NEW PERFLUORINATED BINAP-RHODIUM CATALYSTS AND ASYMMETRIC HYDROGENATION OF KETOESTER IN SUPERCRITICAL CO_2

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The fluorinated BINAP derivative ligands (R)-(+)-2,2'-bis(di-m-(heptadec afluorooctyl)diphenylphosphino)-1,1'-binaphthyl and (R)-6,6'-diheptadecafluoro octyl-2,2'-bis(di-m-(heptadecafluorooctyl)diphenylphosphino)-1,1'-binaphthyl and their Rh(I) complexes were synthesized and characterized by using spectroscopic methods such as IR, ^{1}H, ^{19}F and ^{31}P NMR. The catalysts are slightly soluble in $scCO_2$ at the conditions of 323 ^{o}K, 1800 psi pressure. Catalytic efficiency of catalyst were tested on the ethyl acetoacetate hydrogenation in $scCO_2$ at the conditions of 323 ^{o}K, 1700 psi pressure, substrate/catalyst= 400 (molar ratio). Conversation were determined by chiral GC analysis and observed 54% and 45% respectively.

INTRODUCTION

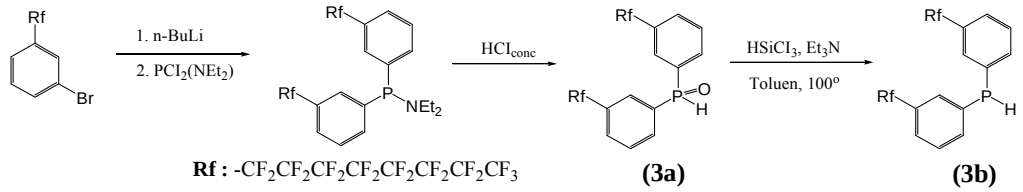
In recent years, the use of supercritical carbon dioxide ($scCO_2$) has found increasing interest as a non-toxic and environmentally at the reaction medium for organic synthesis [1-3]. Of course the most obvious advantage of the use of $scCO_2$ is the replacement of potentially hazardous organic solvents such as benzene, methylene chloride, diethyl ether etc. with environmentally benign and toxicologically harmless carbon dioxide. Working beyond the critical temperature of CO_2 provides attractive option to use the same medium for synthesis, isolation and purification of the product by exploiting the extractive properties of $scCO_2$ [4]. Supercritical carbon dioxide has been used as an alternative medium for a number of asymmetric hydrogenations [5], although catalysts solubility, especially with metal-complexes, has been a problem [6]. It is well known that fluorine groups attached to ligands increase their solubility in $scCO_2$ [7]. Further, the activity of fluorinated Rhodium complexes in the hydroformylation of olefins in $scCO_2$ increased with decreasing basicity of phosphines [8].

Chiral BINAP are among the most useful and popular ligands for catalytic asymmetric reactions [9] and although asymmetric hydrogenation with metal-BINAP complexes is one of the most extensively used reactions in these types of syntheses, only a few examples of fluorinated BINAP ligands have been reported in the literature. There have been different the strategies to synthesize these fluorinated BINAP. One of them, fluorinated Binap was to phosphinate the corresponding fluorinated Binol [10,11]. Even though chiral fluorous Binol can easily be synthesized by Heck reactions [12], Ulmann cross-coupling reactions [13], and lithiation reaction [14]. Another strategy, a fluorinated analog of the BINAP ligand was synthesized with $–OCF_3$ substitution of the aryl groups in BINAP skeleton [15].

The last strategy, this ligand was optained by direct functionalization of BINAP protected by its oxide form [9]. We report herein the synthesis of new perfluoroalkylated-BINAP in homogeneous and $scCO_2$ catalytic hydrogenation of ethyl acetoacetate. These researches indicate that there is a need to study the influence of the fluorous groups on activity and enantioselectivity of chiral Rh-BINAP catalysts for asymmetric hydrogenations reactions.

RESULTS AND DISCUSSIONS

In this study we synthesized two perfluoro analogues of BINAP, **L1** and **L2**, bearing perfluoroalkyl chains on the aryl groups which are found on phosphorus atoms and the naphthyl ring respectively. The chiral (R)-Rf-BINAP, **L1** and (R)-6,6'/Rf-BINAP, **L2** were prepared by the way shown in Scheme 1.



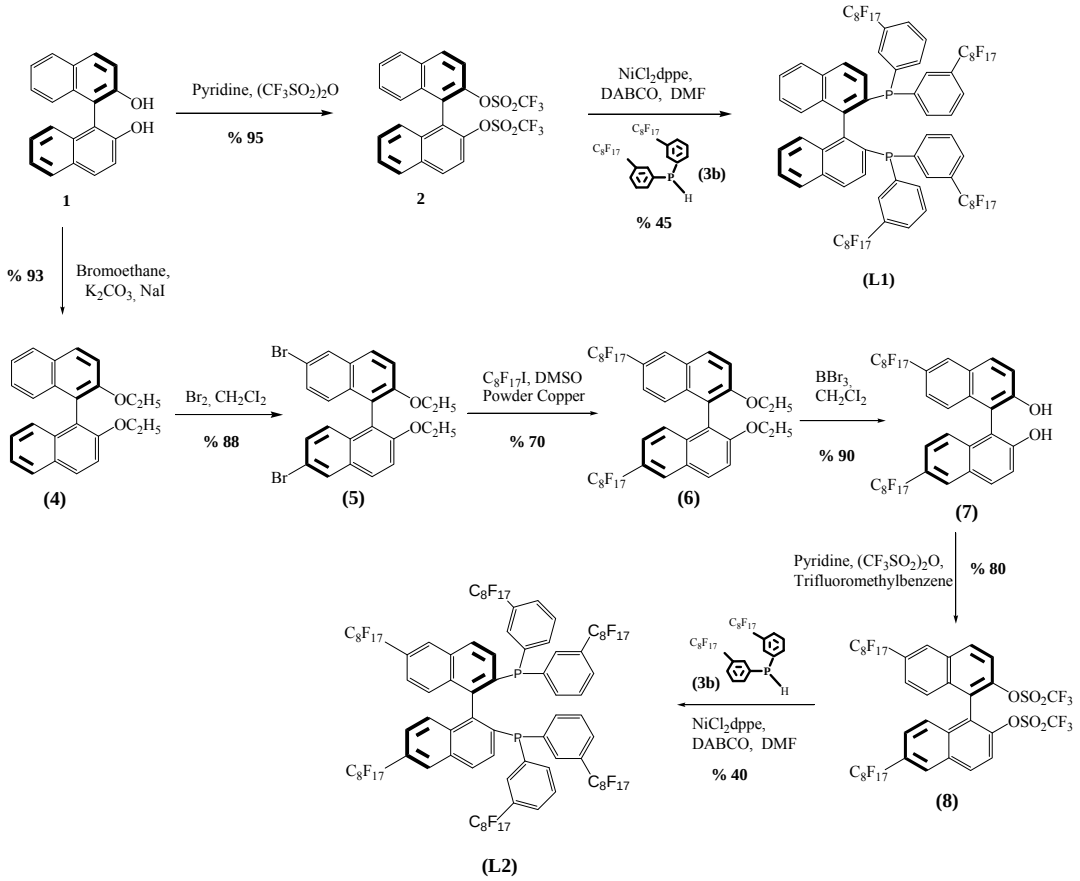
Rf : $-CF_2CF_2CF_2CF_2CF_2CF_2CF_2CF_3$ **(3a)** **(3b)**

Scheme 1.

The intermediate **(3b)** was prepared as solid by lithiation of 1-bromo-3-(heptadecafluorooctyl) benzene with *n*-BuLi in diethyl ether, followed by addition of the resulting solution to dichloro-diethylamino-phosphine, Cl_2PNEt_2 in THF, and subsequent treatment with concentrated HCl [4]. Then produced phosphine-oxide **(3a)** was reduced by using trichlorosilane and triethyl amine the desired bis-[3-(heptadecafluorooctyl)-phenyl]-phosphine **(3b)** in 72% yield.

(R)-(+)-1,1'-bi(2-naphthol) **(1)** was treated with triflic anhydride in the presence of pyridine to form the chiral ditriflate **(2)** [16] and then, it was reacted with bis-[3-(heptadecafluorooctyl)-phenyl]-phosphine **(3b),** $[NiCI_2(dppe)]$, DMF and DABCO [17] to give phosphinylation of chiral compound the perfluoroalkylated (R)-Rf-BINAP **(L1)** in 45 % yield.

The etoxy-protected compound that (R)-2,2'-diethoxy-1,1'-binaphthyl **(4)** was prepared from (R)-(+)-1,1'-bi(2-naphthol) **(1)** by alkylation with bromoethane in acetone. Selective bromination of **(4)** was performed easily at room temperature in CH_2CI_2 to give **(5)** [18]. The attachment of the perfluoroalkyl chain to the etoxy-protected dibromonaphthyl derivate **(5)** was directly available to reacted with $C_8F_{17}I$, DMSO and activated powder copper at 120 ^oC to give **(6).** The following cleavage of the ethoxy group of perfluoro derivate **(6)** with BBr_3 in CH_2CI_2 afforded the (R)-6,6'-diheptadecafluorooctyl-1,1'-binaphthyl-2,2'-diol **(7)** in 90 % yield. The heptadecafluoroalkylated binaphthol **(7)** was treated with triflic anhydride in the presence of pyridine in a mixture of $CH_2Cl_2/C_6H_5CF_3$ to give the (R)-2,2'-bis(trifluoromethanesulfonyloxy)-6,6'-diheptadecafluorooctyl-1,1'-binaphthyl, **(8)** in 80 % yield [19]. Phosphinylation of chiral compound named perfluoroalkylated (R)-6,6'/Rf-BINAP **(L2)** was synthesized in the same way as **(L1)** ligand in 40 % yield.

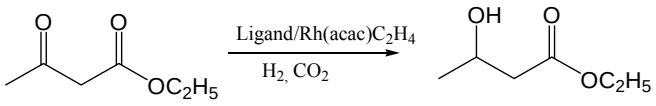


Scheme 2.

Hydrogenation

The catalysts are slightly soluble in $scCO_2$ at the conditions of 323 ^oK, 1800 psi pressure. Hydrogenation reactions were performed in $scCO_2$ a stirred in stainless steel reactor (100 mL) with ligands, substrate and metal catalyst followed by pressurization with hydrogen. By mixing Rh(acac)(C_2H_4) with each one of **L1** and **L2** ligands was tested on hydrogenation of ethyl acetoacetate in $scCO_2$ at 323 K, 1700 psi pressure, substrate/catalyst= 400 (molar ratio). The **L1** ligand together with rhodium gave 54% conversation for the hydrogenation of ethyl acetoacetate. But **L2** ligand gave 45% conversation. Conversation was determined by chiral GC analysis.

Table 1. Hydrogenation of the ethyl acetoacetate by using perfluoroalkylated BINAP ligands



Entry	Ligands	Solvent	Substrate	T (K)	pH_2 (bar)	*Ptotal* (psi)	t (h)	Conversion (%)	TON[a]	TOF[b] (min^{-1})
1	L1	CO_2	ethyl acetoacetate	323	10	1700	3	54	216	72
2	L2	CO_2	ethyl acetoacetate	323	10	1700	3	45	180	60

[a] **TON :** mol of product/mol of catalyst , [b]**TOF :**TON/Time (h)

EXPERIMENTAL

General

Solvents were purified by standard methods which were dried with molecular sieves (4 Å), $CaCl_2$ etc. and were distilled under nitrogen. All synthetic procedures were carried out under an inert argon or nitrogen atmosphere using standard Schlenk techniques and glove box, and using flame-dried glassware. All other chemicals were of reagent grade quality and were used without further purification. The ^{1}H NMR spectra were obtained on a Bruker-Advance DPX 400 spectrometer. IR spectra were recorded on a Perkin Elmer Mattson 1000 FT-IR spectrometer by using KBr pellets in the range of 4000-400 cm^{-1}. Elemental analysis was recorded on a LECO CHNS-932 analyzer. Melting point was determined on a Gallenkamp apparatus in a sealed capillary and is uncorrected. CO_2 with a purity of 99.99% was supplied by BOS Company (Adana, Turkey). The solubility and catalytic studies were performed with stainless steel batch reactor (PARR, 50 ml, windowed and autoclave engineering stirred reactor 100 mL) and syringe pump (ISCO, series D) in $scCO_2$.

(R)-2,2'-bis((trifluoromethanesulfonyl)oxy)-l,l'-binaphthyl, 2 was synthesized as described in the Ref.16. IR (KBr, ν= cm^{-1} : 3068, 2929, 1594, 1509, 1411, 1211, 1137, 941, 827 cm^{-1}, ^{1}H NMR ($CDCl_3$) : δ 7,58 (d, $J_{3,4}$= 9 Hz, H_3), 8,07 (d, J=9 Hz, H_5), 7,94 (d, J=9 Hz, H_4), 7,51 (t, J=7,5 Hz, H_7), 7,34 (t, J=7,5 Hz, H_6), 7,19 (d, J= 8,5 Hz, H_8); Mp : 81-86 °C.

(R)-2,2'-diethoxy-1,1'-binaphthyl, 4 was synthesized as described in the Ref.18. IR (KBr, ν= cm^{-1} : 2974 (-CH2CH3), 1588-1621 (-Ar), 1237 (-C-O), 803 (C-O-C); ^{1}HNMR($CDCl_3$): 1.05 (t, 6H, $-CH_3$), 4.09 (m, 4H, $-CH_2$), 7.15 (d, 2H, J=8 Hz, -ArH), 7.20-7.33 (dd, 4H, J=7.8 Hz, -ArH), 7.49 (d, 2H, J=8.8 Hz, -ArH), 7.85-7.95 (m, 4H, -ArH); Mp: 132-134°C

(*R)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthyl, 5* was synthesized as described in the Ref.18. IR (KBr, ν= cm^{-1}: 3062, 2970, 2925, 1583-1613, 1235, 1053, 800, 685; ^{1}H NMR ($CDCl_3$): δ 1,08 (t, 6H, $-CH_3$), 4,07 (m, 4H, $-CH_2$), 6,98 (d, 2H, -ArH(H_8)), 7,28 (dd, 2H, J=9 Hz, -ArH(H_3)), 7,86 (d, 2H, J=9 Hz, -ArH(H_4)), 8,02 (d, J=2 Hz, 2H, -ArH(H_5)); ^{13}C NMR ($CDCl_3$): δ 14,3 (CH_3), 65,1 (CH_2), 116,3; 116,9 (Ar-C-Br, (C_7)), 117,3 (C_3), 120,1 (1,1'-binaftil C_1), 126,1; 128,2; 130,5 (C_8); 131,1; 132,5, 154,5 ppm; Mp: 159-160 °C

(R)-2,2'-diethoxy-6,6'-diperfluorooctyl-1,1'-binaphthyl, 6 was synthesized as described in the Ref.19. ^{1}H NMR ($CDCl_3$): δ 1.08 (t, *J*=7.0 Hz, 6H, CH_3), 4.10 (m, 4H, CH_2), 6,8-8,2 (Ar-H), ^{19}F NMR ($CDCl_3$): δ -126.1 (s, 4F, CF_2), −122.9 (s, 4F, CF_2), −122.7 (s, 4F, CF_2), −122.2 (s, 4F, CF_2), −121.9 (bs, 8F, CF_2), −109.9 (t, $^3J_{F,F}$=13.8 Hz, 4F, CF_2 Ar), −80.9 (t, $^3J_{F,F}$=9.0 Hz, 6F, CF_3); Mp : 54-55 °C

(R)-6,6'-diperfluorooctyl-1,1-binaphthyl-2,2'-diol, 7 was synthesized as described in the Ref.19. ^{1}H NMR ($CDCl_3$): δ 5.48 (s, 2H, OH), 7.24 (d, *J*=9.0 Hz, 2H, Ar-H), 7.40 (dd, *J*=9.0, 1.8 Hz, 2H, Ar-H), 7.49 (d, *J*=9.0 Hz, 2H, Ar-H), 8.07 (d, *J*=9.0 Hz, 2H, Ar-H), 8.12 (d, *J*=1.8 Hz, 2H, Ar-H); ^{19}F NMR ($CDCl_3$): δ −127.1 (s, 2F, CF_2), −126.6 (s, 2F, CF_2), −124.0 (bs, 4F, CF_2), −122.7 (bs, 8F, CF_2), −122.2 (bs, 8F, CF_2), −110.3 (t, $^3J_{F,F}$=13.8 Hz, 4F, CF_2 Ar), −80.8 (t, $^3J_{F,F}$=9.6 Hz, 6F, CF_3).^{13}C NMR ($CDCl_3$): δ 110.1, 118.9, 120.5, 126.1, 127.9, 132.5, 136.2, 154.8; Mp: 123-127.

(R)-2,2'-bis(trifluoromethanesulfonyloxy)-6,6'–diperfluorooctyl-1,1'-binaphthy, 8 was synthesized as described in the Ref.19. ^{1}H NMR ($CDCl_3$): δ 7.41 (d, *J*=9.0 Hz, 2H, Ar-H), 7.54 (dd, *J*=9.0, 2.0 Hz, 2H, Ar-H), 7.71 (d, *J*=9.0 Hz, 2H, Ar-H), 8.28 (d, *J*=9.0 Hz, 2H, Ar-H), 8.34 (d, *J*=2.0 Hz, 2H, Ar-H); ^{19}F NMR ($CDCl_3$): δ −127.1 (s, 4F, CF_2), −123.8 (s, 4F, CF_2), −123.0 (bs, 8F, CF_2), −122.4 (s, 4F, CF_2), −122.0 (s, 4F, CF_2), −111.6 (t, $^3J_{F,F}$ =13.9

Hz, 4F, CF_2Ar), −81.5 (t, $^3J_{F,F}$=9.5 Hz, 6F, CF_3CF_2), −75.7 (s, 6F, CF_3SO_2). ^{13}C NMR ($CDCl_3$): δ 116.6, 121.0, 121.7, 123.6, 125.9, 128.1, 128.5, 132.1, 133.9, 134.0, 147.7.

Bis-[3-(heptadecafluorooctyl)-phenyl]-phosphine, 3b was synthesized as described in the Ref.4 and Ref. 15. A hexane solution of *n*-BuLi (8 ml, 1.6 M) was added dropwise at -30 °C to a solution of 1-bromo-3-(heptadecafluorooctyl) benzene (5.0 g, 8.69 mmol) in diethyl-ether (50 ml). The mixture was warmed up to 0°C and stirred for 30 min at this temperature. Diethylamino–dichlorophosphine (0.78 g, 4.5 mmol) was added at -40°C via syringe to the resulting intensive yellow solution and then the reaction mixture was slowly allowed to warm to r.t., whereby large amounts of precipitate (presumably LiCl) were formed. The reaction mixture was then treated with 3 ml of HCl_{conc} under vigorous stirring. The organic phase was separated, washed with saturated NaCl solution (3x20 ml) and saturated $NaHCO_3$ solution (3x20 ml), and then dried over $MgSO_4$. The solvents were removed under reduced pressure leading to a pale yellow oil. Spectroscopically pure product was obtained by crystallization from pentane as a white compound. Trichlorosilane (2.7 ml) was added slowly with stirring to bis-[3-(heptadecafluorooctyl)-phenyl]-phosphinoxide, **(3a)** (to 2.25 g, 6.64 mmol), triethyl amine (3.84 ml) and toluene (30 ml) under ice bath, and heated under reflux for 6 h. After cooling, 2N sodium hydroxide solution (133 ml) was added slowly under ice bath. The organic layer was combined with ether and evaporated under vacuum, giving the liquid **3b** (1.7 g, 72%). The spectral properties: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.54 ppm (dd, 4H, $^3J_{H,H}$ = 6.8 Hz, $^3J_{H,P}$ = 6.6 Hz), 7.21 ppm (d, 4H, $^3J_{H,H}$ = 7.6 Hz), 5.35 ppm (d, 1H, $^1J_{H,P}$ = 219.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$) δ: −43.17 ppm (s, decoupled). ^{19}F NMR ($CDCl_3$): δ −127.2 (s, 4F, CF_2), −123.5 (s, 4F, CF_2), −123.1 (bs, 8F, CF_2), −122.5 (s, 4F, CF_2), −121.8 (s, 4F, CF_2), −110.4 (t, $^3J_{F,F}$ =13.9 Hz, 4F, CF_2Ar), −81.2 (t, $^3J_{F,F}$=9.5 Hz, 6F, CF_3)

(R)-(+)-2,2'-bis(di-m-(heptadecafluorooctyl)-phenyl)-phosphino)-1,1'-binaphthyl, L1 was synthesized as described in the Ref.17. To a solution of $NiCl_2$dppe (0.19 g 0.36 mmol) in DMF (10 ml) at room temperature was added **3b** (1.94 g, 1.9 mmol). The solution was heated to 110 ◦C and kept at this temperature for 30 min. (*R*)-(−)-1,1'-Bi-2-naphthol bis (trifluoro methanesulfonate) (2 g, 3,6 mmol) and DABCO (1.62 g 14,4 mmol) in DMF (20 ml) was added slowly to the above solution was kept at 110 °C. Three additional equal portions of **3b** (3 x 1.94 g) were added after 1, 3 and 7 h. The reaction was kept at 110 °C until the starting material (*R*)-(−)-1,1'-Bi-2-naphthol bis (trifluoro methanesulfonate) was completely consumed (3 days) and then the solution was cooled down to 0-5 °C with an ice bath. The desired product was filtered and the filter cake was washed with methanol (2 x 10 mL) and dried under vacuum. **L1** (3.6 g, 43%) was obtained by recrystallizion from a mixture of methanol and DMF. The spectral properties of **L1** are as follows: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.96 ppm (d, 2H, J = 8.3 Hz), 7.67 ppm (m, 4H), 7.54 ppm (m, 4H), 7.45 ppm (m, 4H), 7.36 ppm (d, 2H, J = 8.0 Hz, $^3J_{H,P}$ = 13.2 Hz), 7.32 ppm (m, 4H), 7.10 ppm (m, 4H), 7.06 ppm (m, 4H), ^{31}P NMR (162 MHz, $CDCl_3$) δ: −15.18 ppm (s, decoupled). ^{19}F NMR ($CDCl_3$): δ −127.3 (s, 8F, CF_2), −123.6 (s, 8F, CF_2), −123.3 (bs, 16F, CF_2), −122.5 (s, 8F, CF_2), −121.9 (s, 8F, CF_2), −110.8 (t, $^3J_{F,F}$ =13.9 Hz, 8F, CF_2Ar), −81.4 (t, $^3J_{F,F}$=9.5 Hz, 12F, CF_3)

(R)-6,6'–diheptadecafluorooctyl-2,2'-bis(di-m-(heptadecafluorooctyl)-diphenylphosphino) -1,1'-binaphthyl, L2 Phosphinylation of chiral compound perfluoroalkylated (R)-6,6'/Rf-BINAP (**L2)** was synthesized in the same way as **L1** ligand in 40 % yield. The spectral properties: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.93 ppm (d, 2H, J = 8.3 Hz), 7.61 ppm (m, 2H), 7.54 ppm (m, 4H), 7.46 ppm (m, 2H) 7.45 ppm (m, 4H), 7.35 ppm (d, 2H, J = 8.0 Hz, $^3J_{H,P}$ = 13.2 Hz), 7.18 ppm (m, 2H), 7.10 ppm (m, 4H), 7.06 ppm (m, 4H), ^{31}P NMR (162 MHz, $CDCl_3$) δ: −16.68 ppm (s). ^{19}F NMR ($CDCl_3$): δ −127.4 (s, 8F, CF_2), −123.7 (s, 8F, CF_2), −123.4 (bs, 16F, CF_2), −122.7 (s, 8F, CF_2), −122.2 (s, 8F, CF_2), −110.8 (t, $^3J_{F,F}$ =13.9 Hz, 8F, CF_2Ar), −81.6 (t, $^3J_{F,F}$=9.5 Hz, 12F, CF_3)

CONCLUSION

The solubility properties of fluorinated complexes and perfluorinated complexes are compared. As expected, the perfluorinated complexes are more soluble in $scCO_2$, than fluorinated complexes. The syntheses of fluorinated BINAP derivatives have been performed. Catalytic hydrogenation of ethyl acetoacetate can be carried out with synthesized fluorinated BINP derivatives and $Rh(acac)(C_2H_4)$.

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