J|A|C|S
ARTICLES
Published on Web 04/09/2004

Reversal of Enantioselectivity in the Hydroformylation of Styrene with [2*S*,4*S*-BDPP]Pt($SnCl_3$)Cl at High Temperature Arises from a Change in the Enantioselective-Determining Step

Charles P. Casey,* Susie C. Martins, and Maureen A. Fagan†

Contribution from the Department of Chemistry, University of Wisconsin-Madison, Madison, Wisconsin 53706

Received December 19, 2003; E-mail: casey@chem.wisc.edu

Abstract: Deuterioformylation of styrene catalyzed by [(2*S*,4*S*)-BDPP]Pt($SnCl_3$)Cl at 39 °C gave 3-phenylpropanal (**3**) and 2-phenylpropanal (**2**) (*n*:*i* = 1.8, 71% ee (*S*)-**2**) with deuterium only β to the aldehyde carbonyl and in the formyl group. Small amounts of deuterium were also found in the internal (2.8%), *cis* terminal (1.4%), and *trans* terminal (1.3%) vinyl positions of the recovered styrene. Deuterioformylation of styrene at 98 °C gave 3- (**3**) and 2-phenylpropanal (**2**) (*n*:*i* = 2.3, 10% ee (*R*)-**2**) with deuterium both α and β to the aldehyde carbonyl and in the formyl group. Deuterium was also found in the internal (20%), *cis* terminal (12%), and *trans* terminal (12%) vinyl positions of the recovered styrene. These deuterioformylation results establish that platinum hydride addition to styrene is largely irreversible at 39 °C but reversible at 98 °C. Hydroformylation of (*E*)- and (*Z*)-β-deuteriostyrene at 40 °C, followed by oxidation of the aldehydes to acids, and subsequent derivitization to the (*S*)-mandelate esters confirmed that 84% of 2-phenylpropanal (**2**) arises from platinum hydride addition to the *si*-face of styrene, while 73% of 3-phenylpropanal (**3**) arises from platinum hydride addition to the *re*-face of styrene. At 100 °C, the effect of variable H_2 and CO pressure on *n*:*i*, % ee, and TOF of hydroformylation of styrene was investigated. The results are consistent with enantioselectivity not being fully determined until the final hydrogenolysis of a platinum acyl intermediate.

Introduction

Asymmetric hydroformylation has great utility in the synthesis of optically active substrates.[1] Styrene and its derivatives are important substrates for hydroformylation because oxidation of the resulting optically active aldehydes to 2-arylpropionic acids yields pharmacologically active, anti-inflammatory analgesics such as ibuprofen, ketoprofen, and naproxen.[2] A number of interesting systems for regio- and enantioselective styrene hydroformylation have been developed.[3−6] While excellent progress has been made in finding better catalytic systems, there remains a lack of a fundamental understanding of when and how regioselectivity and enantioselectivity are being controlled. The factors which control selectivity are clearly subtle and vary from one system to another.

Kollár reported a very interesting Pt-catalyzed hydroformylation of styrene in which a change from *S*- to *R*-enantioselectivity was seen as a function of temperature: catalysis by [(2*S*,4*S*)-BDPP]Pt($SnCl_3$)Cl [BDPP = 2,4-bis(diphenylphosphino)pentane] gave the branched aldehyde **2** with 64% ee *S* at 40 °C but 17% ee *R* at 100 °C.[7,8] This highlights the complexity in the mechanism of styrene enantioselective hydroformylation. While Kollár[7] proposed that the reversal of enantioselectivity might be due to a temperature-dependent change in the conformation of the catalyst's six-membered chelate ring,[9] we thought it was more likely that the step in which enantioselectivity is set changed with temperature. According to the proposed mechanism for platinum-catalyzed hydroformylation (Scheme 1),[10,11] the regio- and stereochemistry of the aldehyde products

† Present address: Department of Chemistry, Smith College, Northampton, MA 01063.

(1) For recent reviews, see: (a) Bohnen, H.; Cornils, B. *Adv. Catal.* **2002**, *47*, 1. (b) Breit, B.; Seiche, W. *Synthesis* **2001**, *1*, 1. (c) Eilbracht, P.; Bärfacker, L.; Buss, C.; Hollmann, C.; Kitsos-Rzychon, B. E.; Kranemann, C. L.; Rische, T.; Roggenbuck, R.; Schmidt, A. *Chem. Rev.* **1999**, *99*, 3329. (d) Beller, M.; Cornils, B.; Frohning, C. D.; Kohlpaintner, C. W. *J. Mol. Catal.* **1995**, *104*, 17. (e) Agbossou, F.; Carpentier, J. F.; Mortreux, A. *Chem. Rev.* **1995**, *95*, 2485. (f) Gladiali, S.; Bayon, J. C.; Claver, C. *Tetrahedron: Asymmetry* **1995**, *6*, 1453. (g) Botteghi, C.; Paganelli, S.; Schoinato, A.; Marchetti, M. *Chirality* **1991**, *3*, 355. (h) Consiglio, G.; Pino, P. *Top. Curr. Chem.* **1982**, *105*, 77.

(2) (a) Nugent, W. A.; RajanBabu, T. V.; Burk, M. J. *Science* **1993**, *259*, 479. (b) Rieu, J.-P.; Boucherle, A.; Cousse, H.; Mouzin, G. *Tetrahedron* **1986**, *42*, 4095. (c) Harrison, I. T.; Lewis, B.; Nelson, P.; Rooks, W.; Roxzkowski, A.; Tomolonis, A.; Fried, J. H. *J. Med. Chem.* **1970**, *13*, 203.

(3) Babin, J. E.; Whiteker, G. T. (Union Carbide Chemicals and Plastics Technology Corp., USA). US 5360938 A, 1994.

(4) Buisman, G. J. H.; Kramer, P. C. J.; van Leeuwen, P. W. N. M. *Tetrahedron: Asymmetry* **1993**, *4*, 1625.

(5) RajanBabu, T. V.; Ayers, T. A. *Tetrahedron Lett.* **1994**, *35*, 4295.

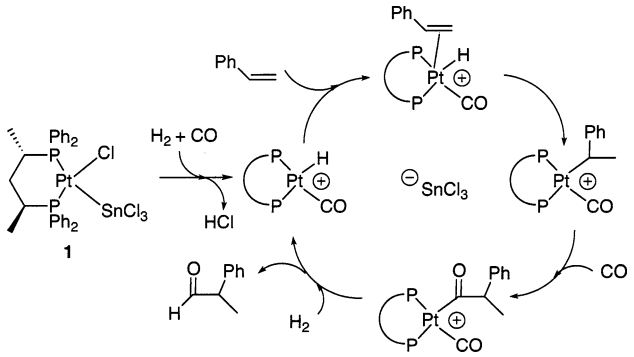
(6) Sakai, N.; Mano, S.; Nozaki, K.; Takaya, H. *J. Am. Chem. Soc.* **1993**, *115*, 7033.

(7) Kollár, L.; Bakos, J.; Tóth, I.; Heil, B. *J. Organomet. Chem.* **1988**, *350*, 277.

(8) Similar reversals of enantioselectivity upon increasing the temperature in the hydroformylation of styrene have been seen with PtCl($SnCl_3$)BINAP [BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl] and PtCl($SnCl_3$)-DIOP [DIOP = 2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane]. (a) Kollár, L.; Sándor, P.; Szalontai, G. *J. Mol. Catal.* **1991**, *67*, 191. (b) Haelg, P.; Consiglio, G.; Pino, P. *J. Organomet. Chem.* **1985**, *296*, 281.

(9) Bosnich reported that chelating diphosphines such as 2,4-bis(diphenylphosphino)pentane and 1,3-bis(diphenylphosphino)butane can adopt various conformations. They attribute the generation of an achiral ligand conformation in the hydrogenation of amino acids to reduced enantioselectivity. MacNeil, P. A.; Roberts, N. K.; Bosnich, B. *J. Am. Chem. Soc.* **1981**, *103*, 2273.

Scheme 1. Simplified Mechanism for Styrene Hydroformylation with [2*S*,4*S*-BDPP]Pt($SnCl_3$)Cl Catalyst



may be set at any one of four stages: (1) irreversible alkene coordination to platinum, (2) reversible alkene coordination followed by irreversible platinum hydride addition to form a platinum alkyl complex, (3) reversible platinum alkyl formation followed by irreversible alkyl migration to CO to form a platinum acyl complex, or (4) reversible platinum acyl formation followed by irreversible platinum acyl hydrogenolysis to yield the aldehyde and regenerate the active platinum hydride, as shown in Scheme 1.

Here, we report deuterioformylation studies and the CO and H_2 pressure dependence of enantioselectivity which show that at low temperature, enantioselectivity is set by largely irreversible platinum hydride addition to styrene, but at high temperature, platinum hydride addition is reversible and enantioselectivity is set by a combination of partially reversible alkyl migration to CO and hydrogenolysis of the platinum acyl intermediate.

Experimental Section

Hydroformylation of Styrene at Variable Pressures of H_2 and CO. Hydroformylations were performed in a 25 mL stainless steel Parr reactor equipped with a magnetic drive stirrer, a Parr 4842 thermocouple, and a ReactIR SiComp cell. Each hydroformylation experiment was performed using octane (0.1 g; 0.875 mmol) as an internal standard for GC analysis. The reactor containing catalyst **1** (20 mg; 0.022 mmol), toluene (6.0 mL), and octane was sealed under 1 atm of N_2. The reactor was then heated to the appropriate temperature, and then pressurized with the respective pressures of CO and H_2. Styrene (1.50 g; 14.4 mmol) was then added via a stainless steel addition funnel by overpressurizing with N_2. Aldehyde formation was monitored at 1730 cm^{-1} using a ASI ReactIR 1000. When it appeared that the absorbance of the aldehyde leveled out, the reaction was stopped; the reactor was slowly vented and then cooled to room temperature. The average pressure loss during the reactions was ~250 psi of synthesis gas. The sample was then analyzed by GC and ^1H NMR spectroscopy. Gas chromatography was performed using a Supelco β-Dex (β-cyclodextrin) 250 chiral capillary column on a Hewlett-Packard 5890A gas chromatograph connected to an HP3390A integrator. The GC flow rate was set to 75 mL/min N_2, an initial temperature of 100 °C (13 min) followed by ramping 30 °C/min to 210 °C. Typical retention times were as follows: 2.20 min octane, 2.39 min toluene, 3.08 min ethylbenzene, 3.58 min styrene, 12.48 min (*R*)-2-phenylpropanal, 12.70 min (*S*)-2-phenylpropanal, and 15.24 min 3-phenylpropanal. The response factors (calculated by correlating the moles of internal standard to its corresponding peak area) for ethylbenzene (1.15), styrene (1.06), 2-phenylpropanal (1.02), and 3-phenylpropanal (1.07) were calibrated relative to octane using standards of commercial samples.

Results

Hydroformylation of Styrene at 40 °C. The hydroformylation of styrene catalyzed by [(2*S*,4*S*)-BDPP]Pt($SnCl_3$)Cl (**1**) was performed at 40 °C with 1000 psi of an analyzed 1:1 mixture of H_2:CO to confirm Kollár's earlier results[7] and to establish a reference for deuterioformylation studies under our experimental conditions. After 5% conversion of styrene, chiral GC analysis showed formation of 3-phenylpropanal (**3**) and 2-phenylpropanal (**2**) [$n{:}i = 2.2$ and 60% ee (*S*)-2-phenylpropanal (**2**-(*S*))]. Under similar reaction conditions, Kollár found $n{:}i = 1.35$ and 64% ee **2**-(*S*)[12] (Scheme 2).

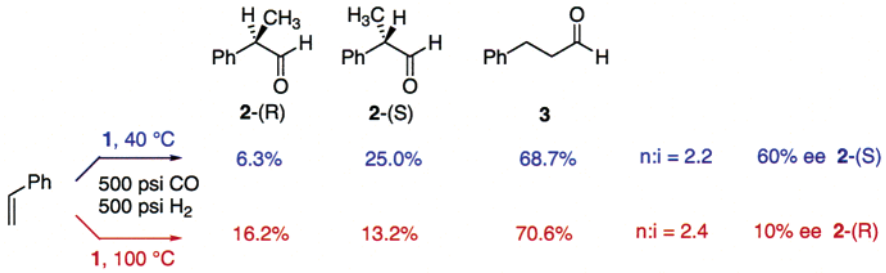
Deuterioformylation of Styrene at 39 °C. To determine whether platinum hydride addition to coordinated styrene is reversible, a deuterioformylation experiment was conducted. If hydride addition is irreversible, deuterium will be incorporated

(10) The exact coordination environments of the platinum hydride, alkyl, and acyl complexes are unknown.

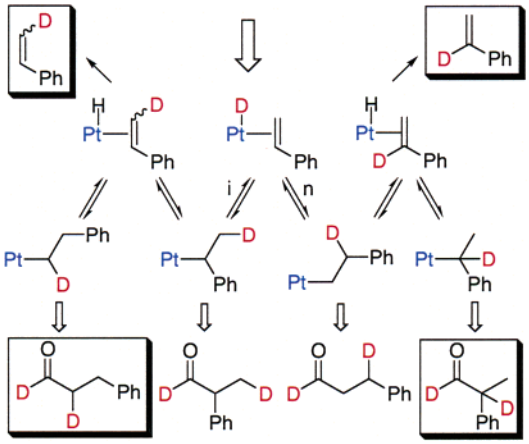
(11) References for the use of Pt−$SnCl_2$ catalysts in hydroformylation, see: (a) Fernandez, D.; Garcia-Seijo, M. I.; Kegl, T.; Petocz, G.; Kollár, L.; Garcia-Fernandez, M. E. *Inorg. Chem.* **2002**, *41*, 4435. (b) Foca, C. M.; dos Santos, E. N.; Gusevskaya, E. V. *J. Mol. Catal. A* **2002**, *185*, 17. (c) van der Veen, L. A.; Keevan, P. K.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Dalton* **2000**, *13*, 2105. (d) Gusevskaya, E. V.; dos Santos, E. N.; Augusti, R.; Dias, A. d. O.; Foca, C. M. *J. Mol. Catal. A* **2000**, *152*, 15. (e) Ellis, D. D.; Harrison, G.; Orpen, A. G.; Phetmung, H.; Pringle, P. G.; deVries, J. G.; Oevering, H. *Dalton* **2000**, *5*, 671. (f) van der Veen, L. A.; Keevan, P. K.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Chem. Commun.* **2000**, *5*, 333. (g) Meessen, P.; Vogt, D.; Keim, W. *J. Organomet. Chem.* **1998**, *551*, 165. (h) Gladiali, S.; Fabbri, D.; Kollár, L. *J. Organomet. Chem.* **1995**, *491*, 91. (i) Ancillotti, F.; Lami, M.; Marchionna, M. *J. Mol. Catal.* **1991**, *66*, 37. (j) Consiglio, G.; Nefkens, S. C. A.; Borer, A. *Organometallics* **1991**, *10*, 2046. (k) Ancillotti, F.; Lami, M.; Marchionna, M. *J. Mol. Catal.* **1990**, *63*, 15. (l) Muller, G.; Sainz, D.; Sales, J. *J. Mol. Catal.* **1990**, *63*, 173. (m) Consiglio, G.; Nefkens, S. C. A. *Tetrahedron: Asymmetry* **1990**, *1*, 417. (n) Ancillotti, F.; Lami, M.; Marchionna, M. *J. Mol. Catal.* **1990**, *58*, 331. (o) Kollár, L.; Bakos, J.; Heil, B.; Sandor, P.; Szalontai, G. *J. Organomet. Chem.* **1990**, *385*, 147. (p) Ancillotti, F.; Lami, M.; Marchionna, M. *J. Mol. Catal.* **1990**, *58*, 345. (q) Scrivanti, A.; Paganelli, S.; Matteoli, U.; Botteghi, C. *J. Organomet. Chem.* **1990**, *385*, 439. (r) Mutez, S.; Paumard, E.; Morteux, A.; Petit, F. *Tetrahedron Lett.* **1989**, *30*, 5759. (s) Kollár, L.; Consiglio, G.; Pino, P. *J. Organomet. Chem.* **1987**, *330*, 305. (t) Moretti, G.; Botteghi, C.; Toniolo, L. *J. Mol. Catal.* **1987**, *39*, 177. (u) Consiglio, G.; Morandini, F.; Scalone, M.; Pino, P. *J. Organomet. Chem.* **1985**, *279*, 193. (v) Clark, H. C.; Jain, V. K.; Rao, G. S. *J. Organomet. Chem.* **1985**, *279*, 181. (w) Cavinato, G.; Toniolo, L. *J. Organomet. Chem.* **1983**, *241*, 275. (x) Tang, S.; Kim, L. *J. Mol. Catal.* **1982**, *14*, 231. (y) Hayashi, T.; Kawabata, Y.; Isoyama, T.; Ogata, I. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3438. (z) Clark, H. C.; Davies, J. A. *J. Organomet. Chem.* **1981**, *213*, 503. (aa) Kawabata, Y.; Hayashi, T.; Ogata, I. *J. Chem. Soc., Chem. Commun.* **1979**, *10*, 462. (ab) Consiglio, G.; Pino, P. *Helv. Chim. Acta* **1976**, *59*, 642 and references therein. For references specifically dealing with the study of reaction intermediates in the hydroformylation of Pt−$SnCl_2$ catalysts, see: (a) Scrivanti, A.; Zeggio, S.; Beghetto, V.; Matteoli, U. *J. Mol. Catal. A* **1995**, *101*, 217. (b) Cavinato, G.; Munno, G. De; Lami, M.; Marchionna, M.; Toniolo, L.; Viterbo, D. *J. Organomet. Chem.* **1994**, *466*, 277. (c) Gomez, M.; Muller, G.; Sainz, D.; Sales, J.; Solans, X. *Organometallics* **1991**, *10*, 4036. (d) Graziani, R.; Cavinato, G.; Casellato, U.; Toniolo, L. *J. Organomet. Chem.* **1988**, *353*, 125. (e) Scrivanti, A.; Botteghi, C.; Toniolo, L.; Berton, A. *J. Organomet. Chem.* **1988**, *344*, 261. (f) Scrivanti, A.; Berton, A.; Toniolo, L.; Botteghi, C. *J. Organomet. Chem.* **1986**, *314*, 369. (g) Scrivanti, A.; Cavinato, G.; Toniolo, L.; Botteghi, C. *J. Organomet. Chem.* **1985**, *286*, 115. (h) Bardi, R.; Piazzesi, A. M.; Cavinato, G.; Cavoli, P.; Toniolo, L. *J. Organomet. Chem.* **1982**, *224*, 407 and references therein. For references with the role of $SnCl_2$ in Pt−$SnCl_2$ hydroformylation catalysts, see: (a) Rocha, W. R.; De Almeida, W. B. *Int. J. Quantum Chem.* **1997**, *65*, 643. (b) Kollár, L.; Kegl, T.; Bakos, J. *J. Organomet. Chem.* **1993**, *453*, 155. (c) Kollár, K.; Sandor, P.; Szalontai, G.; Heil, B. *J. Organomet. Chem.* **1990**, *393*, 153. (d) Ruegg, H. J.; Pregosin, P. S.; Scrivanti, A.; Toniolo, L.; Botteghi, C. *J. Organomet. Chem.* **1986**, *316*, 233. (e) Anderson, G. K.; Clark, H. C.; Davies, J. A. *Inorg. Chem.* **1983**, *22*, 427. (f) Anderson, G. K.; Clark, H. C.; Davies, J. A. *Inorg. Chem.* **1983**, *22*, 434. (g) Anderson, G. K.; Billard, C.; Clark, H. C.; Davies, J. A.; Wong, C. S. *Inorg. Chem.* **1983**, *22*, 439 and references therein. For studies of CO effect on Pt−$SnCl_2$ hydroformylation catalysts, see: (a) Tóth, I.; Kegl, T.; Elsevier, C. J.; Kollár, L. *Inorg. Chem.* **1994**, *33*, 5708. (b) Goel, A. B.; Goel, S. *Inorg. Chim. Acta* **1983**, *77*, L53 and references therein. For temperature-dependent studies of Pt−$SnCl_2$ catalysts, see: Tóth, I.; Guo, I.; Hanson, B. E. *Organometallics* **1993**, *12*, 848 and references therein.

(12) Peak assignments for (*R*)- and (*S*)-2-phenylpropanal were confirmed by oxidation to the respective acids and subsequent derivitization to the (*S*)-methyl mandelate esters. Esters (*R*,*S*)-**4** and (*S*,*S*)-**4** are distinguishable by ^1H NMR spectroscopy.

Scheme 2



Scheme 3. Deuterioformylation Test for the Reversibility of Platinum Hydride Addition to Styrene[a]



[a] Products in boxes require reversible β-hydride elimination.

only β to the aldehyde carbonyl group and in the formyl group. If hydride addition is reversible, deuterium will be incorporated both α and β to the aldehyde carbonyl groups and in the recovered styrene (Scheme 3). For example, platinum deuteride addition to give a secondary alkyl platinum complex will lead to incorporation of deuterium only in the β position of 2-phenylpropanal if the addition is irreversible. However, if the secondary alkyl platinum complex undergoes β-hydride elimination and subsequently re-adds hydride to form a primary alkyl platinum complex, deuterium will be incorporated at the α position of 3-phenylpropanal.

Deuterioformylation of styrene catalyzed by complex **1** was conducted under 600 psi D_2 and 600 psi CO at 39 °C. After 119 h, chiral GC analysis showed that 27% of the styrene had been converted to **3** and **2** with *n*:*i* = 1.8 and 71% ee **2**-(*S*).[13] For **3** and **2**, both ^{1}H and ^{2}H NMR spectroscopy showed the presence of one deuterium β to the carbonyl and one deuterium in the formyl group. No deuterium was observed in the α-positions of either aldehyde regioisomer, although as little as 5% would have been detected by NMR spectroscopy. In the 73% recovered styrene, deuterium was found in the internal (2.8% D), *cis* terminal (1.4% D), and *trans* terminal (1.3% D) vinyl positions. Thus, styrene reacted to give 87% aldehydes and 13% deuterated styrene.

These observations provide evidence that platinum deuteride addition to coordinated styrene is largely irreversible. The initially generated platinum alkyl is mainly converted to β-deuterated aldehydes (Scheme 4, blue). Much more deuterium shows up in recovered styrene than in the α-position of the aldehydes, suggesting that when the platinum alkyl reverts to a platinum hydride styrene complex, the styrene mainly dissociates from platinum. Styrene complexation to platinum is evidently rapid and reversible as compared to platinum hydride addition to the coordinated alkene. The primary deuterated alkyl **A** is converted to aldehyde 8.5 times faster than it eliminates to give α-deuteriostyrene (16.61 mmol/1.96 mmol); taking labeling statistics into account, this indicates that unlabeled **A** would be converted to aldehyde 4.25 (8.5/2) times faster than it eliminates to styrene. Similarly, the secondary deuterated alkyl **B** goes on to aldehyde 4.9 times faster than it eliminates to give β-deuteriostyrene [9.23 mmol/(0.98 mmol + 0.91 mmol)];[14] this indicates that unlabeled **B** would be converted to aldehyde 1.6 (4.9/3) times faster than it eliminates to styrene. At 39 °C, aldehyde stereochemistry is predominantly set by irreversible hydride addition which gives a platinum alkyl that is committed to forming aldehyde. The favored enantiomer is therefore determined by the difference in the relative rates of formation of the (*R*)- and (*S*)-platinum alkyl intermediates, which in turn depends on the equilibrium between the two diastereomeric platinum hydride alkene complexes and their relative rates of conversion to platinum alkyl complexes.

Hydroformylation of (*E*)- and (*Z*)-β-Deuteriostyrene at 39 °C. At 39 °C, platinum hydride preferentially adds to the *si*-face of complexed styrene to form the iso-alkyl that is converted to **2**-(*S*). This was established by analysis of the ratio of enantiomers of **2**-(*S*) and **2**-(*R*) by chiral GC. An unanswered question remained: Is the *n*-aldehyde produced predominantly by hydride addition to the same or opposite alkene enantioface as the iso-aldehyde? To address this question, the hydroformylation of (*E*)-β-deuteriostyrene was carried out and the stereochemistry of the deuterated *n*-aldehydes was determined.

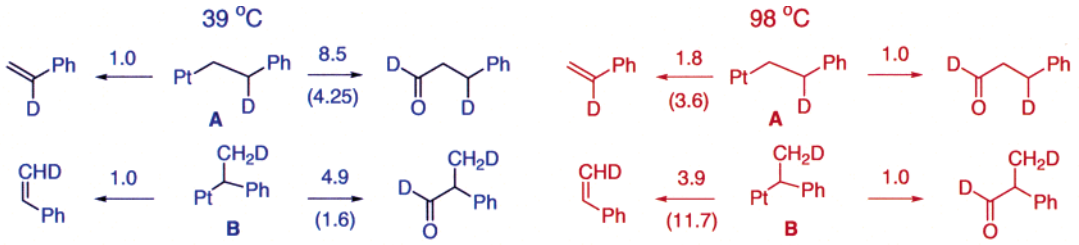
Hydroformylation of (*E*)-β-deuteriostyrene with complex **1** at 39 °C under 1200 psi of 1:1 H_2:CO for 196 h showed that 93% of the styrene converted to **3** and **2** with *n*:*i* = 1.8 and 68% ee **2**-(*S*). Oxidation of the crude aldehyde products with a KH_2PO_4 buffered solution of $KMnO_4$ yielded 84% of 3- and 2-phenylpropanoic acids. Reaction of the acids with methyl (*S*)-(+) mandelate [(*S*)-PhCH(OH)CO_2Me], DCC [1,3-dicyclohexylcarbodiimide], and catalytic DMAP [4-(dimethylamino)pyridine] yielded 61% of mandelate esters **4** and **5** (Scheme 5). The stereochemistry of mandelate esters **5** was previously determined.[15]

The mixture of mandelate esters was analyzed by ^{1}H and ^{2}H NMR spectroscopy. The branched esters were distinguished by

(13) Integrations from ^{1}H and ^{2}H NMR spectroscopy were used to calculate deuterium incorporation into the aldehydes and recovered styrene. NMR samples were prepared in $CDCl_3$ or toluene-d_8 from a solution of the crude hydroformylation mixture (2.0 mL) and an internal standard of 1:1 CH_2Cl_2:CD_2Cl_2 (60 μL).

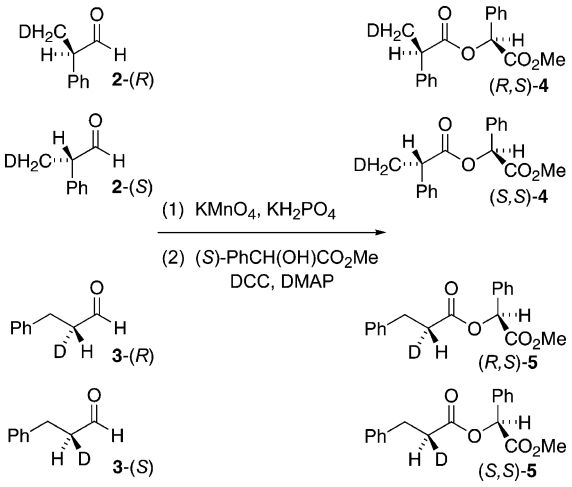
(14) This calculation is further clarified by Scheme 1 in the Supporting Information.

Scheme 4. Relative Rates of Aldehyde Formation As Compared to β-Hydride Elimination at 39 °C (Blue) and at 98 °C (Red)[a]



[a] Numbers in parentheses are corrected for labeling statistics.

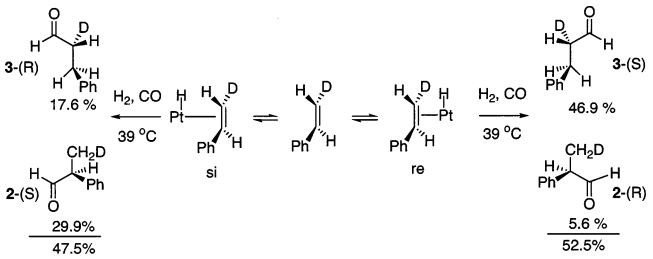
Scheme 5. Derivitization of Chiral Aldehydes by Conversion to Mandelate Esters



the ^{1}H NMR resonances of the C*H*CH$_2$D groups which appear at δ 3.78 (t, 1.0 H, J = 6.9 Hz) for (*R*,*S*)-**4** and at δ 3.69 (t, 5.1 H, J = 6.9 Hz) for (*S*,*S*)-**4**. The diastereomeric excess calculated from these ^{1}H NMR integrations is 67% de, which is similar to the 68% ee **2**-(*S*) measured by chiral GC in the hydroformylation of (*E*)-β-deuteriostyrene. This demonstrates that racemization did not occur in the derivitization process. The straight chain esters were distinguished by the ^{1}H NMR resonances of the C*H*DCO$_2$R groups which appear at δ 2.57 (tt, 0.7 H, $^3J_{HH}$ = 7.4 Hz, $^1J_{HD}$ = 1.8 Hz) for (*S*,*S*)-**5** and at δ 2.47 (m, 0.3 H) for (*R*,*S*)-**5**. This 70:30 ratio of (*S*,*S*)-**5**:(*R*,*S*)-**5** determined from ^{1}H NMR spectroscopy was confirmed by ^{2}H NMR spectroscopy. Simulation of the ^{2}H NMR of CH*D*CO$_2$R resonances of (*R*,*S*)-**5** and (*S*,*S*)-**5** with winDNMR[16] gave the relative amounts of the two diastereomers as 27.3 ± 2% (*R*,*S*)-**5** and 72.7 ± 2% (*S*,*S*)-**5**.

Scheme 6 summarizes the stereochemistry of aldehyde formation. The *n*-aldehyde constitutes 64.5% of the aldehydes, and 73% of it is formed by platinum hydride addition to the *re*-face of styrene. In contrast, the iso-aldehyde constitutes 35.5% of the aldehydes, and 84% of it is formed by platinum hydride addition to the *si*-face of styrene. It is interesting that nearly equal amounts of aldehydes arise from the *si*- (47.5%) and *re*-faces (52.5%) of styrene. Complexation to the *re*-face

Scheme 6. Linear and Branched Aldehydes Arise from Hydride and CO Addition to Opposite Enantiofaces of Styrene



of styrene leads predominantly to a primary alkyl platinum intermediate and results in *n*:*i* selectivity of 8.4, while complexation to the *si*-face leads mainly to a secondary alkyl platinum intermediate and *n*:*i* selectivity of 0.59.

Analysis of the products from hydroformylation of (*Z*)-β-deuteriostyrene led to the same conclusions about the stereochemistry of aldehyde formation.[17]

Hydroformylation of Styrene at 100 °C. The hydroformylation of styrene catalyzed by **1** was performed at 100 °C with 1000 psi of a 1:1 mixture of H$_2$:CO for comparison with Kollár's earlier results.[7] After 4.5 h, chiral GC analysis showed nearly complete conversion of styrene and formation of 63.4% **3**, 14.1% **2**-(*R*), 11.8% **2**-(*S*), and 10% ethylbenzene from hydrogenation (Scheme 2, red). The *n*:*i* = 2.4 and 10% ee **2**-(*R*) are similar to the *n*:*i* = 2.7 and 17% ee **2**-(*R*) reported by Kollár under similar conditions.

Deuterioformylation of Styrene at 98 °C. Deuterioformylation of styrene catalyzed by complex **1** was carried out under 600 psi D$_2$ and 600 psi CO at 98 °C. After 1.6 h, 30% of the styrene had converted to **3** and **2** with *n*:*i* = 2.3 and 10% ee **2**-(*R*) (Scheme 7). Integrations from ^{1}H and ^{2}H NMR spectroscopy showed extensive deuterium incorporation into the α- as well as the β-position of the aldehydes and into all three vinyl positions of styrene. For **3**, 0.12 D was found at the α-position in addition to 0.80 D at the β-position and 0.89 D in the formyl group. Similarly for **2**, 0.10 D was found at the α-position in addition to 0.78 D at the β-position and 0.90 D in the formyl group. In the 67% recovered styrene, deuterium was found in the internal (0.20 D), *cis* terminal (0.12 D), and *trans* terminal (0.12 D) vinyl positions.

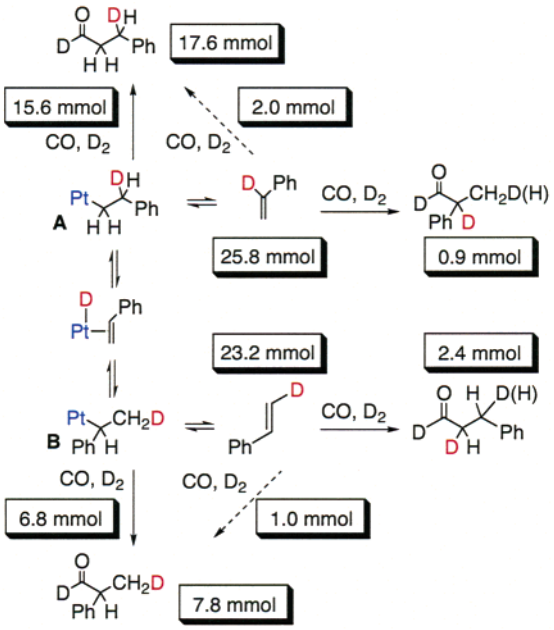
The observation of deuterium in the α-positions of **3**, **2**, and in recovered styrene provides evidence for extensive reversible platinum hydride addition to styrene at 98 °C. The analysis in Scheme 7 shows that the initial primary deuterated alkyl

(15) (a) Parker, D. *J. Chem. Soc., Perkin Trans. 2* **1983**, 83. (b) Giesel, H.; Machacek, G.; Bayerl, J.; Simon, H. *FEBS Lett.* **1981**, *123*, 107. (c) Bartl, K.; Cavalar, C.; Krebs, T.; Ripp, E.; Rétey, J.; Hull, W. E.; Günther, H.; Simon, H. *Eur. J. Biochem.* **1977**, *72*, 247. (d) Hashimoto, H.; Rambeck, B.; Günther, H.; Mannschreck, A.; Simon, H. *Hoppe-Seyler's Z. Physiol. Chem.* **1975**, *356*, 1203. (e) Simon, H.; Rambeck, B.; Hashimoto, H.; Günther, H.; Nohynek, G.; Neumann, H. *Angew. Chem., Int. Ed.* **1974**, *13*, 608.

(16) Reich, H. J. *J. Chem. Educ.* **1995**, *72*, 1086.

(17) A mixture of (*Z*)-β-deuteriostyrene, styrene, phenylacetylene-d_1, and complex **1** was placed under 1200 psi 1:1 H$_2$:CO and reacted at 39 °C for 192 h. GC analysis showed 89% conversion to aldehydes, *n*:*i* = 1.8, and 63% ee (*S*)-2-phenylpropanal. Simulation of the ^{2}H NMR spectrum of 2- and 3-phenylpropanal-derived (*S*)-methyl mandelate esters gave 65.7% (*R*,*S*)-**5** and 34.3% (*S*,*S*)-**5**.

Scheme 7. Deuterioformylation of Styrene at 98 °C



platinum intermediate **A** is converted to β-deuterated 3-phenylpropanal (15.6 mmol) or to α-deuterated styrene (25.8 mmol seen); some α-deuterated styrene was also hydroformylated in situ to give α-deuterated 2-phenylpropanal (0.9 mmol) and (based on the *n*:*i* ratio) additional β-deuterated 3-phenylpropanal (2.0 mmol). Therefore, the primary deuterated alkyl **A** eliminates to give α-deuteriostyrene (25.8 + 0.9 + 2.0 mmol) 1.8 times faster than it is converted to 3-phenylpropanal (**3**) (15.6 mmol) (Scheme 4, red); taking labeling statistics into account, this indicates that unlabeled **A** would eliminate to styrene 3.6 (1.8 × 2) times faster than it is converted to aldehyde. Similarly, the secondary deuterated alkyl **B** eliminates to give β-deuteriostyrene (23.2 + 2.4 + 1.0 mmol) 3.9 times faster than it is converted to 2-phenylpropanal (**2**) (6.8 mmol); taking labeling statistics into account, this indicates that unlabeled **B** would eliminate to styrene 11.7 (3.9 × 3) times faster than it is converted to aldehyde.

When a second deuterioformylation of styrene under 600 psi D_2 and 600 psi CO at 96 °C was carried to longer time (4.5 h), 91% of the styrene was converted to aldehydes and the 2% recovered styrene was almost completely deuterated at the vinyl positions. Chiral GC analysis showed **3** and **2** with *n*:*i* = 2.5 and 11% ee **2**-(*R*). ^{1}H and ^{2}H NMR spectroscopy showed that the α positions of **3** and **2** contained 0.58 and 0.37 D, respectively. The β positions of both aldehydes had more than one deuterium incorporated: **3** had 1.06 D and **2** had 1.74 D. The formyl groups had less than one deuterium: **3** and **2** had 0.69 and 0.75 D, respectively. ^{1}H and ^{2}H NMR spectroscopy of the 2% recovered styrene revealed extensive deuteration of the internal (0.95 D), *cis* (0.69 D), and *trans* (0.75 D) vinyl hydrogens.

These results require extensive β-hydride elimination from the initially formed platinum alkyls. Reversibility is so extensive that recovered styrene is highly deuterated. Deuterioformylation of deuterium exchanged styrene is responsible for α-deuteration and is required for incorporation of more than one D at the β-position. The substantially greater amount of deuterium in the α-position of **3** (0.58 D) than in **2** (0.37 D) is consistent with the greater propensity of the secondary alkyl platinum to β-hydride eliminate.

Table 1. CO Pressure Dependence on the Hydroformylation of Styrene at 100 °C

CO (psi)	H_2 (psi)	*n*:*i*	ee	ethylbenzene	TOF (h^{-1})
200	400	3.18	22% *R*	41%	25
400	400	3.20	19% *R*	21%	142
600	400	3.26	21% *R*	12%	94
800	400	3.13	18% *R*	10%	107
1000	400	3.35	20% *R*	7%	68

A third deuterioformylation of styrene was performed at 600 psi D_2 and 600 psi CO at 96 °C in which aliquots were removed from the reaction mixture every 30 min. ^{1}H and ^{2}H NMR spectroscopy confirmed that the hydrogen content of the formyl groups gradually escalated over the course of the reaction. After 1 h and 10% conversion of styrene, no hydrogen was seen in the formyl groups, but after 2 h and 37% conversion, 12−14% hydrogen was seen in the formyl groups.

The significant hydrogen distribution in the formyl groups originates from cleavage of the platinum acyl intermediates by reaction with HD rather than D_2. Extensive exchange between styrene and D_2 provides a source of HD. HD can arise from reversible platinum alkyl formation, followed by exchange of the platinum hydride with D_2.

Because platinum hydride addition to styrene is mainly reversible at high temperature, the regio- and enantioselectivity of aldehyde formation must arise during a step later in the catalytic cycle, either acyl formation or acyl hydrogenolysis. At 39 °C, the *S*-alkyl platinum intermediate is selectively formed and is mainly converted to **2**-(*S*). At 98 °C, the formation of the alkyl platinum intermediates is largely reversible, and the *R*-alkyl platinum intermediate is converted selectively to an enantiomeric excess of **2**-(*R*).

Hydroformylation of Styrene at 96 °C under 1275 psi CO and 125 psi H_2. If alkyl migration to CO is the step at which enantioselectivity is set and if it is CO-pressure dependent, then an increase in CO pressure should increase the rate of alkyl migration to CO relative to β-hydride elimination and alter the enantioselectivity to favor the formation of more **2**-(*S*). To test this hypothesis, we studied the hydroformylation of styrene at higher CO pressure. To maximize the CO pressure and stay within the convenient limits of tank pressure, the hydroformylation of styrene was studied under the following conditions.

A solution of styrene and **1** in toluene was placed under 1275 psi CO and 125 psi H_2 and heated to 96 °C for 24 h. Chiral GC analysis showed 46% conversion to aldehydes and, unexpectedly, an increase to 21% ee **2**-(*R*) and an increase in the *n*:*i* ratio to 4.3. Because both CO and H_2 pressure were changed simultaneously, it was not clear whether CO pressure, H_2 pressure, or both were contributing to a change in the reaction's selectivity. A systematic study of both CO and H_2 pressure dependence on enantioselectivity and *n*:*i* was clearly needed.

Hydroformylation of Styrene at 100 °C under Variable CO Pressure. The hydroformylation of styrene with **1** at 100 °C was performed at constant 400 psi H_2 pressure while varying CO pressure systematically from 200 to 1000 psi (Table 1). Surprisingly, neither the % ee **2**-(*R*) nor the *n*:*i* ratio varied appreciably as the CO pressure was changed. However, an increase in CO pressure was accompanied by a decrease in the amount of styrene hydrogenation. The turnover frequencies

Table 2. H_2 Pressure Dependence on the Hydroformylation of Styrene at 100 °C

H_2 (psi)	CO (psi)	*n*:*i*	ee	ethylbenzene	TOF (h^{-1})
200	400	3.69	22% *R*	20%	44
400	400	3.20	19% *R*	21%	142
600	400	2.54	15% *R*	21%	163
800	400	2.25	10% *R*	21%	201
1000	400	1.92	6% *R*	24%	443

Table 3. CO Pressure Dependence on the Hydroformylation of Styrene at 50 °C

CO (psi)	H_2 (psi)	*n*:*i*	ee	ethylbenzene	TOF (h^{-1})
200	400	1.92	22% *S*	10%	3
400	400	2.12	40% *S*	7%	5
600	400	2.46	48% *S*	3%	8
800	400	2.51	57% *S*	2%	7
1000	400	2.55	57% *S*	2%	7

Table 4. H_2 Pressure Dependence on the Hydroformylation of Styrene at 50 °C

H_2 (psi)	CO (psi)	*n*:*i*	ee	ethylbenzene	TOF (h^{-1})
200	400	3.11	18% *S*	3%	3
400	400	2.12	40% *S*	7%	5
600	400	1.84	49% *S*	7%	10
800	400	1.54	55% *S*	9%	10
1000	400	1.46	60% *S*	12%	10

(TOF) for aldehyde formation are absolute rates and are consequently more variable than the *n*:*i* ratios and % ee which are relative rates. No systematic variation in TOF as a function of CO pressure was noted.

The decrease in % hydrogenation as CO pressure was increased requires that the transition state for hydrogenation have one fewer CO than the transition state for hydroformylation. While the rate of hydroformylation is zero order in CO, the rate of hydrogenation is inverse order in CO.

Hydroformylation of Styrene at 100 °C under Variable H_2 Pressure. The hydroformylation of styrene with **1** at 100 °C was performed at constant 400 psi CO pressure while varying H_2 pressure systematically from 200 to 1000 psi (Table 2). As the H_2 pressure was increased, the formation of **3** decreased and the formation of both **2**-(*S*) and **2**-(*R*) increased, although **2**-(*S*) increased more than **2**-(*R*). This resulted in a shift of the enantiomeric excess to lower % ee **2**-(*R*) and to a decrease in the *n*:*i* ratio. There was no appreciable hydrogen pressure dependence on the % hydrogenation. The turnover frequency (TOF) increased at higher hydrogen pressure.

The H_2 pressure dependence of the % ee and *n*:*i* ratio requires that enantioselectivity not be fully set until acyl hydrogenolysis. At higher H_2 pressure and 100 °C, the % ee and the *n*:*i* ratio both move toward the values seen at 40 °C where selectivity is controlled by largely irreversible platinum hydride addition. At 40 °C, there is a greater propensity to form the *S*-alkyl platinum intermediate, which is mainly carried on to **2**-(*S*). At 100 °C, the formation of alkyl platinum intermediates is more reversible and selectivity is controlled by a later step in the hydroformylation cycle. The preference for **2**-(*R*) under these conditions is a result of either an equilibrium favoring the (*R*)-acyl intermediate or of a more rapid hydrogenolysis of the (*R*)-acyl intermediate. The shift to lower % ee **2**-(*R*) at higher H_2 pressure is consistent with having more of the initially formed *S*-alkyl platinum intermediate being "locked in" by hydrogenolysis of an *S*-acyl platinum intermediate in equilibrium with it. At lower H_2 pressure, more of the *S*-acyl platinum intermediate has a chance to revert all the way back to free styrene and then proceed on to **2**-(*R*).

The constant % hydrogenation along with the increase in TOF at higher H_2 pressure indicates that the rate-determining steps for both hydrogenation and hydroformylation involve H_2.

Deuterioformylation of 4-Methylstyrene in the Presence of 2- and 3-Phenylpropanal at 96 °C. In several cases, aldehyde formation in hydroformylation has been shown to be reversible.[18] While extensive reversibility of aldehyde formation would have led to 0% ee in the case of hydroformylation of styrene by **1**, the possibility existed that some aldehyde was converted back to styrene. To determine whether aldehyde formation is reversible under our reaction conditions, the deuterioformylation of 4-methylstyrene with complex **1** was performed in a solution containing **2** and **3**. After 4 h at 96 °C under 600 psi D_2 and 600 psi CO, GC analysis revealed that 91% of the 4-methylstyrene was converted to aldehydes. No styrene was observed by ^1H or ^2H NMR spectroscopy, and no deuterium was detected by GC/MS in the recovered **2** and **3**.[19] These results establish that aldehyde formation is irreversible.

Hydroformylation of Styrene at 50 °C under Variable CO Pressure. While platinum alkyl formation at 40 °C under 600 psi CO and 600 psi H_2 was much less reversible than that at 100 °C, some β-hydride elimination occurred to give deuterated styrene (13% of styrene consumed). In light of the pressure dependence of % ee and *n*:*i* at 100 °C, we investigated their dependence at lower temperature. To obtain more convenient rates of hydroformylation, studies were carried out at 50 °C rather than 40 °C.

The hydroformylation of styrene with **1** at 50 °C was performed at constant 400 psi H_2 pressure while varying CO pressure systematically from 200 to 1000 psi (Table 3). In contrast to data at 100 °C where no variation in % ee or the *n*:*i* was seen, the % ee **2**-(*S*) and the *n*:*i* ratio increased as CO pressure was increased at 50 °C. The variation in % ee and *n*:*i* results from an increase in **3**, a decrease in **2**-(*R*), and a little change in **2**-(*S*) as CO pressure is increased. At both 50 and 100 °C, a decrease in CO pressure led to more styrene hydrogenation but no significant change in TOF.

Hydroformylation of Styrene at 50 °C under Variable H_2 Pressure. The hydroformylation of styrene with **1** at 50 °C was performed at constant 400 psi CO pressure while varying H_2 pressure systematically from 200 to 1000 psi (Table 4, Figure 1). The same trends seen at 100 °C were seen at 50 °C. As H_2 pressure increased, a shift toward more **2**-(*S*) was seen which plateaued at about 60% ee **2**-(*S*). The *n*:*i* ratio decreased at higher H_2 pressure and plateaued to a value of 1.5. The variation in % ee and *n*:*i* results from an increase in **2**-(*S*) and a proportional decrease in **3** and **2**-(*R*) as H_2 pressure increased. The TOF increased somewhat at higher H_2 pressure. In contrast to results at 100 °C, an increase in % hydrogenation was seen at higher H_2 pressure.

(18) (a) Lenges, C. P.; Brookhart, M. *Angew. Chem., Int. Ed.* **1999**, *38*, 3533. (b) Brookhart, M.; Lenges, C. P.; White, P. S. *J. Am. Chem. Soc.* **1998**, *120*, 6965. (c) Kondo, T.; Akazome, M.; Tsuij, Y.; Watanabe, Y. *J. Org. Chem.* **1990**, *55*, 1286.

(19) GC/MS showed only the natural abundance of deuterium in the recovered 2- and 3-phenylpropanal [2-phenylpropanal: *m*/*e* (intensity) $[M + 2]^+$ 136 (0.13), $[M + 1]^+$ 135 (1.64), $[M]^+$ 134 (11.70); 3-phenylpropanal: $[M + 2]^+$ 136 (0.63), $[M + 1]^+$ 135 (6.10), $[M]^+$ 134 (44.78)].

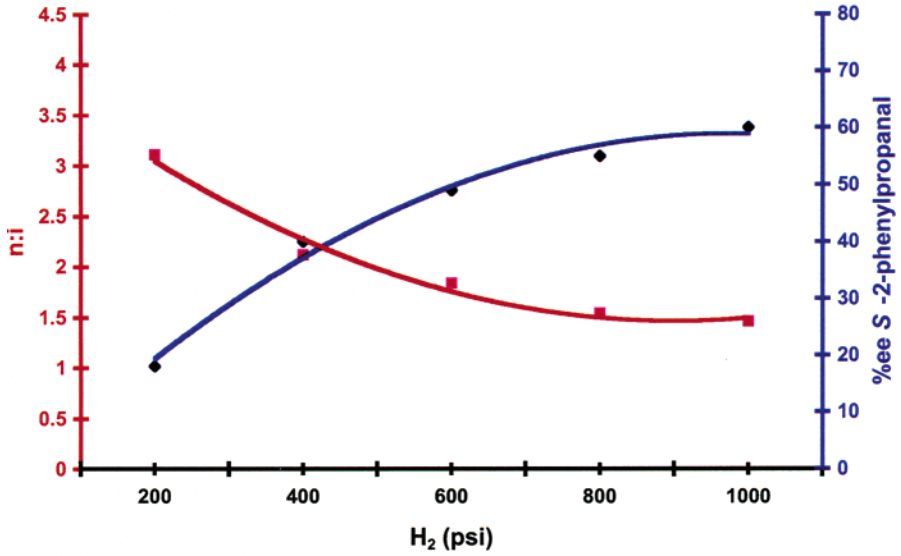


Figure 1. Leveling effect of H_2 pressure on the *n*:*i* and % ee (*S*)-2-phenylpropanal in the hydroformylation of styrene at 50 °C and 400 psi CO.

Discussion

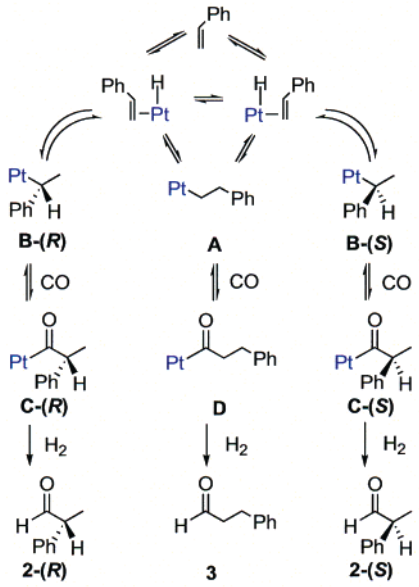
We set out to understand the unusual observation that the enantioselectivity in the hydroformylation of styrene with **1** reverses from 60% ee **2**-(*S*) at 40 °C to 10% ee **2**-(*R*) at 100 °C (Scheme 2). From the beginning, we focused our attention on the stage at which enantioselectivity is set at the two different temperatures.

At 40 °C and equal pressures of syn gas (600 psi CO and 600 psi D_2), deuterioformylation studies showed that the major products had deuterium mainly β to the aldehyde carbonyl. This establishes that the **2**-(*S*) selectivity is set by largely irreversible formation of alkyl platinum intermediates that are converted to aldehydes. The small amount of deuterium found in recovered styrene resulted from competing β-hydride elimination from the alkyl platinum intermediates. It is estimated that the primary alkyl intermediate goes on to aldehyde 4.25 times faster than it eliminates styrene and the secondary alkyl intermediate goes on to aldehyde 1.6 times faster than it eliminates styrene (Scheme 4, blue, taking account of labeling statistics). Finding deuterium in styrene but not in the α-position of aldehydes suggests that intermediate platinum hydride alkene complexes dissociate styrene much faster than they re-form an isomeric platinum alkyl.

In H_2 pressure dependence studies at 50 °C, the fraction of **2**-(*S*) increased as the H_2 pressure increased and plateaued at about 32% **2**-(*S*), 8% **2**-(*R*), and 60% **3** (Scheme 8). These percentages mirror the initial percentages of metal alkyls formed. At high H_2 pressures, acyl formation is less reversible because as the acyl forms, it gets trapped immediately to form aldehyde. This would account for the relatively low *n*:*i* ratio. At lower H_2 pressures, acyl hydrogenolysis is slower, as indicated by the TOF, and is competitive with reversible acyl formation. Slow hydrogenolysis therefore allows time for isomerization of the platinum acyl by reversion all the way back to coordinated or free styrene.

Another level of enantioselective control was discovered in hydroformylation studies at 50 °C under 400 psi H_2 and variable CO pressure. Under these conditions, there is some reversibility in the formation of the *S*-alkyl platinum intermediate **B**-(*S*) because the amount of **2**-(*S*) formed (23%) was significantly

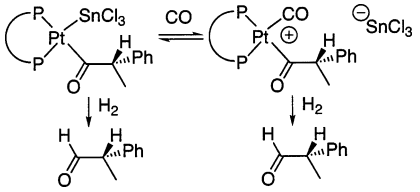
Scheme 8



less than the 30% we associate with initial alkyl formation. As CO pressure was increased from 200 to 1000 psi, the amounts of **2**-(*S*) and **3** increased slightly while the amount of **2**-(*R*) decreased significantly. We suggest that CO shifts the equilibrium of the *n*-alkyl (**A)** toward *n*-acyl (**D)** more than it shifts that of the *R*-alkyl (**B**-(*R*)) to the *R*-acyl (**C**-(*R*)). Therefore, at higher CO pressures, more of the *n*-acyl (**D)** is hydrogenolyzed to aldehyde while more of the *R*-alkyl (**B**-(*R*)) reverts to the pool of styrene, thus increasing the amount of **3** at the expense of **2**-(*R*). This CO dependence emphasizes the importance of the equilibrium between platinum alkyls and platinum acyls.

The rates of β-hydride elimination, platinum acyl formation, and platinum acyl hydrogenolysis are delicately balanced at 50 °C. CO inhibits β-hydride elimination from platinum alkyl, and H_2 takes platinum acyls on to aldehydes. The greatest amount of **2**-(*S*) is formed at lower temperature where β-hydride elimination is disfavored, at high CO pressure where conversion of the *S*-alkyl (**B**-(*S*)) to *S*-acyl (**C**-(*S*)) intermediate is accelerated, and at high H_2 pressure where the *S*-acyl (**C**-(*S*))

Scheme 9. Effect of CO Pressure on the Rates of Hydrogenolysis



intermediate is hydrogenolyzed to **2**-(*S*). It is also possible that the equilibrium between $SnCl_3$ and CO complexes is altered at high CO pressures, and, as a result, the rate of hydrogenolysis may also be affected (Scheme 9).

At 98 °C, deuterioformylation showed extensive deuterium at the α- as well as *β*-positions of the aldehydes and extensive incorporation of deuterium into styrene. This establishes that formation of the alkyl platinum intermediates is reversible and that enantioselectivity is set at a later stage in hydroformylation. The primary alkyl was estimated to *β*-hydride eliminate 3.6 times faster than conversion to *n*-aldehyde, while the secondary alkyl was estimated to eliminate 11.7 times faster than conversion to iso-aldehyde.

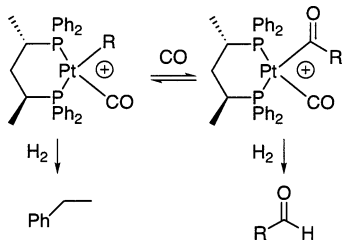
Because the *n*:*i* and % ee **2**-(*R*) decreased as the H_2 pressure increased at 100 °C, this indicates that enantioselectivity is not fully set until hydrogenolysis of intermediate acyl complexes. Upon going from 50 °C under 400 psi CO and 1000 psi H_2 to 100 °C under 400 psi CO and 200 psi H_2, the relative amount of **2**-(*S*) dropped from 32% to 9%, while the amounts of **2**-(*R*) increased from 8% to 13% and **3** increased from 59% to 79%. This suggests that there is partial equilibration of acyl platinum complexes via reversion all the way back to free styrene at high temperature and that the relative rate of hydrogenolysis of the *S*-acyl (**C**-(*S*)) is slower than hydrogenolysis of either the *R*-acyl (**C**-(*R*)) or the *n*-acyl (**D**) at high temperature by a factor of about 6.[20]

Because CO pressure did not affect the rate or selectivity of hydroformylation at 100 °C, the resting state of the catalyst and the transition state for hydrogenolysis must have the same number of CO's. Because higher CO pressures slowed hydrogenation to ethylbenzene, the transition state for hydroformylation has one more CO than the hydrogenation transition state (Scheme 10).

The rates of formation (TOF) of ethylbenzene and of aldehyde both increased at higher H_2 pressures. This indicates that the

(20) This value was obtained by taking the product ratios at 50 °C and high H_2 pressure as the initial ratios for the formation of the corresponding acyl intermediates and comparing them to the product ratios at 100 °C and low H_2 pressure. The formula for calculating the ratio of *R*-acyl cleavage to *S*-acyl cleavage is: $(8y \times 9) = (13 \times 32)$ where $y = 5.8$, the rate at which the *R*-acyl is cleaved as compared to cleavage of the *S*-acyl.

Scheme 10. Higher CO Pressure Increases the Ratio of Hydroformylation to Hydrogenation



slow step in both processes involves H_2. The % hydrogenation to ethylbenzene did not depend on H_2 pressure because both aldehyde formation and hydrogenation depend of H_2 pressure equally.

Why does the selectivity-determining step change as a function of temperature? It all has to do with the greater temperature dependence of a first order reaction ($\Delta H^{\ddagger}$ = larger, $\Delta S^{\ddagger} \approx 0$) as compared to a competing second order reaction ($\Delta H^{\ddagger}$ = smaller, $\Delta S^{\ddagger} \ll 0$). Alkyl formation and *β*-hydride elimination are first order reactions, whereas acyl formation and acyl hydrogenolysis are second order reactions involving CO and H_2, respectively. At 40 °C, the first order elimination of the platinum alkyl back to styrene is slower than its second order reaction with CO to give an acyl complex that is converted on to aldehyde. At 40 °C, selectivity is largely set by the first order formation of platinum alkyls. At 100 °C, the first order elimination of the platinum alkyl back to styrene is accelerated more than the second order acyl formation and the second order hydrogenolysis of the acyl complex. At 100 °C, the selectivity is not determined until the second order hydrogenolysis of the acyl intermediates.

Acknowledgment. Financial support from the Department of Energy, Office of Basic Energy Sciences, is gratefully acknowledged. Grants from the NSF (Grant No. CHE-9629688) and the NIH (Grant No. I S10 RR04981-01) for the purchase of NMR spectrometers and from the NSF (Grant No. CHE-9310428) for the purchase of X-ray instruments are also acknowledged. Douglas R. Powell and Michael A. Kozee are also acknowledged for solving the X-ray crystal structure of the Pt catalyst.

Supporting Information Available: Preparation and characterization of substrates, kinetics experimental details, tables giving X-ray crystallographic data for complex **1**, and graphs (PDF and CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA0318479