Articles

Study of the Effects of Alkali Metal Salts on Styrene Hydroformylation Reactions Catalyzed by Rhodium(I) Complexes of Bis(phosphite) Ligands

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A functionalized α,ω-bis(phosphite-donor) ligand containing two amido groups, **8**, has been prepared from tartaric acid. An *in situ* formed rhodium(I) metallacrown ether complex of **8** has been compared to an *in situ* formed rhodium(I) complex of (*R*,*R*)-Chiraphite for the hydroformylation of styrene. Both Rh(I) complexes are active catalysts, but the complex of (*R*,*R*)-Chiraphite exhibits a higher regioselectivity than does the metallacrown ether catalyst (*iso/n* of 10.1 versus 3.9) as expected. The additions of alkali metal salts to the hydroformylation reactions cause increases in the regioselectivities (approximately 2-fold for both $LiBPh_4 \cdot 3dme$ and $NaBPh_4$ for ligand **8**; 3-fold for both $LiBPh_4 \cdot 3dme$ and $NaBPh_4$ for (*R*,*R*)-Chiraphite) with virtually no effect on the activity. The facts that (1) no change in the *iso/n* ratio is observed upon addition of the noncoordinating salt, $TBA \cdot BPh_4$, (2) $LiBPh_4 \cdot 3dme$ has little effect on the regioselectivity of an *in situ* formed rhodium(I) complex of diphos, and (3) the increase in regioselectivity levels out at high salt:Rh ratios suggest the increase in regioselectivity is due to coordination of the alkali metal salt to the oxygen of a carbonyl ligand and to the phosphite oxygens during the regioselectivity-determining step. This proposal is consistent with the observation of only weak 1:1 coordination of $LiBPh_4 \cdot 3dme$ with a model metallacrown ether, *cis*-$Mo(CO)_4$(**8**) in acetonitrile-d_3.

Introduction

In the past few years, a great deal of effort has been focused on developing active and selective catalysts for alkene hydroformylation (Scheme 1). The vast majority of these catalysts have been rhodium(I) metal complexes with chelating bis(phosphine),[1−8] bis(phosphite),[9−24] bis(phospholane),[4−6,25] or mixed bis(phosphine/phosphite) ligands.[9,17−19] To date, the best regioselectivities (*iso/n* ratios) for the hydroformylation of styrene have been obtained using bis(phosphite) and bis(phospholane) ligands with bulky phosphorus substituents.[25−29] These studies clearly demonstrate that ligands with very sterically constrained ligand

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(1) Stille, J. K.; Su, H.; Brechot, P.; Parrinello, G.; Hegedus, L. S. *Organometallics* **1991**, *10*, 1183.

(2) Consiglio, G.; Nefkens, S. C. A.; Borer, A. *Organometallics* **1991**, *10*, 2046.

(3) Dieguez, M.; Pereira, M. M.; Masdeu-Bulto, A. M.; Claver, C.; Bayon, J. C. *J. Mol. Catal. A: Chem.* **1999**, *143*, 111.

(4) Axtell, A. T.; Cobley, C. J.; Klosin, J.; Whiteker, G. T.; Zanotti-Gerosa, A.; Abboud, K. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 5834.

(5) Nelson, R. C.; Landis, C. R. *Chim. Oggi* **2006**, *24*, 36.

(6) Clark, T. P.; Landis, C. R.; Freed, S. L.; Klosin, J.; Abboud, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 5040.

(7) Cobley, C. J.; Klosin, J.; Qin, C.; Whiteker, G. T. *Org. Lett.* **2004**, *6*, 3277.

(8) Axtell, A. T.; Klosin, J.; Abboud, K. A. *Organometallics* **2006**, *25*, 5003.

(9) Beghetto, V.; Scrivanti, A.; Matteoli, U. *Catal. Commun.* **2001**, *2*, 139.

(10) Cobley, C. J.; Gardner, K.; Klosin, J.; Praquin, C.; Hill, C.; Whiteker, G. T.; Zanotti-Gerosa, A.; Petersen, J. L.; Abboud, K. A. *J. Org. Chem.* **2004**, *69*, 4031.

(11) Cserepi-Szucs, S.; Huttner, G.; Zsolnai, L.; Szolosy, A.; Hegedus, C.; Bakos, J. *Inorg. Chim. Acta* **1999**, *296*, 222.

(12) Dieguez, M.; Pamies, O.; Claver, C. *J. Org. Chem.* **2005**, *70*, 3363.

(13) Dieguez, M.; Pamies, O.; Claver, C. *Chem. Commun.* **2005**, 1221.

(14) Dieguez, M.; Pamies, O. P.; Claver, C. *Chem. Rev.* **2004**, *104*, 3189.

(15) Dieguez, M.; Ruiz, A.; Claver, C. *J. Chem. Soc., Dalton Trans.* **2003**, 2957.

(16) Kadyrov, R.; Heller, D.; Selke, R. *Tetrahedron: Asymmetry* **1998**, *9*, 329.

(17) Deerenberg, S.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Organometallics* **2000**, *19*, 2065.

(18) Deerenberg, S.; Pamies, O.; Dieguez, M.; Claver, C.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Org. Chem.* **2001**, *66*, 7626.

(19) Deerenberg, S.; Schrekker, H. S.; van Strijdonck, G. P. F.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Fraanje, J.; Goubitz, K. *J. Org. Chem.* **2000**, *65*, 4810.

(20) Kostas, I. D.; Vallianatou, K. A.; Holz, J.; Borner, A. *Appl. Organomet. Chem.* **2005**, *19*, 1090.

(21) van der Vlugt, J. I.; van Duren, R.; Batema, G. D.; den Heeten, R.; Meetsma, A.; Fraanje, J.; Goubitz, K.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Vogt, D. *Organometallics* **2005**, *24*, 5377.

(22) van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741.

(23) vanRooy, A.; Kamer, P. C. J.; vanLeeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J.; Veldman, N.; Spek, A. L. *Organometallics* **1996**, *15*, 835.

(24) Vanrooy, A.; Orij, E. N.; Kamer, P. C. J.; Vanleeuwen, P. W. N. M. *Organometallics* **1995**, *14*, 34.

(25) Klosin, J.; Landis, C. R. *Acc. Chem. Res.* **2007**, *40*, 1251.

(26) Babin, J. E.; Whiteker, G. T. WO 9303839, 1993.

(27) Dieguez, M.; Pamies, O.; Ruiz, A.; Castillon, S.; Claver, C. *Chem. Commun.* **2000**, 1607.

(28) Dieguez, M.; Pamies, O.; Ruiz, A.; Castillon, S.; Claver, C. *Chem.−Eur. J.* **2001**, *7*, 3086.

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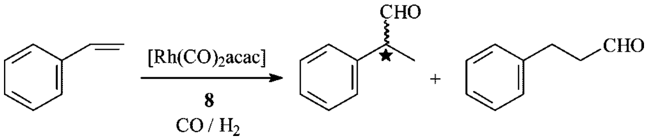
Scheme 1. Hydroformylation of Styrene Using 8



backbones, **1**−**5** in Figure 1, give reasonably high regioselectivities under conditions that also give reasonable reaction rates and high conversions. They further demonstrate that even higher regioselectivities (*iso/n* ≥ 60:1) can be obtained at lower degrees of conversion and, in some cases, with milder reaction conditions.[25]

The catalysts containing bis(phosphite) ligands are particularly interesting because Powell and co-workers have demonstrated that bis(phosphite) ligands are capable of binding alkali metal cations. Powell and McLain have also demonstrated that binding of the Li^+ and Na^+ to carbonyl ligands can result in the activation of carbonyl ligands toward nucleophilic attack, as shown in Figure 2.[30−35] Thus, if a migratory-insertion reaction involving a carbonyl is either the rate- or regioselectivity-determining step in the catalytic mechanism, the presence of a hard metal cation could significantly increase either the reaction rate or the regioselectivity.

Surprisingly, the effects of alkali metal cations on hydroformylation reactions catalyzed by bis(phosphite) complexes have not been studied. In this article, we report the effects of alkali metal cations on the hydroformylation of styrene catalyzed by a Rh(I) complex of Chiraphite, one of the best commercially available bis(phosphite) ligands, and also by a Rh(I) complex of a flexible bis(phosphite) ligand derived from tartaric acid. This ligand forms metallacrown ethers[36−41] when chelated to transition metals. The flexible backbone may result in multiple conformations and low regioselectivities;[42] however it also has the potentially offsetting advantage that it has additional binding sites for alkali metal cations. The catalytic results obtained with the bis(phosphite) ligands are compared to those obtained with 1,2-bis(diphenylphosphino)ethane, a ligand that cannot bind alkali metal cations. Finally, the ability of a *cis*-$Mo(CO)_4$ metallacrown ether containing the flexible bis(phosphite) ligand derived from tartaric acid to bind to Li^+ or Na^+ has been evaluated and is discussed in light of the catalytic results.

Experimental Section

Materials and Methods. All reactions were carried out under a dry N_2 atmosphere using the appropriate Schlenk glassware and techniques. Both THF and Et_3N were dried by distillation from sodium benzophenone ketyl. Ethanolamine and styrene were purchased from Aldrich and distilled. Dimethyl 2,3-*O*-isopropylidene-L-tartrate, $LiBPh_4 \cdot 3dme$, $NaBPh_4$, tetrabutylammonium tetraphenylborate ($TBA \cdot BPh_4$), and anhydrous MeOH were purchased from Aldrich and used as received. (*R*,*R*)-Chiraphite (**1**) and 1,2-bis(diphenyphosphino)ethane (**10**) were purchased from Strem Chemicals and used as received. The 2,2′-biphenylylenephosphochloridite ester, $Rh(CO)_2acac$, and $Mo(CO)_4(nbd)$ were prepared by literature methods.[43−47] All NMR spectra were recorded on a Bruker DRX400 spectrometer. The chloroform-*d* and acetonitrile-d_3 solvents were obtained from Cambridge Isotopes and were opened and handled under N_2. The $^{31}P\{^1H\}$ NMR spectra were referenced to external 85% phosphoric acid, and both the ^{13}C and the ^1H NMR spectra were referenced to internal $SiMe_4$.

(4*R*,5*R*)-Bis[*N*-(2′-hydroxyethyl)amido]-2,2-dimethyl-1,3-dioxolane, $(C_5H_8O_2)[C(O)NHCH_2CH_2OH]_2$ (7). To a 250 mL round-bottom flask equipped with a stir bar were added 4.00 g (18.3 mmol) of dimethyl 2,3-*O*-isopropylidene-L-tartrate, 4.47 g (7.32 mmol) of ethanolamine, and 100 mL of anhydrous MeOH. The mixture was stirred at room temperature for 11 days, after which time the reaction was shown to be complete by ^1H NMR. The reaction mixture was evaporated to dryness to yield 4.91 g (97.4%) of **7** as a white solid. ^1H NMR ($CDCl_3$): δ 7.29 (t, 2H, $|^3J(HH)|$ 5.1 Hz, NH), 4.60 (s, 2H, CH), 3.72 (t, 4H, $|^2J(HH)|$ 5.1 Hz, CH_2O), 3.46 (dt, 4H, $|^3J(HH)|$ 5.0 Hz, $|^3J(HH)|$ 5.0 Hz, CH_2N), 3.11 (bs, 2H, OH), 1.51 (s, 6H, CH_3). ^{13}C NMR ($CDCl_3$): δ 170.97 (s, CO), 112.99 (s, $\underline{C}(CH_3)_2$), 78.12 (s, CH), 61.95 (s, CH_2O), 42.46 (s, CH_2N), 26.38 (s, CH_3).

(4*R*,5*R*)-Bis[*N*-(2′-(5,7-dioxa-6-phosphadibenzo[*a*,*c*]cycloheptan-6-yloxy)ethyl)amido]-2,2-dimethyl-1,3-dioxolane, $(C_5H_8O_2)[C(O)NHCH_2CH_2OP(O_2C_{12}H_8)_2]_2$ (8). A 250 mL round-bottom flask was charged with 0.51 g (1.9 mmol) of the diol **7**, 0.53 mL (3.8 mmol) of dry Et_3N, and 100 mL of dry THF. Then, a solution of 0.95 g (3.8 mmol) of 2,2′-biphenylylenephosphochloridite ester in 40 mL of THF was added dropwise with stirring over a period of 30 min, causing a white precipitate to form. The solution was stirred for an additional 30 min and then was filtered through a 1 cm bed of Celite in a 60 cc medium sintered glass funnel under nitrogen. The resulting filtrate was evaporated to dryness to yield 1.2 g (92%) of **8** as a white solid. ^{31}P NMR ($CDCl_3$): δ 137.54 (t, $|^3J(PH)|$ 7.0 Hz). ^1H NMR ($CDCl_3$): δ 7.0−7.7 (m, 16H, $\underline{H}_{Ar}$), 4.53 (s, 2H, $C\underline{H}$), 3.96 (dt, 4H, $|^3J(PH)|$ 7.3 Hz, $|^3J(HH)|$ 5.2 Hz, $C\underline{H}_2O$), 3.43 (dt, 4H, $|^3J(HH)|$ 5.0 Hz, $|^3J(HH)|$ 5.0 Hz, $C\underline{H}_2N$), 1.51 (s, 6H, $C\underline{H}_3$). ^{13}C NMR ($CDCl_3$): δ 170.46 (s, $\underline{C}{=}O$), 150.21 (d, $|^2J(PC)|$ 5.7 Hz, $\underline{C}_{Ar}O$), 150.09 (d, $|^2J(PC)|$ 5.3 Hz, $\underline{C}_{Ar}O$), 131.38 (d, $|^3J(PC)|$ 3.3 Hz, $\underline{C}_{Ar}C_{Ar}$), 131.31 (d, $|^3J(PC)|$ 3.3 Hz, $\underline{C}_{Ar}C_{Ar}$), 130.64 (s, $\underline{C}_{Ar}H$), 130.02 (s, $\underline{C}_{Ar}H$), 125.88 (s, $\underline{C}_{Ar}H$), 122.34 (d, $|^4J(PC)|$ 2.1 Hz, $\underline{C}_{Ar}H$), 113.09 (s, $\underline{C}Me_2$), 77.19 (s, $\underline{C}HO$), 63.87 (d, $|^2J(PC)|$ 3.1 Hz, $\underline{C}H_2O$), 40.58 (d, $|^3J(PC)|$ 3.8 Hz, $\underline{C}H_2N$), 26.65 (s, $\underline{C}H_3$).

***cis*-$Mo(CO)_4\{(C_5H_8O_2)[C(O)NHCH_2CH_2OP(O_2C_{12}H_8)_2]_2\}_2$, *cis*-$Mo(CO)_4(8)$ (9).** To a 100 mL round-bottom flask were added 0.123 g (0.410 mmol) of $Mo(CO)_4(nbd)$ and 50 mL of degassed CH_2Cl_2. This solution was stirred until all of the $Mo(CO)_4)(nbd)$ had

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(29) Dieguez, M.; Pamies, O.; Ruiz, A.; Claver, C. *New J. Chem.* **2002**, *26*, 827.

(30) Cornils, B.; Herrmann, W. A. *Applied Homogeneous Catalysis with Organometallic Compounds: A Comprehensive Handbook in Two Volumes*; VCH: New York, 1996; p 2 v (xxxvi, 1246 pp).

(31) Powell, J.; Gregg, M.; Kuksis, A.; May, C. J.; Smith, S. J. *Organometallics* **1989**, *8*, 2918.

(32) Powell, J.; Kuksis, A.; May, C. J.; Meindl, P. E.; Smith, S. J. *Organometallics* **1989**, *8*, 2933.

(33) Powell, J.; Kuksis, A.; May, C. J.; Nyburg, S. C.; Smith, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 5941.

(34) Shriver, D. F. *J. Organomet. Chem.* **1975**, *94*, 259.

(35) McLain, S. J. *J. Am. Chem. Soc.* **1983**, *105*, 6355–7.

(36) Butler, J. M.; Jablonsky, M. J.; Gray, G. M. *Organometallics* **2003**, *22*, 1081.

(37) Duffey, C. H.; Lake, C. H.; Gray, G. M. *Inorg. Chim. Acta* **2001**, *317*, 199.

(38) Duffey, C. H.; Lake, C. H.; Gray, G. M. *Organometallics* **1998**, *17*, 3550.

(39) Gray, G. M. *Comments Inorg. Chem.* **1995**, *17*, 95.

(40) Hariharasarma, M.; Lake, C. H.; Watltins, C. L.; Gray, G. M. *J. Organomet. Chem.* **1999**, *580*, 328.

(41) Smith, D. C.; Lake, C. H.; Gray, G. M. *J. Chem. Soc., Dalton Trans.* **2003**, 2950.

(42) Cobley, C. J.; Froese, R. D. J.; Klosin, J.; Qin, C.; Whiteker, G. T.; Abboud, K. A. *Organometallics* **2007**, *26*, 2986.

(43) Verizhnikov, L. V.; Kirpichnikov, P. A. *Zh. Obshch. Khim.* **1967**, *37*, 1355.

(44) Ehrl, W.; Rinck, R.; Vahrenkamp, H. *J. Organomet. Chem.* **1973**, *56*, 285.

(45) Gray, G. M.; Fish, F. P.; Duffey, C. H. *Inorg. Chim. Acta* **1996**, *246*, 229.

(46) Varshney, A.; Gray, G. M. *Inorg. Chem.* **1991**, *30*, 1748.

(47) Varshavskii, Y. S.; Cherkasova, T. G. *Zh. Neorg. Khim.* **1967**, *12*, 1709.

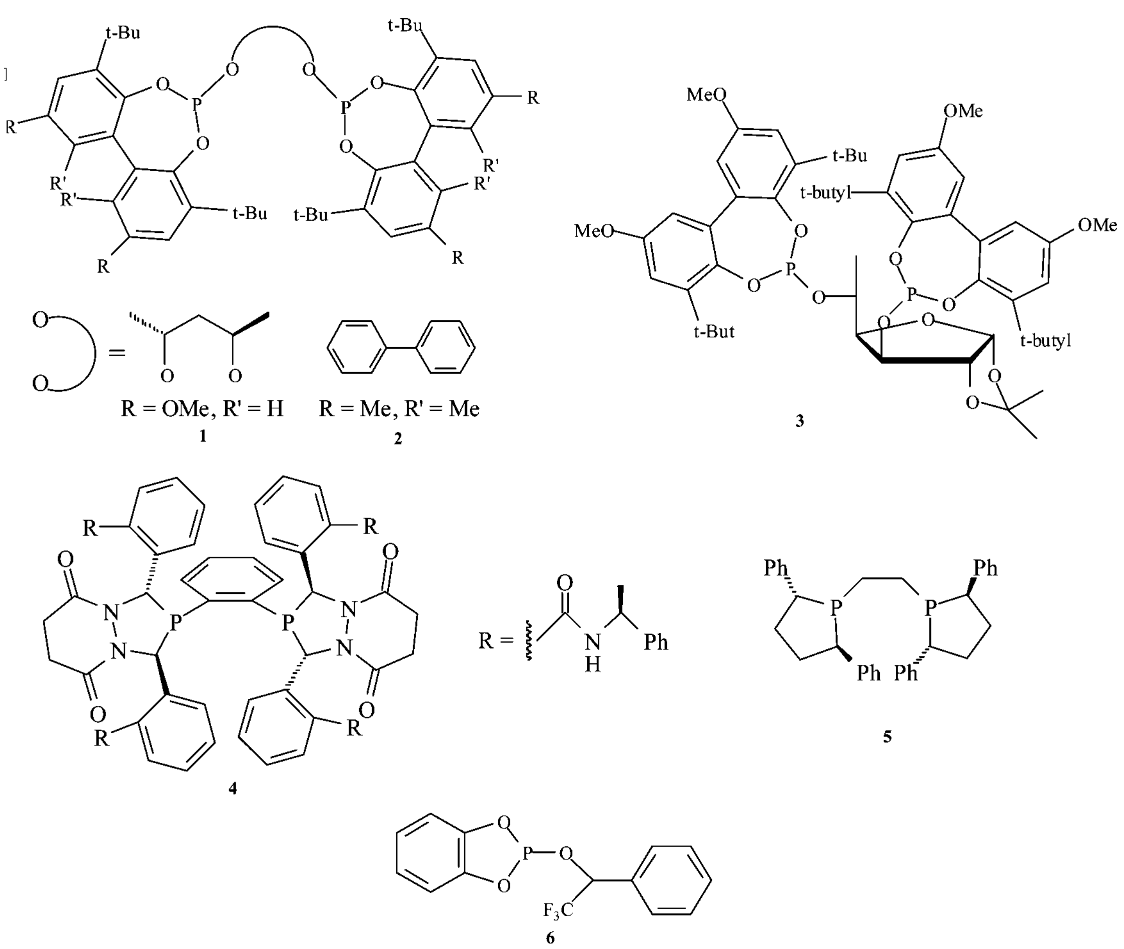


Figure 1. Ligands whose Rh(I) complexes are highly regioselective catalysts for the hydroformylation of styrene.

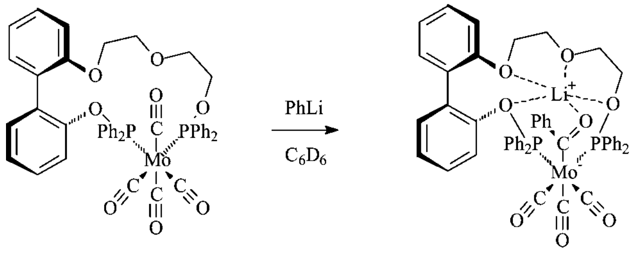


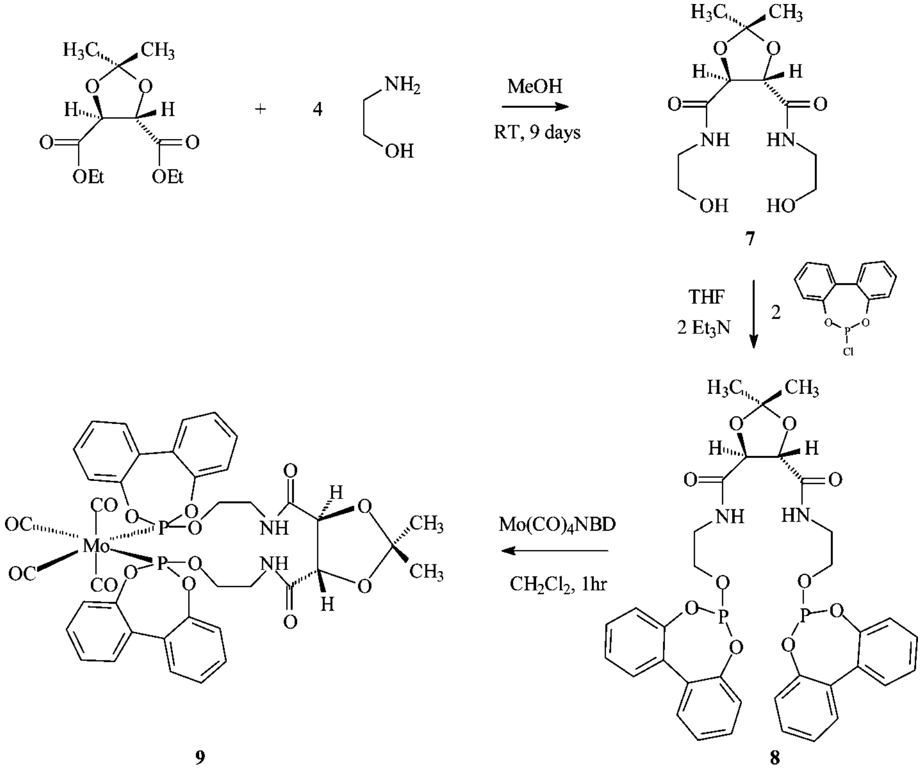
Figure 2. Activation of carbonyl ligands toward nucleophilic attack in metallacrown ethers.

dissolved, at which time 0.300 g (0.410 mmol) of **8** was added in one portion. The reaction mixture was stirred for 30 min, resulting in a pale yellow solution. A ^{31}P{^{1}H} NMR spectrum of the reaction mixture was then taken and exhibited the single resonance of the product. The mixture was evaporated to dryness and placed on the pump to ensure removal of all excess norbornadiene and solvent. The resulting dark yellow solid was taken up in CH_2Cl_2 and run through a ~1 cm thick pad of silica gel in a 15 cc medium sintered glass funnel under nitrogen. This colorless solution was again evaporated to dryness to yield 0.290 g (75.7%) of crude **9** as a white solid. Recrystallization from a dichloromethane/hexanes mixtures yielded analytically pure **9** as a white, microcrystalline solid. Anal. Calcd for $C_{47}H_{34}N_2O_{10}P_2Mo$: C, 51.33; H, 3.76. Found: 51.16; H, 3.84. ^{31}P{^{1}H} NMR ($CDCl_3$): δ 167.58 (s). ^{1}H NMR ($CDCl_3$): δ 7.0−7.7 (m, 16H, $\underline{H}_{Ar}$), 4.44 (s, 2H, $C\underline{H}$), 4.22 (dt, 4H, $|^3J(\mathrm{PH})|$ 7.3 Hz, $|^3J(\mathrm{HH})|$ 5.2 Hz, $C\underline{H}_2O$), 3.14 (dt, 4H, $|^3J(\mathrm{HH})|$ 5.0 Hz, $|^3J(\mathrm{HH})|$ 5.0 Hz, $C\underline{H}_2N$), 1.48 (s, 6H, $C\underline{H}_3$). ^{13}C{^{1}H} NMR ($CDCl_3$): 210.56 (*trans* $\underline{C}O$, dd, $|^2J(\mathrm{PC}) + {}^2J(\mathrm{PC'})|$ 29 Hz), 206.49 (*cis* $\underline{C}O$, t, $|^2J(\mathrm{PC})|$ 11 Hz), 170.21 (CO), 148.33 (d, $|^2J(\mathrm{PC})|$ 5.7 Hz, $\underline{C}_{Ar}O$), 147.64 (d, $|^2J(\mathrm{PC})|$ 5.3 Hz, $\underline{C}_{Ar}O$), 131.37 (d, $|^3J(\mathrm{PC})|$ 3.3 Hz, $\underline{C}_{Ar}C_{Ar}$), 130.78 (d, $|^3J(\mathrm{PC})|$ 3.3 Hz, $\underline{C}_{Ar}C_{Ar}$), 128.64 (s, $\underline{C}_{Ar}H$), 127.95 (s, $\underline{C}_{Ar}H$), 125.96 (s, $\underline{C}_{Ar}H$), 120.55 (d, $|^4J(\mathrm{PC})|$ 2.1 Hz, $\underline{C}_{Ar}H$), 117.09 (s, $\underline{C}Me_2$), 77.19 (s, $\underline{C}HO$), 65.97 (d, $|^2J(\mathrm{PC})|$ 3.1 Hz, $\underline{C}H_2O$), 41.28 (d, $|^3J(\mathrm{PC})|$ 3.8 Hz, $\underline{C}H_2N$), 27.69 (s, $\underline{C}H_3$).

Procedure for the Determination of Binding Stoichiometry from a Job Plot. Two stock solutions, each 0.025 M in 5.0 mL of acetonitrile-d_3, were prepared (110 mg of *cis*-$Mo(CO)_4$(**8**) or 17 mg of LiI). These stock solutions were used to prepare nine solutions in NMR tubes with varying ratios of complex to salt. In each case the total concentration of the sample remained constant. Each NMR sample was then analyzed by ^{31}P NMR using the Bruker DRX400 spectrometer. The resulting data were then plotted as the change in chemical shift ($\Delta\delta$) times the concentration of Mo complex versus the mole fraction (χ) of LiI. As with all Job plots, the binding stoichiometry was determined on the basis of the point at which the curve reaches a maximum.

Procedure for the Rhodium-Catalyzed Hydroformylation of Styrene. The catalysis reactions were carried out using a Parr Series 4560 minireactor connected to a high-pressure gas burette that introduced gas to the reactor at a constant pressure. The digitized reactor temperature, burette temperature, and burette pressure were monitored using Agilent Benchlink Data Logger software on a PC connected to an Agilent data acquisition switch unit. In a typical run, a solution of $Rh(CO)_2(acac)$ (3.37×10^{-5} mol) and the alkali metal salt, if used, in 12.0 mL of dry THF and a solution of ligand (4.04×10^{-5} mol) in 10.0 mL of dry THF were separately added to the reactor via needle transfer under nitrogen pressure through the substrate inlet valve. Next, the reactor was purged three times with a 1:1 H_2/CO gas (syngas) mixture and then pressurized to 20 atm with syngas and heated to 80 °C with mechanical stirring. The reactor was maintained under these

Scheme 2. Synthesis of Compounds 7−9



conditions for 45 min to allow for precatalyst equilibration and then was cooled to 40 °C before the pressure was vented. Styrene (0.0337 mol) was then injected into the reactor through the substrate inlet valve, after which the reactor was pressurized to 20 atm with syngas and heated to 80 °C. The reaction progress was then monitored using the Agilent software. The data obtained from the pressure drop versus time were fitted using Graphical Analysis version 3.4[48] with an exponential function to determine the pseudo-first-order rate constant. The regioselectivities and percent conversions of the catalytic reactions were determined by ^{1}H NMR. In the presence of large amounts of Li^+ and Na^+ and at long reaction times (generally overnight), an alkali metal-catalyzed aldol condensation reaction of the linear aldehyde was sometimes observed. If the proton resonance of the aldol product at 9.57 ppm was observed, its integrated intensity was doubled and added to that of the resonance for the linear aldehyde before the *iso/n* ratio was calculated.

Results and Discussion

The bis(phosphite) ligand **8** was synthesized in two steps from inexpensive starting materials as shown in Scheme 2. This procedure gave a high yield of **8**, and the ^{1}H, ^{13}C, and ^{31}P NMR spectra of **8** exhibited only the expected resonances. This allowed the bis(phosphite) ligand **8** to be used in the catalysis reactions without further purification.

The results for the hydroformylation of styrene with the Rh(I) catalysts with various phosphorus-donor ligands and both with and without an alkali metal salt are listed in Table 1. For each set of reaction conditions, two catalytic runs were carried out. In all cases, the differences in the rate constants were less than 11%, and the differences in the regioselectivities were less than 9%.

Table 1. Hydroformylation of Styrene Using 8, (*R*,*R*)-Chiraphite (1), and DPPE (10) as Ligands[d]

ligand + cation	conv %[a]	*iso/n*[a]	fitted *k* (s^{-1})[b]
8	>99	3.9	3.4×10^{-4}
8	>99	3.9	3.1×10^{-4}
32 equiv of $LiBPh_4$(**8**)	>99	6.1	3.3×10^{-4}
32 equiv of $LiBPh_4$(**8**)	>99	6.3	3.1×10^{-4}
8 equiv of $LiBPh_4$(**8**)	>99	7.1	2.8×10^{-4}
8 equiv of $LiBPh_4$(**8**)	>99	6.8	3.3×10^{-4}
4 equiv of $LiBPh_4$(**8**)	>99	5.6	2.4×10^{-4}
4 equiv of $LiBPh_4$(**8**)	>99	5.5	3.0×10^{-4}
2 equiv of $LiBPh_4$(**8**)	>99	4.3	2.8×10^{-4}
2 equiv of $LiBPh_4$(**8**)	>99	5.2	3.2×10^{-4}
1 equiv of $LiBPh_4$(**8**)	>99	4.2	3.2×10^{-4}
1 equiv of $LiBPh_4$(**8**)	>99	4.0	2.9×10^{-4}
32 equiv of $NaBPh_4$(**8**)	>99	6.6	2.9×10^{-4}
32 equiv of $NaBPh_4$(**8**)	>99	6.5	3.0×10^{-4}
8 equiv of $NaBPh_4$(**8**)	>99	5.4	2.9×10^{-4}
8 equiv of $NaBPh_4$(**8**)	>99	5.6	2.7×10^{-4}
2 equiv of $NaBPh_4$(**8**)	>99	4.7	2.5×10^{-4}
2 equiv of $NaBPh_4$(**8**)	>99	4.7	2.3×10^{-4}
32 equiv of TBA·BPh_4(**8**)	>99	3.5	2.0×10^{-4}
(*R*,*R*)-Chiraphite (**1**)	>99	10.1	5.0×10^{-4}
(*R*,*R*)-Chiraphite (**1**) w/32 equiv of $LiBPh_4$	>99	33.6	5.0×10^{-4}
(*R*,*R*)-Chiraphite (**1**) w/32 equiv of $NaBPh_4$	>99	16.6	5.0×10^{-4}
dppe (**10**)[c]	61	1.8	2.2×10^{-5}
dppe (**10**)[c] w/32 equiv of $LiBPh_4$	61	2.2	1.9×10^{-5}

[a] Conversion % and *iso/n* ratio were determined when pressure change was no longer observed using ^{1}H NMR. [b] Rate constant (*k*) was obtained from a first-order fit of pressure drop versus time using Graphical Analysis software.[48] [c] dppe is 1,2-bis(diphenylphosphino)ethane. [d] Conditions: ligand/Rh = 1.2, substrate/Rh = 1000. Hydrogenation was not observed in any of the experiments. All reactions were performed at 80 °C and 20 atm of CO/H_2.

It is very difficult to compare the results for the Rh(I) catalyst containing phosphite ligand **8** in Table 1 to those for reported in the literature for related systems because the reaction conditions used in the various references are quite different. The differing reaction conditions have significant effects both

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(48) *Graphical Analysis*; Vernier Software & Technology: Beaverton, OR, 2005.

Table 2. Comparative Ligands in the Hydroformylation of Styrene

ligand$^{\mathrm{ref}}$	substrate:Rh	*T* (°C)	*iso*/*n*	activity[a]
8 (w/32 equiv of $LiBPh_4$)	1000:1	80	12.4	1188 h^{-1}
1[25]	300:1	35	47	54%
1[25]	300:1	70	13	98%
2[25]	300:1	35	68	40%
2[25]	300:1	70	17	100%
2[25]	1000:1	70	16.9	95%
3[28]	1000:1	20	37.5	15 h^{-1}
4[25]	5000:1	80	6.6	100%
4[25]	30000:1	60	30	42%
4[25]	30000:1	80	13	85%
5[25]	5000:1	80	45.0	57%
5[25]	30000:1	80	45.0	33%
6[48]	4000:1	40	22.8	55 h^{-1}
6[48]	4000:1	100	1.3	2000 h^{-1}

[a] Activity is listed as a percent conversion after 3 h reaction time or as an initial turnover frequency (TOF), i.e., mol styrene per mol Rh per hour.

on reaction rates and on regioselectivities. Recently, Klosin and Landis have reported a comprehensive comparison of the rates, regioselectivities, and enantioselectivities of Rh(I) catalysts of a variety of bis(phosphorus-donor) ligands for the simultaneous hydroformylations of styrene, allyl cyanide, and vinyl acetate.[25] Although this study allows Rh(I) catalysts containing the various ligands to be compared, the reaction conditions and the manner in which the activities of the catalysts are reported makes direct comparison with our results very difficult. Thus, to compare the activity of the Rh(I) catalyst of our ligand, **8**, to those in the Klosin and Landis study, we have also evaluated a Rh(I) catalyst containing the commercially available (*R*,*R*)-Chiraphite ligand, **1**, under our reaction conditions. We chose **1** for comparison both because it is commercially available and because it is one of the most active and regioselective ligands in the Klosin and Landis study. As shown by the data in Table 1, the Rh(I) catalysts containing **1** and **8** have similar activities, with the Rh(I) catalyst containing **1** being slightly more active.

Comparisons of regioselectivities are also difficult because milder reaction conditions invariably result in higher regioselectivities. In the Klosin and Landis study, the most regioselective catalysts are Rh(I) complexes of **2**, **4**, and **5**, and selected data for these catalysts are given in Table 2. The Rh(I) complex of **2** gives a very high *iso/n* (68) under mild reaction conditions that result in a low conversion. However, the *iso/n* drops to 17 under conditions that are more comparable to those in this study. For comparison, the Rh(I) catalyst containing **1** gives a 13 *iso/n* under the same conditions and a 10.1 *iso/n* under our reaction conditions (Table 1). The Rh(I) catalyst containing **5** gives a 45 *iso/n* under conditions that are comparable to those in this study, but the conversion is lower (54%). A highly regioselective catalyst not in the Klosin and Landis study is the Rh(I) complex of **3** (Figure 1), developed by Diéguez et al.[27−29] This catalyst exhibits excellent regioselectivity for the *iso* product of styrene (37.5 *iso/n*) at 20 °C and 10 atm; however the turnover frequency (TOF) is only 15, corresponding to a pseudo-first-order rate constant of 4.2×10^{-6} s^{-1}.[49] Finally, the Rh(I) complex of the monophosphite ligand **6** developed by Odinets et al.,[50] which is also not in the Klosin and Landis study, exhibits a high regioselectivity (22.8 *iso/n*) at 40 °C and 100 atm, but the activity of the catalyst is low, with an initial TOF of 55, corresponding to a rate constant of about 3.8×10^{-6} s^{-1}. When the reaction temperature is raised to 100 °C, the initial TOF increases to 2000 ($k = 1.4 \times 10^{-4}$ s^{-1}), which is comparable to that of the Rh(I) complex of **8**, but the regioselectivity decreases to 1.3 *iso/n*, which is significantly lower than that of the Rh(I) complex of **8**. These results indicate that, as expected, the catalysts containing ligands with rigid backbones (**1**, **2**, **3**, **4**, **5**) exhibit higher regioselectivities than do catalysts of ligands with flexible backbones such as **8** or monodentate ligands such as **6**.

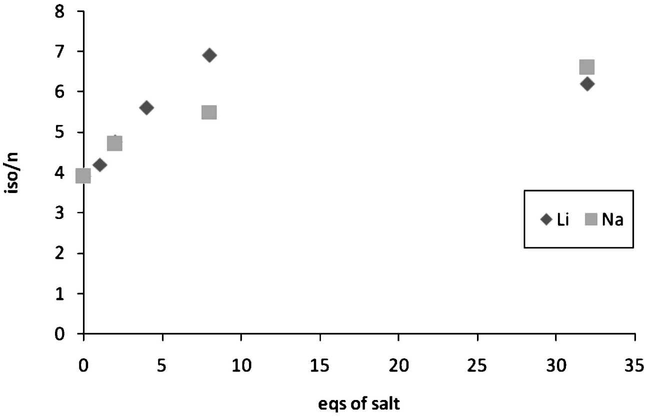

Figure 3. Dependence of the regioselectivity on the amount of salt used in the catalytic hydroformylation of styrene using a Rh(I) complex of **8** as the catalyst.

The most interesting feature of the catalytic data reported in this paper is that the addition of alkali metal salts to the Rh(I) complexes containing either **1** or **8** significantly improves the regioselectivity of the catalyst without lowering the reaction rate. Both the amount and the nature of the alkali metal cation have a significant effect on the regioselectivity, as shown by the data in Table 1 and the plot in Figure 3.

The increase in the regioselectivity in the presence of alkali metal salts does not appear to be due to an increase in the ionic strength of the solution. No increase in the regioselectivity is observed in the presence of an equal concentration of the noncoordinating salt $TBA \cdot BPh_4$, and the two alkali metal salts have different effects on the regioselectivities at the same concentrations. Further, an ionic strength effect might be expected to be linear with concentration at the relatively low concentrations of salts in these solutions (from 1.3×10^{-3} M for a 1:1 Rh:salt ratio to 4.1×10^{-2} M for a 1:32 Rh:salt ratio), but Figure 3 clearly shows that it is not.

As discussed in the Introduction, the most likely explanation for the effect of alkali metal salts on the regioselectivity of the hydroformylation reaction is that equilibrium exists between the alkali metal cation coordinated to the THF and the alkali metal coordinated to the oxygen of a carbonyl ligand. The coordination of the alkali metal cation to the oxygen to a carbonyl ligand activates that ligand toward migratory insertion. The different effects of the alkali metal cations could be due either to the different charge to size ratios of the Li^+ and Na^+ cation or to differing abilities of the catalysts to bind the Li^+ and Na^+ or to a combination of both factors.

To gain more insight into the effect of high salt concentrations on the regioselectivity of metallacrown ether catalysts, discussed above, the effects of alkali metal salts on the regioselectivities of the Rh(I) complexes of **1** and **8** were compared. As shown in Table 1, the addition of 32 equiv of $LiBPh_4$ increases the regioselectivity of the Rh(I) complex of **1** from 10.1 *iso/n* to 33.6 *iso/n*, while the addition of 32 equiv of $NaBPh_4$ increases

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(49) Initial turnover frequencies were converted to pseudo-first-order rate constants using the following equation: $TOF_o = k[S]_o/[C]$, where [S] is the substrate concentration and [C] is the catalyst concentration.

(50) Odinets, R.; Kegl, T.; Sharova, E.; Artyushin, O.; Goryunov, E.; Molchanova, G.; Lyssenko, K.; Mastryukova, T.; Roschenthaler, G. V.; Keglevich, G.; Kollar, L. *J. Organomet. Chem.* **2005**, *690*, 3456.

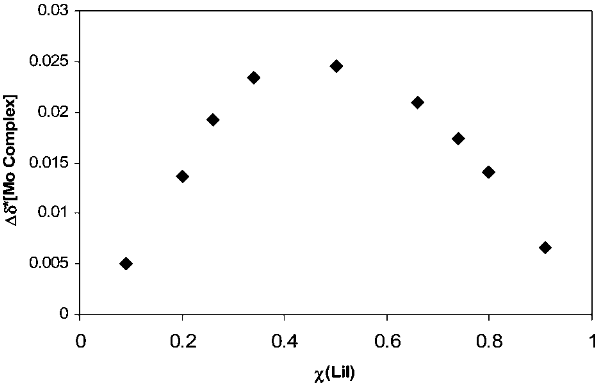

Figure 4. Job plot of **3** with LiI showing 1:1 binding stoichiometry.

the regioselectivity to 16.6 *iso/n*. The relative increases (3.3 × for $LiBPh_4$ and 1.6 × for $NaBPh_4$) are roughly twice those for the Rh(I) complex of **8** with $LiBPh_4$ (1.5×) but approximately the same as those for this complex with $NaBPh_4$ (1.5×). These differences in the effects of the alkali metal cations on the regioselectivities of the Rh(I) complexes of **1** and **8** suggest that the effect is not solely due to the coordination of the alkali metal cation to a carbonyl oxygen but that coordination to the complex is also playing a role. To further support this, the effect of $LiBPh_4$ on the hydroformylation of styrene was studied with a Rh(I) complex of dppe (**10**), a ligand that has no oxygen donor groups to coordinate to the Li^+. When 32 equiv of $LiBPh_4$ was added, only a slight increase in regioselectivity was observed (1.2×). This strongly suggests that interactions of the alkali metal cation with the oxygens of the phosphites facilitate the interaction of the cation with the carbonyl oxygens to enhance the regioselectivity. The ability of phosphite oxygens to coordinate alkali metal cations has previously been demonstrated by Powell and co-workers.[32] It is less obvious as to whether interactions with other functional groups in ligand **8**, similar to those shown in Figure 2, are affecting this process.

If the hypothesis as to the mode of action of the alkali metal cations is correct, metallacrown ethers containing **8** should only weakly bind Li^+ and Na^+. To determine if this is the case, the *cis*-$Mo(CO)_4$(**8**) metallacrown ether, **9**, was synthesized as shown in Scheme 2. Binding of Li^+ and Na^+ to **9** in acetonitrile-d_3 was measured using $^{31}P\{^1H\}$ NMR spectroscopy. Significant shifts in the $^{31}P\{^1H\}$ NMR resonance of **9** were observed upon addition of $LiBPh_4 \cdot 3dme$, but no shifts were observed upon addition of $NaBPh_4$. A Job plot for the binding of $LiBPh_4 \cdot 3dme$ by **9**, shown in Figure 4, indicates that the stoichiometry of the complex is 1:1. The relatively smooth curve of the Job plot suggests that **9** only weakly binds Li^+ cations. The fact that **9** binds Li^+ but not Na^+ is consistent with the greater effect of Li^+ on the regioselectivity, but this datum is not sufficient to exclude an effect based solely upon the smaller charge to size ratio of Li^+. The weak binding is consistent with the large excesses of the alkali metal salts that are needed to maximize the regioselectivity of the catalysis because the bis(phosphite) catalyst probably does not efficiently compete for the cations with the strongly coordinating THF solvent that is used in the catalytic reactions.

Conclusion

We have shown that a Rh(I) complex containing an α,ω-bis(phosphite) ligand with two amido groups, **8**, is an active catalyst for the hydroformylation of styrene. More importantly, we have demonstrated that the regioselectivity of this catalyst and of a Rh(I) complex of (*R*,*R*)-Chiraphite, **1**, another bis(phosphite) ligand, can be greatly improved by the addition of hard metal cations without adversely affecting the activities of the catalysts. The facts that higher relative increases in regioselectivities are observed only for Rh(I) complexes of bis(phosphite) ligands and not for Rh(I) complexes of bis(phosphine) ligands and that a $Mo(CO)_4$ metallacrown ether complex of **8** is a weak binder for Li^+ suggest that cation binding by the bis(phosphite) ligands is having a positive effect on the regioselectivity. If this is the case, it may be possible to observe even larger increases in regioselectivities by developing bis(phosphite) ligand complexes that more strongly bind alkali metal cations and/or by using alkali metal salts in solvents that do not strongly coordinate to the alkali metal cations. In addition, it may also be possible to increase the activity of the catalysts by modifying the linker group and/or phosphite substituents. Finally, it may be possible to develop these catalysts for enantioselective hydroformylation. Although **8** is chiral, it seems unlikely that the chiral centers are within suitable range of the metal center to allow for any enantioselectivity.[51] However, introduction of additional chiral centers in the phosphite backbone and/or the phosphite substituents could lead to ligands that can perform enantioselective catalysis. It will also be interesting to see if the addition of cations can have an effect on the enantioselectivities similar to that of with the current work on increasing regioselectivities. These issues will be addressed in future papers.

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(51) Freixa, Z.; Bayon, J. C. *J. Chem. Soc., Dalton Trans.* **2001**, 2067.