Supplementary Material (ESI) for Chemical Communication

Supporting information

Highly enantioselective hydroformylation of dihydrofurans catalyzed by hybrid phosphine phosphonite-rhodium complexes

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1. General remarks: Reaction manipulations involving moisture sensitive compounds were carried out under an atmosphere of dry argon using Schlenk technique. Solvents were dried by standard procedures unless otherwise mentioned.[1] The monophosphine **5** was prepared according to the literature procedure.[2] The starting materials 1,1-disubstitued H_8-BINOL and substituted BINOL's were synthesized as reported earlier.[3] All other chemicals/reagents were purchased from commercial suppliers and used without further purification. NMR spectra were recorded on 400 MHz Bruker Avance and 300 MHz Varian instruments at 298K unless mentioned otherwise; Chemical shifts are referenced to ext. TMS (^{1}H, ^{13}C) or 85% H_3PO_4 (Ξ = 40.480747 MHz, ^{31}P). Coupling constants are given as absolute values. High-resolution fast atom bombardment mass spectrometric (HRMS-FAB) measurements were carried out on a JEOL JMS SX/SX 102A spectrometer. Samples were loaded in a 3-nitrobenzyl alcohol matrix and bombarded with xenon atoms. Melting points were recorded on a Gallenkamp melting point apparatus in argon sealed capillary. Chiral GC separations were recorded on an Interscience Trace GC Ultra instrument with a Supelco BETA–DEX 225 column (internal diameter 0.25mm, 10 m column, film thickness 0.25µm).

2. Synthesis and characterization of compound 6:

Phosphine **5** (730 mg, 1.246 mmol) was dissolved in 10 mL of diethyl ether and the resulting solution was cooled to -78˚C. Next, *tert*-BuLi (1.56 mL of 1.6 M hexane solution, 2.492 mmol) was added drop wise to the above mixture and resulting yellowish-orange solution was allowed to warm to room temperature over 1 h. The reaction mixture was stirred for an additional 15 min. at room temperature before being cooled to -65 ˚C and bis(diethylamino)chlorophosphine (0.32 mL, 1.495 mmol) was added. The faint yellow solution was allowed to warm up to room temperature and stirred for another 2 h. The precipitate formed was filtered over a pad of neutral alumina, washed with diethyl ether (3 × 10 mL), solvent was evaporated in vacuum to obtain **6** as a solid in 85% yield (720 mg).

^{1}H NMR (C_6D_6, 300 MHz, 298K): δ = 7.7-7.4 (m, 7H, Ar), 7.3-7.0 (m, 6H, Ar), 6.97 (m, 1H, Ar), 3.40-3.10 (m, 8H, NCH_2), 1.71 (s, 6H, Me_2), 1.42 (s, 9H, *tert*-Bu), 1.19 (s, 9H, *tert*-Bu), 1.13 (t, $^2J_{H\text{-}H}$ = 7 Hz, 12H, NCH_3).

^{13}C NMR (C_6D_6, 300 MHz, 298K): δ = 152.1(d, $^2J_{P\text{-}C}$ = 17.8 Hz, *C*O-Xant), 150.2 (d, $^2J_{P\text{-}C}$ = 16.6 Hz, *C*O-Xant), 145.5 (s, *C*-Xant), 144.9 (s, *C*-Xant), 138.7 (d, $^2J_{P\text{-}C}$ = 14.8 Hz, *C*PPh_2), 134.4 (d, $^1J_{P\text{-}C}$ = 19.9 Hz, *C*PPh_2), 130.6 (s, *C*-Xant), 130.3 (m, *C*-Xant), 130.1 (m, *C*PPh_2), 129.9 (s, *C*-Xant), 125.1 ($^1J_{P\text{-}C}$ = 18.9 Hz, *C*-Xant), 123.0 (s, *C*-Xant), 121.7 (s, *C*PPh_2), 43.6 (dd, $^2J_{P\text{-}C}$ = 19.0 Hz, $^1J_{C\text{-}C}$ = 2.1 Hz, P*C*H_2), 35.2 (t, *C*-Xant), 34.7 (s, *C*t-Bu), 34.6 (s, *C*t-Bu), 31.8 (s, C(*C*H_3)$_3$), 31.5 (s, C(*C*H_3)$_2$), 31.5 (s, C(*C*H_3)$_3$), 25.8 (s, *C*(CH_3)$_2$), 14.9 (d, $^3J_{P\text{-}C}$ = 2.9 Hz, PN(CH_2*C*H_3)$_2$).

^{31}P NMR (C_6D_6, 300 MHz, 298K): δ = 92.4 (d, $^6J_{P\text{-}P}$ = 17.1 Hz), -15.1 (d, $^6J_{P\text{-}P}$ = 17.1 Hz).

HRMS (FAB$^+$) m/z calculated for $[C_{43}H_{58}ON_2P_2+H]$ = 681.4103 $[MH]^+$; obs.: 681.4102.

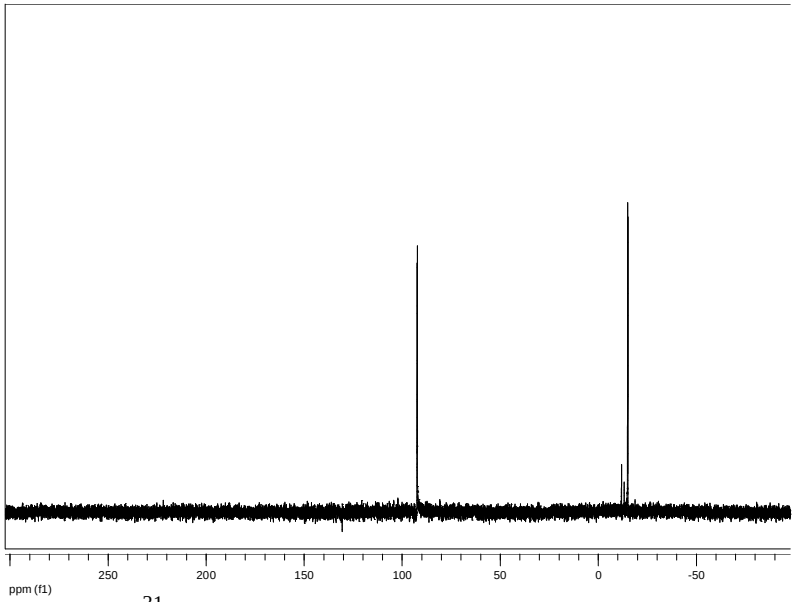


Figure S1: ^{31}P NMR of **6** in benzene-d_6 displaying two doublets.

3a. Synthesis and characterization of compound 7a:

650 mg (0.9548 mmol) of compound **6** was dissolved in 12 ml of dry toluene and 273 mg of *S*-BINOL (0.9546 mmol) was added to it. The reaction mixture was refluxed at 110ºC under argon atmosphere for 16 hours. Finally, solvent was evaporated in vacuum, to yield a solid material, which was re-dissolved in 10 ml of toluene and the volatiles were evaporated again. The solid was dissolved in 10 ml of pentane and stored overnight at -20 °C to give white precipitate, which was isolated in excellent yield (90%) by a quick filtration under inert conditions.

^{1}H NMR ($CDCl_3$, 300 MHz, 298K): δ = 8.15-7.70 (m, 4H, PPh_2), 7.60-7.10 (m, 22H, PPh_2+Ar), 1.70 (br. s, 3H, Me_2), 1.63 (br. s, 3H, Me_2), 1.14 (br. s, 9H, *tert*-Bu), 0.76 (br. s, 9H, *tert*-Bu).

^{31}P NMR ($CDCl_3$, 300 MHz, 298K**):** δ = 179.7 (d, $^6J_{P\text{-}P}$ =29.3 Hz), -15.3 (d, $^6J_{P\text{-}P}$ =29.3 Hz).

HRMS (FAB$^+$) m/z calculated for $[C_{55}H_{50}O_3P_2+H]^+$ = 821.3313 $[MH]^+$; obs.: 821.3311.

3b. Synthesis and characterization of compound 7b:

The ligand **7b** was synthesized following similar procedures as reported for ligand **7a**, (*S*) 3,3'-dimethyl-[1, 1'-binaphthalene]-2, 2'-diol was used instead of *S*-BINOL and the mixture was refluxed for 60 h.

^{1}H NMR ($CDCl_3$, 300 MHz, 298K): δ = 7.85-7.00 (m, 24H, PPh_2+Ar), 2.60-2.40 (br. s, 6H, BINOL-Me_2), 1.65 (br. s, 6H, Me_2), 1.16 (br. s, 9H, *tert*-Bu), 1.07 (br. s, 9H, *tert*-Bu), traces of solvent impurities were also observed.

^{31}P NMR (C_6D_6, 300 MHz, 298K): δ = 172.9(d, $^{6}J_{P\text{-}P}$ = 33.8 Hz), -15.18(d, $^{6}J_{P\text{-}P}$ = 33.8 Hz).

HRMS (FAB^{+}) m/z calculated for $[C_{57}H_{54}O_3P_2+H]^{+}$ = 849.3626 $[MH]^{+}$; obs.: 849.3625.

3c. Synthesis and characterization of compound 7c:

3,3'-diphenyl-5,5',6,6',7,7',8,8'-octahydro-[1,1'-binaphthalene]-2,2'-diol (*S*) (418 mg 0.936 mmol) was added to a solution of bis-phosphine **6** (580 mg, 0.852 mmol in 15 mL of toluene). A catalytic amount of tetrazole (0.045 mmol) was added and the mixture was refluxed at 120 °C for 60 h. The faint yellow solution was cooled to room temperature, filtered through a glass frit and concentrated to give **7c** as a white solid. The crude powder was purified by chromatography (using Chromatotron) with 98:2 mixture of hexane and triethyl amine, which afforded pure **7c** in 92% (767 mg, 0.784 mmol) yield.

^{1}H NMR (C_6D_6, 300 MHz, 298K): δ = 7.86 (d, $^{3}J_{P\text{-}H}$ = 8.1 Hz, 2H, PPh_2), 7.74 (m, 2H, PPh_2), 7.64 (m, 2H, Ar), 7.48 (s, 1H, Ar), 7.46 (s, 2H, Ar), 7.37 (m, 2H, Ar), 7.28-7.18 (m, 7H, Ar), 7.18-7.08 (m, 4H, Ar), 7.0-6.90 (m, 3H, Ar), 6.54 (t, $^{3}J_{H\text{-}H}$ = 7.4 Hz, 1H, Ar), 3.0-2.60 (m, 8H, CH_2-8H-BINOL), 1.9-1.7 (m, 8H, CH_2-8H-BINOL, 1.67 (s, 6H, Me_2), 1.33 (s, 9H, *tert*-Bu), 1.18 (s, 9H, *tert*-Bu).

^{13}C NMR (C_6D_6, 300 MHz, 298K): δ = 152.8(d, $^{2}J_{P\text{-}C}$ = 22.0 Hz, *C*O-Xant), 152.5 (s, *C*O-Xant), 150.28 (d, $^{2}J_{P\text{-}C}$ = 15.8 Hz, *C*O-Xant) 150.26 (d, $^{2}J_{P\text{-}C}$ = 15.5 Hz, *C*O-8H-BINOL), 150.24 (d, $J_{P\text{-}C}$ = 2.5 Hz, *C*-Xant), 150.22 (d, $J_{P\text{-}C}$ = 2.3 Hz, *C*-8H-BINOL), 150.17 (s, *C*-Xant), 146.7 (d, $J_{P\text{-}C}$ = 1.8 Hz, *C*-Xant), 145.4 (s, *C*-Xant), 144.7 (d, $J_{P\text{-}C}$ = 4.8 Hz, *C*-Xant), 144.1 (s, *C*-Xant), 138.8 (s, *C*-Xant), 138.2 (d, $J_{P\text{-}C}$ = 14.7 Hz, *C*PPh_2), 137.5-137.4 (m), 136.7 (s), 135.5 (s, *C*-8H-BINOL), 135.2 (s, *C*-8H-BINOL), 134.5 (d, $J_{P\text{-}C}$ = 1.7 Hz, *o*-*C*PPh_2), 134.3 (m, Ar), 134.2 (d, $J_{P\text{-}C}$ = 1.7 Hz, *o*-*C*PPh_2), 133.4 (s), 132.9 (d, $J_{P\text{-}C}$ = 2.6 Hz, *C*-Xant), 132.8 (s), 131.8 (s, *C*-Ar), 131.7 (s, *C*-Ar), 131.4(d, $J_{P\text{-}C}$ = 2.2 Hz, *C*-8H-BINOL), 130.2 (s, *C*-Ar), 130.1 (s, *C*-Ar), 129.9 (s, *C*H_2), 129.5 (d, $J_{P\text{-}C}$ = 0.8 Hz, *C*-Ar), 129.2 (m, *C*-Ar), 128.9 (s, *C*-Ar), 128.8 (s, *C*PPh_2), 126.9 (s, C-Ar), 126.7 (s, C-Ar), 126.5 (s, C-Ar), 125.6 (s, CH_2),

125.1 (s, CH_2), 124.6 (d, $J_{P\text{-}C}$ = 1.9 Hz, *C*-Xant), 124.5 (d, $J_{P\text{-}C}$ = 0.9 Hz, *C*-Xant), 123.9 (s, *C*-Xant), 121.7 (m, *C*-8H-BINOL), 35.1 (m, CH_3), 34.7 (s, $C[CH_3]_3$), 34.6 (m, CH_3), 34.5 (s, $C[CH_3]_3$), 31.5 (CH_2), 30.0 (CH_2), 29.5 (CH_2), 23.5-23.0 (m, CH_2).

^{31}P NMR (C_6D_6, 300 MHz, 298K): δ = 167.7 (d, $^6J_{P\text{-}P}$ = 34.3 Hz), -13.8 (d, $^6J_{P\text{-}P}$ = 34.3 Hz);

HRMS (FAB$^+$) m/z calculated for $[C_{67}H_{66}O_3P_2+H]$ = 981.4565 $[MH]^+$; obs.: 981.4572.

mp: 198 °C (dec.).

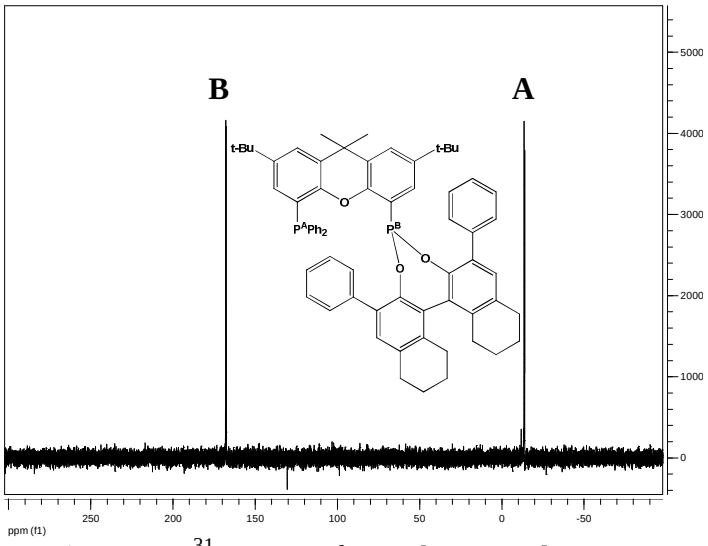


Figure S2: ^{31}P NMR of **7c** in benzene-d_6.

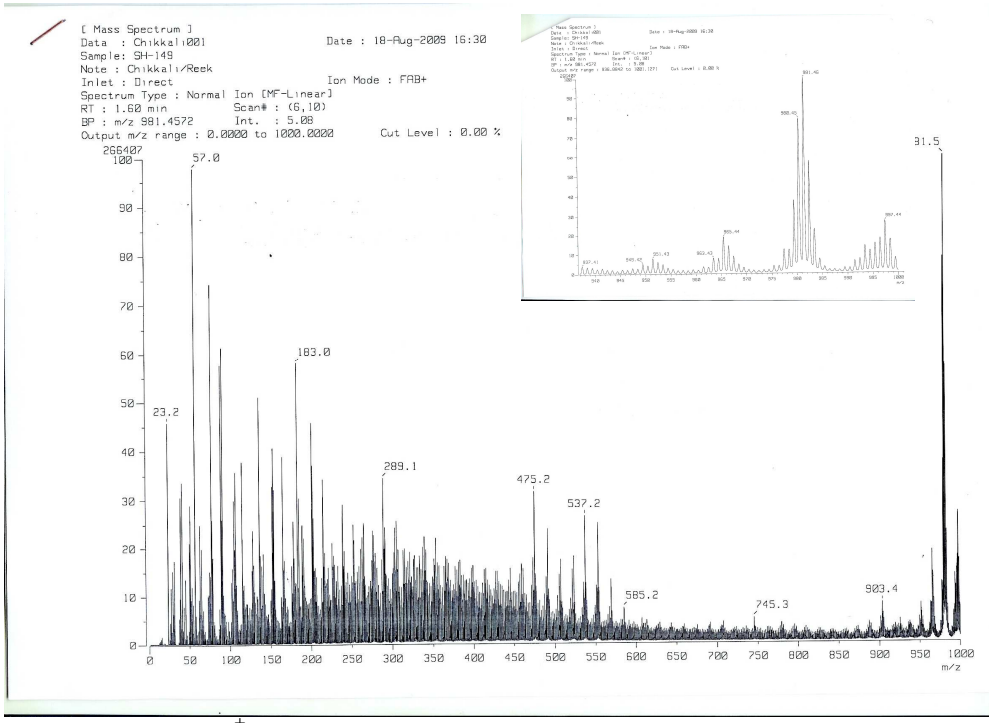


Figure S3: MS (FAB^+) spectrum of **7c** with an expanded view in the top right corner.

4. Synthesis and characterization of complex 8:

A mixture of $[Rh(CO)_2Cl]_2$ (10.53 mg, 0.0271 mmol) and **7c** (53.2 mg, 0.0542 mmol) was placed in a 25 mL schlenk tube, dry dichloromethane (2 mL) added and the reaction mixture was stirred at room temperature. After 2 h the volatiles were stripped off in vacuum and the yellowish orange solid was isolated in near quantitative yield (58.81 mg, 0.0512 mmol, 94%).

^{31}P NMR (CH_2Cl_2, 300 MHz, 298K): δ = 162.2 (dd, $^1J_{Rh\text{-}P}$ = 202 Hz, $^2J_{P\text{-}P}$ = 532 Hz), 20.6 (dd, $^1J_{Rh\text{-}P}$ = 127.5 Hz, $^2J_{P\text{-}P}$ = 532 Hz).

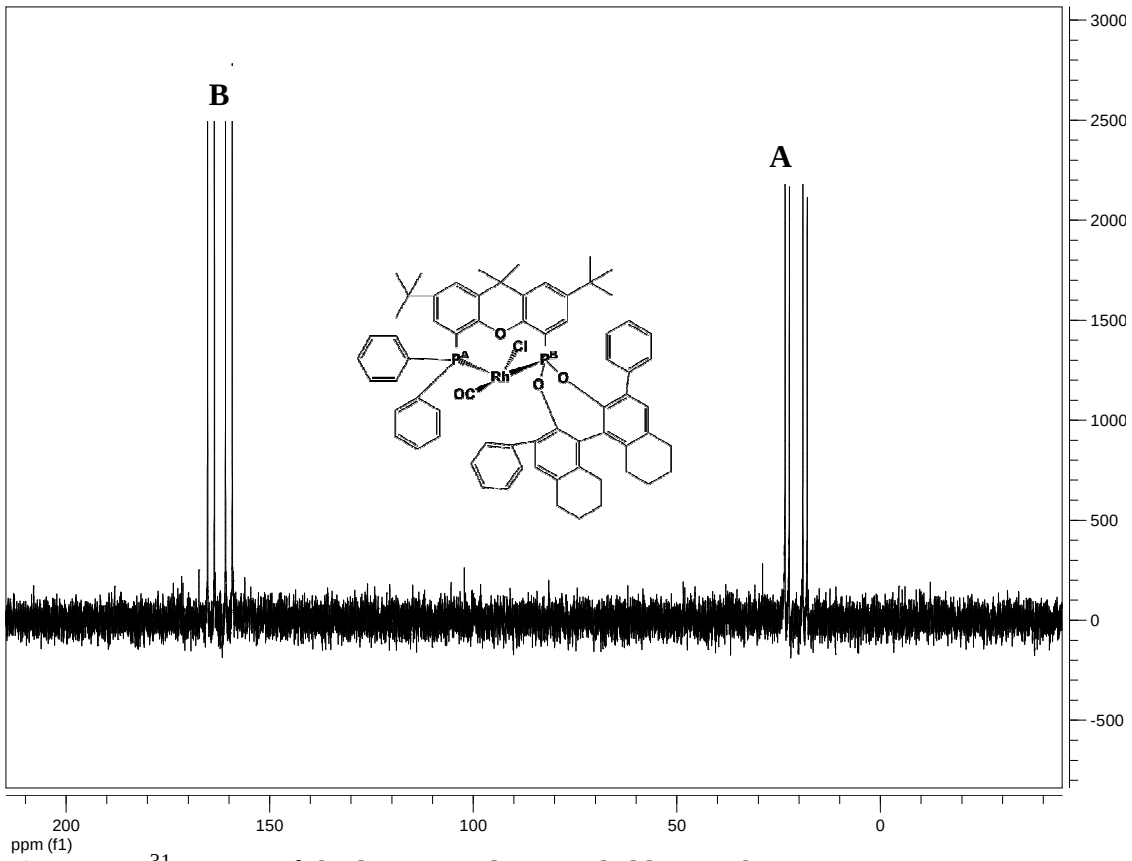
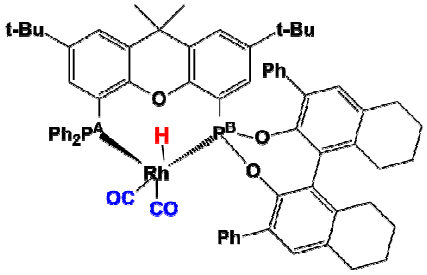


Figure S4: ^{31}P NMR of rhodium complex **8** in dichloromethane.

5. In situ investigations on rhodium complex 9:

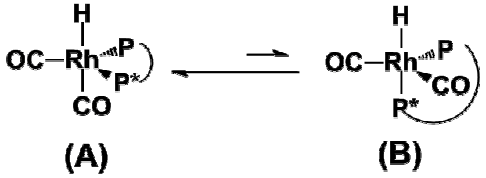
In our quest for catalytically active species, we prepared complex **[RhH(7c) $(CO)_2$]** (**9**) and the *in situ* protocol follows as: The hybrid ligand **7c** (20 mg, 0.0202 mmol) and [Rh(acac)$(CO)_2$] (5.212 mg, 0.0202 mmol) was dissolved in 1 mL of dry toluene-d_8 in a 2 mL glass vial under inert atmosphere. The vial was immediately transferred to a stainless steel autoclave and was purged three times with 30 bars of syngas pressure. Finally, the autoclave was pressurized to 20 bars and heated to 45 °C for 16 h with constant stirring. Next, the autoclave was slowly cooled to room temperature, the vial content transferred to a



high pressure NMR tube and the tube was pressurised to 5 bars of syngas. The following high pressure NMR (HP-NMR) data were collected on a 300 MHz DRX instrument.

^{1}H HP-NMR (Toluene-d_8, 300 MHz, 298K): δ = -9.0 ($^{2}J_{P^*\text{-}H}$ = 35 Hz, $^{2}J_{P\text{-}H}$ = 8.0 Hz, $^{1}J_{Rh\text{-}H}$ = 4.1 Hz (see Fig.S5).

^{31}P HP-NMR (Toluene-d_8, 300 MHz, 298K): δ = 173.9 (dd, $^{2}J_{P\text{-}P}$ = 95 Hz, $^{1}J_{Rh\text{-}P}$ = 203 Hz), 19.5 ($^{2}J_{P\text{-}P}$ = 95 Hz, $^{1}J_{Rh\text{-}P}$ = 130.6 Hz). The above NMR and coupling constant assignments are derived from a set of high pressure NMR experiments (please refer to Fig. S5-S10).
An expanded view of the hydride signal is presented in figure S5. The coupling constants were extracted from ^{31}P NMR (Fig. S6), ^{1}H [^{31}P-decoupled] (Fig. S7), ^{31}P NMR [^{1}H-coupled] (Fig. S8). Figure S9 and S10 display 2D ^{1}H ^{31}P correlation spectra with the phosphine and phosphonite regions expanded, respectively.
The *in situ* HP-NMR investigations strongly indicate that the two species (A) and (B) (see Scheme 1) are in equilibrium with the predominant species being (A).



Scheme 1: equatorial-equatorial and equatorial-axial equilibrium under hydroformylation conditions.

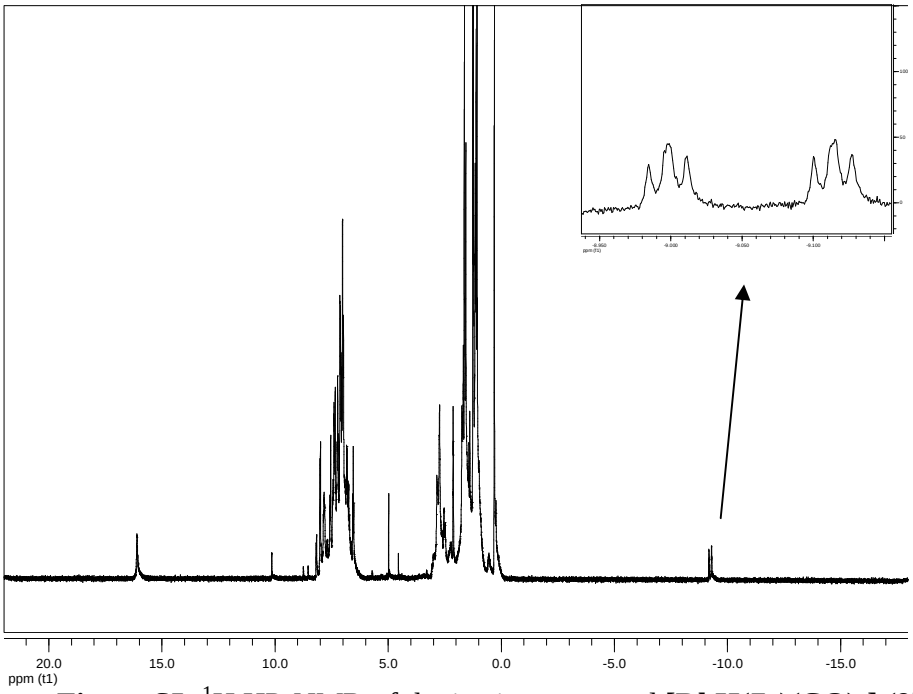


Figure S5: ^{1}H HP-NMR of the in situ generated **[RhH(7c)(CO)$_2$] (9)**, expanded view of the hydride signal is presented in the top right corner.

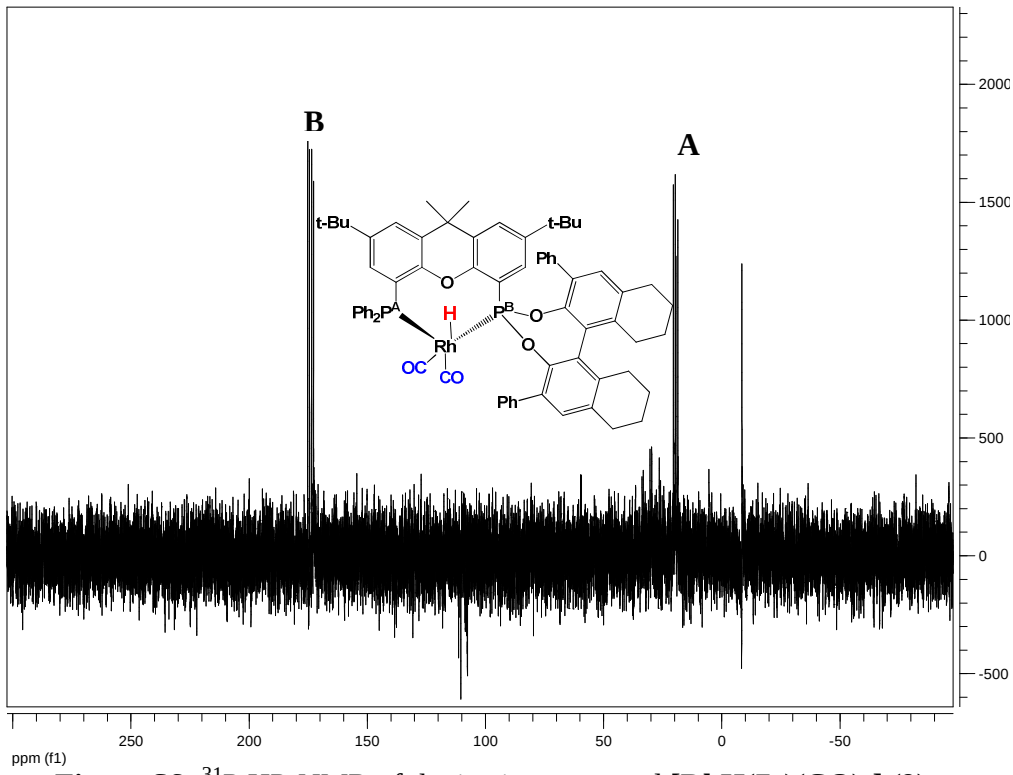


Figure S6: ^{31}P HP-NMR of the in situ generated **[RhH(7c)(CO)$_2$] (9)**.

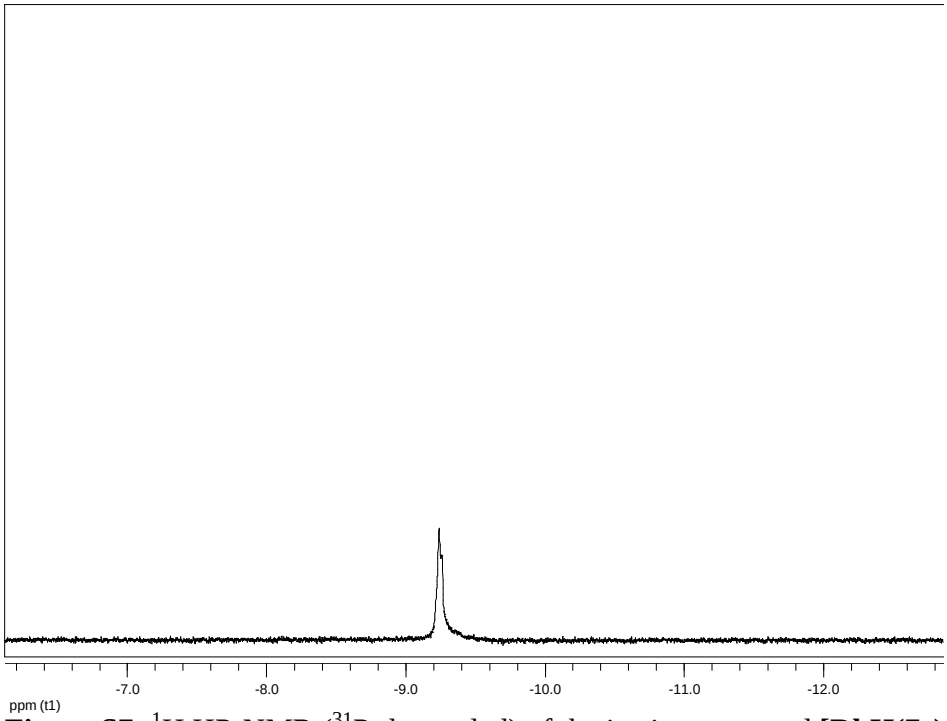


Figure S7: ^{1}H HP-NMR (^{31}P-decoupled) of the in situ generated **[RhH(7c)(CO)$_2$] (9)** complex, expanded view of the hydride region.

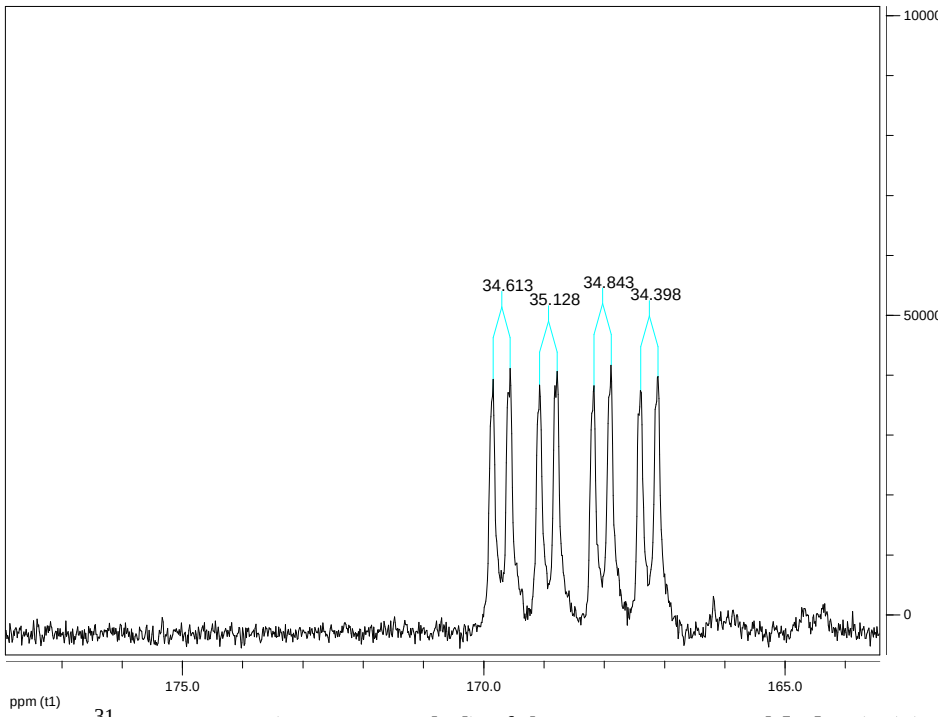


Figure S8: ^{31}P HP-NMR (proton-coupled) of the in situ generated **[RhH(7c)(CO)$_2$] (9)**, expanded view of the phosphonite region.

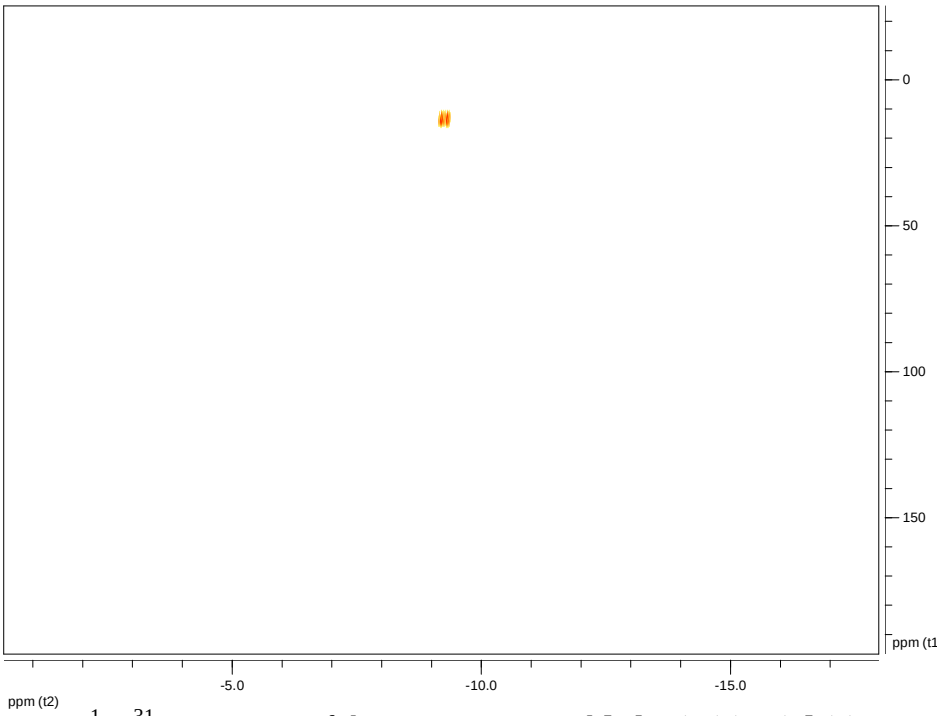


Figure S9: ^{1}H-^{31}P HP-NMR of the in situ generated **[RhH(7c)(CO)$_2$] (9)**, expanded view of the hydride-phosphine cross peaks.

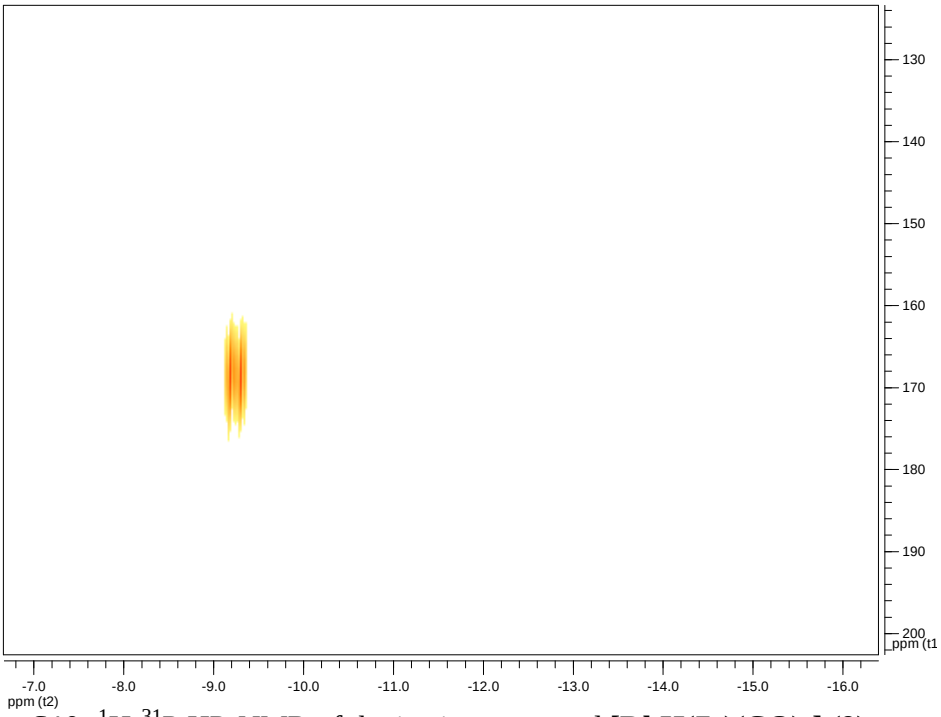


Figure S10: ^{1}H-^{31}P HP-NMR of the in situ generated **[RhH(7c)(CO)$_2$] (9)**, expanded view of the hydride-phosphonite cross peaks.

6. General hydroformylation procedure: The reactions were performed in a stainless steel autoclave containing inserts for five 2 mL glass vials with Teflon stirring bars. The vials were charged with appropriate amounts of solvent, substrate, metal precursor and ligand (see Table 1). Before starting the catalytic reactions, the charged autoclave was purged three times with appropriate pressure of syngas and then pressurized to the desired pressure. After catalysis the autoclave was cooled to 0 ºC, pressure was reduced to 1 bar, catalysis was either quenched (by the addition of tri-t-butyl phosphine) or the reaction solution was directly analyzed. The conversion was determined by ^{1}H NMR in $CDCl_3$ at room temperature and regio-, stereo-selectivities were determined by chiral-GC.

7. Determination of enantiomeric excess and absolute configuration of 3 and 4: A control experiment using Xantphos ligand and [Rh(acac)$(CO)_2$] as precursor was performed following the general procedure reported in section 6. This produced all four isomers of **3** and **4** (see fig. S11). The reaction mixture was diluted with dichloromethane in a 1 mL GC vial. The enantiomeric purity was determined on a chiral Trace GC Ultra instrument. 2,3- and 2,5-dihydrofurans: Supelco BETA–DEX 225, initial temperature 50 °C, hold for 0.10 min.; ramp 1, 15 °C/min. to 150 °C, hold 0.2 min.; ramp 2, 100 °C/min. to 215 °C. 2-Carbaldehyde t_R = 4.8 min., t_R = 5.0 min. and 3-Carbaldehyde t_R (*S*) = 5.3 min., t_R (*R*) = 5.6 min. The absolute configuration of **3** (3-carbaldehyde) was established by comparing the chiral-GC traces of an authentic sample [prepared according to the procedures reported by Nozaki et al,[4]{using (*S*,*R*) BINAPHOS as ligand}] with those obtained from runs 1-19. The ee and absolute configuration of **4** was not determined.

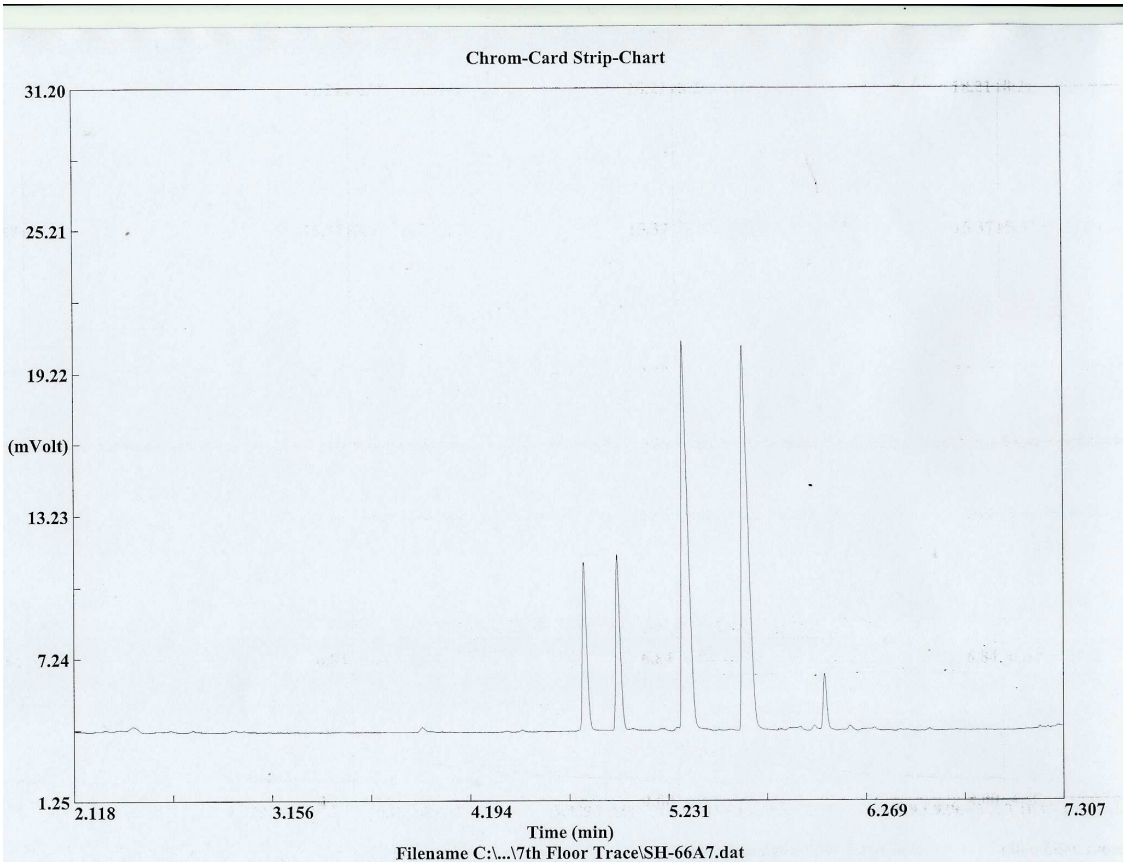


Figure S11: Chiral GC trace (displaying all four isomers) of a control sample prepared using Xantphos and [Rh(acac)$(CO)_2$] precursor.

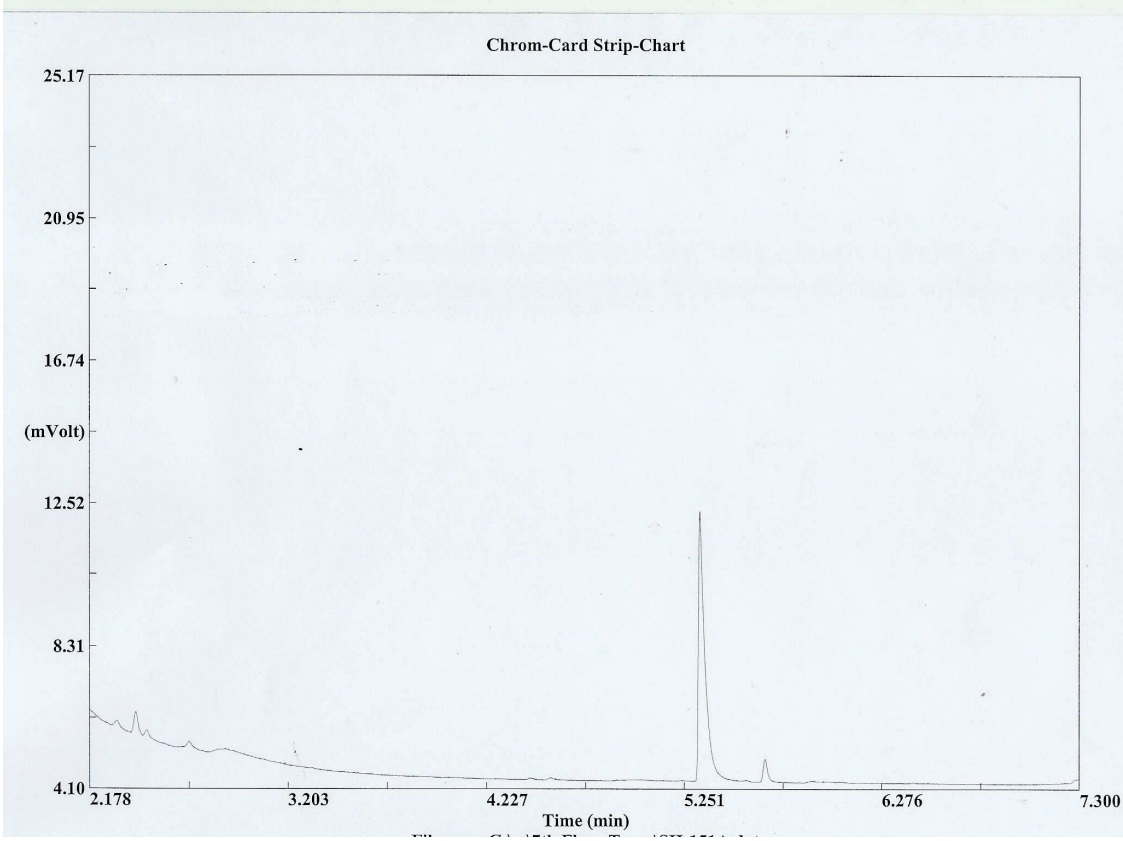


Figure S12: Chiral GC trace obtained from a sample of run 8.

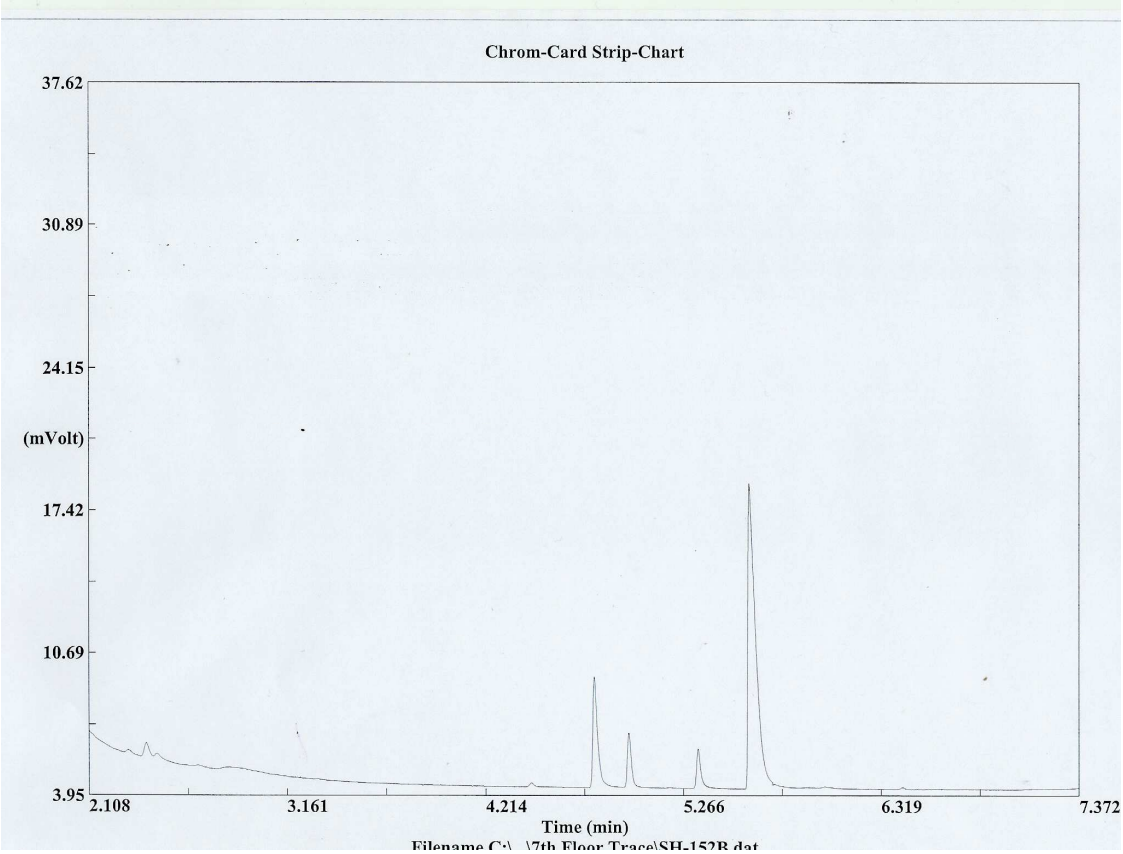


Figure S13: Chiral GC trace obtained from a sample of run 16.

8. References:

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