J|A|C|S
COMMUNICATIONS

Published on Web 06/07/2002

Kinetic and Thermodynamic Preferences for the Diastereoselective Oxidative Addition of H_2 to *trans*-Ir(P*R_3)$_2$(CO)Cl: Monodentate Chiral Phosphines May Impart Exceptional Degrees of Diastereoselectivity

Jun Ho Shin and Gerard Parkin*

Department of Chemistry, Columbia University, New York, New York 10027

Received February 28, 2002; Revised Manuscript Received April 24, 2002

Oxidative addition of dihydrogen is a crucial step in transition-metal-catalyzed reactions involving H_2. Olefin hydrogenation is one such reaction, and the asymmetric version catalyzed by chiral rhodium−phosphine complexes has experienced considerable commercial impact, as exemplified by Monsanto's synthesis of L-DOPA.[1,2] A particularly interesting feature of these asymmetric rhodium-catalyzed reactions is that the selectivity is counter to the preference of the catalyst to bind to a particular face of the prochiral olefin,[1,3,4] such that the reactions have been proposed to occur by an "anti-lock-and-key" mechanism.[4b] Oxidative addition of H_2 is generally recognized to be the rate-determining and enantiomer-determining step in these reactions,[4] and the selectivity is therefore dictated by the dramatically enhanced reactivity of H_2 towards the minor component olefin adduct. To account for the overall selectivity, the susceptibility of the diastereomeric adducts towards oxidative addition of H_2 has been estimated to differ by a substantial factor of ca. 600 in rate constant.[4a] However, well-defined examples of oxidative addition of H_2 that exhibit selectivity of this magnitude are unprecedented. In this paper, we provide the first report that chiral *mono*phosphine ligands are capable of imparting a high degree of diastereoselectivity in the oxidative addition of H_2 to a metal center and that the selectivity exceeds that for certain bidentate phosphine ligands.

The reaction of H_2 with Vaska's complex, *trans*-Ir(PPh_3)$_2$(CO)Cl, is the classic example of oxidative addition. Vaska-type complexes, therefore, provide an excellent system to determine the ability of chiral phosphine ligands to impart diastereoselectivity in the oxidative addition of H_2. For this purpose, we have employed the monodentate chiral phosphines PhP[(C$_5$Me$_4$)]$_2$,[5] PhP[Me$_2$C$_4$H$_6$],[6] and PhP[Pr$^i_2$C$_4$H$_6$][7] (Scheme 1).

Trans-Ir(P*R_3)$_2$(CO)Cl derived from racemic P*R_3 consists of a pair of *R*,*S* and *R*,*R*/*S*,*S* diastereomers,[8] and oxidative addition of H_2 to this mixture yields *three* diastereomers (one of which exists as an enantiomeric pair). The formation of three diastereomers from a mixture composed of two diastereomers is a consequence of oxidative addition of H_2 to the *meso* isomer, (*R*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)Cl, resulting in a structure in which the iridium is a "pseudoasymmetric center".[9] The term "pseudoasymmetric center" is used to describe a stereogenic center in an achiral molecule, and is given the notation *r* or *s*. Thus, the two diastereomers derived from addition of H_2 to (*R*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)Cl may be classified as *R*,*r*,*S* and *R*,*s*,*S*, differing only in the configuration at iridium (Scheme 1).[10]

Significantly, the barriers to both oxidative addition and reductive elimination are highly dependent upon the diastereomer under consideration, as illustrated in Figure 1.[11] Of most interest, there is a significant difference in the barrier for oxidative addition of H_2 to the two faces of the *meso* isomer, (*R*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)Cl. For example, the rate constant for oxidative addition of H_2 to one face of (*R*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)Cl (P*R_3 = PhP[Pr$^i_2$C$_4$H$_6$]) is a factor of at least ∼60 greater than that to the other face.[12] However, despite the extreme kinetic selectivity, the kinetically favored product is *not* the thermodynamic product, and the kinetic product transforms to a 1:3 equilibrium mixture with the thermodynamic product over a period of days (as illustrated in Figure 1 for PhP[(C$_5$Me$_4$)]$_2$).[13] The kinetics of reductive elimination of H_2 from the (*R*,*r*,*S*)- and (*R*,*s*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)ClH_2 diastereomers exhibit even greater differences than those for the oxidative addition (Figure 2). Thus, the rate constants for reductive elimination of H_2 from the *R*,*r*,*S* and *R*,*s*,*S* diastereomers of *trans*-Ir(P*R_3)$_2$(CO)ClH_2 (P*R_3 = PhP[Pr$^i_2$C$_4$H$_6$]) differ by a factor of ∼170.[11,14]

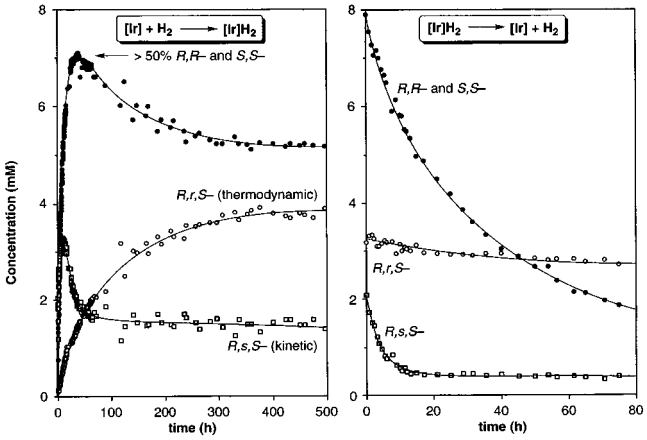
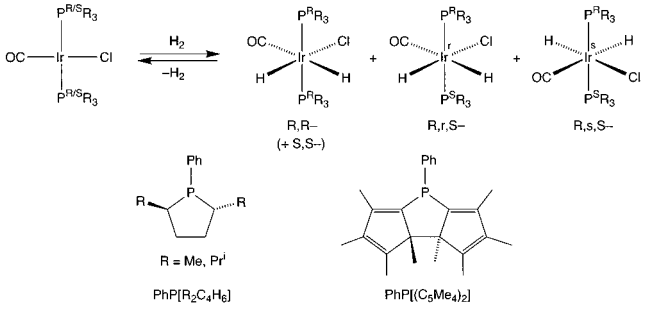


Figure 1. Kinetics plots for oxidative addition of H_2 to *trans*-Ir(P*R_3)$_2$(CO)Cl and reductive elimination from *trans*-Ir(P*R_3)$_2$(CO)ClH_2 (P*R_3 = PhP[(C$_5$Me$_4$)]$_2$).

Scheme 1



* To whom correspondence should be addressed. E-mail: parkin@chem.columbia.edu.

10.1021/ja026059i CCC: $22.00

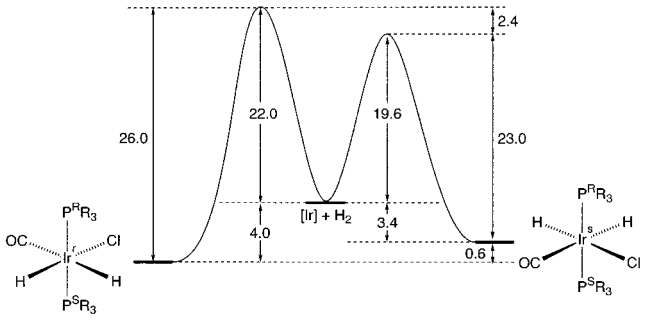


Figure 2. Free energy surface for addition of H_2 to the two faces of (*R*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)Cl (P*R_3 = PhP[Pr$^i_2$$C_4H_6$]). Values in kcal mol^{-1} at 300 K and the *r*/*s* configuration is arbitrary.

The extremely high kinetic facial selectivity for oxidative addition of H_2 observed here contrasts markedly with the selectivity that has been observed previously for related square planar Vaska-type complexes that employ bidentate chiral phosphine ligands. For example, oxidative addition of H_2 to *cis*-Ir(chiraphos)(CO)Br yields a 2.1:1 mixture of diastereomers,[15] while the corresponding reaction of [(*S*)-binap]Ir(PPh$_3$)Cl gives a 1:1 mixture of diastereomers.[16] Thus, chiral *mono*phosphine ligands are capable of achieving a kinetic diastereoselectivity which greatly exceeds that of certain bidentate phosphine ligands.

In light of previous studies on iridium complexes, it is also significant that the kinetic and thermodynamic products of oxidative addition of H_2 to (*R*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)Cl are different. For example, Eisenberg has noted that the kinetic and thermodynamic products for oxidative addition of H_2 to the two faces of *cis*-Ir(chiraphos)(CO)Br are the same.[15,17] Furthermore, Landis has also observed that the kinetic and thermodynamic diastereomers for oxidative addition of H_2 to a series of [Ir(bisphosphine)(1,5-COD)]$^+$ complexes to give [Ir(bisphosphine)(1,5-COD)H$_2$]$^+$ are generally the same; only for [Ir(chiraphos)(1,5-COD)]$^+$ are the kinetic (1.8:1) and thermodynamic (1:6.1) selectivities of H_2 addition inverted.[18] The kinetic diastereoselectivity for the monodentate phosphine systems reported here (~60:1 for P*R_3 = PhP[Pr$^i_2$$C_4H_6$]), thus greatly rivals the one other system, namely [Ir(chiraphos)(1,5-COD)]$^+$ (1.8:1), for which the kinetic and thermodynamic products of oxidative addition are different.[19] The favorable kinetic discrimination that (*R*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)Cl exhibits towards a molecule as small as H_2 thus bodes well for further applications of chiral monodentate phosphine ligands in asymmetric catalysis, an area that has been neglected by comparison to the use of multidentate phosphine ligands, until recently.[20]

In conclusion, the oxidative addition of H_2 to the two faces of the *meso* isomer (*R*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)Cl proceeds with a high degree of kinetic diastereoselectivity, thus demonstrating that monodentate phosphine ligands are capable of providing an effective kinetic discrimination for a substrate as small as H_2. However, (i) the kinetically favored dihydride complex is *not* favored thermodynamically, and (ii) the kinetic discrimination is significantly greater than the thermodynamic discrimination. The magnitude of the inversion of the kinetic and thermodynamic selectivities is greater than has previously been experimentally observed for other iridium complexes of bidentate phosphine ligands. Considering the small size of the H_2 reactant, these observations underscore the importance of not assuming that the energies of diastereomeric intermediates reflect the energies of related diastereomeric transition states in asymmetric transformations.

Acknowledgment. We thank the U. S. Department of Energy, Office of Basic Energy Sciences (DE-FG02-93ER14339) for support of this research, and Nicholas Johnson (Chirotech Technology Ltd.) for a gift of (3*R*,6*R*)- and (3*S*,6*S*)-(2,7-dimethyloctane-3,6-diol) used in the preparation of PhP[Pr$^i_2$$C_4H_6$].

Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Knowles, W. S. *J. Chem. Educ.* **1986**, *63*, 222−225.
(2) Burk, M. J. *Acc. Chem. Res.* **2000**, *33*, 363−372.
(3) Brown, J. M. *Hydrogenation of Functionalized Carbon-Carbon Double Bonds*; Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 1, pp 119−182.
(4) (a) Landis, C. R.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 9, 1746−1754. (b) Feldgus, S.; Landis, C. R. *J. Am. Chem. Soc.* **2000**, *122*, 12714−12727.
(5) Shin, J. H.; Bridgewater, B. M.; Churchill, D. G.; Parkin, G. *Inorg. Chem.* **2001**, *40*, 5626−5635.
(6) Burk, M. J.; Feaster, J. E.; Harlow, R. L. *Organometallics* **1990**, *9*, 2653−2655.
(7) Burk, M. J.; Feaster, J. E.; Nugent, W. A.; Harlow, R. L. *J. Am. Chem. Soc.* **1993**, *115*, 10125−10138.
(8) For brevity, we use *R* and *S* nomenclature to describe the enantiomers of P*R_3 although the chirality is due to the configuration of two stereogenic carbon centers.
(9) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley-Interscience: New York, 1994; pp 123−124.
(10) The designator (*R*,*r*,*S*)- is arbitrarily assigned to the thermodynamically more stable of the two isomers.
(11) Rate and equilibrium constant data at 300 K for PhP[Pr$^i_2$$C_4H_6$] derivatives: $k_{RR} = k_{SS} = 1.0(1) \times 10^{-2}$ M^{-1} s^{-1}, $k_{RrS} = 6.0(3) \times 10^{-4}$ M^{-1} s^{-1}, $k_{RsS} = 3.5(4) \times 10^{-2}$ M^{-1} s^{-1}; $k_{-RR} = 8.3(2) \times 10^{-6}$ s^{-1}, $k_{-RrS} = 7.0(2) \times 10^{-7}$ s^{-1}, $k_{-RsS} = 1.2(1) \times 10^{-4}$ s^{-1}; $K_{RR} = K_{SS} = 1.2(1) \times 10^3$ M^{-1}, $K_{RrS} = 8.6(2) \times 10^2$ M^{-1}, $K_{RsS} = 2.9(1) \times 10^2$ M^{-1}. See Supporting Information for data for other derivatives.
(12) One outcome of the markedly different rates of oxidative addition is that the combined amount of (*R*,*R*)- and (*S*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)ClH$_2$ isomers formed at the point at which H_2 uptake is complete *exceeds* the amount of (*R*,*R*)- and (*S*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)Cl present initially due to phosphine exchange between the square planar isomers. However, it should be noted that the rate of oxidative addition is not influenced by addition of P*R_3, consistent with the notion that reaction with H_2 occurs with the square planar complex.
(13) The oxidative addition of H_2 to *trans*-Ir(P*R_3)$_2$(CO)Cl (P*R_3 = PhP[(C$_5$Me$_4$)]$_2$) is characterized by an inverse equilibrium isotope effect, with $K_H/K_D = 0.55$ at 300 K. For other examples of such isotope effects, see: Hascall, T.; Rabinovich, D.; Murphy, V. J.; Beachy, M. D.; Friesner, R. A.; Parkin, G. *J. Am. Chem. Soc.* **1999**, *121*, 11402−11417.
(14) It should be noted that the observed rate constants for the slow elimination of H_2 from the thermodynamically favored (*R*,*r*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)ClH$_2$ isomers correspond to an upper limit. Specifically, it is possible that the reductive elimination from (*R*,*r*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)ClH$_2$ is so slow that it occurs by an alternative mechanism. For example, loss of H_2 from (*R*,*r*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)ClH$_2$ could be catalyzed by isomerization to (*R*,*s*,*S*)-*trans*-Ir(P*R_3)$_2$(CO)ClH$_2$ (possibly involving P*R_3 dissociation). Alternatively, reductive elimination could be facilitated by bimolecular dihydride transfer to four coordinate Ir(P*R_3)$_2$(CO)Cl. See, for example: Kunin, A. J.; Johnson, C. E.; Maguire, J. A.; Jones, W. D.; Eisenberg, R. *J. Am. Chem. Soc.* **1987**, *109*, 2963−2968.
(15) Kunin, A. J.; Farid, R.; Johnson, C. E.; Eisenberg, R. *J. Am. Chem. Soc.* **1985**, *107*, 5315−5317.
(16) Tani, K.; Nakajima, K.; Iseki, A.; Yamagata, T. *Chem. Commun.* **2001**, 1630−1631.
(17) It should be noted that high geometric (i.e., *nonfacial*) diastereoselectivities for oxidative addition of H_2 parallel to the P−Ir−Br and P−Ir−CO bonds of *cis*-Ir(chiraphos)(CO)Br have been observed, and that the kinetic and thermodynamic selectivities for these two modes of addition are inverted (ref 15).
(18) Kimmich, B. F. M.; Somsook, E.; Landis, C. R. *J. Am. Chem. Soc.* **1998**, *120*, 10115−10125.
(19) High kinetic selectivities were obtained for (*R*,*R*)-Me-DuPhos (47:1), (*R*)-BINAP (>50:1), and (*R*)-Tol-BINAP (>50:1), but the kinetic and thermodynamic products are the same in these cases. See ref 18.
(20) (a) Lagasse, F.; Kagan, H. B. *Chem. Pharm. Bull.* **2000**, *48*, 315−324. (b) Komarov, I. V.; Börner, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 1197−1200. (c) Hayashi, T. *Acc. Chem. Res.* **2000**, *33*, 354−362.

JA026059I