6**, ($S_{Re}S_C$)-**7**, and ($S_{Re}R_C$)-**7** as catalyst precursors for enantioselective hydrosilylations of ketones. To more thoroughly compare the newer systems ($S_{Re}S_C$)-**7** and ($S_{Re}R_C$)-**7**, described for the first time in the preceding paper,[12] to the single-stereocenter species (*S*)-**5** and (*S*)-**6**, some asymmetric hydrogenations of dehydroamino acid derivatives are also reported.

Scheme 1. Catalytic Enantioselective Hydrosilylation of Aromatic Ketones with the Rhodium Catalysts in Figure 1



Results

As shown in Scheme 1, four aromatic ketones of the formula $PhCOCH_2R$ (**9a**−**d**) were selected for hydrosilylation experiments. Three have progressively larger carbonyl substituents (methyl, ethyl, propyl) and the fourth a polar chloride group. The silane Ph_2SiH_2 was chosen for its ready availability, ease of handling, and good performance in other enantioselective hydrosilylations.[6−9,16] Although high yields of the corresponding silyl ethers $Ph_2HSiOCH(Ph)CH_2R$ (**10a**−**d**) were anticipated, minor amounts of silyl enol ethers $Ph_2HSiOC(Ph)=CHR$ (**11a**−**d**) are often observed.[16,17] The product distribution is easily assayed by NMR.[17,18]

(10) (a) Kromm, K.; Zwick, B. D.; Meyer, O.; Hampel, F.; Gladysz, J. A. *Chem. Eur. J.* **2001**, *7*, 2015. (b) Preliminary communication of some of the work in the preceding paper: Zwick, B. D.; Arif, A. M.; Patton, A. T.; Gladysz, J. A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 910; *Angew. Chem.* **1987**, *99*, 921.

(11) Kromm, K.; Hampel, F.; Gladysz, J. A. *Helv. Chim. Acta* **2002**, *85*, 1778.

(12) Kromm, K.; Hampel, F.; Gladysz, J. A. *Organometallics* **2002**, *21*, 4264.

(13) As described in the preceding paper,[12] ($S_{Re}S_C$)-**3** and ($S_{Re}S_C$)-**7** were prepared from a precursor enantiomeric to that used for ($S_{Re}R_C$)-**3** and ($S_{Re}R_C$)-**7**. For ease of comparison, the configurations of ($S_{Re}R_C$)-**3** and ($S_{Re}R_C$)-**7**, and all derived products, have been inverted in the text, tables, and graphics. The Experimental Section describes all work as it was actually conducted (i.e., with ($R_{Re}S_C$)-**7** and not ($S_{Re}R_C$)-**7** as given elsewhere).

(14) Brunner, H.; Wachter, J.; Schmidbauer, J.; Sheldrick, G. M.; Jones, P. G. *Organometallics* **1986**, *5*, 2212.

(15) Selected recent references: (a) Kudis, S.; Helmchen, G. *Angew. Chem., Int. Ed.* **1998**, *37*, 3047; *Angew. Chem.* **1998**, *110*, 3210. (b) Bolm, C.; Muñiz, K. *Chem. Soc. Rev.* **1999**, *28*, 51. (c) Pasquier, C.; Pélinski, L.; Brocard, J.; Mortreux, A.; Agbossou-Niedercorn, F. *Tetrahedron Lett.* **2001**, *42*, 2809. (d) Son, S. U.; Park, K. H.; Lee, S. J.; Chung, Y. K.; Sweigart, D. A. *Chem. Commun.* **2001**, 1290. (e) Bolm, C.; Kesselgruber, M.; Hermanns, N.; Hildebrand, J. P.; Raabe, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 1488; *Angew. Chem.* **2001**, *113*, 1536. (f) Jones, G.; Richards, C. J. *Organometallics* **2001**, *20*, 1251.

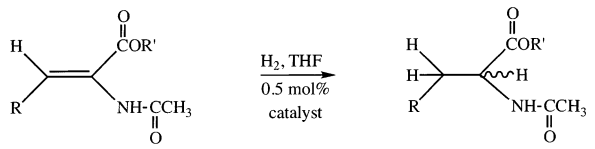
(16) (a) Brunner, H.; Obermann, U. *Chem. Ber.* **1989**, *122*, 499. (b) Hayashi, T.; Yamamoto, K.; Kasuga, K.; Omizu, H.; Kumada, M. *J. Organomet. Chem.* **1976**, *113*, 127.

Table 1. Data for the Reactions in Scheme 1[a]

entry	educt	catalyst	*T* (°C)	conversn (%) **10** + **11**	conversn (%) **10**[b]	yield (**12**) (%)[c]	ee (%)	con-fign[d]
1	**9a**	(*S*)-**5**	25	91	89	83	44	*R*
2	**9b**	(*S*)-**5**	25	82	79	72	38	*R*
3	**9c**	(*S*)-**5**	25	81	80	75	47	*R*
4	**9d**	(*S*)-**5**	25	90	84	60	48	*R*[e]
5a	**9a**	(*S*)-**6**	25	98	95	75	63	*R*
5b	**9a**	(*S*)-**6**	25	96	91	78	60	*R*
6	**9a**	(*S*)-**6**	0	88	81	68	55	*R*
7	**9a**	(*S*)-**6**	−20	56	49	38	25	*R*
8	**9b**	(*S*)-**6**	25	95	93	70	62	*R*
9	**9b**	(*S*)-**6**	0			50	60	*R*
10	**9b**	(*S*)-**6**	−20			53	23	*R*
11	**9c**	(*S*)-**6**	25	96	92	68	60	*R*
12	**9c**	(*S*)-**6**	0			75	58	*R*
13	**9c**	(*S*)-**6**	−20			62	32	*R*
14	**9d**	(*S*)-**6**	25	95	89	72	92	*R*[e]
15	**9d**	(*S*)-**6**	0			68	87	*R*[e]
16	**9d**	(*S*)-**6**	−40			54	42	*R*[e]
17	**9a**	($S_{Re}S_C$)-**7**	26			65	23	*R*
18	**9b**	($S_{Re}S_C$)-**7**	26			72	11	*R*
19	**9c**	($S_{Re}S_C$)-**7**	26			60	15	*R*
20	**9d**	($S_{Re}S_C$)-**7**	26			64	35	*R*[e]
21	**9a**	($S_{Re}R_C$)-**7**	24	96	92	82	41	*R*
22	**9b**	($S_{Re}R_C$)-**7**	24			78	46	*R*
23	**9c**	($S_{Re}R_C$)-**7**	24			76	62	*R*
24	**9d**	($S_{Re}R_C$)-**7**	24	88	77	68	58	*R*[e]

[a] Analytical methods are detailed in the Experimental Section. [b] Hydrolysis was carried out after 14-16 h, except for entries 5a and 21 (1 h). [c] Isolated yield. [d] By optical rotation. [e] Tentative assignment; see reference 20.

Scheme 2. Catalytic Enantioselective Hydrogenation of Dehydroamino Acids[a]



13a-c **a:** R = H, R' = H **b:** R = Ph, R' = H **c:** R = Ph, R' = CH_3 **14a-c**

Entry	Educt	Catalyst	T [°C]	Yield[b] [%]	TOF [h^{-1} (s^{-1})]	TON	ee [%]	Config. (**14**)
1	**13a**	($S_{Re}S_C$)-**7**	30	85	2000 (0.56)	170	37	*S*
2	**13b**	($S_{Re}S_C$)-**7**	30	88	850 (0.24)	176	62	*S*
3	**13c**	($S_{Re}S_C$)-**7**	30	91	1600 (0.44)	182	31	*S*
4	**13a**	($S_{Re}R_C$)-**7**	30	90	2300 (0.64)	180	93	*R*
5	**13b**	($S_{Re}R_C$)-**7**	30	88	900 (0.25)	176	94	*R*
6	**13c**	($S_{Re}R_C$)-**7**	30	92	2800 (0.78)	184	97	*R*
7	**13a**	(*S*)-**6**	23	93	1750 (0.49)	186	62	*S*
8	**13b**	(*S*)-**6**	23	86	2970 (0.83)	172	72	*S*
9	**13c**	(*S*)-**6**	23	98	2100 (0.58)	196	65	*S*
10	**13a**	(*S*)-**5**	23	82	280 (0.08)	164	92	*S*
11	**13b**	(*S*)-**5**	23	70	100 (0.03)	140	93	*S*
12	**13c**	(*S*)-**5**	23	94	300 (0.08)	188	88	*S*

[a] Analytical methods are detailed in the Experimental Section. [b] Isolated yield.

Accordingly, reactions were carried out at 24−26 °C with a slight excess of Ph_2SiH_2 and 1 mol % of (*S*)-**5**, (*S*)-**6**, ($S_{Re}S_C$)-**7**, or ($S_{Re}R_C$)-**7**, as summarized in Scheme 1 and Table 1. With entries 5a and 21 (Table 1), NMR analyses showed >95% conversions after 1 h. However, the other hydrosilylations were slower, especially with (*S*)-**5**. However, in all cases conversions reached >95% over 12 h. The ratios of silyl ethers **10a**−**d** to silyl enol ethers **11a**−**d** were nearly always greater than 10:1. After 14−16 h, hydrolytic workups and chromatography gave the alcohols HOCH(Ph)CH_2R (**12a**−**d**) in 83−60% isolated yields. Enantiomeric purities were assayed by chiral HPLC or GLC, as described in the Experimental Section. Entries 5a and 5b illustrate typical levels of reproducibility. The absolute configurations of **12a**−**c** were determined from the signs of the optical rotations.[19,20] Importantly, catalysts with identical relative configurations at rhenium gave alcohols with identical relative (and coincidentally absolute) configurations at carbon.

At 24−26 °C, the catalyst precursor (*S*)-**6**, with only a rhenium stereocenter, gives the highest enantioselectivities (entries 5, 8, 11, and 14). These range from 60% to 63% ee for the simple alkyl-substituted ketones **9a**−**c** to 92% ee for chlorinated ketone **9d**. Interestingly, the diastereomeric phenyl-substituted analogues ($S_{Re}S_C$)-**7** and ($S_{Re}R_C$)-**7** are distinctly inferior. The latter affords ee values (41−62%) that are slightly higher than those of (*S*)-**5** (38−48%). However, ($S_{Re}S_C$)-**7** gives still poorer enantioselection (11−35% ee). These trends are further analyzed in the Discussion. In contrast to the hydrosilylation results, (*S*)-**5** gave higher enantioselectivities than (*S*)-**6** in hydrogenations.[10a]

For the best catalyst, (*S*)-**6**, lower reaction temperatures were investigated. Since the effect upon ee values was of primary interest, reaction times were kept constant. As would be expected, the yields of alcohols **12a**−**d** decreased (compare entries 5−7, 8−10, 11−13, and 14−16). Although many reactions exhibit higher stereoselectivities at lower temperatures, the ee values of **12a**−**d** dropped dramatically (23−42%, −20 to −40 °C). Experiments were also conducted with decreased catalyst loadings. For example, **9a** was reacted as above at 25 °C, but with 0.1 mol % of (*S*)-**6**. NMR analysis after 72 h showed a 58% conversion to **10a** and **11a** (47% conversion to **10a**). This corresponds to a turnover number (TON) of 470, as opposed to 98 in entry 5a of Table 1.

We next tested the new catalyst precursors ($S_{Re}S_C$)-**7** and ($S_{Re}R_C$)-**7** in enantioselective hydrogenations. As shown in Scheme 2, three typical dehydroamino acid derivatives, **13a**−**c**, were selected for screening. Hydrogenations were conducted at 30 °C (entries 1−6) under conditions similar to those reported for (*S*)-**6** and (*S*)-**5** previously (entries 7−12). Turnover frequencies were

(17) (a) Brunner, H. In *Synthetic Methods of Organometallic and Inorganic Chemistry*; Herrmann, W. A., Ed.: Georg Thieme: Stuttgart, New York, 2002; Vol. 10, Chapter 4. (b) The abbreviations "DH" (degree of hydrosilylation, corresponding to total conversion to **10** and **11**) and "CY" (chemical yield, corresponding to conversion to **10**) are often used.

(18) Literature NMR data are as follows. **10a** and **11a**: ref 16a. **10a**,**b**: ref 16b. **11c**: Ojima, I.; Kogure, T. *Organometallics* **1982**, *1*, 1390. The silyl ether **10d** and alcohol **12d** are reported in ref 6d.

(19) MacLeod, R.; Welch, F. J.; Mosher, H. S. *J. Am. Chem. Soc.* **1960**, *82*, 876.

(20) The configuration given for **12d**, which has previously been prepared in high enantiomeric purity,[6d] is provisional and based upon (1) the order of chromatographic elution and (2) the dominant enantiomer obtained for **12a**−**c**.

calculated from the rate of H_2 uptake, which was complete within 0.5 h for entries 1−6. The protected amino acids **14a**−**c** were isolated in 92−85% yields. Enantiomeric purities and absolute configurations were determined as described in the Experimental Section.

Complex ($S_{Re}S_C$)-**7** gave enantioselectivities (37/62/31% ee, entries 1−3) that were much lower than those of (*S*)-**6** (62/72/65% ee, entries 7−9), which lacks the phenyl group and carbon stereocenter. In both cases, *S* enantiomers of **14a**−**c** dominated. Gratifyingly, ($S_{Re}R_C$)-**7** gave enantioselectivities that were much higher (93/94/97% ee, entries 4−6) and exceeded those of (*S*)-**5** (92/93/88% ee, entries 10−12), the previous "record holder" in this series. However, (*S*)-**5** gave *S* enantiomers of **14a**−**c**, whereas ($S_{Re}R_C$)-**7** gave *R* enantiomers. This shows that the relative carbon configurations of **14a**−**c** (and coincidentally the absolute configurations as well) are determined by the relative carbon configurations of ($S_{Re}S_C$)-**7** and ($S_{Re}R_C$)-**7**. Possible implications are analyzed in the Discussion.

Finally, entry 6 of Scheme 2 was repeated, but with lower catalyst loadings. When 0.2 mol % of ($S_{Re}R_C$)-**7** was employed, an 89% yield of **14c** was obtained (96% ee), corresponding to a TON of 435 (H_2 uptake complete within 1 h). When 0.0125 mol % was employed, a 78% yield of **14c** was obtained (98% ee), corresponding to a TON of 6230. However, some **13c** remained (82% conversion). Since H_2 uptake had ceased prior to workup (16 h), this indicates catalyst deactivation.

Discussion

The preceding data establish that the rhodium/rhenium chelate complexes in Figure 1 are effective catalyst precursors for the hydrosilylation of ketones and, presumably, other types of unsaturated organic molecules. The new complexes ($S_{Re}S_C$)-**7** and ($S_{Re}R_C$)-**7** are also, like (*S*)-**5** and (*S*)-**6**,[10] catalyst precursors for the hydrogenation of protected dehydroamino acids, and presumably related systems. Catalyst (*S*)-**5** is somewhat less active, both for hydrogenations (TOF data, Scheme 2) and hydrosilylations.[21] However, the others are qualitatively similar. Therefore, discussion will focus upon trends in the enantioselectivities.

In this regard, we had anticipated that one of the new catalysts ($S_{Re}S_C$)-**7** and ($S_{Re}R_C$)-**7** might function as a "matched" diastereomer and the other as a "mismatched" diastereomer, with respect to the single-stereocenter catalyst (*S*)-**6**. In other words, the carbon stereocenter might be expected to reinforce the product enantiomer favored by the rhenium stereocenter of (*S*)-**6** in one diastereomer and exert an opposite influence in the other. This is clearly not the case with ketone hydrosilylation, as both ($S_{Re}S_C$)-**7** and ($S_{Re}R_C$)-**7** are inferior to (*S*)-**6**. One possible rationale is that the geometry of the configuration-determining step with (*S*)-**6** is greatly altered by the introduction of the phenyl groups. The crystal structure of racemic **6** shows it to be a very congested molecule, the conformation of which might easily be altered by substituents.[10a] However, suitable crystals of ($S_{Re}S_C$)-**7** and ($S_{Re}R_C$)-**7** could not be obtained for comparison.[12]

(21) Such trends sometimes reflect the rate of initiation. See: Börner, A.; Heller, D. *Tetrahedron Lett.* **2001**, *42*, 223.

There are only a few detailed mechanistic studies of ketone hydrosilylations catalyzed by chiral rhodium complexes.[22] Several distinct mechanisms remain consistent with available data, usually with two possible configuration-determining steps. Unfortunately, this renders the basis for enantioselection a matter of speculation and precludes any deeper analysis of our ee trends. Others have observed lower ee values at lower temperature and have interpreted this (with other data) in terms of competing configuration-determining steps.[22a] It also deserves emphasis that structural data for rhodium(I) catalyst precursors are of limited relevance to key intermediates in the catalytic cycle.

The mechanism of hydrogenation of dehydroamino acid derivatives by chiral rhodium diphosphine complexes has been studied in detail, and the configuration-determining steps have been elucidated.[23] With (*S*)-**5** and (*S*)-**6**, the effects of pressure and temperature upon enantioselectivities have been measured.[10a] The data suggest that these are among the many catalysts for which the less stable of two diastereomeric π-C=C adducts is more reactive,[23] and ($S_{Re}S_C$)-**7** and ($S_{Re}R_C$)-**7** are likely similar. With the last two, "matched" and "mismatched" relationships can be read into the ee values, but not in the originally envisioned sense. The catalyst that gives the highest ee values, ($S_{Re}R_C$)-**7**, yields product configurations opposite to those of the other catalysts. Since all catalysts have identical relative configurations at rhenium, the carbon stereocenter in ($S_{Re}R_C$)-**7** can be viewed as configuration-determining. The diastereomeric catalyst ($S_{Re}S_C$)-**7** delivers opposite enantiomers with lower ee values, consistent with a mismatched rhenium configuration that exerts a counteractive influence.

Although such relationships may, in view of the caveats noted above, be coincidental, they provide methodical constructs for the synthesis and testing of new catalysts. There is no simple way to remove the rhenium stereocenters in **7**, as the two-electron donor ligand PPh_3 cannot be replaced by the three-electron-donor ligand NO or vice versa. However, an analogous series of catalysts could be based upon iron or ruthenium templates of the formula (η^5-$C_5H_4PPh_2$)M(L)(L′)($CHRPPh_2$). Here, L/L′ would be two-electron-donor ligands that could be different or equal, allowing catalyst families with all possible combinations of metal and carbon stereocenters. Regardless, it is not in retrospect surprising that the carbon stereocenter in **7**, which is closer to the catalytically active rhodium, exerts a greater influence on the configurations of the hydrogenation products.

Our results can be compared with a variety of literature data, and some chiral ferrocene-based chelate ligands previously employed for rhodium-catalyzed ketone hydrosilylations using Ph_2SiH_2 are given in Figure 2. Ligand **A** represents a large family pioneered by Ito and can give very high enantioselectivities.[6] However, they function as trans-spanning ligands, yielding an entirely different class of catalyst. The

(22) (a) Haag, D.; Runsink, J.; Scharf, H.-D. *Organometallics* **1998**, *17*, 398. (b) See also: Zheng, G. Z.; Chan, T. H. *Organometallics* **1995**, *14*, 70.

(23) (a) Rossen, K. *Angew. Chem., Int. Ed.* **2001**, *40*, 4611; *Angew. Chem.* **2001**, *113*, 4747. (b) Landis, C. R.; Hilfenhaus, P.; Feldgus, S. *J. Am. Chem. Soc.* **1999**, *121*, 8741.

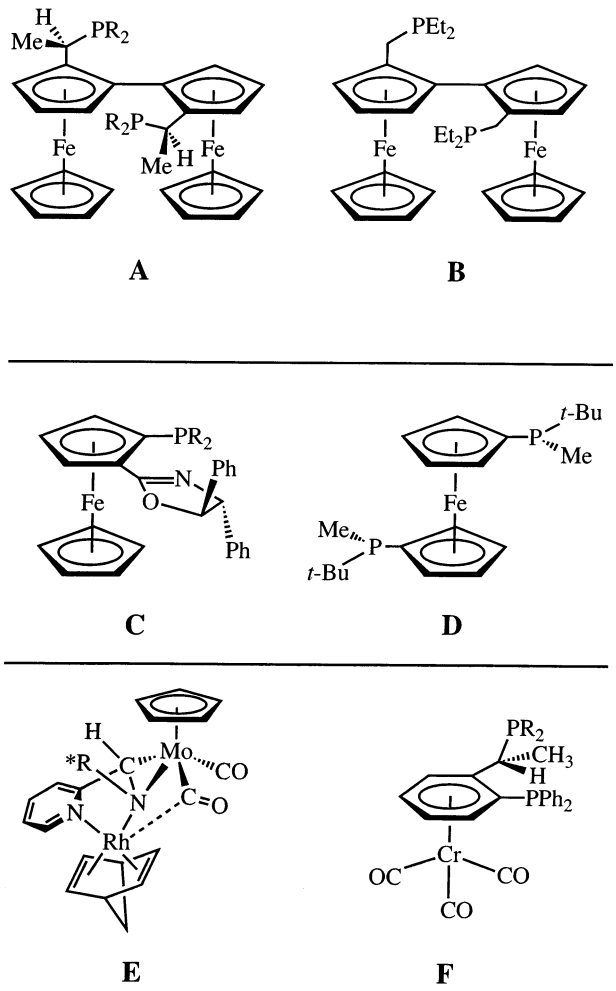


Figure 2. Other relevant chiral ligands or catalysts containing "spectator" transition metals.

related diphosphine **B**, which contains only planar chirality elements, gives alcohols **12a**−**d** in 94%, 88%, 89%, and 88% ee.[6d] The phosphorus/nitrogen donor ligand **C** must give chelates with cis geometries and affords **12a**,**b** in 91% and 23% ee.[7a,b] Curiously, the analogous iridium catalyst gives the opposite enantiomer of **12a** in 96% ee. The chiral-at-phosphorus diphosphine **D** must also give a cis chelate and yields **12a** in 89% ee.[8c]

To our knowledge, there is only one other catalyst for the hydrosilylation of ketones involving a chiral chelate ligand based upon a non-ferrocenylmetal template. The novel rhodium complex **E** (Figure 2) features a molybdenum stereocenter and a carbon stereocenter in the substituent R*.[14] However, enantioselectivities were for some reason quite low. More recently, chiral monodentate ligands containing (arene)chromium tricarbonyl moieties have been used for enantioselective hydrosilylations of alkenes.[24] We also find monophosphine analogues of (*S*)-**5** and (*S*)-**6** to be effective ligands for a variety of metal-catalyzed reactions.[25] To our knowledge, **F** is the only chelate ligand based upon a nonferrocenylmetal template to be used for enantioselective alkene hydrogenation.[26] Rhodium catalysts, generated in situ, converted alkene **13b** (Scheme 2) to **14b** in 66% ee (R = Ph) to 78% ee (R = Cy).

There is also the question of how our results compare with the best enantioselective hydrosilylation and hydrogenation catalysts, irrespective of nature. The catalyst precursor ($S_{Re}R_C$)-**7** gives results quite close to the current art in hydrogenation.[23,27] However, many complexes perform similarly in this crowded field of contestants. Except for ketone **9d**, (*S*)-**6** gives hydrosilylation products with ee values somewhat lower than those of the catalysts described above, as well as other systems.[2a,b,3b] However, in view of the many diversity elements in our catalysts, and the modular and general nature of the syntheses described in the preceding papers,[10a,12] we view these as promising beginnings. For historical calibration, the first test reaction selected for the first ferrocene-based chiral chelating ligand was rhodium-catalyzed ketone hydrosilylation. From the humble initial results (5−49% ee),[8a] many highly enantioselective catalysts have been developed.

Analyses in the preceding papers also show that the rhenium-containing diphosphines and rhodium complexes in Figure 1 can be accessed in comparable numbers of steps and yields as popular ferrocene-containing analogues.[10a,12] Further, the donor atoms are more basic than in the corresponding organic ligands, a feature known to accelerate certain metal-catalyzed reactions. Finally, palladium chelates of (*R*)-**1** and (*S*)-**2** are effective catalyst precursors for enantioselective Heck reactions, although in these cases the ee values are disappointingly low.[11]

In conclusion, this study has extended the application of architecturally novel chiral chelate ligands that feature a non-metallocene "spectator" metal fragment in metal-catalyzed enantioselective organic synthesis. Elegant complementary efforts have been described by other laboratories.[15,26] Future reports will detail extensions to chiral monodentate ligands and bidentate ligands with a multitude of metal-containing spectator units.[28]

Experimental Section

General Data.[13] Benzene and THF were distilled from CaH_2 and Na/O=CPh_2, respectively, and stored under N_2. Ph_2SiH_2 (Fluka, ~97%), acetophenone, propiophenone, and butyrophenone were used as received. The γ-chlorobutyrophenone was protected from light and freshly distilled before use. Protected dehydroamino acids and catalysts were obtained as described previously.[10a,12] Liquid chromatography was conducted on a Thermoquest instrument package (pump/autosampler/detector P4000/AS 3000/UV6000LP). Other general procedures were reported earlier.[10a]

Catalytic Hydrosilylations (Table 1). A glass vial was charged under argon with the ketone **9** (1.00 mmol; typical was entry 8, 0.134 g of **9b**), catalyst (1.0 mol %; entry 8, 0.013 g of (*S*)-**6**), THF (2 mL), and Ph_2SiH_2 (0.221 g, 1.20 mmol) and sealed with a screw cap. The sample was stirred (16 h) at the temperature in Table 1 (23−26 °C, glovebox; −20 to −40 °C, thermostated cooling bath outside of glovebox). In entries where conversions are given, aliquots were removed (1 and/or

(24) Weber, I.; Jones, G. B. *Tetrahedron Lett.* **2001**, *42*, 6983.
(25) Eichenseher, S.; Kromm, K.; Delacroix, O.; Gladysz, J. A. *Chem. Commun.* **2002**, 1046.
(26) Vasen, D.; Salzer, A.; Gerhards, F.; Gais, H.-J.; Stürmer, R.; Bieler, N. H.; Togni, A. *Organometallics* **2000**, *19*, 539.
(27) Tang, W.; Zhang, X. *Angew. Chem., Int. Ed.* **2002**, *41*, 1612; *Angew. Chem.* **2002**, *114*, 1682 and references therein.
(28) Alvey, L. J.; Delacroix, O.; Wallner, C.; Meyer, O.; Hampel, F.; Szafert, S.; Lis, T.; Gladysz, J. A. *Organometallics* **2001**, *20*, 3087.

12 h) and dried by oil pump vacuum (1 h). The residues were dissolved in $CDCl_3$ and ^1H NMR signals of **9** integrated against those of **10** and **11**.[18,29] After 14−16 h, samples were stirred with K_2CO_3-saturated methanol (1 mL, 0.5 h) to generate alcohols **12**. The solvents were removed by oil pump vacuum and the residues chromatographed (silica gel, 8 × 1 cm column, 9:1 v/v hexanes/ethyl acetate) to give pure **12**. Yields (Table 1) were not corrected for any removed aliquots. The alcohols were dissolved in methanol (ca. 0.010 g in 2 mL) and the ee values determined by HPLC (Chiralcel OD with cellulose carbamate on silica gel; 92:8 v/v hexanes/2-propanol (isocratic) for **12a**−**c**, 96:4 v/v hexanes/2-propanol (isocratic) for **12d**). The signs of the optical rotations of **12a**−**c** gave the absolute configuration of the dominant enantiomer.[19,20]

Catalytic Hydrogenations (Scheme 2). A 100 mL flask was charged with **13** (3.00 mmol; typical was entry 5, 0.616 g of **13b**), catalyst (0.50 mol %; entry 5, 0.021 g of ($R_{Re}S_C$)-**7**),[13] and THF (25 mL) and attached to a gas buret. The light orange solution was freeze−pump−thaw degassed. A H_2 atmosphere was introduced, and the solution was vigorously stirred. Within 1 min, H_2 uptake began. TOF values were calculated from rates through 50−60% conversions. After uptake ceased (entry 5, 62 mL, 2.8 mmol; theory, 67 mL), ca. 0.5 mL aliquots were removed for assaying ee values, and the remaining **14** was isolated by a standard workup (entry 5: 0.547 g/2.64 mmol of **14b**, 88%).[30] Aliquots of **14a**,**b** were treated with methanol (2 mL) and ethereal diazomethane (yellow endpoint) to give methyl esters.[31] Aliquots of **14c** were taken to dryness and extracted with ether, and the extracts were filtered through a silica gel plug, concentrated, and passed through a syringe filter. The ester from **14a** was analyzed by GLC (FS-LIPODEX E (octakis(2,6-di-*O*-pentyl-3-*O*-butyryl)-γ-cyclodextrin on fused silica gel, 25 × 0.25 glass capillary column, 130 °C, N_2 carrier flow 20 mL min^{-1}, split flow 38 mL min^{-1}, split ratio 1:25). The esters from **14b**,**c** were analyzed by HPLC (Chiralcel OD with cellulose carbamate on silica gel; 98:2 v/v isohexane/2-propanol (isocratic)). Product configurations were assigned by comparison to the retention times of samples characterized earlier.[10a]

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(29) ^1H NMR (400 MHz, $CDCl_3$):[18] (a) **9a** at δ 2.40 (s, CH_3), **10a** at δ 5.40 (s, SiH), 4.99 (q, J = 7 Hz, OCH), and 1.50 (d, J = 7 Hz, CH_3), **11a** at δ 5.62 (s, SiH), 4.92 (d, J = 3 Hz, =C*H*H′), and 4.54 (d, J = 3 Hz, =CH*H*′); (b) **9b** at δ 2.95 (q, J = 7 Hz, CH_2) and 1.18 (t, J = 7 Hz, CH_3), **10b** at δ 5.35 (s, SiH), 4.60 (t, J = 6 Hz, OCH), 1.78 (m, CH_2), and 0.84 (t, J = 7 Hz, CH_3), **11b** at δ 5.55 (s, SiH), 4.52 (q, J = 7 Hz, =CH), and 1.85 (d, J = 7 Hz, CH_3); (c) **9c** at δ 3.02 (t, J = 7 Hz, C(O)-CH_2), 1.87 (m, CH_2), and 1.10 (t, J = 7 Hz, CH_3), **10c** at δ 5.47 (s, SiH), 4.88 (dd, J = 7, 5 Hz, CH), 1.96−1.76 (m, CH_2), 1.52−1.35 (m, CH_2), and 0.95 (t, J = 7 Hz, CH_3), **11c** at δ 5.60 (s, SiH), 4.76 (dd, J = 7, 5 Hz, =CH), 2.00 (m, CH_2), and 1.02 (t, J = 7 Hz, CH_3); (d) **9d** at δ 3.64 (t, J = 6 Hz, C(O)CH_2), 3.14 (m, J = 7 Hz, CH_2Cl), and 2.19 (quint, J = 6 Hz, CH_2), **10d** at δ 5.25 (s, SiH), 4.72 (dd, J = 4, 3 Hz, CH), 3.38 (m, OCHC*H*$_2$), and 1.92−1.68 (m, $2CH_2$), **11d** at δ 5.52 (s, SiH), 4.64 (t, J = 6 Hz, =CH), and 1.75−1.65 (m, $2CH_2$), **12d** at δ 4.69 (t, J = 5 Hz, OCH), 3.55 (m, CH_2Cl), and 1.92−1.82 (m, $2CH_2$).

(30) Riley, D. P.; Shumate, R. E. *J. Org. Chem.* **1980**, *45*, 5187.

(31) The solvent was removed under vacuum, the residue was extracted with ether, and the extract was filtered through a silica gel plug. The solvent was removed from the filtrate, the residue extracted with ether (**14a**) or methanol (**14b**), and the extract passed through a syringe filter.