Supercritical and Liquid Solvent Effects on the Enantioselectivity of Asymmetric Cyclopropanation with Tetrakis[1-[(4-*tert*-butylphenyl)-sulfonyl]-(2*S*)-pyrrolidinecarboxylate]dirhodium(II)

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Abstract: The enantioselectivity of the cyclopropanation of styrene and methyl phenyldiazoacetate in the presence of a dirhodium carboxylate catalyst was found to be dependent on both the dielectric constant and the coordinating ability of the solvent. The enantiomeric excess is pressure dependent in supercritical fluoroform, changing from as low as 40% ee at pressures above 100 bar to nearly 80% ee at pressures near the critical point. The pressure dependence is caused by the changing dielectric constant of the fluoroform. Reactions in some coordinating liquid solvents had greater enantioselectivities than expected on the basis of dielectric constant alone. The crystal structure of the catalyst was obtained along with spectroscopic data in order to elucidate the causes of the solvent-dependent enantioselectivity.

Introduction

The choice of solvent can have a dramatic effect on the enantioselectivity of asymmetric homogeneous catalysis.[1−5] To understand and optimize solvent-dependent enantioselectivity, one normally performs a solvent study in which the reaction is tested in a variety of different solvents and the results are rationalized by noting relationships between the properties of the solvent and the selectivity. A complication with this approach is that solvents differ in more than one property; individual properties of the solvent can be difficult to isolate. For example, a change from a solvent with a low dielectric constant (ϵ_r) to a solvent with a high ϵ_r will usually be accompanied by a change in the coordinating ability, Lewis basicity, acidity, and other properties of the solvent.[6−8] This problem can be overcome by utilizing supercritical fluids (SCFs). Because the solvent properties of supercritical fluids are pressure dependent, selected solvent properties can be varied while keeping the chemical nature of the solvent unchanged.

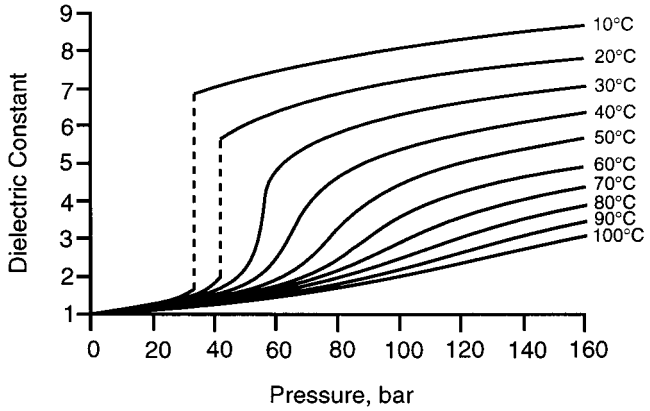

Figure 1. The dielectric constant of fluoroform as a function of pressure and temperature.[63] Curves for temperatures below 70 °C were drawn from published data,[9,64] while the curves for T ≥ 70 °C are based upon the equation of Rhodes et al.[65] and published densities.[66,67]

For example, the dielectric constant of supercritical fluoroform ($scCHF_3$) is a strong function of pressure at 30 °C; it is a medium-polar solvent ($\epsilon_r = 7$) at 120 bar but a relatively nonpolar solvent ($\epsilon_r = 3$) at 52 bar (Figure 1).[9] Supercritical solvent studies are complementary to liquid studies in that one can use the results in SCFs to isolate the effect of a property such as the dielectric constant and consequently elucidate the effects of the other properties. Liquid solvents, on the other hand, have the advantages of ease of use and a wider range of dielectric constants. The information derived from combined supercritical and liquid solvent studies can be used to elucidate the role of solvent and to optimize the selectivity.

The tunable properties of supercritical solvents offer an exciting new method of performing solvent studies. Chemical synthesis in supercritical fluids has become an important new field in chemistry and chemical engineering,[10,11] and the effect of pressure on solvent properties and therefore reaction perfor-

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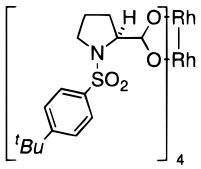
mance in supercritical fluids is one of the factors which is most often explored. Pressure dependence of catalytic selectivity in SCFs has been observed previously and attributed to dilution[12] or changes in tuning functions or activation volumes of competing transition states.[13,14] The effect of the dielectric constant change of SCFs on the selectivity of homogeneous catalysis has not been explored nor has the effect of pressure on enantioselective homogeneous catalysis in SCFs.[15] We set out to demonstrate a case of pressure-dependent enantioselective homogeneous catalysis in a SCF and then to demonstrate the utility of such a discovery as part of a solvent study.

Asymmetric cyclopropanation, a synthetically important reaction,[3,16] has been shown to exhibit interesting solvent effects in liquid reactions.[2−5,17] One of the most successful cyclopropanation catalysts is the complex tetrakis[1-[(4-*tert*-butylphenyl)-sulfonyl]-(2*S*)-pyrrolidinecarboxylate]dirhodium(II) ([Rh_2(TBSP)$_4$], **1**) developed by Davies[2,3] as a hexane-soluble analogue of McKervey's tetrakis[1-[phenylsulfonyl]-(2*S*)-pyrrolidinecarboxylate]dirhodium(II) catalyst.[18]



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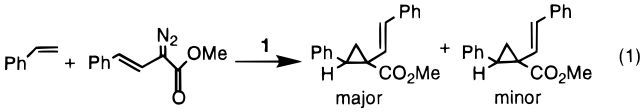
Cyclopropanation involving diazo decomposition in the presence of this catalyst was studied by Davies[2,3] (eq 1) and Doyle[4] (eq 2). Both studies found a dramatic increase in the



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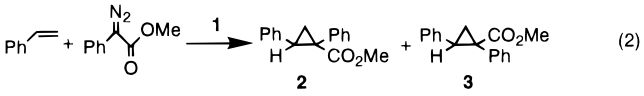

(2)

enantiomeric excess (ee) of the major diastereomer upon changing the reaction solvent from methylene chloride to pentane, from 74% ee to 90% ee and from 61% ee to 85% ee, for eqs 1 and 2, respectively. Davies proposed that the solvent effect was due to the difference between the dielectric constants of the two solvents (CH_2Cl_2, $\epsilon_r = 9.08$; C_5H_{12}, $\epsilon_r = 1.84$),[19] although this is not the only property by which CH_2Cl_2 and pentane differ (they also differ in their ability to coordinate to metal complexes).[20−22] We suspected therefore that the enantiomeric excess might be pressure dependent in supercritical fluoroform (scCHF$_3$; $T_c = 25.9$ °C, $P_c = 48.2$ bar). A communication describing our preliminary findings was published recently.[23] Here, we present, along with a complete analysis of the pressure dependent enantioselectivity, new data which describe coordination effects on selectivity. This study provides additional insight into the solvent -dependent enantioselectivity seen with the [Rh_2(TBSP)$_4$] catalyst.

Experimental Section

Materials. The [Rh_2(*S*-TBSP)$_4$] catalyst was prepared according to the literature method[24] for the pressure dependence studies. However, for the later coordinating effect studies (Tables 1 and 2), commercially available catalyst was used (Aldrich). The styrene (Aldrich) contained 10−15 ppm of 4-*tert*-butyl catechol, which was not removed by distillation because this was found to have no effect on the enantioselectivity of the reaction. The methyl phenyldiazoacetate was synthesized from phenylglycine methyl ester and isoamyl nitrite.[25] The CHF_3 (AGA Specialty Gas, 99.995% pure) and CO_2 (Air Products and Chemicals, Inc., 99.9999% pure) were passed through an oxygen trap (Alltech) before use. Nitrous oxide (Nellcor Puritan Bennett, 99.998%, $O_2 < 2$ ppm) was used as received. Liquid solvents (98−99% pure) were purchased from a variety of manufacturers and were dried by distillation from sodium benzophenone ketyl (hexane, THF) or molecular sieves (DMF, CH_2Cl_2, NEt_3, MeCN). Chloroform (Spectrophotometric grade with amylene inhibitor) was dried with oven-dried K_2CO_3. The trialkyl phosphines and triethylphosphine oxide were stored and used under nitrogen in a drybox.

Equipment/Spectroscopy. The supercritical experimental apparatus is presented schematically in Figure 2. The gases were pressurized via an ISCO syringe pump (model 500D) and were delivered through 1/16 in. stainless steel HPLC tubing and a Rheodyne model 7725 HPLC injector to the reaction vessel. The reactions were carried out in a Parr 160 mL stainless steel vessel fitted with a pressure transducer, thermocouple, burst disk, and two reagent addition ports. The apparatus also includes an acetone reservoir and a wash pump to allow cleaning of the gas lines. The injector was cleaned after every reaction. The vessel was heated by a water bath fitted with a Fisher Isotemp recirculator. A magnetic stirrer custom-made by Glas-Col was placed underneath the water bath and directly below the vessel; tests showed that this stirrer was able to reproducibly couple with a magnetic stir bar inside the vessel. All enantiomeric excesses were determined by

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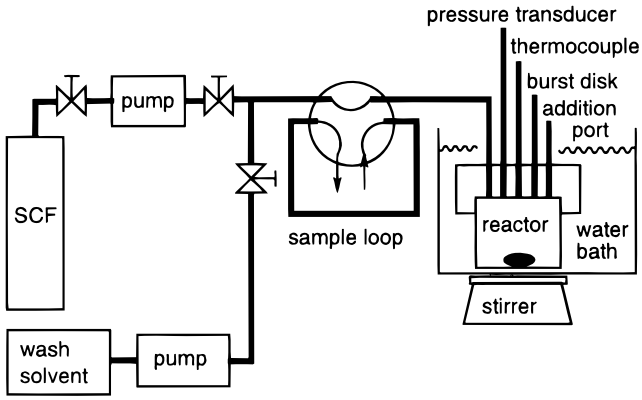

Figure 2. Experimental apparatus.

GC on a Chirasil-Dex CB column (25 m × 0.25 mm × 0.25 μm, T = 170 °C, split ratio 7.7).

All liquid UV/vis measurements were obtained with a Hewlett-Packard 8452A diode array spectrophotometer for solutions in 1.0 cm path length quartz cuvettes. Airtight cuvettes filled under nitrogen were used for solutions containing trialkyphosphines or triethylphosphine oxide. The UV/vis measurements in SCFs were obtained in a 160 mL vessel with diametrically opposed sapphire windows (path length = 14.3 cm) on an Olis (Rapid Scanning Monochromator) spectrometer. All NMR data was collected on a General Electric 300 MHz spectrophotometer.

Cyclopropanation in SCFs. To the 160 mL steel vessel were added 440 μmol of styrene and 0.69 μmol of $[Rh_2(TBSP)_4]$ along with a stirbar. The vessel was placed in a water bath at the desired temperature and allowed to equilibrate (30 °C for reactions in $scCHF_3$ and 35 °C for reactions in $scCO_2$). The vessel was purged with the gas to be used and stirring was started. The vessel was then pressurized to above the critical pressure but below the desired pressure. After allowing for the temperature of the vessel to equilibrate for 10 min, 56 μmol of methyl phenyldiazoacetate was added via the HPLC injector and carried into the vessel with the remaining amount of SCF. To stop the reaction (usually after 1 h), the vessel was cooled in a dry ice/acetone bath until the pressure dropped to <5 bar, vented, and allowed to warm to room temperature. The vessel was opened; the colorless liquid inside was dissolved in acetone and analyzed by GC.

Cyclopropanation in Liquid Solvents. The liquid-phase reactions were performed by dissolving styrene (440 μmol), $[Rh_2(TBSP)_4]$ (0.69 μmol), and any added ligand (14 μmol, 20 mol per mol of catalyst) into 4 mL of solvent in a 10 mL vial at room temperature under nitrogen. The mixture was stirred until the catalyst appeared to be dissolved, and then the methyl phenyldiazoacetate (56 μmol) was added. The reaction time required depended on the solvent, but all reactions were given at least 1 h. The reaction was considered complete when the bright orange of the diazoacetate completely disappeared.

Cyclopropanation in Liquid Nitrous Oxide. SAFETY WARNING: Nitrous oxide is a thermodynamically powerful oxidant. Never mix high concentrations of organic compounds with liquid or supercritical N_2O. Explosions have occurred with a 9 vol % solution of ethanol in scN_2O, with a mixture of 25 mL of cyclohexene in 75 mL of scN_2O, and with a mixture of 1 g of ground coffee in 2.5 mL of scN_2O.[26−29] To minimize the risk, we choose to keep the combustible substrate to microscale quantities and *very low concentrations*. In addition, we employ a burst disk, blast shield, and eye protection in all experiments. Diluting N_2O with CO_2 may further enhance the safety. Combustible cosolvents should not be used with compressed N_2O under any circumstances. Never use an oil-based compressor to pressurize nitrous oxide; if the N_2O were to leak into the oil, an explosion could result.[27]

Styrene (440 μmol), $[Rh_2(TBSP)_4]$ (0.69 μmol), and a stirbar were placed, under air, into a flat-bottomed glass liner (5.5 cm diameter) in a 160 mL steel vessel equipped with diametrically opposed sapphire windows. Methyl phenyldiazoacetate (56 μmol) was placed in a 0.7 mL microbeaker inside the glass liner. The vessel was purged with N_2O and then placed in a water bath at 28 °C. Liquid nitrous oxide was pumped into the vessel until the liquid level rose above the top of the microbeaker. Stirring was then started. To stop the reaction after 2 h, the vessel was very slowly vented and then opened; the colorless liquid inside was dissolved in acetone and analyzed by GC.

Solubility Studies. Solubility of the substrates in $scCO_2$ (35 °C) or $scCHF_3$ (30 °C) was verified by the following methods. The dissolution of the styrene and diazoacetate (twice the concentration used for cyclopropanation reactions) was confirmed visually in a 160 mL vessel fitted with sapphire windows. The reagents were found to be dissolved completely by 51 bar. For this reason the lowest pressure used for the catalytic experiments was 52 bar. The solubility was verified in this manner for both of the substrates separately and for a mixture of the styrene and methyl phenyldiazoacetate in the proportions used in experiments but again at double the normal concentration. Because of the small quantity of catalyst used, the catalyst solubility could not be detected visually. The solubility of the catalyst in $scCHF_3$ was confirmed by UV/vis spectroscopy by dissolving the catalyst in the SCF in the sapphire-windowed vessel. The absorbance (at 290 nm) at 51 bar was identical to the absorbance at 122 bar, indicating that all of the 1.3 mg (0.90 μmol) had dissolved at both pressures. As a further demonstration that the catalyst was homogeneous,[30] the catalyst was put into a small beaker in the vessel and the vessel was pressurized to 60 bar for 1 h without stirring. The beaker was then removed from the vessel and a reaction was performed in the vessel without the addition of more catalyst. That the reaction proceeded asymmetrically is considered evidence that the active catalyst was soluble.

Crystallography. $[Rh_2(TBSP)_4(DMF)_2]$ crystals were grown in a 7 in. NMR tube in the following manner. About 1 mL of a concentrated solution of $[Rh_2(TBSP)_4]$ in toluene was placed into the NMR tube, and 20 μL of dimethylformamide was added to this portion and allowed to mix. About 1 mL of pentane was slowly layered on top of the toluene solution. The NMR tube was capped and allowed to sit for 2 weeks. Long, thin, blue needles formed. A needle of dimensions 0.05 × 0.05 × 0.35 mm was mounted in the CRYO Industries cold stream of a Bruker SMART 1000 diffractometer equipped with a sealed Mo tube and graphite monochromator. Approximately a $^1/_2$ sphere of data (98% completeness) were collected to a maximum 2Θ of 63°. No decay in the intensities of 50 standard frames was observed. Of 76 290 reflections measured, 24 884 were unique, R(int) = 0.114. The structure was solved using direct methods. Refinement was by full-matrix least-squares methods, based on F^2, using all data. Hydrogen atoms were located on a difference map and constrained during refinement. The solvent molecules of toluene and *n*-pentane occupy the same site. They were initially refined as rigid groups but were fixed in the final cycles of refinement. No chemically significant peaks were present in the final difference map. No extinction or absorption corrections were applied. The handedness of the structure was determined by calculation of the Flack parameter, −0.02(2). Crystallographic programs were those of SHELXTL 5.1.[31] Tables of neutral atom scattering factors, f' and f'', and absorption coefficients are from International Tables for Crystallography.[32]

Results

The asymmetric cyclopropanation reaction in eq 2 proceeds readily in $scCHF_3$, producing compound **2** and no traces of diastereomer **3**. The reaction was performed in $scCHF_3$ at several pressures, and the enantiomeric excess (ee) of the product was

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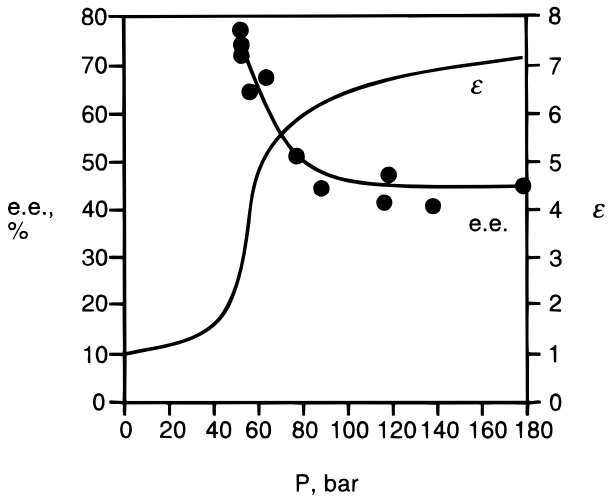

Figure 3. The dependence of the dielectric constant[9,64] of fluoroform and the enantiomeric excess of cyclopropanation performed in $scCHF_3$ on the pressure of fluoroform at 30 °C.

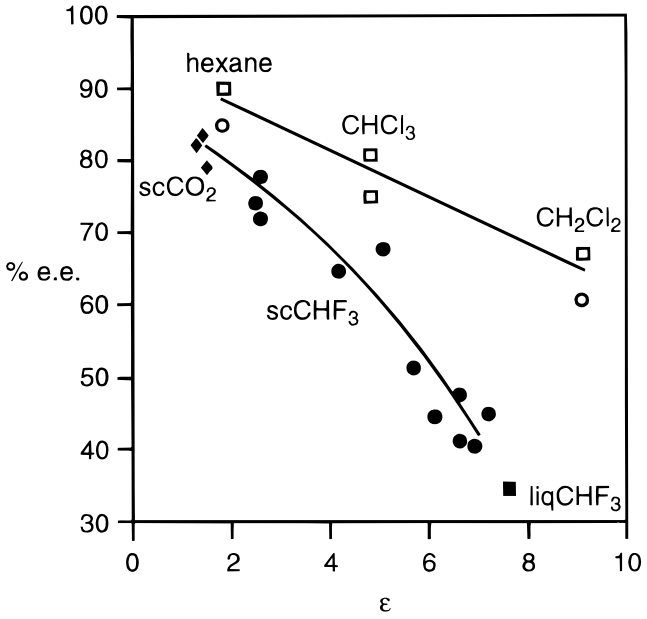

Figure 4. The dependence of the enantiomeric excess of **2** on the dielectric constant of $scCHF_3$ (●), $scCO_2$ (◆), liquid CHF_3 (■), or noncoordinating liquid solvents (literature[4] data ○, our data □). The two data points for $CHCl_3$ correspond to the amylene- (lower point) and ethanol-stabilized (upper point) solvents.

found to be a function of the pressure at which the reaction was performed (Figure 3). The ee is as low as 40% at pressures above 100 bar and as high as 78% at pressures close to the critical point. This is the first example of pressure-dependent enantioselectivity in homogeneous catalysis in SCFs or indeed in any medium at pressures below thousands of bar. As seen in the plot of ee vs dielectric constant (Figure 4), the results in CHF_3 show the same trend as the results in noncoordinating liquid solvents. This suggests that the pressure-dependent enantioselectivity is due to dielectric constant effects rather than other pressure-related effects such as dilution or solute−solvent clustering. As further evidence, when the reaction is performed in $scCO_2$ (T_c = 31 °C, P_c = 73.8 bar) at 35 °C, the enantioselectivity is essentially pressure independent (Figure 5), as expected because the dielectric constant of $scCO_2$ changes only very slightly with pressure.[33] Although the dielectric constant dependence was evident, it was unclear why the selectivity in

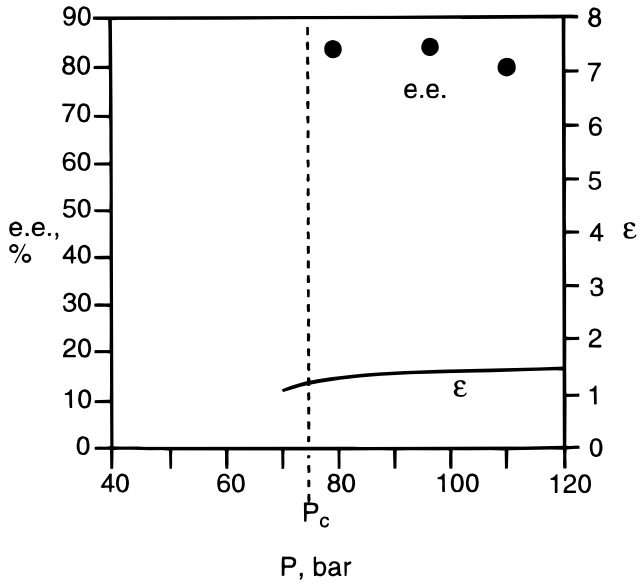

Figure 5. The dependence of the dielectric constant of carbon dioxide[33] and the enantiomeric excess of cyclopropanation performed in $scCO_2$ on the pressure of carbon dioxide at 35 °C.

SCFs was slightly lower than in liquids. We therefore tested the effects of the following: temperature, injection method, ability of the steel vessel walls to catalyze the reaction, and the role of trace water. These studies are described in the Supporting Information. The conclusions were that the temperature and injection method have only a negligible effect on the ee but that the use of a steel vessel lowers the ee, possibly because of a competing steel-catalyzed cyclopropanation.

Coordination Effects. The effect of solvent coordinating ability can be isolated from the effect of the dielectric constant by comparing two solvents with differing coordinating ability but identical dielectric constants. The reaction was performed in THF (ϵ_r = 7.6 at 25 °C)[34] to see if its coordinating ability causes the selectivity to differ from CHF_3 at the same dielectric constant. With the help of published dielectric constant data,[9] we were able to tune the dielectric constant of CHF_3 to match that of THF. The dielectric constant matches when the CHF_3 is at 25 °C and 156 bar (Figure 1), which happens to be just inside the liquid portion of the CHF_3 phase diagram. Because of the extremely dilute conditions, the reagent contribution to the dielectric constant of the medium could be neglected. The enantiomeric excess of the product of the reaction in the liquid CHF_3 was 35%, which falls along the line for the results in $scCHF_3$ (Figure 4). Surprisingly, the enantioselectivity in THF was 81%, far higher than the result in CHF_3 and higher than would be expected (∼70%) in a noncoordinating liquid solvent with a dielectric constant of 7.6. These results demonstrate that the dielectric constant is not the only parameter which controls the ee; another parameter such as coordinating ability is involved.

Other potentially coordinating solvents, including acetonitrile, triethylamine, *N*,*N*-dimethylformamide (DMF), and compressed liquid nitrous oxide (N_2O), also had an effect on the enantioselectivity (Table 1). The enantioselectivity was found to vary over a wide range and have no correlation to the dielectric constant of the solvent, probably because the other solvent properties overwhelm the dielectric constant effect. For example,

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Table 1. Enantiomeric Excess of Product **2** after Cyclopropanation with $[Rh_2(TBSP)_4]$ in Various Solvents[a]

slvent	additive	color	ee, %
hexane	none	green	90
hexane	$OP(Oct)_3$	green	90
hexane	$OPPh_3$	green	90
hexane	$OP(OEt)_3$	green	89
hexane	$OPEt_3$	green	82
hexane	$P(mes)_3$	green	90
hexane	(*R*)-BINAP	orange	90
hexane	(*S*)-BINAP	orange	89
hexane	PCy_3	orange	88
hexane	PPh_3	orange	46
hexane	PEt_3	yellow	21
hexane	H_2O	green	67
hexane	$H_2O + OP(Oct)_3$[c]	green	89
hexane	$H_2O + OP(Oct)_3$[d]	green	65
N_2O[b]	none	green	84
THF	none	green	81
MeCN	none	purple	73
DMF	none	blue	69
CH_2Cl_2	none	green	67
NEt_3	none	purple	55

[a] Performed in glassware at 20 °C. Additive:**1** molar ratio = 20:1. [b] Performed in a glass liner inside a steel vessel at 28 °C. [c] H_2O:$OP(Oct)_3$:**1** molar ratio = 16:20:1. [d] H_2O:$OP(Oct)_3$:**1** molar ratio = 100:20:1.

the ee of the product from a run in acetonitrile was 73%, much higher than would be expected for a solvent of a dielectric constant of 36. The trend in ee is hexane > N_2O > THF ≫ MeCN > DMF ≈ CH_2Cl_2 > NEt_3. The trend in dielectric constants is N_2O ≈ hexane < NEt_3 ≪ THF < CH_2Cl_2 ≪ MeCN ≈ DMF. The trend in donor number is CH_2Cl_2 < MeCN < THF < DMF < NEt_3 (value not known for hexane or N_2O) while the trend in acceptor number is hexane ≈ NEt_3 < THF < DMF < MeCN ≈ CH_2Cl_2 (value not known for N_2O).[6] It is evident that the enantioselectivity does not correlate with any of these properties (nor does it correlate to other related[8] solvent scales). If one were to compare the observed ee to the predicted ee (based on the dielectric constant), one could group the solvents into those that gave a much greater ee than predicted (DMF, MeCN), those that gave a moderate increase (THF), and those that gave a moderate decrease (NEt_3). The difference between observed and predicted ee correlates to neither the donor number nor the acceptor number of the solvent.

Solutions of coordinating reagents in hexane were also tested as reaction media. The reagents were triethylphosphine, tricyclohexylphosphine, trimesitylphosphine, triphenylphosphine, (*R*)-(+)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (*R*-BINAP), (*S*)-(−)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (*S*-BINAP), triethylphosphine oxide, triphenylphosphine oxide, and tri-*n*-octylphosphine oxide. The results are listed in Table 1. The bulkiest phosphine ligands (trimesitylphosphine, tricyclohexylphosphine, and the BINAP ligands) did not seem to affect the ee significantly. However, the smaller phosphines (PPh_3 and PEt_3) caused a significant drop in the ee and caused the formation of several unidentified byproducts. Phosphine oxides and triethyl phosphate had no detrimental effect and in fact greatly enhanced the ee of reactions performed in solvents that had not been rigorously dried.

Product yield was also affected by the presence of coordinating reagents. In hexane, the conversion was 100% (after 1 h) and the spectroscopically determined yield was 84%, with the remainder being unidentified byproducts. In somewhat more coordinating solutions, the yield was slightly lower (61% in MeCN after 5 h). However, in the presence of strongly basic coordinating reagents, the yields and conversions dropped dramatically; with PPh_3 for example, the product mixture contained only 5% of **2** and 20% starting material, while with NEt_3 the mixture contained less than 1% of **2** and 68% starting material, despite the fact that these reactions were run for 48 h.

Table 2. The Wavelengths (λ, nm) and Extinction Coefficients (ϵ, $cm^{-1}\ M^{-1}$) of the UV/Vis Maxima for $[Rh_2(TBSP)_4]$ in Various Solvents, with or without Additives[a]

solvent	additive	color	λ_{max1} (ϵ)	λ_{max2} (ϵ)
$CHCl_3$	none	green	612 (250)	440 (140)
$CHCl_3$	$OP(n\text{-}Oct)_3$	green	622 (240)	442 (130)
$CHCl_3$	$OPEt_3$	green	618 (220)	442 (130)
$CHCl_3$	$OPPh_3$	green	614 (270)	438 (170)
$CHCl_3$	$OP(OEt)_3$	green	612 (270)	440 (170)
$CHCl_3$	(*R*)-BINAP	orange	544 (300)	
$CHCl_3$	(*S*)-BINAP	orange	578 (500)	
$CHCl_3$	$P(mes)_3$	green	610 (250)	440 (150)
$CHCl_3$	PPh_3[b]	orange	472 (1,600)	325 (8,700)
$CHCl_3$	PEt_3	yellow	354 (4,700)	
$CHCl_3$	PCy_3	purple[c]	552 (230)	
DMF	none	blue	590 (320)	454 (110)
THF	none	green	596 (260)	448 (130)
MeCN	none	purple	556 (280)	444 (170)
CH_2Cl_2	none	green	656 (390)	424 (290)
NEt_3	none	purple	548 (460)	404 (250)

[a] Additive:**1** molar ratio = 20:1. Spectra with additives were measured in $CHCl_3$ rather than hexane because of the greater solubility of **1** in $CHCl_3$. [b] Additive:**1** molar ratio = 10:1. [c] The solution in $CHCl_3$ is orange for a few seconds and then turns purple. In pentane and hexane it is orange.

Although solutions of **1** in CH_2Cl_2, pentane, hexane, and THF are bright green, solutions of complex **1** are a wide variety of colors in the presence of coordinating solvents or reagents (Tables 1 and 2), the color changes presumably being indicative of reactions between the solvent or additive and the rhodium complex. The UV/vis maxima for the catalyst in different solvents or in $CHCl_3$ with added coordinating ligands were measured (Table 2). The λ_{max} for the two peaks in the visible region were 612 and 440 nm in $CHCl_3$. The peak at 440 nm did not change greatly with different coordinating species (other than phosphines). Only with NEt_3 did the λ_{max} change significantly, where the peak was slightly blue-shifted. The 612 nm peak varied widely depending on the solvent. It ranged from as low as 556 nm in MeCN to as high as 656 nm in CH_2Cl_2. In the presence of most phosphines, the spectrum completely changed. Interestingly, a few solvents or additives had little or no effect on the spectrum; these included CH_2Cl_2, $CHCl_3$, THF, the phosphine oxides, and trimesitylphosphine. One can conclude that these solvents or reagents failed to bind to the Rh complex or bound so weakly that they did not significantly affect the electronic properties of the complex.

The Effect of Water. The enantioselectivity we obtained in Na/benzophenone-dried alkane (hexane or pentane) was significantly greater than that reported in the literature[4] and also greater than we found in commercially available "anhydrous" alkane. We therefore tested the effect of controlled amounts of water on the enantioselectivity in hexane and found that the ee dropped precipitously (Table 1). However, the addition of phosphine oxides or triethyl phosphate counteracted the effect of water. It is therefore not necessary to use rigorously dried hexane if instead one adds 20 equiv of tri-*n*-octylphosphine oxide.

Rates of Reaction. The orange color of the diazoacetate took longer to disappear in some reactions performed in coordinating solvents or in the presence of coordinating additives such as DMF, NEt_3, THF, and PEt_3 (but not trimesitylphosphine or the phosphine oxides). NMR spectroscopy was used to track the progress of the reaction in $CDCl_3$, CD_3CN, and d_8-THF ([diazoacetate] = 11 mM, [**1**] = 0.14 mM, [styrene] = 44 mM,

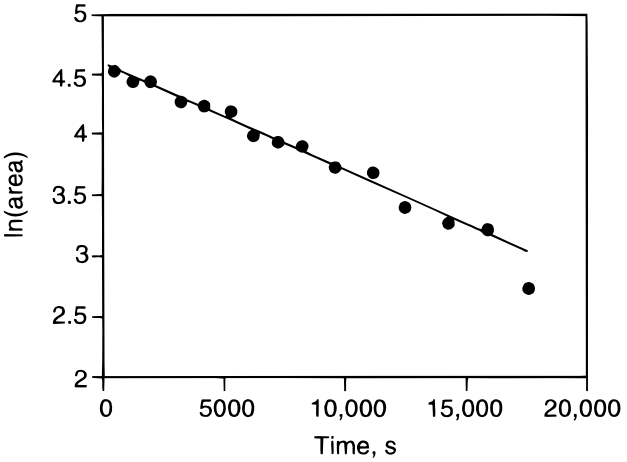

Figure 6. Log plot of the area of the methyl peak for methyl phenyldiazoacetate in the ^{1}H NMR spectrum in CD_3CN as a function of time during the cyclopropanation reaction at 20 °C.

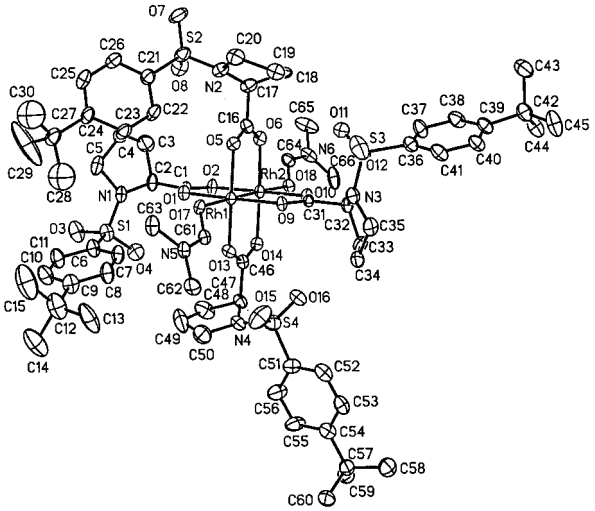

Figure 7. Crystallographically determined molecular structure of $[Rh_2(TBSP)_4(DMF)_2]\cdot 0.5$toluene$\cdot 0.5n$-pentane. The hydrogen atoms and the solvate molecules have been omitted.

$T = 20$ °C). The peaks monitored were the methyl peaks of the diazoacetate and the cyclopropane methyl ester (at 3.90 and 3.66 ppm, respectively, in $CDCl_3$). At the addition of the diazoacetate, the vial was shaken and then transferred to an NMR tube where the first scan was taken. At approximately 15 min intervals, the NMR tube was shaken and then another scan was taken. In $CDCl_3$, the reaction went so quickly that by the time the first scan was taken (approximately 5 min after the start of the reaction), the reaction was essentially complete. Therefore, assuming first-order kinetics, $k_{obs} \geq 1 \times 10^{-2}$ s^{-1}. In CD_3CN, the reaction took much longer, more than 5 h. The log plot (Figure 6) was found to be linear for at least 2 half-lives, showing that the reaction was first order with respect to the diazoacetate. The observed rate constant, 9.6×10^{-5} s^{-1}, was 2 orders of magnitude lower than in $CDCl_3$. In THF, the reaction was also slow with an observed rate constant of 2.2×10^{-4} s^{-1}.

Crystal Structure of $[Rh_2(TBSP)_4]$. Crystals of the bis(*N*,*N*-dimethylformamide) adduct of $[Rh_2(TBSP)_4]$ were prepared and crystallographically characterized in order to determine the Rh−Rh bond length and to note the orientation of the ligands (Figures 7 and 8, Tables 3 and 4). Although this catalyst is commercially available, its X-ray structure has not previously been published, but an illustration of the structure of the bis-(H_2O) adduct of the closely related complex tetrakis(*N*-benzenesulfonyl-L-prolinate)dirhodium(II) has been published.[35,36]

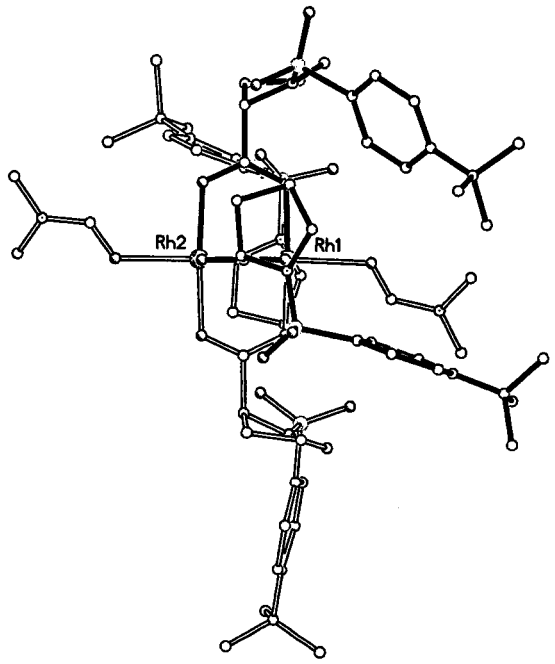

Figure 8. Crystallographically determined molecular structure of $[Rh_2(TBSP)_4(DMF)_2]\cdot 0.5$toluene$\cdot 0.5n$-pentane. A view emphasizing the placement of the *tert*-butylphenylsulfonylprolinate ligands relative to the Rh(1)−O(1)−O(5)−O(9)−O(13) surface. The hydrogen atoms and the solvate molecules have been omitted.

Table 3. Crystal Data and Structure Refinement for $[Rh_2(TBSP)_4(DMF)_2]\cdot 0.5$Toluene$\cdot 0.5n$-Pentane

identification code	mn1028
empirical formula	$C_{72}H_{104}N_6O_{18}Rh_2S_4$
formula weight	1675.67
temperature	91(2) K
wavelength	0.71073 Å
crystal system	orthorhombic
space group	$P2_12_12_1$
unit cell dimensions	$a = 10.6911(5)$ Å, $\alpha = 90°$ $b = 24.4434(11)$ Å, $\beta = 90°$ $c = 29.7425(13)$ Å, $\gamma = 90°$
volume	7772.5(6) Å^3
Z	4
density (calculated)	1.432 Mg/m^3
absorption coefficient	0.602 mm^{-1}
F(000)	3504
crystal size	$0.35 \times 0.05 \times 0.05$ mm^3
crystal color and habit	blue needle
diffractometer	Bruker SMART 1000
Θ range for data collection	1.60−31.52°
index ranges	$-15 \leq h \leq 15$, $-35 \leq k \leq 35$, $-43 \leq l \leq 43$
reflections collected	24950
independent reflections	24884 [R(int) = 0.1144]
completeness to theta = 31.52°	98.0%
absorption correction	none
max. and min. transmission	0.9705 and 0.8169
solution method	SHELXS-97 (Sheldrick, 1990)
refinement method	SHELXL-97 (Sheldrick, 1997) full matrix least-squares on F^2
data/restraints/parameters	24884/0/868
goodness-of-fit on F^2	0.902
final *R* indices [$I > 2\sigma(I)$]	R1 = 0.0590, wR2 = 0.1096
R indices (all data)	R1 = 0.1310, wR2 = 0.1306
absolute structure parameter	-0.02(2)
largest diff. peak and hole	1.850 and −1.174 e.Å^{-3}

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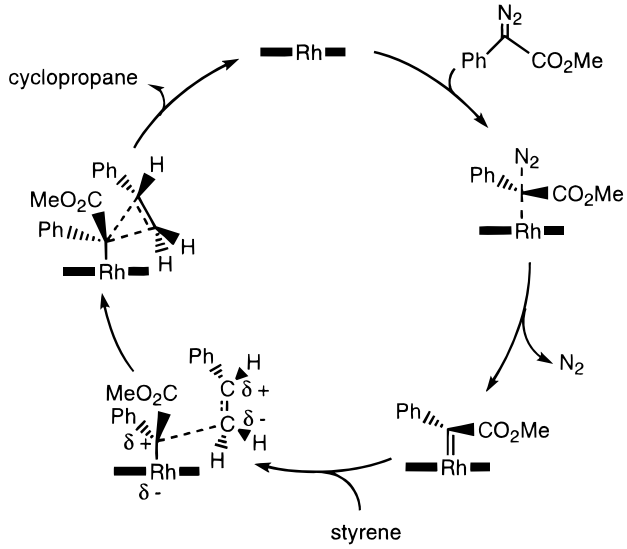
Table 4. Selected Bond Lengths [Å] and Angles [deg] for $[Rh_2(TBSP)_4(DMF)_2]\cdot 0.5Toluene\cdot 0.5n\text{-}Pentane$

Rh(1)−Rh(2)	2.3910(5)	Rh(2)−O(10)	2.020(3)
Rh(1)−O(13)	2.020(3)	Rh(2)−O(2)	2.040(3)
Rh(1)−O(5)	2.040(3)	Rh(2)−O(14)	2.056(3)
Rh(1)−O(1)	2.043(3)	Rh(2)−O(6)	2.060(3)
Rh(1)−O(9)	2.055(3)	Rh(2)−O(18)	2.262(3)
Rh(1)−O(17)	2.264(3)		
O(13)−Rh(1)-O(5)	177.28(14)	O(10)−Rh(2)-O(2)	177.05(13)
O(13)−Rh(1)-O(1)	89.16(14)	O(10)−Rh(2)-O(14)	90.53(14)
O(5)−Rh(1)-O(1)	89.70(14)	O(2)−Rh(2)-O(14)	89.53(15)
O(13)−Rh(1)-O(9)	90.90(14)	O(10)−Rh(2)-O(6)	90.23(15)
O(5)−Rh(1)-O(9)	90.07(13)	O(2)−Rh(2)-O(6)	89.49(15)
O(1)−Rh(1)-O(9)	175.79(13)	O(14)−Rh(2)-O(6)	175.56(13)
O(13)−Rh(1)-O(17)	89.34(14)	O(10)−Rh(2)-O(18)	86.53(12)
O(5)−Rh(1)-O(17)	93.12(14)	O(2)−Rh(2)-O(18)	96.41(12)
O(1)−Rh(1)-O(17)	89.61(12)	O(14)−Rh(2)-O(18)	92.23(14)
O(9)−Rh(1)-O(17)	94.60(12)	O(6)−Rh(2)-O(18)	92.19(14)
O(13)−Rh(1)-Rh(2)	88.99(10)	O(10)−Rh(2)-Rh(1)	88.87(9)
O(5)−Rh(1)-Rh(2)	88.51(10)	O(2)−Rh(2)-Rh(1)	88.19(9)
O(1)−Rh(1)-Rh(2)	88.11(9)	O(14)−Rh(2)-Rh(1)	87.65(10)
O(9)−Rh(1)-Rh(2)	87.67(9)	O(6)−Rh(2)-Rh(1)	87.98(10)
O(17)−Rh(1)-Rh(2)	177.20(9)	O(18)−Rh(2)-Rh(1)	175.40(8)

Extensive data has been published on the effect of various ligands L on the Rh−Rh bond length in $Rh_2(O_2CR)_4L_2$ (R = Me or Pr).[37−42] The Rh−Rh distances found by crystallography vary from 2.4505 (L = PPh_3, R = Me)[43] down to 2.366 (L = none, R = Pr).[44] The Rh−Rh bond distance found in complex **1** is 2.3910 Å, which is near the short end of the range but comparable to that found[45] in the complex $Rh_2(O_2CCH_3)_4(DMF)_2$ and longer than the estimated Rh−Rh bond length of $Rh_2(O_2CR)_4$ in solution (2.33 Å).[39]

Although in solution the floppy tails of the carboxylate ligands are likely to be continuously and rapidly changing conformation, the solid-state structure gives a snapshot of one possible conformation. The proline portion of the ligands was found to be fairly ordered; all of the proline rings were oriented such that the four sulfonyl sulfur atoms were coplanar with Rh(1) and the four oxygen atoms attached thereto. If viewed down the Rh(2)−Rh(1) bond, these sulfonylproline fragments appear to form a swastika-type arrangement. Rotation about the N−S bond should allow the *tert*-butylphenyl groups to swing freely in solution. In the solid state, two of these *tert*-butylphenyl groups extend past Rh(1) so that they appear to be roughly parallel to the DMF ligand on that Rh. The other two *tert*-butylphenyl groups are oriented out and away from the dirhodium core. The ability of these groups to swing so far away from the active sites on either Rh suggests that they have essentially no steric effect on the active sites. The sulfonyl groups, on the other hand, are oriented to be able to influence reactions of ligands bound to Rh(1). The closest distance between a sulfonyl oxygen and the DMF oxygen atom is 4.5 Å between O(15) and O(17). This represents the distance between the sulfonyl O atom and the electrophilic carbon of a carbene intermediate; too far for any kind of interaction but potentially close enough to supply steric hindrance to an incoming olefin.

Scheme 1



Discussion

Cyclopropanation with dirhodium tetracarboxylates[46,47] has been studied quite extensively in terms of mechanism and structure/selectivity relationships.[3,16,48−50] Rhodium(II) carboxylates have two open sites for catalysis, one on each electronically unsaturated rhodium. In the currently accepted mechanism for rhodium-catalyzed cyclopropanation (Scheme 1),[16,48] the diazoacetate binds to the metal and releases the dinitrogen to form a carbene. This step is rate determining.[51] The electrophilic carbene can react with a nucleophilic olefin to form a cyclopropane ring. This is generally thought to occur in a nonsynchronous manner where the carbene first interacts with the more electron rich olefinic carbon.[3] In asymmetric cyclopropanation, the chirality transfer is from the chiral carboxylate ligands, which block some orientations of the incoming olefin. There has been much research into the relationship between the catalyst/alkene structure and diastereoselectivity[16] and some research into the effects of structure on the enantioselectivity.[3,50] For reaction 2, the *E* diastereomer **2** is favored as is common with diazocarbonyl substrates and is formed with excellent diastereoselectivity. The enantioselectivity is found to depend greatly on the nature of the chiral ligands. For the $[Rh_2(TBSP)_4]$ catalyst and its analogues, it was determined that the stuctural features that most enhanced the enantioselectivity were the aliphatic ring attached to the carboxylate group and the existence of the arylsulfonyl group.[3]

(36) X-ray structures of three other chiral dirhodium carboxylate catalysts have appeared: $[Rh_2((R)\text{-}\alpha\text{-methoxy-}\alpha\text{-phenylacetate})_4(THF)_2]$,[36a] $[Rh_2((S)\text{-mandalate})_4(EtOH)_2]$,[36a] and $[Rh_2(N\text{-phthaloyl-}(S)\text{-phenylalaninate})_4(4\text{-}t\text{butylpyridine})_2]$.[36b] (a) Agaskar, P. A.; Cotton, F. A.; Falvello, L. R.; Han, S. *J. Am. Chem. Soc.* **1986**, *108*, 1214−1223. (b) Hashimoto, S.; Watanabe, N.; Sato, T.; Shiro, M.; Ikegami, S. *Tetrahedron Lett.* **1993**, *34*, 5109.

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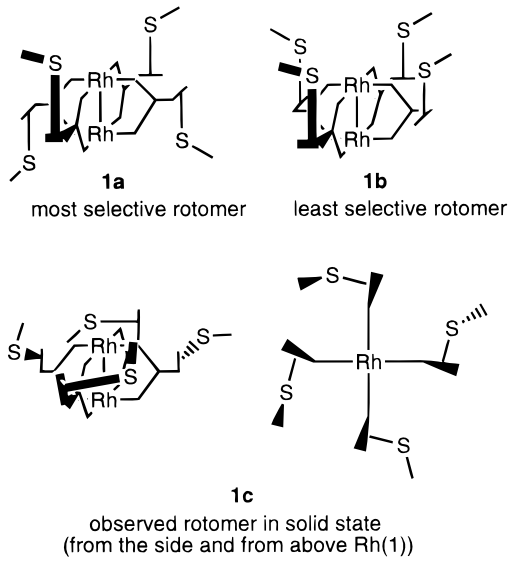
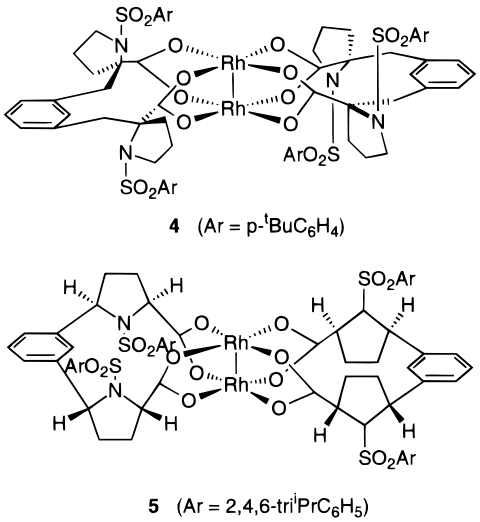
Scheme 2



Scheme 3



Pressure-Dependent Enantioselectivity. The results confirm that the dependence of the dielectric constant of a SCF upon pressure can cause the enantioselectivity of homogeneous catalysis to be pressure dependent.[22] Because all SCFs have pressure-dependent dielectric constants and many reactions have dielectric-constant-dependent enantioselectivity, one can predict the following. At any temperature close to but above T_c, the enantioselectivity of an asymmetric synthesis near the critical pressure of the reaction mixture may deviate from that at higher pressure. If the principal cause of the deviation for a particular system is known, then the direction of the deviation can be predicted. In particular, if the cause of the deviation is the pressure dependence of the dielectric constant of the SCF, then *the enantioselectivity in supercritical fluids will be greater near the critical pressure than at higher pressures if the enantioselectivity in liquids is greater in nonpolar rather than in polar solvents*. This prediction will be true for all supercritical fluids, because they all have lower dielectric constants near P_c than at higher pressures. However, the magnitude of the deviation in enantioselectivity will be proportional to the magnitude of the change in dielectric constant (a property of the SCF) and proportional to the magnitude of the dielectric-constant dependence observed in liquid solvents (a property of the reaction). While the change in dielectric constant is large in SCFs which have significant dipole moments, it is small in $scCO_2$. Thus, one would not expect a significant pressure dependence in $scCO_2$ based on dielectric constant change. It may be possible, however, to obtain a large dielectric constant change by pressure changes on a mixture of $scCO_2$ with a polar cosolvent. This is the subject of future research.

The Effect of Noncoordinating Solvents. There has been a small amount of work on solvent effects in enantioselective cyclopropanation, most notably the elegant work by Davies and co-workers.[2,3] Davies has proposed two possible explanations for the solvent effects on enantioselectivity seen in this system. The first explanation invokes steric arguments, in which the chiral ligands are stabilized as different rotomers in different solvents. The carboxylate groups have free rotation about the proline carboxylate C−C bond and the N−S bond between the proline nitrogen and the sulfonyl group. Therefore, the floppy ligands could potentially have many orientations. Davies suggests that the greatest chiral induction would be obtained from the rotomer shown as **1a** in Scheme 2 due to its high symmetry and more hindered catalytic sites. Other possible rotomers, such as the one shown as **1b** in Scheme 2, leave one rhodium site sterically unencumbered and therefore achiral (the rotomer found for $[Rh_2(TBSP)_4(DMF)_2]$ in the solid state is shown as **1c**). The rationale is that in pentane a highly selective rotomer such as **1a** is stabilized, while in CH_2Cl_2 a less selective rotomer closer to **1b** is the predominant form. In support of this theory is Doyle's finding that with rigid dirhodium carboxamide ligands no solvent-dependent enantioselectivity was seen.[4] To test this theory, Davies[17] synthesized catalysts **4** and **5**, similar to the most highly selective dirhodium catalysts but with carboxylate ligands tethered to each other to hinder rotation (Scheme 3). Although catalyst **4** did not have solvent-dependent enantioselectivity for reaction 1, strong solvent dependence was observed for catalyst **5** (from 74% ee in pentane to 90% in CH_2Cl_2) and the trend was opposite to that observed with **1** or related catalysts. The reason for this is not at all clear. It appears, nevertheless, that the solvent dependence is caused by more factors than just rotation within the carboxylate ligands.

The other explanation that Davies has suggested involves electronic effects. It has been amply demonstrated that changing the electronic nature of both the substrates and catalyst can affect selectivity.[2−5,16,49,50] The electronic nature of the substrate and catalyst can affect the charge separation at the transition state in which the carbene attracts the more electron rich carbon atom of the olefin while the other alkene carbon becomes more electropositive (Scheme 1). Davies[3] suggested that the solvent polarity could play a role in the timing of the transition state. According to this explanation, solvents of high dielectric constant favor an early transition state in which the styrene molecule is farther away from the rhodium and therefore in a less chiral environment. In pentane, the charge separation is not stabilized at greater distances, the transition state must be later, and the olefin must be closer to the carbene and therefore in a more chiral environment.

Our results in both supercritical fluids and noncoordinating solvents confirm a dependence of the enantioselectivity on the dielectric constant. Even with the new data, it is difficult to determine whether the dependence is due to steric or electronic effects.

The Effect of Coordinating Solvents or Reagents. The new results demonstrate convincingly that in coordinating solvents or in solutions of coordinating reagents the dielectric constant is not the sole factor affecting the selectivity. It is obvious that in some manner the ability of the solvent or additive to coordinate affects the enantioselectivity. However, there is no

obvious trend. Some solvents, such as THF and acetonitrile, cause the enantioselectivity to be greater than one would expect on the basis of the dielectric constants of the solvents. Other solvents or mixtures such as NEt_3 or PPh_3/hexane cause the enantioselectivity to be poorer than expected. The ee does not correlate exactly to any single characteristic property of the solvent (such as donor number or $E_T(30)$). How does the coordinating ligand affect selectivity? The two possibilities are still steric and electronic effects.

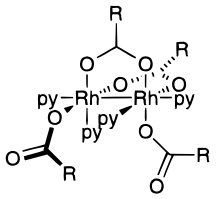
For the steric argument, one might suggest that the coordinating solvent or ligands bind to one site and influence the arrangement of the chiral auxiliaries so that catalysis occurring at the other Rh is in a sterically altered environment. Such an argument would suggest that a very large phosphine bound to one Rh would force the prolinate ligands to the other Rh and therefore increase the enantioselectivity. The results are not definitive. PPh_3 (cone angle[52] = 145°) and trimesitylphosphine (212°) were tested, but the trimesitylphosphine was too large; the failure of the UV/vis spectrum to change upon addition of that phosphine indicates that it did not bind to the complex (Table 2). PCy_3 and PEt_3 were also tested; they are electronically similar to each other, but the former is sterically much larger (a cone angle of 170° compared to 132°). The UV spectral changes show that both reacted with the catalyst. The ee of the cyclopropanation in the presence of PCy_3, however, is much greater than that in the presence of PEt_3. In general, the larger phosphines gave better enantioselectivity than the smaller phosphines, but no phosphine raised the ee above that observed in the absence of phosphine.

The possibility of the coordinating species influencing the selectivity due to electronic effects is likely. Three possible ways that the coordinating solvent can affect the electronic properties of the catalyst are (1) coordination to one rhodium affects the electronic density at the other rhodium, therefore possibly changing the nature of rhodium−carbene bond and thus the electronic nature of the transition state, (2) coordinating species may disrupt the dirhodium tetracarboxylate core, and (3) coordinating species might interact directly with the carbene. These three scenarios will now be discussed.

(1) Presumably, in the presence of excess coordinating ligand (L), the diadduct $[Rh_2(TBSP)_4L_2]$ is formed. This should be a catalytically inactive species (hence the slower reaction in strongly coordinating solvents) and would become active only upon loss of 1 equiv of L. Thus, the catalysis (carbene formation and subsequent cyclopropanation) would take place at the unsaturated Rh, while 1 equiv of L would remain bound to the other Rh. The presence of this bound ligand L could affect the catalyst by donating electron density into the Rh−Rh σ^* antibonding orbital and therefore weaken the Rh−Rh bond and increase the electron density at both metals. For example, PPh_3 donates electron density far better than weaker ligands such as H_2O and hence the Rh−Rh distance is much greater in the bis(PPh_3) adduct[41,43] than the bis(H_2O) adduct[42,53] of dirhodium tetracarboxylates. The existence of the axial ligand on one Rh atom in $LRh(\mu\text{-}O_2CR)_4Rh{=}CPhCO_2Me$ could therefore change the electrophilicity and ability of the other Rh to stabilize charge as well as change the nucleophilicity of the carbene carbon. While this is probably true in the present system, it is not sufficient to explain the results. Although weakly coordinating ligands in general allowed high ee's while strongly coordinating ligands did not, a few strongly coordinating ligands (PCy_3 and BINAP) allowed high ee's. In addition, almost all coordinating solvents allowed higher ee's than would have been expected on the basis of their dielectric constants.

Pirrung and co-workers found a relationship between the electronic nature of the carboxylate ligands on dirhodium catalysts and the selectivity between ylide formation and C−H insertion.[49] They found that the $\Delta\Delta G^{\ddagger}$ between the transition states for the two pathways varied with the nature of the carboxylate ligands. It was found that the selectivity depended directly on the polarizability of the carboxylate ligands, where the best selectivity was seen with carboxylate ligands of low field effects and high polarizability. The polarizability was hypothesized to help stabilize the carbene intermediate and accept back-bonding electron donation. While electronic effects of this type may be involved with a few of the coordinating ligands, it is difficult to adapt this theory to explain the effect of most of the coordinating solvents or reagents on the enantioselectivity of cyclopropanation. For example, triethylphosphine is more polarizable than triethylamine, but both greatly decrease the enantioselectivity.

(2) In the presence of particularly donating ligands, one or more of the carboxylates in $[Rh_2(TBSP)_4L_2]$ could become monodentate (dangling), reducing the number of chiral ligands proximate to the active site. Pyridine, for example, reacts with $[Rh_2(O_2CCF_3)_4]$ at room temperature to form $[Rh_2(O_2CCF_3)_4(py)_4]$ with two dangling carboxylates (structure **6**).[54] $[Rh_2(O_2CR)_4(PPh_3)_2]$ reacts even further (eq 3, L = RCO_2H, R = CF_3), resulting eventually in a complex containing two orthometalated and bridging $Ph_2PC_6H_4^-$ ligands.[54−56] This isomerization sequence is known to take place even at room temperature.[54] While we have no direct evidence for the formation of dangling carboxylates or orthometalated phosphines in the cyclopropanation, the time period required for the cyclopropanation in the presence of PPh_3 is so long that there could be time for partial isomerization of the bis(PPh_3) adduct.



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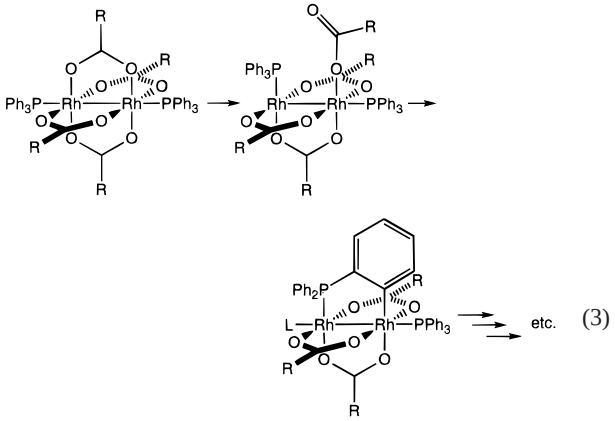

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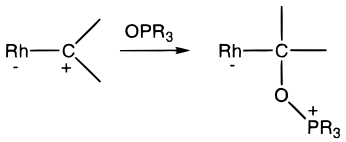
Dangling carboxylate ligands are even more likely to form if a bidentate additive is added. For example, (*R*)-(+)-2,2′-bis-(diphenylphosphino)-1,1′-binaphthyl (*R*-BINAP) and its *S*-enantiomer were able to bind to [Rh_2(*S*-TBSP)$_4$], as indicated by a change in the color and spectrum. The *R*-BINAP and *S*-BINAP adducts of [Rh_2(S-TBSP)$_4$] had similar UV/vis. spectra, but the spectra were significantly different from that of the PPh_3 adduct. The BINAP adducts also catalyzed the cyclopropanation with far greater enantioselectivity than the PPh_3 adduct. These observations strongly suggest that the manner of binding of BINAP differed significantly from the manner of binding of PPh_3. We suggest that the BINAP ligand was likely to have chelated and thereby forced at least one of the carboxylate ligands into a dangling position. The reason this does not cause a decrease in the enantioselectivity is not known.

(3) The third possibility is that the coordinating solvent or additive might directly interact with the carbene before or even during the transition state of the cyclopropanation. For example, it is likely that the electrophilic carbene would attract the Lewis basic phosphine oxide. This could stabilize the carbene in the form of an ylide (eq 4). While there is no precedent for an ylide



(4)

of exactly this type, trimethylamine oxide is known to accelerate carbonyl substitution by nucleophilic attack on the carbonyl carbon[57] (trialkyphosphine oxides are believed to accelerate reactions of metal carbonyl by binding to the metal and not by forming an ylide with the carbonyl).[58,59] Rhodium carboxylates are known to act as catalysts for the formation of oxonium ylides from diazo compounds and ethers.[16] In fact, dirhodium tetracarboxylate-catalyzed ylide formation between a carbene and an ether group can compete with cyclopropanation.[60] Ylide formation in this manner could protect the carbene from adventitious water, which would explain the beneficial effects of phosphine oxides in the presence of trace water.[61]

Free ylide formation may also occur in the presence of phosphines[62] or amines[16] plus a catalyst; this may be the reason for the very low yields and large number of byproducts observed when the cyclopropanation was performed in the presence of PPh_3, PEt_3, and NEt_3.

Further study will be required to determine the reasons for the widely differing enantioselectivities in the presence of these various coordinating solvents and additives. It is likely that more than one reason is involved; the manner in which PPh_3 lowers the enantioselectivity should be different from the manner in which weaker ligands increase the enantioselectivity. Nevertheless, the results are promising because they indicate new ways in which enantioselectivity can be enhanced.

Conclusions

1. The dependence of the dielectric constant of a SCF upon pressure can cause the enantioselectivity of homogeneous catalysis to be pressure dependent. Cyclopropanation in fluoroform has been described as the first example of this effect on homogeneous catalysis. Predictions have been made that future examples will be found, in which, at a temperature close to but above T_c, the enantioselectivity near the critical pressure of the reaction mixture will deviate from that at higher pressure. If the cause of the deviation is the pressure dependence of the dielectric constant of the SCF, then the enantioselectivity in supercritical fluids will be greater near the critical pressure than at higher pressures if the enantioselectivity in liquids is greater in nonpolar rather than in polar solvents.

2. This pressure dependence was used as part of a combined liquid/supercritical solvent study for the purposes of mechanistic understanding and selectivity optimization for the cyclopropanation reaction. Our results in both supercritical fluids and noncoordinating solvents confirm a strong dependence of the enantioselectivity on the dielectric constant of the medium. However, in coordinating solvents or solvent/additive mixtures, the dielectric constant is not the sole factor affecting the selectivity. In fact, the enantioselectivity in such solutions is, in some manner, strongly dependent on the coordinating ability or nucleophilicity of the solvent or additive L. Although coordinating solvents enhance the enantioselectivity relative to what one would expect on the basis of the dielectric constant, the best enantioselectivity was obtained in solvents or in the presence of reagents which showed no UV/vis evidence of binding to the catalyst. Three different explanations are offered for the effect of coordinating solvents or reagents; coordination of the solvent to form a L$Rh(\mu$-$O_2CR)_4Rh$=$CPhCO_2Me$ complex, disruption of the $Rh_2(O_2CR)_4$ core to create dangling carboxylates, or coordination of L to the carbene to form an ylide. There is as yet insufficient evidence to distinguish between these; it is possible that all three occur with different coordinating species.

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Supporting Information Available: Description of tests of the effects of temperature, injection method, trace water, and steel vessel walls on enantioselectivity of cyclopropanations in SCFs. Tables of atomic coordinates, equivalent isotropic displacement parameters, anisotropic displacement parameters, bond lengths, and bond angles for [Rh_2(TBSP)$_4$(DMF)$_2$]·0.5toluene·0.5*n*-pentane. Log plot for reaction 2 in THF-d_8. This material is available free of charge via the Internet at http://pubs.acs.org.

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