Polyhedron 84 (2014) 120–135

Contents lists available at ScienceDirect

Polyhedron

journal homepage: www.elsevier.com/locate/poly

Extending the range of pentasubstituted cyclopentadienyl compounds: The synthesis of a series of tetramethyl(alkyl or aryl)cyclopentadienes (Cp^{*R}), their iridium complexes and their catalytic activity for asymmetric transfer hydrogenation

David M. Morris, Michael McGeagh, David De Peña, Joseph S. Merola *

Department of Chemistry, Virginia Tech, 306 Hahn Hall North, Blacksburg, VA 24061, United States

ARTICLE INFO

Article history:
Received 10 April 2014
Accepted 26 June 2014
Available online 8 July 2014

This paper is dedicated to Professor John Bercaw on the occasion of his 70th birthday. Your friendship and advice over the years has always been good and always valuable.

Keywords:
Iridium
Cyclopentadiene
Amino acid
Half-sandwich compounds
ATH

ABSTRACT

Tetramethyl(alky or aryl)cyclopentadienes were synthesized and the organometallic half-sandwich iridium complexes of the form [(η^5-Cp^{*R})Ir(aa)Cl], Cp^{*R} = tetramethyl(phenyl)cyclopentadienyl (Cp^{*Ph}), tetramethyl(benzyl)cyclopentadienyl (Cp^{*Bn}), tetramethyl(2-propyl)cyclopentadienyl (Cp^{*iPr}), or tetramethyl(cyclohexyl)cyclopentadienyl (Cp^{*Cy}) were prepared and characterized. The complexes adopt a piano stool configuration, forming diastereomers, with ratios similar to reported [(η^5-Cp^*)Ir(aa)Cl] complexes. The complexes display an intermolecular hydrogen bonding network in the solid state. These complexes were tested for the asymmetric transfer hydrogenation of several ketones, showing that the R of the Cp^{*R} drastically impacts both selectivity and rate of reaction. Additionally, severe solvent effects are displayed when the reaction media is changed from aqueous to organic solvent.

© 2014 Elsevier Ltd. All rights reserved.

1. Introduction

The discovery of ferrocene [1] in 1951 is arguably the starting point for the modern era of organometallic chemistry. The history of that discovery and the early years of ferrocene chemistry are nicely related by Kauffman [2], by Werner [3], and by Wilkinson [4] in a personal recounting. Fischer and Wilkinson were awarded the Nobel Prize in Chemistry in 1973 for their investigations into the syntheses and chemistry of a wide variety of metallocene compounds. One of the more intriguing aspects of ferrocene is the enhanced reactivity of the cyclopentadienyl ring toward a number of reactions, especially electrophilic aromatic substitution [5].

The enhanced reactivity of the unsubstituted cyclopentadienyl rings attached to metals made the cyclopentadienyl ligand less than desirable for examining some chemistry at the metal since the Cp ring often became involved in reactions at the metal center [6]. 1,2,3,4,5-pentamethylcyclopenta-1,3-dienyl, (Cp^*), is one of the most common ancillary ligands in organometallic chemistry due to its steric bulk, good electron density and the full methyl substitution blocks some direct reactions of the metal with the ligand due to the absence of cyclopentadienyl C–H bonds. One of the first Cp^* metal complexes was made by reaction between $IrCl_3 \cdot 3H_2O$ and hexamethyldewarbenzene [7]. A complete review of Cp^* complexes would be massive, but recent publications show that Cp^* may be used in complexes for transfer hydrogenation [8–11], water oxidation [12–14], anti-cancer activity [15,16], and anti-microbial activity [17]. The development of much early metal chemistry was made possible in large part to the use of pentamethylcyclopentadiene. The contributions of Bercaw and a host of co-workers for the development of an efficient synthesis of pentamethylcyclopentadiene [18] and the use of pentamethylcyclopentadienyl complexes of metal compounds across the periodic table have been critical in the development of modern organometallic chemistry [19,20].

Further modification of the penta-alky substituted cyclopentadienyl ligands could have potential utility, especially in the realm of catalytic chemistry. Asymmetrically penta-substituted cyclopentadienyl ligands, specifically C_5Me_4R variants, would provide the opportunity to probe the effect of changing a single substitution and note any changes in catalytic activity and/or selectivity. One of the most successful and intriguing of catalytic systems is

* Corresponding author.
E-mail address: jmerola@vt.edu (J.S. Merola).

http://dx.doi.org/10.1016/j.poly.2014.06.053
0277-5387/© 2014 Elsevier Ltd. All rights reserved.

asymmetric transfer hydrogenation (ATH), for which a share of the Nobel Prize was awarded to Ryoji Noyori in 2001 [21]. Noyori and co-workers have shown that half-sandwich compounds of ruthenium are excellent catalysts for ATH [22–24]. It has been postulated that interaction of ATH substrates with the methyl groups of C_6Me_6 ruthenium compounds plays an important role in the enantioselectivity of the products [25]. This led us to test C_5Me_4R systems for ATH catalysis and determine if varying the R group would have an effect on the activity or selectivity of Cp*Ir(aa)Cl complexes, where aa = aminoacidato ligands.

Although some substitutionally-modified Cp* type ligands have been reported, an extended series of these ligands is not readily available. Because of this there has been limited reporting on functionalized Cp* complexes for both catalysis and biological activity studies.[26–29] Bercaw and Threlkel reported on the specific variants C_5Me_4R with R = ethyl, propyl, butyl and phenyl [18]. Modification to the Cp portion of the molecule allows tailoring of the hydrophobicity and sterics of the organometallic complex. Sadler has shown previously that modification to the Cp* moiety effects cytotoxicity, hydrolysis and pK_a of Ir organometallic complexes [16]. Mintz and co-workers have shown that addition of vinyl Grignard to 2,3,4,5-tetramethylcyclopent-2-enone provides good yields of pentamethylfulvene that, in turn, can provide a route to C_5Me_4R complexes [30]. We decided upon an approach utilizing 2,3,4,5-tetramethycyclopent-2-enone with Grignard reagents followed by dehydration because of the wide availability of commercial Grignard reagents and the ease of synthesis of many others. As we were developing this chemistry, as mentioned above, Sadler and co-workers reported on the syntheses of C_5Me_4R compounds with R = phenyl and naphthyl using the same general methodology [31]. Wills and co-workers have also used this tetramethylcyclopentenone route to make amino aryl pentamethylcyclopentadienyl complexes with a diamine tethered to the ring thus tethering the asymmetric diamine ligand to the tetramethylcyclopentadienyl ligand [32]. The work reported herein is the first on tetramethylcyclopentadienyl ligands with benzyl, isopropyl and cyclohexyl groups and their iridium complexes as well as the examination of the iridium complexes for ATH catalysis.

2. Experimental

2.1. Materials and methods

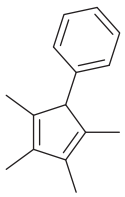
Unless otherwise stated, synthetic work was carried out in air with untreated solvents. Commercially available reagents were obtained from the following sources: $IrCl_3xH_2O$ from Pressure Chemical, Pittsburgh, PA 15201. Sodium formate, pinacolone, *L*-alanine, *L*-proline, benzylmagnesium chloride, and 2,3,4,5-tetramethylcyclopent-2-en-1-one were purchased from Alfa Aesar, Ward Hill, MA 01835. Reagent grade solvents and *L*-phenylglycine, *L*-piperidine-2-carboxylic acid, *L*-phenylalanine, cyclohexylmagnesium bromine, phenylmagnesium chloride, 2-propylmagnesium bromide, 2,2-dimethyl-1-phenylpropan-1-one, and acetophenone were purchased from Sigma–Aldrich, St. Louis, MO 63103. Glycine was purchased from Qiagen Sciences, Germantown, MD 20874. *N*,*N*-dimethylglycine was purchased from Spectrum Chemical, Gardena, CA 90248. Deuterated solvents for NMR spectroscopy were obtained from Cambridge Isotope Laboratories, Tewksbury, MA 01876. *L*-azetidine-2-carboxylic acid was purchased from Indofine Chemical, Hillsborough, NJ 08844. Elemental analyses were performed by Atlantic Microlabs, Norcross, GA. All compounds were dried *in vacuo* at 100 °C for at least 12 h before submitting for elemental analysis. In some complexes, the elemental analysis indicated solvent retention, especially H_2O, even after this treatment.

^1H and ^{13}C NMR spectra were collected on a Varian MR-400 NMR spectrometer. For many of the ^1H spectra reported below, a number of factors made assignment of coupling constants difficult: overlap of major/minor isomer peaks, non-first order behavior and some very complex multiplets. In some cases while coupling constants could be read for one of the protons, the coupling proton was often obscured. Thus there are some listings with *J* values for one proton without the same corresponding *J* value for the coupled proton for the reasons just described. Also, in a number of cases, the non-first order systems could not be modeled adequately and so are described as multiplets(m). GC chromatograms were collected on a Hewlett Packard 5890 equipped with a CP-Chiral-Sil–Dex CB 25 × 0.25 column. HRMS were collected on an Agilent 6220 Accurate Mass TOF LC-MS. X-ray crystallographic data were collected at 100 K on an Oxford Diffraction Gemini diffractometer with an EOS CCD detector and Mo Kα radiation. Crystals were coated in Paratone® oil and mounted on a fiber under nitrogen at 100 K. Data collection and data reduction were performed using Agilent's CrysAlisPro soft-ware [33], Structure solution and refinement were performed with SHELXS and SHELXL [34], and Olex2 was used for graphical representation of the data [35].

2.2. Cyclopentadiene ligand syntheses

2.2.1. Synthesis of (2,3,4,5-tetramethylcyclopenta-2,4-dien-1-yl)benzene (D1)

To a stirred solution of 2,3,4,5-tetramethyl-2-cyclopentenone (2.00 g, 15.2 mmol) in anhydrous THF (20 mL) was added a solution of phenylmagnesium bromide (6.4 mL of a 3.0 M solution 19.1 mmol) in THF. The mixture was refluxed for 3 h, then cooled to 0 °C and quenched with HCl (20 mL of a 1.0 M solution, 20 mmol). This solution was warmed to room temperature and stirred for 1 h. The products were washed with water (30 mL × 3), and the organic layer was dried over $MgSO_4$. The products were concentrated under reduced pressure, and purified by column chromatography (silica gel, hexanes) to afford 2.064 g (68.5%) of the products as an orange liquid.



.

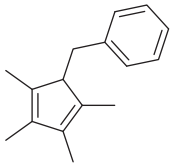
Major isomer: ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.28 (m, 2H), 7.25–7.14 (m, 3H), 3.19 (dddt, *J* = 9.3, 7.6, 5.8, 1.7 Hz, 1H), 2.02 (d, *J* = 1.8 Hz, 3H), 1.93 (d, *J* = 1.0 Hz, 3H), 1.86 (dt, *J* = 2.4, 1.1 Hz, 3H), 0.95 (d, *J* = 7.7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.70, 140.68, 137.14, 134.97, 128.42, 128.05, 125.35, 50.08, 14.72, 12.65, 11.90, 11.07 ppm.

HRMS/ESI$^+$ (*m*/*z*): Calc. for $C_{15}H_{19}$ 199.1481. Found: 199.1475.

2.2.2. Synthesis of ((2,3,4,5-tetramethylcyclopenta-2,4-dien-1-yl)methyl)benzene (D2)

To a stirred solution of 2,3,4,5-tetramethyl-2-cyclopentenone (5.00 g, 36.2 mmol) in anhydrous THF (20 mL) was added a solution of benzylmagnesium bromide (45.3 mL of a 1.0 M solution 45.3 mmol) in THF. The mixture was refluxed for 4 h, then cooled to 0 °C and quenched with HCl (15 mL of a 1.0 M solution, 15 mmol). This solution was warmed to room temperature and stirred for 1 h. The products were washed with water

(30 mL × 3), and the organic layer was dried over $MgSO_4$. The products were concentrated under reduced pressure, and purified by column chromatography (silica gel, hexanes) to afford 7.124 g (92.7%) of the product as a yellow liquid.



Isomer 1: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.04 (m, 5H), 6.10 (s, 1H), 2.52 (q, J = 7.7 Hz, 2H), 1.90 (s, 3H), 1.61 (s, 3H), 1.06 (d, J = 2.3 Hz, 3H), 1.04 (d, J = 2.2 Hz, 3H) ppm.

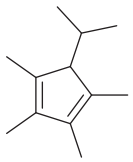
Isomer 2: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.04 (m, 5H), 3.68–3.53 (m, 2H), 2.60 (q, J = 7.4 Hz, 1H), 1.80 (s, 6H), 1.79 (s, 3H), 1.75 (s, 3H) ppm.

Isomer 3: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.03 (m, 5H), 3.76 (d, J = 15.3 Hz, 1H), 3.44 (d, J = 15.2 Hz, 1H), 2.98–2.88 (m, 1H), 1.89–1.86 (m, 3H), 1.79 (d, J = 1.6 Hz, 3H), 1.76–1.74 (m, 3H), 0.98 (d, J = 7.6 Hz, 3H) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{16}H_{21}$ 213.1638. Found: 213.1635.

2.2.3. Synthesis of 5-isopropyl-1,2,3,4-tetramethylcyclopenta-1,3-diene (D3)

To a stirred solution of 2,3,4,5-tetramethyl-2-cyclopentenone (2.50 g, 18.09 mmol) in anhydrous THF (30 mL) was added a solution of 2-propylmagnesium bromide (7.34 mL of a 2.9 M solution, 22.60 mmol) in THF. The mixture was refluxed for 24 h, then cooled to 0 °C and quenched with HCl (30 mL of a 1.0 M solution, 30 mmol). This solution was then stirred for 1.5 h. The organic phase was washed with water (30 mL × 3), and the organic layer was dried over $MgSO_4$. The products were concentrated under reduced pressure and purified by column chromatography (silica gel, hexanes) to afford 1.102 g (37.1%) of the product as a yellow liquid.

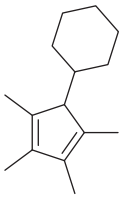


Major isomer: ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.83 (CpC), 134.84 (CpC), 62.71 (Cp**C**H), 28.07 (Me_2**C**H), 18.91 (CH_3), 13.22 (CpMe), 10.96 (CpMe).

HRMS/ESI$^+$ (m/z): Calc. for $C_{12}H_{21}$ 165.1638. Found: 165.1627.

2.2.4. (2,3,4,5-tetramethylcyclopenta-2,4-dien-1-yl)cyclohexane (D4)

To a stirred solution of 2,3,4,5-tetramethyl-2-cyclopentenone (4.00 g, 28.9 mmol) in anhydrous THF (20 mL) was added a solution of cyclohexylmagnesium chloride (18.1 mL of a 2.0 M solution, 36.2 mmol) in THF. The mixture was refluxed for 2 h. The mixture was cooled to 0 °C and quenched with HCl (40 mL of a 1.0 M solution, 40 mmol). This solution was then stirred for 1 h. The organic phase was washed with water (30 mL × 3), and the organic layer was dried over $MgSO_4$. The products were concentrated under reduced pressure and purified by column chromatography (silica gel, hexanes) to afford 4.825 g (71.4%) of the product as a yellow liquid.



^{1}H unassignable due to signal overlap between isomers. ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.11, 135.65, 134.92, 133.88, 62.55, 49.68, 39.23, 38.49, 32.88, 32.29, 30.14, 29.64, 27.25, 26.85, 26.38, 14.97, 14.07, 13.38, 11.39, 11.00 ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{17}H_{31}$ 204.1878. Found: 204.1891.

2.3. Synthesis of Cp^{*R} chloro-bridged dimers

2.3.1. Synthesis of $[(\eta^5\text{-}C_5Me_4C_6H_5)IrCl_2]_2$ (**1**)

0.200 g (0.569 mmol) of $IrCl_3 \times 3H_2O$ was combined with (2,3,4,5-tetramethylcyclopenta-2,4-dien-1-yl)benzene (0.135 g 0.683 mmol) in methanol (1 mL) in a microwave pressure tube. The reaction mixture was heated to 115 °C at 150 watts and 88 psi and held there for 30 min. Upon cooling, an orange powder formed and was collected by filtration. This orange powder was washed with cold methanol and hexanes to yield 0.1187 g (45.3%) of **1**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62–7.53 (m, 4H, ArH), 7.4.–7.32 (m, 6H, ArH), 1.72 (s, 12H, 4 CpMe), 1.63 (s, 12H, 4 CpMe) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 130.18 (ArC), 129.79 (ArC), 128.62 (ArC), 128.42 (ArC), 93.43 (CpC), 85.48 (CpC), 10.33 (CpMe), 9.60 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{30}H_{34}[^{193}Ir]_2Cl_3$ 885.0979. Found: 885.1018.

Anal. Calc. for $C_{30}H_{34}Cl_4Ir_2$: C, 39.130; H, 3.720. Found: C, 38.11; H, 3.61%.

2.3.2. Synthesis of $[(\eta^5\text{-}C_5Me_4CH_2C_6H_5)IrCl_2]_2$ (**2**)

1.000 g (2.84 mmol) of $IrCl_3 \times 3H_2O$ was combined with (2,3,4,5-tetramethylcyclopenta-2,4-dien-1-yl)methylbenzene 0.9033 g (4.25 mmol) in methanol (30 mL) in a 100 mL Schlenk flask. The reaction was refluxed for 48 h. Upon cooling, an orange powder formed and was collected by filtration. This orange powder was washed with cold methanol and hexanes to yield 0.3543 g of a first crop. Solvent was reduced to half volume and the flask was stored overnight with refrigeration and a second crop of crystals were collected (0.1878 g) for a combined yield of 0.542 g (42.3%) of **2**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.24 (m, 4H, ArH), 7.22–7.16 (m, 2H, ArH), 7.12–7.05 (m, 4H, ArH), 3.55 (s, 4H, $2CH_2$), 1.63 (s, 12H, 4CpMe), 1.61 (s, 12H, 4CpMe) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.79 (ArC), 128.70 (ArC), 128.21 (ArC), 126.73 (ArC), 87.52 (CpC), 86.76 (CpC), 85.80 (CpC), 30.41 (CH_2), 9.78 (CpMe), 9.35 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{32}H_{38}Cl_3Ir_2$ 913.1298. Found: 913.1347.

Anal. Calc. for $C_{32}H_{38}Cl_4Ir_2$; C, 40.50; H, 4.04. Found: C, 40.40; H, 3.98%.

2.3.3. Synthesis of $[(\eta^5\text{-}C_5Me_4iPr)IrCl_2]_2$ (**3**)

1.000 g (2.84 mmol) of $IrCl_3 \times 3H_2O$ was combined with 5-isopropyl-1,2,3,4-tetramethylcyclopenta-1,3-diene (0.699 g 4.25 mmol) in methanol (30 mL) with stirring. The mixture was refluxed for 48 h. Solvent was reduced to half volume and the reaction was cooled to 0 °C produce an orange solid. The product was isolated by filtration and washed with cold methanol to yield 1.37 g (56.7%) of **3**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (sept, J = 7.1 Hz, 2H, 2 (Me_2-C***H***), 1.67 (s, 12H, 4CpMe), 1.59 (s, 12H, 4CpMe), 1.28 (d, J = 7.1 Hz, 12H, 2CH**Me**$_2$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 25.24 (Me_2**C**H), 20.58 (Me_2CH), 10.21 (CpMe), 9.51 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{24}H_{38}Cl_4[^{193}Ir]_2$ Na; 875.0878. Found: 875.0898.

Anal. Calc. for $C_{24}H_{36}Cl_4Ir_2$; C, 33.80; H, 4.49. Found: C, 33.98; H, 4.62%.

2.3.4. Synthesis of [(η^5-$C_5Me_4C_6H_{10}$)$IrCl_2$]$_2$ (**4**)

2.00 g (5.67 mmol) of $IrCl_3 \times 3H_2O$ was combined with 1.74 g (8.51 mmol) of (2,3,4,5-tetramethylcyclopenta-2,4-dien-1-yl)cyclohexane in 50 mL of methanol with stirring. The mixture was refluxed for 48 h. After 48 h the reaction mixture was cooled in an ice bath to produce an orange powder. The powder was isolated on a frit and washed with cold methanol and ether (1.23 g). Removal of solvent and overnight storage at 4 °C produced a second crop of crystals what were isolated as stated previously, (0.05 g). Combined yield was 1.28 g (48.5%) of **4**.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (tt, J = 12.1, 3.2 Hz, 2H, CH_2), 1.96–1.85 (m, 4H, 2CH_2), 1.80–1.70 (m, 4H, 2CH_2), 1.66 (s, 12H, 2CpMe), 1.62–1.59 (m, 2H, CH_2), 1.58 (s, 12H, 2CpMe), 1.43–1.19 (m, 8H, 4CH_2), 1.13 (tt, J = 12.6, 3.5 Hz, 2H, CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 90.57 (CpC), 85.85 (CpC), 84.73 (CpC), 35.60 (Cp-**C**H), 30.72 (CH_2), 26.93 (CH_2), 26.03 (CH_2), 10.51 (CpMe), 9.56 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{30}H_{50}Cl_4[^{193}Ir]_2N$ 950.1950. Found: 950.1946.

Anal. Calc. for $C_{30}H_{46}Cl_4Ir_2$ C, 38.62; H, 4.970. Found: C, 38.77; H, 4.92%.

2.4. Synthesis of amino acid complexes

2.4.1. General procedure for synthesis of [(η^5-Cp^{*R})Ir(aa)Cl] complexes

A round bottom flask was charged with appropriate amounts of the respective [Cp^{*R} $IrCl_2$]$_2$, amino acid, sodium hydrogen carbonate, and methanol with magnetic stirring. The initially orange solution changed to yellow over the course of approximately 30 min. The solvent was then removed under reduced pressure. The product was extracted away from unreacted amino acid and sodium hydrogen carbonate with dichloromethane (3 × 10 mL) and filtered. The complexes were recrystallized from dichloromethane and ether or hexanes and collected on a frit as yellow crystalline powders.

2.4.2. Synthesis of [(η^5-$C_5Me_4C_6H_5$)Ir(L-alaninate)Cl] complex (**5**)

Following the general procedure: 0.1000 g (0.109 mmol) of [(η^5-$C_5Me_4C_6H_5$)$IrCl_2$]$_2$ was combined with 0.0203 (0.228 mmol) of *L*-alanine and 0.0192 g (0.228 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **5**, 0.0578 g (51.9% yield). **5** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, CDCl3) δ 7.51–7.43 (m, 2H, ArH), 7.39–7.30 (m, 3H, ArH), 6.23 (br s, 1H, NH), 3.54 (br s, 1H, NH), 3.47–3.33 (m, 1H, CH), 1.69 (s, 6H, 2CpMe, 1.67 (s, 3H, CpMe), 1.65 (s, 3H, CpMe), 1.43 (d, J = 6.9 Hz, 3H, CH3) ppm. ^{13}C NMR (101 MHz, CDCl3) δ 182.70 (COO), 130.43 (ArC), 130.29 (ArC), 128.84 (ArC), 128.75 (ArC), 91.97 (CpC), 91.45 (CpC), 82.92 (CpC), 82.83 (CpC), 81.94 (CpC), 53.04, (CH), 21.61, CH3, 10.04 (CpMe), 9.89 (CpMe), 9.35 (CpMe), 9.26 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52–7.43 (m, 2H, ArH), 7.40–7.30 (m, 3H, ArH), 4.48 (d, J = 6.3 Hz, 2H, NH_2), 3.45–3.35 (m, 1H, αCH), 1.82 (s, 3H, CpMe), 1.80 (s, 3H, CpMe), 1.77 (s, 3H, CpMe), 1.77 (s, 3H, CpMe), 1.34 (d, J = 7.2 Hz, 3H, CH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.44 (COO), 130.72 (ArC), 130.54 (ArC), 128.48 (ArC), 128.34 (ArC), 92.53 (CpC), 91.70 (CpC), 82.33 (CpC), 81.50 (CpC), 81.31 (CpC), 51.50 (CH), 19.86 (CH_3), 9.97 (CpMe), 9.94 (CpMe), 9.35 (CpMe), 9.15 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{18}H_{23}[^{193}Ir]NO_2$; 478.1358. Found: 478.1391.

Anal. Calc. for $C_{18}H_{23}ClIrNO_2 \cdot H_2O$, C, 40.71; H, 4.74. Found: C, 40.62; H, 4.47%.

2.4.3. Synthesis of [(η^5-$C_5Me_4C_6H_5$)Ir(L-phenylglycinate)Cl] complex (**6**)

Following the general procedure: 0.1000 g (0.109 mmol) of [(η^5-$C_5Me_4C_6H_5$)$IrCl_2$]$_2$ was combined with 0.0345 (0.228 mmol) of *L*-phenylglycine and 0.0192 g (0.228 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **6**, 0.1176 g (94.2% yield). **6** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.69–7.61 (m, 2H, ArH), 7.43–7.36 (m, 3H, ArH), 7.36–7.22 (m, 5H, ArH), 6.98–6.84 (m, 1H, NH), 4.42–4.29 (m, 1H, αCH), 4.16–4.03 (m, 1H, NH), 1.89 (s, 3H, CpMe), 1.78 (s, 3H, CpMe), 1.73 (s, 3H, CpMe), 1.69 (s, 3H, CpMe) ppm. ^{13}C NMR (101 MHz, DMSO-d_6) δ 181.61 (COO), 140.56 (ArC), 131.66 (ArC), 131.02 (ArC), 129.44 (ArC), 128.73 (ArC), 128.54 (ArC), 128.38 (ArC), 127.94 (ArC), 92.14 (CpMe), 90.72 (CpMe), 83.07 (CpMe), 81.29 (CpMe), 81.06 (CpMe), 59.40 (CH), 9.14 (CpMe), 9.05 (CpMe), 8.94 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.71–7.61 (m, 2H, ArH), 7.43–7.36 (m, 3H, ArH), 7.36–7.22 (m, 5H, ArH), 5.54–5.42 (m, 1H, NH), 5.32–5.18 (m, 1H, NH), 4.60–4.53 (m, 1H, αCH), 1.74 (s, 3H, CpMe), 1.72 (s, 3H, CpMe), 1.66 (s, 3H, CpMe), 1.65 (s, 3H, CpMe) ppm. ^{13}C NMR (101 MHz, DMSO-d_6) δ 181.61 (COO), 141.54 (ArC), 131.64 (ArC), 131.05 (ArC), 129.14 (ArC), 128.84 (ArC), 128.66 (ArC), 128.45 (ArC), 92.08 (CpC), 90.28 (CpC), 82.52 (CpC), 81.65 (CpC), 80.72 (CpC), 60.68 (CH), 10.11 (CpMe), 9.88 (CpMe), 9.79 (CpMe), 9.73 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{23}H_{25}Cl[^{193}Ir]Cl$; 575.1198. Found: 575.1238.

Anal. Calc. for $C_{23}H_{25}ClIrNO_2 \cdot H_2O$, C, 46.57; H, 4.59. Found: C, 46.91; H, 4.41%.

2.4.4. Synthesis of [(η^5-$C_5Me_4C_6H_5$)Ir(L-phenylalaninate)Cl] complex (**7**)

Following the general procedure: 0.1000 g (0.109 mmol) of [(η^5-$C_5Me_4C_6H_5$)$IrCl_2$]$_2$ was combined with 0.0377 (0.228 mmol) of *L*-phenylalanine and 0.0192 g (0.228 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **7**, 0.055 g (43.0% yield). **7** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.19 (m, 8H, ArH), 7.18–7.10 (m, 2H, ArH), 4.12 (br s, 1H, NH), 3.98–3.84 (m, 1H, αCH), 3.76 (br s, 1H, NH), 3.24 (dd, J = 14.4, 6.6 Hz, 1H, C*H*H), 3.06 (dd, J = 14.4, 5.2 Hz, 1H, CH*H*), 1.63 (s, 3H, CpMe), 1.62 (s, 3H, CpMe), 1.58 (s, 3H, CpMe), 1.49 (s, 3H, CpMe) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.42 (COO), 135.87 (ArC), 130.08 (ArC), 129.70 (ArC), 129.34 (ArC), 129.22 (ArC), 128.92 (ArC), 128.47 (ArC), 127.49 (ArC), 90.57 (CpC), 89.89 (CpC), 84.30 (CpC), 81.92 (CpC), 81.42 (CpC), 55.03 αC, 38.47, CH_2, 9.66 (CpMe), 9.58 (CpMe), 8.81 (CpMe), 8.79 (CpMe) ppm.

Note* significant overlap is observed between benzyl protons in the spectra.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.19 (m, 8H, ArH), 7.18–7.12 (m, 2H, ArH), 4.43–4.24 (m, 1H, NH), 3.71–3.61 (m, 1H, NH), 3.57–3.48 (m, 1H, αCH), 3.00 (d, J = 9.9 Hz, 1H, CH*H*), 1.77 (s, 3H, CpMe), 1.75 (s, 3H, CpMe), 1.67 (s, 3H, CpMe), 1.63 (s, 3H, CpMe) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.32 (COO), 136.88 (ArC), 130.27 (ArC), 130.06 (ArC), 129.40 (ArC), 129.17 (ArC), 129.10 (ArC), 128.58 (ArC), 91.10 (CpC), 90.59 (CpC), 83.80 (CpC), 82.32 (CpC), 58.44 (αC), 40.73 (CH_2), 9.95 (CpMe), 9.80 (CpMe), 9.17 (CpMe), 9.09 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{24}H_{27}NO_2$ [^{193}Ir] 554.1666. Found: 554.1632.

Anal. Calc. for $C_{24}H_{27}ClIrNO_2$; C, 48.93; H, 4.62. Found: C, 49.10; H, 4.76%.

2.4.5. Synthesis of [(η^5-$C_5Me_4C_6H_5$)Ir(L-prolinate)Cl] complex (**8**)

Following the general procedure: 0.1000 g (0.109 mmol) of [(η^5-$C_5Me_4C_6H_5$)IrCl$_2$]$_2$ was combined with 0.0281 (0.244 mmol) of *L*-proline and 0.0205 g (0.244 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **8**, 0.1102 g (94.1% yield). **8** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.41 (m, 2H, ArH), 7.40–7.33 (m, 3H, ArH), 4.79–4.65 (m, 1H, NH), 4.11–3.98 (m, 1H, αCH), 3.31–3.20 (m, 1H, N-CH), 2.68 2.75–2.62 (m, 1H, N-CH), 2.25–2.14 (m, 1H, CH*H*), 2.04–1.92 (m, 1H, C*H*H), 1.77 (s, 3H, CpMe), 1.75 (s, 3H, CpMe), 1.74 (s, 3H, CpMe), 1.66 (s, 3H, CpMe), 1.65–1.54 (m, 2H, CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.45 (COO), 130.52 (ArC), 130.10 (ArC), 128.88 (ArC), 128.51 (ArC), 91.44 (CpC), 91.12 (CpC), 85.38 (CpC), 80.90 (CpC), 80.68 (CpC), 62.54 (αC), 54.53 (N–C), 29.09 (CH_2), 26.94 (CH_2), 10.52 (CpMe), 9.68 (CpMe), 9.16 (CpMe), 9.09 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.79 (s, 3H, CpMe), 1.68 (s, 3H, CpMe), 1.67 (s, 3H, CpMe) ppm. (Significant overlap with major isomer obscures other peaks).

HRMS/ESI$^+$ (m/z): Calc. for $C_{20}H_{26}NO_2$ [^{193}Ir]Cl 540.1276. Found: 540.1231.

Anal. Calc. for $C_{20}H_{25}ClIrNO_2{\cdot}H_2O$; C, 43.12; H, 4.88. Found: C, 43.52; H, 4.88%.

2.4.6. Synthesis of [(η^5-$C_5Me_4C_6H_5$)Ir(L-piperidine-2-carboxylate)Cl] complex (**9**)

Following the general procedure: 0.1000 g (0.109 mmol) of [(η^5-$C_5Me_4C_6H_5$)IrCl$_2$]$_2$ was combined with 0.0295 (0.228 mmol) of *L*-piperidine-2-carboxylic acid and 0.0192 g (0.228 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **9**, 0.1133 g (94.3% yield). **9** was identified based on the following information:

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.47 (m, 2H, ArH), 7.41–7.32 (m, 3H, ArH), 4.00 (br s, 1H, NH), 3.46–3.33 (m, 1H, N-CH), 3.09 (td, J = 11.8, 3.1 Hz, 1H, αCH), 2.82 (qd, J = 12.4, 3.1 Hz, 1H, N-CH), 2.28–2.13 (m, 1H, CH*H*), 2.08–1.83 (m, 1H, C*H*H), 1.77 (s, 3H, CpMe), 1.73 (s, 3H, CpMe), 1.68 (s, 3H, CpMe), 1.65 (s, 3H, CpMe), 1.58–1.38 (m, 4H, CH_2–CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.93 (COO), 130.34 (ArC), 130.28 (ArC), 128.79 (ArC), 128.46 (ArC), 94.89 (CpC), 93.02 (CpC), 82.46 (CpC), 81.44 (CpC), 79.33 (CpC), 66.15 (αC), 53.27 (N–C), 30.83 (CH_2), 27.71 (CH_2), 23.57 (CH_2), 10.56 (CpMe), 10.05 (CpMe), 9.38 (CpMe), 9.13 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.47 (m, 2H, ArH), 7.40–7.31 (m, 3H, ArH), 4.36 (br s, 1H, NH), 3.90–3.76 (m, 1H, N-CH), 3.30–3.16 (m, 1H, N-CH), 3.04–2.94 (m, 1H, αCH), 2.28–2.13 (m, 1H, CH*H*), 2.00–1.92 (m, 1H, C*H*H), 1.75 (s, 3H, CpMe), 1.70 (s, 3H, CpMe), 1.69 (s, 3H, CpMe), 1.64 (s, 3H, CpMe), 1.57–1.38 (m, 4H, CH_2–CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.92 (COO), 130.73 (ArC), 130.14 (ArC), 128.46 (ArC), 128.32 (ArC), 91.96 (CpC), 83.64 (CpC), 81.42 (CpC), 62.48 (αC), 52.24 (N–C), 31.53 (CH_2), 29.00 (CH_2), 23.70 (CH_2), 9.70 (CpMe), 9.55 (CpMe), 8.90 (CpMe), 8.74 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{21}H_{27}O_2$[^{193}Ir] 518.1666. Found: 518.1677.

Anal. Calc. for $C_{21}H_{27}ClIrNO_2{\cdot}CH_2Cl_2$; C, 41.48; H, 4.58. Found: C, 40.63; H, 4.50%.

2.4.7. Synthesis of [(η^5-$C_5Me_4CH_2C_6H_5$)Ir(L-phenylalaninate)Cl] complex (**10**)

Following the general procedure: 0.1000 g (0.105 mmol) of [(η^5-$C_5Me_4CH_2C_6H_5$)IrCl$_2$]$_2$ was combined with 0.0360 g (0.221 mmol) of *L*-phenylalanine and 0.0186 g (0.221 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **10**, 0.1187 g (93.4% yield). **10** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.25 (m, 6H, ArH), 7.05–7.01 (m, 2H, ArH), 4.30 (br s, 1H, NH), 4.01 (br s, 1H, NH), 3.94–3.83 (m, 1H, αCH), 3.40 (dd, J = 14.2, 6.1 Hz, 1H, CH*H*), 3.33–3.21 (m, 2H, CH_2), 3.10 (dd, J = 14.2, 5.2 Hz, 1H, C*H*H), 1.57 (s, 3H, CpMe), 1.55 (s, 3H, CpMe), 1.54 (s, 3H, CpMe), 1.53 (s, 3H, CpMe) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.76 (COO), 137.16 (ArC), 136.20 (ArC), 129.90 (ArC), 129.28 (ArC), 128.72 (ArC), 128.09 (ArC), 126.77 (ArC), 86.17 (CpC), 85.68 (CpC), 84.39 (CpC), 83.81 (CpC), 83.17 (CpC), 55.06 (αC), 38.47 (Cp-***C***H$_2$-Ar), 29.71 (CH_2), 9.16 (CpMe), 8.82 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.25 (m, 6H, ArH), 7.24–7.13 (m, 2H, ArH), 7.10–7.06 (m, 2H, ArH), 5.11 (br s, 1H, NH), 3.71–3.58 (m, 1H, NH), 3.62–3.51 (m, 1H, αCH), 3.46 (s, 2H, CH_2), 1.71 (s, 3H, CpMe), 1.69 (s, 3H, CpMe), 1.68 (s, 3H, CpMe), 1.67 (s, 3H, CpMe) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.77 (ArC), 137.13 (ArC), 129.58 (ArC), 129.10 (ArC), 128.70 (ArC), 128.19 (ArC), 127.53 (ArC), 85.63 (CpC), 84.66 (CpC), 84.16 (CpC), 58.49 (αC), 40.45 (CH_2), 30.03 (Cp-***C***H$_2$-Ar), 9.49 (CpMe), 9.12 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{25}H_{29}ClIrNO_2$; 603.1511. Found: 603.1597.

Anal. Calc. for $C_{25}H_{29}ClIrNO_2$; C, 49.78; H, 4.85. Found: C, 50.01; H, 5.04%.

2.4.8. Synthesis of [(η^5-$C_5Me_4CH_2C_6H_5$)Ir(L-prolinate)Cl] complex (**11**)

Following the general procedure: 0.1000 g (0.105 mmol) of [(η^5-$C_5Me_4CH_2C_6H_5$)IrCl$_2$]$_2$ was combined with 0.0255 (0.221 mmol) of *L*-proline and 0.0186 g (0.221 mmol) of sodium hydrogen carbonate in methanol (20 mL) to give **11**, 0.1032 g (88.5% yield). **11** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.25 (m, 2H, ArH), 7.23–7.16 (m, 1H, ArH), 7.13–7.05 (m, 2H, ArH), 4.92 (br s, 1H, NH), 4.10–3.98 (m, 1H, N-CH), 3.63–3.56 (m, 1H, N-CH), 3.49 (s, 2H, CH_2), 2.93 (qd, J = 11.0, 5.8 Hz, 1H, CH*H*), 2.32–2.18 (m, 2H, CH_2), 2.17–1.81 (m, 2H, CH_2), 1.70 (s, 3H CpMe), 1.69 (s, 3H CpMe), 1.67 (s, 3H CpMe), 1.67 (s, 3H, CpMe) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.55 (COO), 137.02 (ArC), 128.75 (ArC), 128.10 (ArC), 126.79 (ArC), 86.25 (CpC), 85.71 (CpC), 84.41 (CpC), 84.36 (CpC), 83.73 (CpC), 62.53 (N-C), 54.98 (αC), 30.14 (Cp-***C***H$_2$-Ar), 28.79 (CH_2), 27.12 (CH_2), 9.64 (CpMe), 9.55 (CpMe), 9.29 (CpMe), 9.23 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.73 (s, 1H, CpMe), 1.72 (s, 1H, CpMe), 1.71 (s, 1H, CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{21}H_{28}Cl$[^{193}Ir]NO_2; 554.1432. Found: 554.1431.

Anal. Calc. for $C_{21}H_{27}ClIrNO_2{\cdot}CH_2Cl_2$; C, 41.41; H, 4.58. Found: C, 41.27; H, 4.74%.

2.4.9. Synthesis of [(η^5-$C_5Me_4CH_2C_6H_5$)Ir(L-azetidine 2-carboxylate)Cl] complex (**12**)

Following the general procedure: 0.1000 g (0.105 mmol) of [(η^5-$C_5Me_4CH_2C_6H_5$)IrCl$_2$]$_2$ was combined with 0.0255 (0.221 mmol) of *L*-azetidine-2-carboxylic acid and 0.0186 g (0.221 mmol) of sodium hydrogen carbonate in methanol (30 mL) with slight heating to give **12**, 0.0936 g (82.4% yield). **12** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.25 (m, 2H, ArH), 7.23–7.16 (m, 1H, ArH), 7.13–7.06 (m, 2H, ArH), 5.55 (br s,

1H, NH), 4.62–4.43 (m, 1H, αCH), 4.35–4.24 (m, 1H, N-CH), 3.95–3.83 (m, 1H, N-CH), 3.52 (s, 2H, CH_2), 3.04–2.90 (m, 1H, CH*H*), 2.50–2.36 (m, 1H, C*H*H), 1.73 (s, 3H, CpMe), 1.71 (s, 3H, CpMe), 1.71 (s, 3H, CpMe), 1.70 (s, 3H, CpMe) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.09 (ArC), 128.74 (ArC), 128.10 (ArC), 126.78 (ArC), 86.06 (CpC), 85.40 (CpC), 84.28 (CpC), 84.23 (CpC), 83.72 (CpC), 60.76 (N-C), 51.29 (αC), 30.03 (Cp-***C***H_2-Ar), 26.26 (CH_2), 9.43 (CpMe), 9.38 (CpMe), 9.08 (CpMe), 9.06 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.96–4.80 (m, 1H, N-CH), 4.16–3.99 (m, 1H, NH), 2.77–2.64 (m, 1H, CH*H*), 2.64–2.55 (m, 1H, C*H*H), 1.68 (s, 3H, CpMe), 1.67 (s, 3H, CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{20}H_{26}Cl[^{193}Ir]NO_2$; 540.1276. Found: 540.1258.

Anal. Calc. for $C_{20}H_{25}ClIrNO_2$; C, 44.56; H, 4.67. Found: C, 44.41; H, 4.76%.

2.4.10. Synthesis of [(η^5-$C_5Me_4CH_2C_6H_5$)Ir(L-piperidine-2-carboxylate)Cl] complex (**13**)

Following the general procedure: 0.1000 g (0.105 mmol) of [(η^5-$C_5Me_4CH_2C_6H_5$)$IrCl_2$]$_2$ was combined with 0.0224 (0.221 mmol) of *L*-piperidine-2-carboxylic acid and 0.0186 g (0.221 mmol) of sodium hydrogen carbonate in methanol (20 mL) with slight heating to give **13**, 0.1102 g (92.2% yield). **13** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.25 (m, 2H, ArH), 7.24–7.17 (m, 1H, ArH), 7.10–7.04 (m, 2H, ArH), 3.92 (br s, 1H, NH), 3.61–3.50 (m, 1H, N-CH), 3.48 (s, 2H, CH_2), 3.18–3.10 (m, 1H, αCH), 2.30–2.20 (m, 1H, N-CH), 2.03–1.91 (m, 1H, CH*H*), 1.88–1.75 (m, 2H, CH_2), 1.69 (s, 3H, CpMe), 1.69 (s, 3H CpMe), 1.68 (s, 3H CpMe), 1.67 (s, 3H, CpMe), 1.59–1.37 (m, 4H, CH_2–CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.76 (COO), 136.72 (ArC), 128.82 (ArC), 127.99 (ArC), 126.91 (ArC), 86.35 (CpC), 86.20 (CpC), 84.76 (CpC), 84.25 (CpC), 83.96 (CpC), 66.39 (N-C), 53.85 (αC), 30.79 (CH_2), 30.29 (Cp-***C***H_2-Ar), 27.82 (CH_2), 23.62 (CH_2), 9.73 (CpMe), 9.65 (CpMe), 9.36 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.25 (m, 2H, ArH), 7.24–7.17 (m, 1H, ArH), 7.15–7.11 (m, 2H, ArH), 3.82–3.71 (m, 1H, N-CH), 3.45–3.37 (m, 1H, αCH), 3.10–2.97 (m, 1H, N-CH), 2.13–2.05 (m, 1H, CH*H*), 1.72 (s, 3H, CpMe), 1.67 (s, 3H, CpMe), 1.64 (s, 3H, CpMe), 1.59–1.38 (m, 4H, CH_2-CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 128.90 (ArC), 128.48 (ArC), 9.25 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{22}H_{29}[^{193}Ir]NO_2$; 532.1822. Found: 532.1830.

Anal. Calc. for $C_{22}H_{29}IrNO_2{\cdot}H_2O$; C, 45.16; H, 5.34. Found: C, 45.78; H, 5.43%.

2.4.11. Synthesis of [(η^5-C_5Me_4iPr)Ir(glycinate)Cl] complex (**14**)

Following the general procedure: 0.1000 g (0.173 mmol) of [(η^5-C_5Me_4iPr)$IrCl_2$]$_2$ was combined with 0.0198 (0.246 mmol) of glycine and 0.0207 g (0.246 mmol) of sodium hydrogen carbonate in methanol to give **14**, 0.0963 g (88.3% yield). **14** was identified based on the following information:

^{1}H NMR (400 MHz, Methanol-d_4) δ 3.49–3.27 (m, 2H, CH_2), 2.63 (sept, J = 7.1 Hz, 1H, (Me_2C***H***), 1.75 (s, 3H, CpMe), 1.73 (s, 3H, CpMe), 1.66 (br s, 6H, 2CpMe), 1.31 (overlapping doublets, $J_1 \approx J_2$ = 7.0, 6H, CH**Me**$_2$) ppm. ^{13}C NMR (101 MHz, Methanol-d_4) δ 185.47 (COO), 88.37 (CpC), 88.27 (CpC), 85.99 (CpC), 83.65 (CpC), 82.59 (CpC), 44.19 (αC), 24.93 (Me_2**C**H), 20.09 (CH_3), 19.84 (CH_3), 8.51 (CpMe), 8.25 (CpMe), 7.53 (CpMe), 7.43 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{15}H_{25}IrNO_2$; 444.1515. Found: 444.1492.

Anal. Calc. for $C_{14}H_{23}ClIrNO_2$; C, 36.16; H, 4.99. Found: C, 35.98; H, 4.94%.

2.4.12. Synthesis of [(η^5-C_5Me_4iPr)Ir(N,N-dimethyl-glycinate)Cl] complex (**15**)

Following the general procedure: 0.1000 g (0.173 mmol) of [(η^5-C_5Me_4iPr)$IrCl_2$]$_2$ was combined with 0.0254 (0.246 mmol) of *N*,*N*-dimethyl-glycine and 0.0207 g (0.246 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **15**, 0.0859 g (74.4% yield). **14** was identified based on the following information:

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.06 (d, J = 14.6, 1H, CH*H*), 3.07 (s, 3H, N-CH_3), 2.95 (d, J = 14.6 Hz, 1H, C*H*H), 2.92 (s, 3H, N-CH_3), 2.58 (sept, J = 7.4 Hz, 1H, Me_2C***H***), 1.68 (s, 3H, CpMe), 1.65 (s, 3H, CpMe), 1.57 (s, 3H, CpMe), 1.56 (s, 3H, CpMe), 1.29 (overlapping doublets, J = 7.4 Hz, 6H, CH**Me$_2$**) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.40 (COO), 87.73 (CpC), 87.47 (CpC), 86.77 (CpC), 85.10 (CpC), 81.88 (CpC), 66.32 (αC), 56.26 (N-CH_3), 50.65 (N-CH_3), 25.16 (Me_2**C**H), 20.58 (CH_3), 20.35 (CH_3), 9.91 (CpMe), 9.42 (CpMe), 9.23 (CpMe), 9.02 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{16}H_{28}Cl[^{193}Ir]NO_2$; 494.1432. Found: 494.1455.

Anal. Calc. for $C_{16}H_{27}ClIrNO_2$; C, 38.98; H, 5.52. Found: C, 39.01; H, 5.43%.

2.4.13. Synthesis of [(η^5-C_5Me_4iPr)Ir(L-alaninate)Cl] complex (**16**)

Following the general procedure: 0.1000 g (0.173 mmol) of [(η^5-C_5Me_4iPr)$IrCl_2$]$_2$ was combined with 0.0220 (0.246 mmol) of *L*-alanine and 0.0207 g (0.246 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **16**, 0.0762 g (68.2% yield). **16** was identified based on the following information: Significant signal overlap is observed for this complex for the 2-propyl portion of the Cp ring.

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (br s, 1H, NH), 3.50–3.40 (m, NH), 3.41–3.33 (m, 1H, αCH), 2.63 (sept, J = 7.3, 1H, (Me_2C***H***), 1.71–1.64 (m, 12H, 4CpMe), 1.44 (d, J = 6.7 Hz, 3H, CH_2), 1.28 (overlapping doublets, J = 7.3 Hz, 6H, CH**Me**$_2$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.21 (COO), 89.01 (CpC), 88.77 (CpC, 85.77 (CpC), 83.18 (CpC), 82.40 (CpC), 52.97 (αC), 25.07 (Me_2**C**H), 21.71 (CH_3), 21.32 (CH_3), 10.03 (CpMe), 9.87 (CpMe), 9.26 (CpMe), 9.19 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.94 (br s, 1H, NH), 4.45–4.23 (m, 1H, NH), 3.70–3.56 (m, 1H, αCH), 2.63 (h, J = 7.1, 1H, (Me_2C***H***), 1.78–1.71 (m, 12H, 4CpMe), 1.40 (d, J = 7.2 Hz, 3H, CH_3), 1.28 (overlapping doublets, J = 7.1 Hz, 6H, CH**Me**$_2$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.72 (COO), 88.97 (CpC), 88.71 (CpC), 85.58 (CpC), 83.06 (CpC), 82.55 (CpC), 51.60 (αC), 21.35 (CH_3), 21.26 (CH_3), 19.63 (CH_3), 10.08 (CpMe), 9.85 (CpMe), 9.30 (CpMe), 9.13 (CpMe) ppm.

Anal. Calc. for $C_{15}H_{25}ClIrNO_2$; C, 3.61; H, 5.26. Found: C, 37.37; H, 5.36%.

2.4.14. Synthesis of [(η^5-C_5Me_4iPr)Ir(L-phenylalaninate)Cl] complex (**17**)

Following the general procedure: 0.1000 g (0.173 mmol) of [(η^5-C_5Me_4iPr)$IrCl_2$]$_2$ was combined with 0.0410 (0.246 mmol) of *L*-phenylalanine and 0.0207 g (0.246 mmol) of sodium hydrogen carbonate in methanol (30 mL) to produce **17**, 0.1071 g (82.3% yield). **17** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.25 (m, 5H, ArH), 4.20 (br s, 1H, NH), 3.97–3.91 (m, 1H, NH), 3.87 (tt, J = 7.6, 5.2 Hz, 1H, αCH), 3.39 (dd, J = 14.3, 5.4 Hz, 1H, CH), 3.06 (dd, J = 14.3, 5.0 Hz, 1H, CH), 2.43 (sept, J = 7.1 Hz, 1H, Me_2C***H***), 1.59 (s, 3H, CpMe), 1.55 (s, 3H, CpMe), 1.49 (s, 3H, CpMe), 1.48 (s, 3H, CpMe), 1.16 (overlapping doublets J = 7.1 Hz, 6H, CH**Me**$_2$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.34 (COO), 136.12 (ArC), 129.90 (ArC), 129.25 (ArC), 127.49 (ArC), 88.40 (CpC), 87.79 (CpC), 85.88 (CpC), 83.44 (CpC), 82.38 (CpC), 54.88 (αC), 38.40 (CH_2), 25.05 (Me_2**C**H), 21.14 (CH_3), 21.04 (CH_3), 9.58 (CpMe), 9.54 (CpMe), 8.79 (CpMe), 8.76 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.25 (m, 5H, ArH), 4.88–4.75 (m, 1H, NH), 3.66–3.51 (m, 2H, NH, αCH), 3.45 (dd, J = 14.7, 3.1 Hz, 1H, CH), 3.04 (dd, J = 14.7, 3.1 Hz, 1H, CH), 2.56 (sept, J = 7.1 Hz, 1H, Me_2CH), 1.71 (s, 3H, CpMe), 1.68 (s, 3H CpMe), 1.64 (s, 3H CpMe), 1.63 (s, 3H CpMe), 1.26 (overlapping doublets, J = 7.1 Hz, 6H, $CHMe_2$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.52 (COO), 136.99 (ArC), 129.47 (ArC), 129.10 (ArC), 127.09 (ArC), 88.67 (CpC), 88.46 (CpC), 86.17 (CpC), 83.16 (CpC), 82.68 (CpC), 58.50 (αC), 40.67 (CH_2), 25.12 (Me_2CH), 21.29 (CH_3), 21.26 (CH_3), 9.84 (CpMe), 9.81 (CpMe), 9.15 (CpMe), 9.11 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{21}H_{28}Cl[^{193}Ir]NNaO_2$; 577.133. Found:, 577.1385.

Anal. Calc. for $C_{21}H_{29}ClIrNO_2$; C, 45.44; H, 5.27. Found: C, 45.67; H, 5.25%.

2.4.15. Synthesis of [(η^5-C_5Me_4*i*Pr)Ir(L-prolinate)Cl] complex (**18**)

Following the general procedure: 0.1000 g (0.173 mmol) of [(η^5-C_5Me_4*i*Pr)$IrCl_2]_2$ was combined with 0.0339 (0.293 mmol) of *L*-proline and 0.0246 g (0.293 mmol) of sodium hydrogen carbonate in methanol (20) to produce **18**, 0.0839 g (70.8% yield). **18** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.68 (br s, 1H, NH), 4.08–3.98 (m, 1H, αCH), 3.64–3.52 (m, 1H, N-CH), 3.00–2.86 (m, 1H, N-CH), 2.57 (sept, J = 7.1 Hz, 1H, (Me_2CH), 2.30–2.17 (m, 1H, CH*H*), 2.06–1.86 (m, 3H, CH_2-C*H*H), 1.71 (s, 3H, CpMe), 1.70 (s, 3H, CpMe), 1.65 (s, 3H, CpMe), 1.62 (s, 3H, CpMe), 1.29 (overlapping doublets, J = 7.1 Hz, 6H, $CHMe_2$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.41 (COO), 89.20 (CpC), 87.81 (CpC), 86.16 (CpC), 84.18 (CpC), 82.24 (CpC), 62.46 (αC), 54.92 (NC), 28.83 (CH_2), 27.19 (CH_2), 25.07 (Me_2CH), 21.03 (CH_3), 20.92 (CH_3), 9.96 (CpMe), 9.83 (CpMe), 9.26 (CpMe), 9.20 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.42–4.25 (m, 1H, NH), 3.82–3.62 (m, 1H, αCH), 3.82–3.65 (m, 1H, N-CH), 2.79–2.62 (m, 1H, C*H*H), 1.75 (s, 3H, CpMe), 1.73 (d, 3H, CpMe), 1.68 (s, 3H, CpMe), 1.66 (s, 3H, CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{17}H_{28}Cl[^{193}Ir]Cl$; 506.1432. Found: 506.1432.

Anal. Calc. for $C_{17}H_{27}ClIrNO_2$; C, 40.43; H, 5.39. Found: C, 40.82; H, 5.56%.

2.4.16. Synthesis of [(η^5-$C_5Me_4C_6H_{10}$)Ir(glycinate)Cl] complex (**19**)

Following the general procedure: 0.1000 g (0.107 mmol) of [(η^5-$C_5Me_4C_6H_{10}$)$IrCl_2]_2$ was combined with 0.0170 (0.225 mmol) of glycine and 0.019 g (0.225 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **19**, 0.0634 g (57.5% yield). **19** was identified based on the following information:

^{1}H NMR (400 MHz, Methanol-d_4) δ 5.82 (br s, 1H, NH), 4.92 (br s, 1H, NH), 3.51–3.39 (m, 1H, CH*H*), 3.39–3.31 (m, 1H, C*H*H), 2.21 (tt, J = 12.4, 3.2 Hz, 1H, Cp-C***H***), 1.92–1.83 (m, 2H, CH_2), 1.83–1.77 (m, 2H, CH_2), 1.75 (s, 3H, CpMe), 1.73 (s, 3H, CpMe), 1.67–1.62 (m, 6H, 2CpMe), 1.58–1.43 (m, 2H, CH_2), 1.42–1.15 (m, 4H, $2CH_2$) ppm. ^{13}C NMR (101 MHz, Methanol-d_4) δ 185.46 (COO), 88.62 (CpC), 84.28 (CpC), 83.61 (CpC), 44.31 (αC), 35.46 (Cp-***C***H), 31.08 (CH_2), 30.94 (CH_2), 26.70 (CH_2), 25.71 (CH_2), 8.80 (CpMe), 8.50 (CpMe), 7.47 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{18}H_{29}[^{193}Ir]NO_2$ 484.1828. Found: 484.1832.

Anal. Calc. for $C_{17}H_{27}ClIrNO_2{\cdot}H_2O$: C, 39.03; H, 5.59. Found: C, 39.05; H, 5.54%.

2.4.17. Synthesis of [(η^5-$C_5Me_4C_6H_{10}$)Ir(L-alaninate)Cl] complex (**20**)

Following the general procedure: 0.1000 g (0.107 mmol) of [(η^5-$C_5Me_4C_6H_{10}$)$IrCl_2]_2$was combined with 0.0210 (0.225 mmol) of *L*-alanine and 0.019 g (0.225 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **20**, 0.0089 g (80.0% yield). **20** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 (br s, 1H, NH), 3.52–3.34 (m, 2H, NH, αCH), 2.17 (ddt, J = 15.6, 12.4, 3.1 Hz, 1H, Cp-C***H***), 1.88–1.77 (m, 4H, $2CH_2$), 1.77–1.71 (m, 12H, 4CpMe), 1.47 (d, J = 6.7 Hz, 3H, CH_3), 1.45–1.41 (m, 1H, CH*H*), 1.36–1.22 (m, 4H, $2CH_2$), 1.15 (ddd, J = 16.3, 8.3, 3.6 Hz, 1H, C*H*H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.20 (COO), 89.77 (CpC), 89.28 (CpC), 83.97 (CpC), 82.86 (CpC), 82.22 (CpC), 52.97 (aC), 35.42 (Cp-***C***H), 31.56 (CH_2), 27.00 (CH_2), 25.99 (CH_2), 21.70 (CH_3), 10.34 (CpMe), 10.15 (CpMe), 9.27 (CpMe), 9.22 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.59–4.48 (m, 1H, NH), 4.46–4.32 (m, 1H, NH), 3.75–3.62 (m, 1H, αCH), 2.17 (tt, J = 12.4, 3.2 Hz, 1H, Cp-C***H***), 1.88–1.77 (m, 4H, $2CH_2$), 1.71–1.64 (m, 12H, 4CpMe), 1.45–1.41 (m, 2H, CH_2), 1.40 (d, J = 7.2 Hz, 3H, CH_3), 1.30 (ddt, J = 17.2, 13.9, 6.9 Hz, 2H, CH_2), 1.16 (tt, J = 12.8, 3.2 Hz, 2H, CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.73 (COO), 89.68 (CpC), 89.32 (CpC), 83.72 (CpC), 82.79, 82.35 (CpC), 51.60 (αC), 35.48 (Cp-***C***H), 31.51 (CH_2), 27.00 (CH_2), 25.99 (CH_2), 19.65 (CH_3), 10.38 (CpMe), 10.12 (CpMe), 9.32 (CpMe), 9.15 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{18}H_{30}Cl[^{193}Ir]NO_2$ 520.1589. Found: 520.1603.

Anal. Calc. for $C_{18}H_{29}ClIrNO_2{\cdot}H_2O$: C, 40.25; H, 5.82. Found: C, 41.00; H, 5.78%.

2.4.18. Synthesis of [(η^5-$C_5Me_4C_6H_{10}$)Ir(L-phenylglycinate)Cl] complex (**21**)

Following the general procedure: 0.1000 g (0.107 mmol) of [(η^5-$C_5Me_4C_6H_{10}$)$IrCl_2]_2$ was combined with 0.0342 (0.225 mmol) of *L*-phenylglycine and 0.019 g (0.225 mmol) of sodium hydrogen carbonate in methanol (30 mL) to give **21**, 0.1072 g (86.2% yield). **21** was identified based on the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.31 (m, 2H, ArH), 7.24–7.16 (m, 4H, ArH), 6.39 (br s, 1H, NH), 4.20 (dd, J = 10.0, 7.6 Hz, 1H, αCH), 3.65 (br s, 1H, NH), 2.18 (tt, J = 12.2, 3.1 Hz, 1H, Cp-C***H***), 1.89–1.75 (m, 4H, $2CH_2$), 1.73 (s, 3H, CpMe), 1.71 (s, 3H, CpMe), 1.68 (s, 3H, CpMe), 1.65 (s, 3H, CpMe), 1.32–1.22 (m, 4H, $2CH_2$), 1.20–1.06 (m, 2H, CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 181.24 (COO), 140.63 (ArC), 129.28 (ArC), 128.90 (ArC), 128.86 (ArC), 128.06 (ArC), 89.74 (CpC), 89.37 (CpC), 84.20 (CpC), 83.60 (CpC), 82.55 (CpC), 58.76 (αC), 35.50 (Cp-***C***H), 31.60 (CH_2), 27.01 (CH_2), 25.86 (CH_2), 10.33 (CpMe), 10.19 (CpMe), 10.17 (CpMe), 10.11 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.32 (m, 1.9 Hz, 2H, ArH), 7.24–7.16 (m, 4H, ArH), 4.73 (br s, 1H, NH), 4.53 (dd, J = 7.9, 4.9 Hz, 1H, αCH), 4.11 (br s, 1H, NH), 2.09 (tt, J = 12.4, 3.2 Hz, 1H, Cp-C***H***), 1.89–1.76 (m, 4H, $2CH_2$), 1.64 (s, 3H, CpMe), 1.60 (s, 3H, CpMe), 1.55 (s, 3H, CpMe), 1.52 (s, 3H, CpMe), 1.48–1.32 (m, 4H, $2CH_2$), 1.18–1.06 (m, 2H, CH_2) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.70 (COO), 138.90 (ArC), 129.28 (ArC), 128.86 (ArC), 128.77 (ArC), 128.06 (ArC), 89.70 (CpC), 89.64 (CpC), 83.60 (CpC), 82.96 (CpC), 82.69 (CpC), 61.08 (αC), 35.39 (Cp-***C***H), 31.57 (CH_2), 26.93 (CH_2), 26.01 (CH_2), 10.17 (CpMe), 10.11 (CpMe), 9.27 (CpMe), 9.00 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{23}H_{32}Cl[^{193}Ir]O_2$ 582.1745. Found: 582.1726.

Anal. Calc. for $C_{23}H_{31}ClIrNO_2{\cdot}H_2O$: C, 46.10; H, 5.55. Found: C, 46.39: H, 5.50%.

2.4.19. Synthesis of [(η^5-$C_5Me_4C_6H_{10}$)Ir(L-phenylalaninate)Cl] complex (**22**)

0.1000 g (0.107 mmol) of [(η^5-$C_5Me_4C_6H_{10}$)$IrCl_2]_2$ was combined with 0.0373 (0.225 mmol) of *L*-phenylalanine and 0.019 g (0.225 mmol) of sodium hydrogen carbonate in a round bottom flask. Upon addition of 30 mL methanol and a magnetic stir bar the mixture slowly turned yellow over the course of 30 min. Solvent was removed and the product extracted using dichloromethane (3 × 10 mL). This solution was filtered to remove any

excess amino acid or sodium hydrogen carbonate. The product was recrystallized from dichloromethane and ether, and isolated on a frit as a yellow solid, 0.1081 g (84.9% yield) of **22**. **22** was identified based on the following information.

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.25 (m, 5H, ArH), 4.25–4.07 (m, 1H, NH), 3.97–3.76 (m, 2H, NH, αCH), 3.38 (dd, J = 14.3, 4.9 Hz, 1H, CH*H*), 3.06 (dd, J = 14.3, 4.6 Hz, 1H, *C*HH), 2.02 (tt, J = 12.2, 3.1 Hz, 1H, Cp-C***H***), 1.84–1.71 (m, 4H, $2CH_2$), 1.60 (s, 3H, CpMe), 1.55 (s, 3H, CpMe), 1.49 (s, 3H, CpMe), 1.48 (s, 3H, CpMe), 1.44–1.03 (m, 6H, $3CH_2$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.22 (COO), 136.07 (ArC), 129.87 (ArC), 129.23 (ArC), 127.51 (ArC), 88.91 (CpC), 88.16 (CpC), 84.16 (CpC), 83.34 (CpC), 82.27 (CpC), 54.85 (αC), 38.43 (CH_2), 35.47 (Cp-***C***H), 31.46 (CH_2), 31.29 (CH_2), 26.96 (CH_2), 25.89 (CH_2), 9.89 (CpMe), 9.87 (CpMe), 8.81 (CpMe), 8.77 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.25 (m, 5H, ArH), 3.64–3.56 (m, 1H, NH), 3.55–3.42 (m, 2H, NH, αCH), 3.03–2.98 (m, 1H, CH*H*), 2.11 (tt, J = 12.4, 3.2 Hz, 1H, Cp-C***H***), 1.83–1.71 (m, 4H, $2CH_2$), 1.70 (s, 3H, CpMe), 1.67 (s, 3H, CpMe), 1.65 (s, 3H, CpMe), 1.63 (s, 3H, CpMe), 1.45–1.01 (m, 6H, $3CH_2$) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 180.23 (COO), 137.08 (ArC), 129.38 (ArC), 129.14 (ArC), 127.12 (ArC), 89.29 (CpC), 84.54 (CpC), 82.75 (CpC), 58.70 (αC), 40.79 (CH_2), 35.58 (Cp-***C***H), 31.56 (CH_2), 27.01 (CH_2), 26.95 (CH_2), 10.13 (CpMe), 9.18 (CpMe), 9.12 (CpMe) ppm.

HRMS/ESI$^+$ (m/z): Calc. for $C_{24}H_{33}Cl[^{193}Ir]NO_2$ 595.1824. Found: 595.1871.

Anal. Calc. for $C_{24}H_{33}ClIrNO_2$: C, 48.43; H, 5.59. Found: C, 48.38; H, 5.77%.

2.4.20. Synthesis of [(η^5-$C_5Me_4C_6H_{10}$)Ir(L-prolinate)Cl] complex (**23**)

0.1000 g (0.107 mmol) of [(η^5-$C_5Me_4C_6H_{10}$)$IrCl_2$]$_2$ was combined with 0.0259 g (0.225 mmol) of *L*-proline and 0.019 g (0.225 mmol) of sodium hydrogen carbonate in a round bottom flask. Upon addition of 30 mL methanol and a magnetic stir bar the mixture slowly turned yellow over the course of 30 min. Solvent was removed and the product extracted away using dichloromethane (3 × 10 mL). This solution was filtered to remove any excess amino acid or sodium hydrogen carbonate. The product was recrystallized from dichloromethane and ether, and isolated on a frit as a yellow solid to yield 0.0810 g (67.8%) of **23** identified on the basis of the following information:

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.56 (br s, 1H, NH), 4.10–3.97 (m, 1H, αCH), 3.60–3.51 (m, 1H, N-CH), 2.98–2.85 (m, 1H, N-CH), 2.29–2.17 (m, 1H, CH*H*), 2.12 (tt, J = 12.4, 3.0 Hz, 1H, Cp-C***H***), 2.06–1.89 (m, 2H, CH_2), 1.89–1.75 (m, 4H, $2CH_2$), 1.71 (s, 3H, CpMe), 1.70 (s, 3H, CpMe), 1.69–1.65 (m, 2H, CH_2), 1.64 (s, 3H, CpMe), 1.62 (s, 3H, CpMe), 1.51–1.35 (m, 2H, CH_2), 1.36–1.21 (m, 2H, CH_2), 1.21–1.09 (m, 1H, *C*HH) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.16 (COO), 90.11 (CpC), 88.29 (CpC), 84.15 (CpC), 83.98 (CpC), 81.92 (CpC), 62.44 (αC), 54.83 (CH_2), 35.73 (Cp-***C***H), 31.35 (CH_2), 31.30 (CH_2), 28.79 (CH_2), 27.22 (CH_2), 27.06 (CH_2), 26.03 (CH_2), 10.31 (CpMe), 10.09 (CpMe), 9.32 (CpMe), 9.22 (CpMe) ppm.

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (br s, 1H, NH), 3.81–3.72 (m, 1H, αCH), 3.24–3.11 (m, N-CH, 1H), 1.73 (s, 3H, CpMe), 1.72 (s, 3H, CpMe), 1.66 (s, 3H, CpMe) ppm. Other signals not detectable due to signal overlap.

HRMS/ESI$^+$ (m/z): Calc. for $C_{20}H_{31}Cl[^{193}Ir]NO_2$ 545.1673. Found: 545.1684.

Anal. Calc. for $C_{20}H_{31}ClIrNO_2$: C, 44.06; H, 5.73. Found: C, 44.72; H, 6.01%.

2.5. Asymmetric transfer hydrogenation

2.5.1. General procedure for catalytic reduction of ketones

In a 2 dram vial, 4×10^{-4} mmol of catalyst was dissolved in water (2 mL), and allowed to equilibrate to reaction temperature with stirring for 30 min. Sodium formate, (0.2 mmol) and 3,3-dimethylbutan-2-one, (0.04 mmol) were added. The reaction was maintained at set temperature until the total reduction of the ketone was achieved or conversion of the ketone ceased (monitored by GC). The product was extracted with diethyl ether (3 × 2 mL), the extracts were dried over $MgSO_4$, and evaporated under reduced pressure. The product was purified by TLC with hexanes/ethyl acetate mixture. Enantiomeric excess was determined by chiral GC.

(*S*)-3,3-dimethylbutan-2-ol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (q, J = 6.4 Hz, 1H), 1.44 (s, 1H), 1.10 (d, J = 6.4 Hz, 3H), 0.87 (s, 9H) ppm. T = 75 °C, P = 15 psi, retention times: tR = 7.163 min, tS = 7.384 min.

(*R*)-2,2-dimethyl-1-phenylpropan-1-ol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.28 (m, 5H), 4.38 (s, 1H), 0.91 (s, 12H) ppm. T = 120 °C, P = 15 psi, tR = 9.633 min, tS = 10.016 min.

(*R*)-1-phenylethan-1-ol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.25 (m, 3H), 7.23–7.18 (m, 2H), 4.83 (q, J = 6.5 Hz, 1H), 1.43 (d, J = 6.5 Hz, 3H) ppm. T = 140 °C, P = 15 psi retention times: tR = 8.471 min, tS = 9.137 min.

3. Results and discussion

3.1. General comments and naming scheme

Chart 1 lists the abbreviations and numbering scheme used for the various ligands and complexes discussed in this paper.

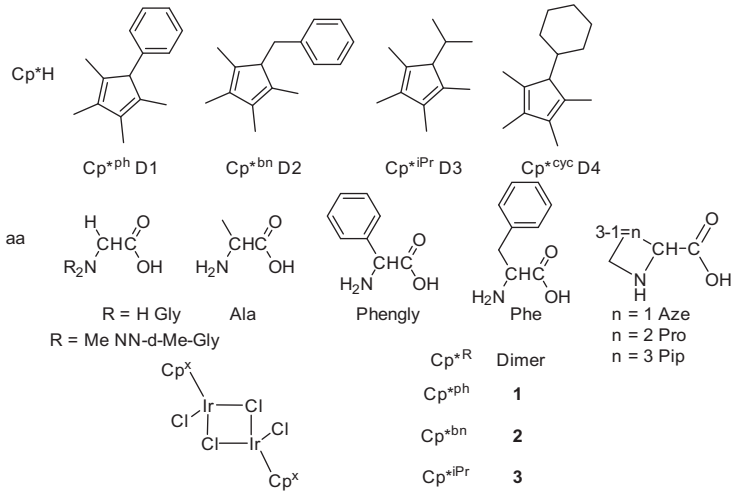
3.2. Cyclopentadienyl ligand synthesis

The Cp^{*R} variants were synthesized via reaction of 1.25–1.50 molar equivalents of a Grignard reagent and 2,3,4,5-tetramethylcylopent-2-enone in anhydrous THF (Scheme 1). This reaction results in an alcohol product which is then dehydrated to its respective diene using HCl. Purification of the final Cp^{*R} variant is carried out with column chromatography on silica gel using hexanes as the eluent. Yields ranged from fair to excellent, with the product being a combination of several isomers. The ^{1}H NMR spectra of the pentasubstituted dienes are fairly complex due to signal overlap of the multiple isomers that are produced (for an example of isomers, see Scheme 2). Yields are summarized in Table 1.

3.3. Synthesis of chloro-bridged iridium complexes

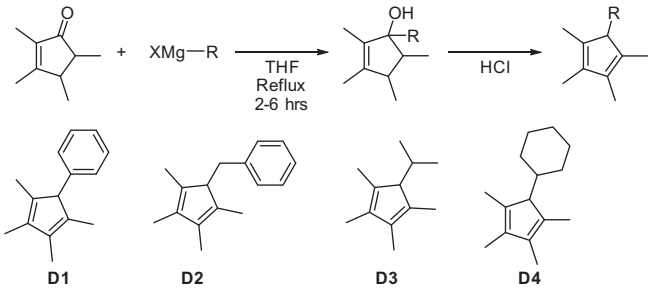
With the HCp^{*R} variants in hand, a standard reaction of the dienes with $IrCl_3 \times 3H_2O$ was performed in refluxing methanol to obtain the respective chloro-bridged iridium dimer complexes. Upon complexation, the NMR pattern observed for the diene is simplified with each Cp^{*R} isomer becoming aromatic and planar on the metal. As an example, the ^{1}H spectra of complex **3**(Cp^{*iPr}) is shown in Fig. 1. Yields of the chloride complexes range from fair to good and are summarized in Table 2. All iridium dimer complexes were isolated as orange powders with overall appearances and behaviors the same as the standard [$IrCp^*Cl_2$]$_2$ dimer. The various dimer complexes were characterized by NMR spectroscopy, HRMS, CH analysis, and X-ray crystallography when able. Complex **1**(Cp^{*Ph}) was previously reported by Sadler et al. [16], but we found that the yield of this compound could be improved by carrying out the synthesis in a microwave reactor, 60% yield with microwave compared with 39% under methanol reflux conditions.

The dimers **2**–**4** exhibit similar structures, each with bridging chlorides and with an inversion center that relates the unique portion of the dimer to the other half. The bond lengths of these chlorides are 2.4549(7), 2.4444(13), and 2.4393(11), for **2**(Cp^{*Bn}), **3**(Cp^{*iPr}), and **4**(Cp^{*Cy}), respectively. There is no π–π interaction



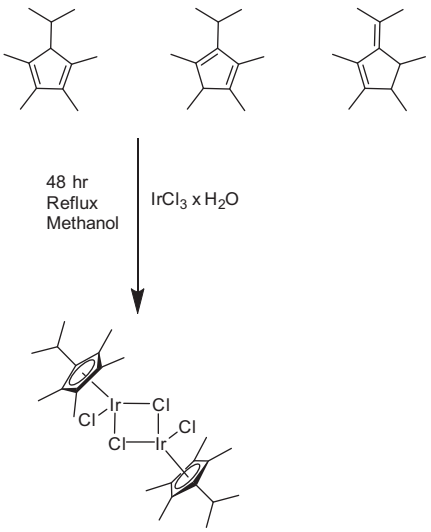
Complex	aa	Cp*R
5	Ala	Cp*ph
6	Phengly	Cp*ph
7	Phe	Cp*ph
8	Pro	Cp*ph
9	Pip	Cp*ph
10	Phe	Cp*bn
11	Pro	Cp*bn
12	Aze	Cp*bn
13	Pip	Cp*bn
14	Gly	Cp*iPr
15	NN-di-Me-Gly	Cp*iPr
16	Ala	Cp*iPr
17	Phe	Cp*iPr
18	Pro	Cp*iPr
19	Gly	Cp*cyc
20	Ala	Cp*cyc
21	Phengly	Cp*cyc
22	Phe	Cp*cyc
23	Pro	Cp*cyc

Chart 1. Iridium tetramethyl(R)cyclopentadienyl amino acid complexes.



Scheme 1. Synthesis of tetramethyl(R)cyclopentadienes.

observed for complex **2**(Cp^{*Bn}), unlike what was seen in earlier work with complex **1**(Cp^{*Ph}), which has a weak interaction with the symmetry related phenyl group in a neighboring molecule. Most interesting is that in the case of **4**(Cp^{*Cy}), two different chair configurations of the cyclohexane ring are observed in the structure when the disorder is appropriately modeled. The crystal structures for the dimers characterized crystallographically are displayed in Fig. 2.



Scheme 2. Synthesis of complex **3**(Cp^{*iPr}).

Table 1
Percent yields of tetramethyl(R)cyclopentadienyl ligands.

R group	% Yield
Phenyl D1	69
Benzyl D2	94
Isopropyl D3	37
Cyclohexyl D4	41

Table 2
Percent yields of iridium dimer complexes.

Complex	Yield%
1 (Cp^{*Ph})	60
2 (Cp^{*Bn})	40
3 (Cp^{*iPr})	57
4 (Cp^{*Cy})	49

3.4. Synthesis of amino acid complexes

Complexes **5**–**23** were synthesized in a fashion similar to other piano stool amino acid complexes reported previously.[22,23,36–40] All complexes adopt the three-legged piano-stool (half-sandwich) configuration, as expected. As is the case with Cp*Ir amino acid complexes previously reported, the iridium atom becomes a pseudo-tetrahedral chiral center upon coordination of the amino acid, resulting in diastereomers that differ at configuration of the metal when using an enantiomerically pure amino acid. Since homo chiral amino acids were used, these complexes will only differ in configuration at the metal center. In the case of glycine, two enantiomers form. The diastereomers formed from enantiomerically pure amino acids are distinguishable by both ^{1}H and ^{13}C NMR spectroscopies. Yields and isolated diastereomer ratios are shown in Table 3.

The diastereomer ratios obtained for these modified complexes are similar to what has been reported for the Cp* variants. Diastereomer selectivity is dependent for the most part on the amino acid ligand used, with ring-based systems such as *L*-proline and *L*-azetidine-2-carboxylic acid having the highest selectivity, whereas the less bulky *L*-alanine produces the least selectivity. The Cp^{*R} variant seems to have very little effect on the diastereomer ratio compared with (η^5-Me_5C_5)Ir(aa)Cl complexes presumably because a large R group such as benzyl or cyclohexyl on the ring may rotate away from the bulkiest portion of the amino acid ligand (see crystal structure discussion below.) These ratios remained unchanged over time in solution, as observed by NMR spectroscopy.

The major configurations of these complexes, (S_C, S_{Ir}) or (S_C, R_{Ir}) are the same as those reported for unmodified (η^5-Me_5C_5)Ir(aa)-Cl complexes, and was determined through NOE experiments. For example, irradiation of the Cp^{*R} methyls of the major component for complex **22**(Cp^{*Cy}) results in the enhancement of the phenyl protons of the phenylalaninate portion of the complex. Irradiation of the minor component Cp^{*R} methyls results in no such enhancement (Fig. 3). Complexes **7**(Cp^{*Ph}), **10**(Cp^{*Bn}), and **17**(Cp^{*iPr}) exhibit similar results, indicating that the major component for each *L*-phenylalaninate complex is S_CS_{Ir}. The ^{1}H NMR spectrum of **17**(Cp^{*iPr}) displays markedly different splitting patterns and chemical shifts for the diastereotopic 2-propyl methyl groups between the two diastereomers, with the major component having greater steric clash due to placement of the phenyl ring up and near the Cp* portion of the molecule (Fig. 4). For the Cp^{iPr} complexes, the diastereotopic methyl groups display as a pair of overlapping doublets. In some cases, the overlap of the major and minor isomer peaks for these resonances lead to a complex signal from which it is difficult to extract coupling information.

In the case of alkylated amino acids with only one hydrogen on the nitrogen, such as *L*-proline, the nitrogen becomes a chiral site upon chelation as well, leading to the possibility of $S_{Ir}S_CS_N$, $R_{Ir}S_CS_N$, $R_{Ir}S_CR_N$, and $S_{Ir}S_CR_N$ configurations. It was found that, in the smaller ring systems of **8**(Cp^{*Ph}), **11**(Cp^{*Bn}), **12**(Cp^{*Bn}), **18**(Cp^{*iPr}), and **23**(Cp^{*Cy}), the chirality of the nitrogen is the same as the chirality of the carbon center, leading to the formation of $R_{Ir}S_CS_N$ and $S_{Ir}S_CS_N$ configurations for the complexes. The major components in each case are $S_{Ir}S_CS_N$, which is determined by measuring the NOE interaction between the N-CH_2 groups and the Cp^{*R} methyls. The minor component, though difficult to observe, displays an interaction between the Cp* methyls and the amine proton, Fig. 5. These configurations are again what has been shown for (η^5-Me_5C_5)Ir(aa)Cl complexes.

The larger ring system of *L*-piperidine-2-carboxylate displays the opposite chirality on the nitrogen, with configurations of $S_{Ir}S_C$-R_N and $R_{Ir}S_CR_N$. NOE experiments showed that the major

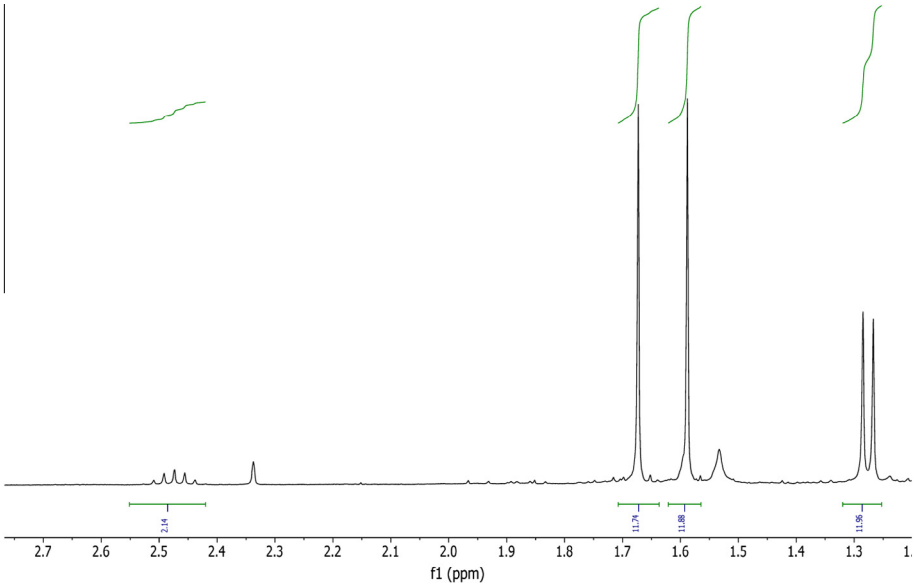


Fig. 1. ^{1}H NMR spectrum of **3**(Cp^{*iPr}).

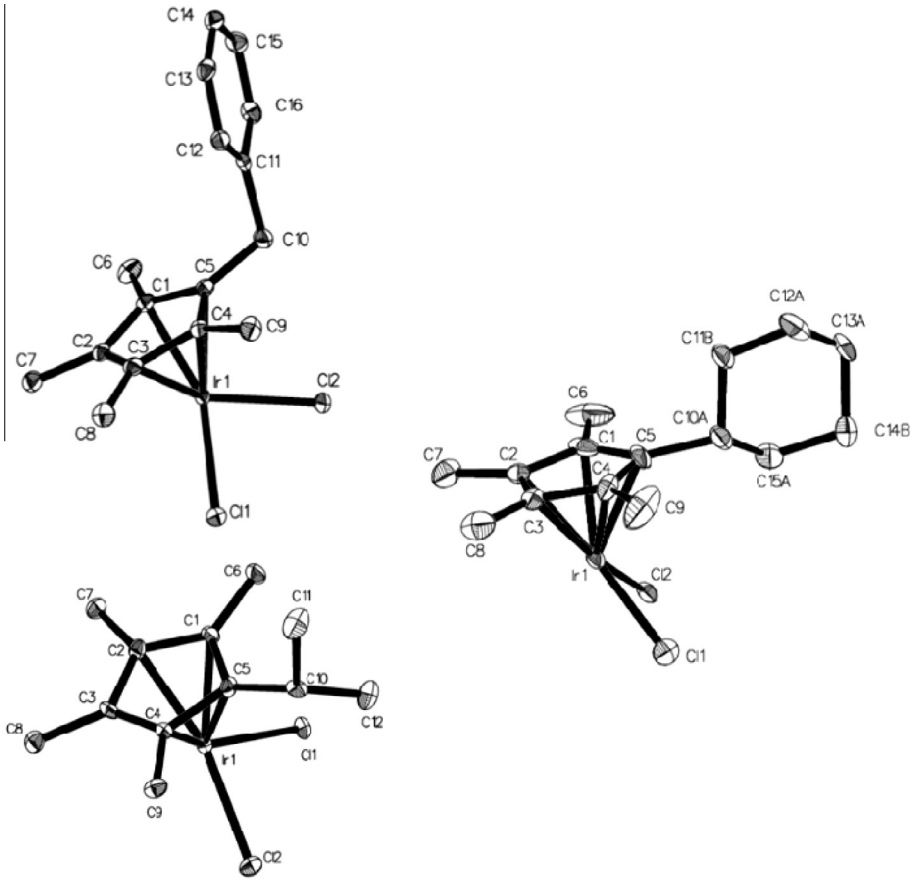


Fig. 2. Thermal ellipsoid plots of the asymmetric units of complexes **2**(Cp^{*Bn}), **3**(Cp^{*iPr}), and **4**(Cp^{*Cy}). Hydrogens omitted for clarity. Ellipsoids shown at 50%.

Table 3
Yields and diastereomeric ratios of isolated complexes.

AA(Compound #)	Yield%	Ratio	AA(Compound #)	Yield%	Ratio
Cp^{*Ph}			Cp^{*Bn}		
Ala (**5**)	52	54	Phe (**10**)	93	69
Phengly (**6**)	43	68	Pro (**11**)	77	85
Phe (**7**)	94	55	Aze (**12**)	98	69
Pro (**8**)	94	89	Pip (**13**)	83	88
Pip (**9**)	94	69			
Cp^{*iPr}			Cp^{*Cy}		
Gly (**14**)	88	na	Gly (**19**)	59	na
N,N-dimeth-Gly (**15**)	74	na	Ala (**20**)	80	56
Ala (**16**)	68	50	Phe (**21**)	85	68
Phe (**17**)	82	71	Phengly (**22**)	80	58
Pro (**18**)	71	83	Pro (**23**)	69	88

component has an interaction between the amine proton and the Cp^{*R} methyls, precisely the opposite from the smaller ring systems. The minor component displays interactions between the alpha carbon proton and the Cp^{*R} methyls. NOE interactions are displayed in Fig. 6.

3.5. Crystal structures

None of the NOE experiments show an interaction between the R group on the Cp^{*R} ligand and the amino acid ligand. This leads to the conclusion that the R group's steric bulk forces it away from the sterically demanding amino acid and chloride ligands. This is seen not only in a lack of NOE interactions, but in the solid state as well. In the case of complexes formed from **1**(Cp^{*Ph}), **3**(Cp^{*iPr}), and **4**(Cp^{*Cy}) the R group of the Cp^{*R} moiety is forced in-between the chlorine and nitrogen to relieve the steric interaction. Complexes formed from **2** with the Cp^{*Bn} ligand adopt a configuration similar to Cp^{*} complexes, with the benzyl portion having freedom of rotation

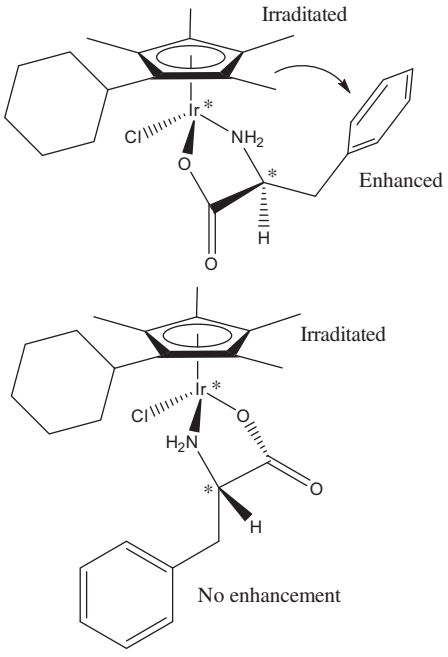


Fig. 3. NOE effects for complex **22**(Cp^{*Cy}), displaying interaction of Cp^{*Cy} methyls and the phenyl portion of phenylalaninate.

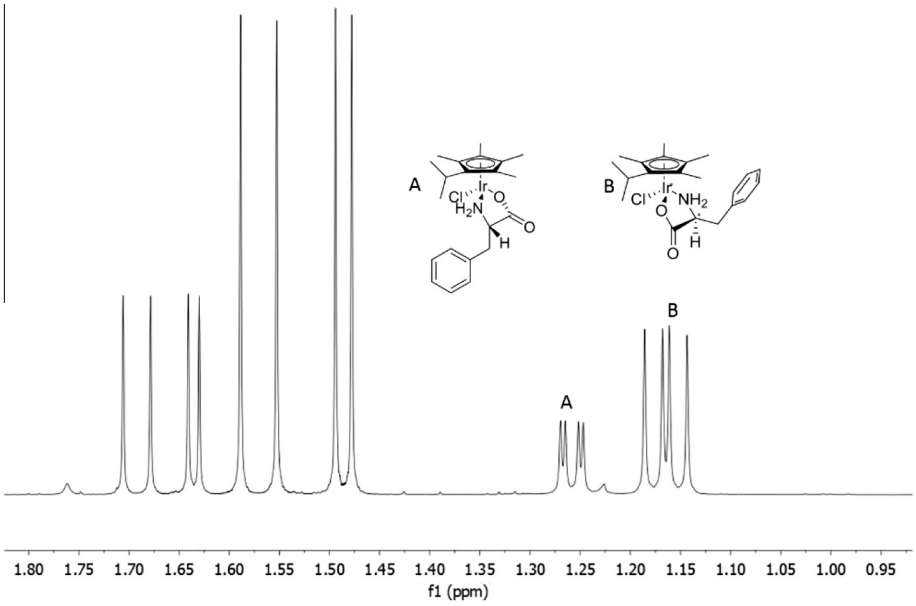


Fig. 4. Splitting pattern differences between the 2-propyl groups of the isomers of complex **17**(Cp^{*iPr}).

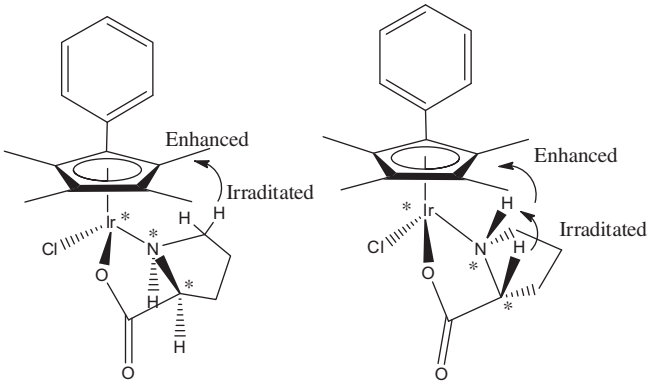


Fig. 5. Observed NOE enhancement of irradiated protons, showing absolute configuration of complex **8**(Cp^{*Ph}).

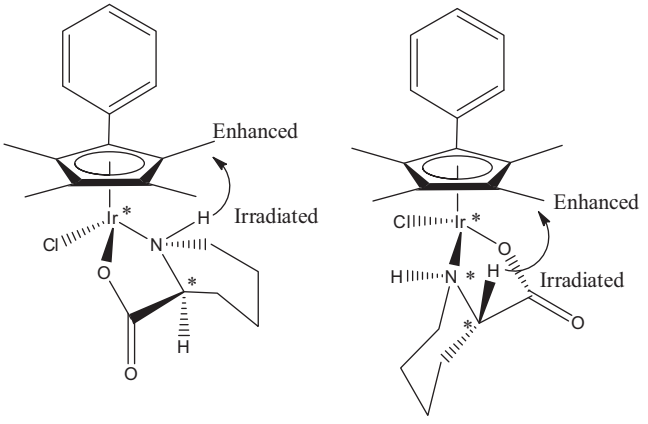


Fig. 6. NOE of complex **9**(Cp^{*Ph}), showing enhancement of Cp^{*Ph} methyls with the amine proton or αH is irradiated.

placing the phenyl group in a position anti with respect to the metal. Complex **14** with the Cp^{*iPr} ligand displays hindered rotation in the proton NMR spectra yielding peaks as described in the NMR section. The chloro-bridged dimer complex **3** with the same Cp^{*iPr} ligand lacks this spectral feature, indicating that interactions with the amino acid ligand are what is inducing this hindered rotation.

Comparison of the bond lengths and angles of the *L*-prolinate based complexes shows a significant lengthening of the Ir–Cl bond in the case of **8**(Cp^{*Ph}) compared to **11**(Cp^{*Bn}) and **18**(Cp^{*iPr}). Distances from the centroid to the iridium are nearly identical, with complex **8**(Cp^{*Ph}) being shorter by 0.01 angstroms. Complexes **11**(Cp^{*Bn}) and **18**(Cp^{*iPr}) are nearly identical to the unmodified complex, which has a distance of 1.766 Å. Ir-N bonds are also nearly identical between **8**(Cp^{*Ph}), **11**(Cp^{*Bn}), and **18**(Cp^{*iPr}), but shorter than the unmodified complex (2.140 Å). Ir–O bond lengths are similar between the phenyl and benzyl complexes of **8** and **11**, but the 2-propyl based **18** has a lengthening of more than 0.3 Å. All Ir–O bonds in these complexes are significantly longer than the Cp^* complex (2.086 Å). Bond lengths and angles are summarized in Table 4.

Unlike the crystal structures obtained of the (η^5-Me_5C_5)Ir(Pro)Cl complex by Beck and co-workers [41] only one diastereomer is present in the lattice in the cases of **8**(Cp^{*Ph}), **11**(Cp^{*Bn}), and **18**(Cp^{*iPr}) (see Fig. 7). The water molecule found in the Beck structure that hydrogen bonds between the two diastereomers is not present in any of these structures. However, a hydrogen-bonding network still persists, being formed through the amine proton and the carbonyl oxygen of a symmetry related complex in the lattice (see Fig. 8) such as that found in complex **18**. The network is also seen in complexes **12**(Cp^{*Bn}) and **13**(Cp^{*Bn}), which also show one diastereomer in the crystal lattice. The hydrogen bond lengths vary slightly between the 5 complexes, with the *L*-prolinate based complexes have the shortest lengths of 2.050, 2.027, and 1.935 Å for **8**(Cp^{*Ph}), **11**(Cp^{*Bn}), and **18**(Cp^{*iPr}), respectively. Complexes **12**(Cp^{*Ph}) and **13**(Cp^{*Ph}) have slightly longer bonds of 2.166 and 2.139 Å, respectively.

Because only a single diastereomer is present in the crystal structure for complexes **8**(Cp^{*Ph}), **11**(Cp^{*Bn}), **12**(Cp^{*Bn}), **13**(Cp^{*Bn}), and **18**(Cp^{*iPr}), yet there is an observed second diastereomer observed in the NMR spectra. Finding a single diastereomer in a solid state structure is not uncommon and may simply reflects that the compounds pack more efficiently as a single diastereomer. No

Table 4
Selected bond lengths and angles of complexes **8**(Cp^{*Ph}), **11**(Cp^{*Bn}), and **18**(Cp^{*iPr}).

	8(Cp^{*Ph})	**11**(Cp^{*Bn})	**18**(Cp^{*iPr})
Ir–Cl	2.434(4)	2.3999(7)	2.416(1)
Ir–O	2.12(1)	2.111(2)	2.155(3)
Ir–N	2.12(1)	2.127(2)	2.129(3)
Ir–W	1.755	1.767	1.76
C5–C10	1.50(2)	1.490(5)	1.513(6)
Cl–Ir–O	86.9(3)	86.92(7)	86.14(8)
Cl–Ir–N	83.4(3)	84.35(7)	86.34(9)
O–Ir–N	78.4(4)	77.44(9)	76.5(1)
Cl–Ir–W*	125.03	127.08	125.75
O–Ir–W	129.91	126.91	129.58
N–Ir–W	135.72	136.38	134.95

W = Centroid of pentamethylcyclopentadienyl ligand.

great pains were taken to screen other crystals for ones that would contain the other diastereomer. Fully alkylated amino acids such as N-methyl-*L*-proline produce exclusively one diastereomer in solution, as reported by Carmona et al. [36].

The complexes are soluble in water, though to less of a degree as the hydrophobicity of the Cp^{*R} group is increased, with Cp^{*iPr} > Cp^{*Ph} > Cp^{*Bn} > Cp^{*Cy} being the trend. Potential chloride disassociation and subsequent formation of a mono-aqua cation as well as the hydrogen bonding interactions between the NH and CO groups assists in this solubility. Mono-aqua cation formation is commonly seen in similar piano stool complexes [9,12,42,43].

3.6. Asymmetric transfer hydrogenation using amino acid catalysts

Asymmetric transfer hydrogenation (ATH) of both aliphatic and aromatic ketones was performed using complexes **8**(Cp^{*Ph}), **9**(Cp^{*Ph}), **11**(Cp^{*Bn}), **12**(Cp^{*Bn}), **13**(Cp^{*Bn}), **15**(Cp^{*iPr}), **18**(Cp^{*iPr}), **23**(Cp^{*Cy}). Prior work has shown that the ring based systems are the most selective, at least in the case of aromatic substrates [22,23,44,45]. This is due to only one active hydride complex being formed under ATH conditions. The second diastereomer places the proton and hydride at too great of a distance to reduce the ketone substrate.

The *L*-prolinate, *L*-piperidine-2-carboxylate, and *L*-azetidine-2-carboxylate variants were tested for the catalytic reduction of pinacolone and acetophenone to 3,3-dimethylbutan-2-ol and 1-phenylethan-1-ol, respectively. The reactions were carried out in both water with sodium formate and 2-propanol with sodium hydroxide as base. In the case of water-based reactions the substrate/catalyst/formate ratios were 1/.1/5 with 2 mL of water and no inert protection. The 2-propanol based reactions have a substrate/catalyst/base ratio of 1/.1/.2 and must be conducted under inert atmosphere conditions.

The aliphatic substrate pinacolone reduction proceeds best in aqueous media, in regards to both enantiomeric selectivity and rate of reduction. Of the complexes **8**(Cp^{*Ph}), **11**(Cp^{*Bn}), **18**(Cp^{*iPr}), and **23**(Cp^{*Cy}), **11**(Cp^{*Bn}) had the highest selectivity, though at a reduced rate of reaction. The cyclohexyl and isopropyl based systems had the same selectivity, though complex **23**(Cp^{*Cy}) reached only 36% conversion at 44 h. The phenyl based system reduces both rate of reduction and selectivity. The reduction in rate is most likely brought about through the steric hindrance of the Cp^{*R} group. The mechanism implied by Noyori goes through a six membered transition state formed through the metal hydride, amine proton, and the C=O of the substrate.[25] The positioning of the R groups on the Cp^* ring conflicts with this, with the phenyl system being the most rigid, leading to reduced conversion. The loss in selectivity can be justified through a similar process. The smaller ring system of complex **12**(Cp^{*Bn}) produces an ee% of 92 with a conversion of 40% at 44 h. Most interesting to note is that when the reaction is performed with complex **18**(Cp^{*iPr}) in 2-propanol only one percent conversion is witnessed after 27 h, even under inert conditions. The selectivity is also decreased by 10%. A summary of the reduction of pinacolone is presented in Table 5.

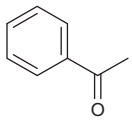
Acetophenone reduction also gains a rate enhancement when performed in water, as seen prior by Xiao [46]. The differences in percent conversion at similar times of 21 and 25 h is staggering, for example complex **18**(Cp^{*iPr}) reaches full conversion is 21 h in water, with the 2-propanol-based reaction only reaching 11 percent in 24.5 h. In the case of the *L*-prolinate based variants the trend observed with the pinacolone reduction is retained, with the sterically hindered variants of **8**(Cp^{*Ph}) and **23**(Cp^{*Cy}) having the lowest conversion. Selectivity in these *L*-prolinate complexes is low, generally below 20 percent. Interestingly, while performing the reaction in 2-propanol reduced selectivity in the case of pinacolone, the trend is reversed for the aromatic acetophenone. Complex **18**(Cp^{*iPr}) goes from a near racemic mixture in water to an ee% of 70 percent in 2-propanol. Of the other variants tested, the complex **13**(Cp^{*Bn}), had the highest selectivity of 75, in 2-propanol. Complex **15**(Cp^{*iPr}), containing a fully methylated amine, reached 5 percent conversion at 48 h. This is interesting since the rate determining step in the classic mechanism is the concerted transfer of the hydride and hydrogen to the ketone. Since conversion still takes place with a methylated ligand, the hydrogen source must be solvent itself, not an amine proton. A step-wise mechanism, which has been presented by several groups prior to this study, accounts for the reduction when no amine protons are present [9,47,48]. A summary of the reduction of acetophenone is displayed in Table 6.

Table 5
Asymmetric transfer hydrogenation[a] of pinacolone.

Entry	Complex	Ketone	*T* (h)	Conv%[c]	ee%[d]	Conf.[e]
1	**8**		44	9	63	S
2	**11**		44	32	80	S
3	**18**		44	60	74	S
4[b]	**18**		27	1	65	S
5	**23**		44	36	74	S
6	**12**		44	40	92	S
7	**13**		50	58	43	R

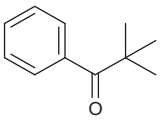
[a] Performed in water at 40 °C, substrate/catalyst/formate ratios were 1/.1/5 with 2 mL of water and no inert protection.
[b] Performed in 2-propanol at 40 °C, substrate/catalyst/base ratio of 1/.1/.2.
[c] Determined by GC.
[d] Determined by chiral GC.
[e] Comparison against literature values.

Table 6
Asymmetric transfer hydrogenation[a] of acetophenone.

Entry	Complex	Ketone	*T* (h)	Conv%[c]	ee%[d]	Conf.[e]
9	**8**[a]		21	50	0	Na
10	**8**[b]		25	13	5	R
11	**11**[a]		21	81	6	R
12	**11**[b]		25	14	10	R
13	**18**[a]		21	99	4	R
14	**18**[b]		24.5	11	70	R
15	**23**[a]		21	75	20	R
16	**23**[b]		25	26	4	R
17	**12**[b]		48	85	17	S
18	**9**[b]		25.5	38	46	S
19	**13**[b]		45	84	75	S
20	**15**[a]		48	5	0	Na

[a] Performed in water at 40 °C, substrate/catalyst/formate ratios were 1/.1/5 with 2 mL of water and no inert protection.
[b] Performed in 2-propanol at 40 °C, substrate/catalyst/base ratio of 1/.1/.2.
[c] Determined by GC.
[d] Determined by chiral GC.
[e] Comparison against literature values.

Table 7
Asymmetric transfer hydrogenation[a] of 2,2-dimethyl-1-phenylpropan-1-one.

Entry	Complex	Ketone	T (h)	Conv%[c]	ee%[d]	Conf.[e]
20	**8**		13	4	51	R
21	**11**		13	13	61	R
22	**18**		13	18	70	R
23	**18**[b]		43	2	18	R
24	**23**		13	9	57	R
25	**9**		13	17	67	S
26	**13**		13	52	69	S
27	**13**[b]		43	40	37	S
28	**12**		48	7	43	R

[a] Performed in water at 40 °C, substrate/catalyst/formate ratios were 1/.1/5 with 2 mL of water and no inert protection.
[b] Performed in 2-propanol at 40 °C, substrate/catalyst/base ratio of 1/.1/.2.
[c] Determined by GC.
[d] Determined by chiral GC.
[e] Comparison against literature values.

The reduction of 2,2-dimethyl-1-phenylpropan-1-one achieved the best selectivity when performed in water, similar to pinacolone. Again, complex **18**(Cp^{*iPr}) had the best selectivity between the *L*-prolinate based variants, though conversion was very low, and seemingly ceased at 13 h. The *L*-piperidine-2-carboxylate based **13**(Cp^{*Bn}) achieved a conversion and selectivity of 52 and 69, respectively on a similar time frame. **12**(Cp^{*Bn}), while having the highest selectivity in the reduction of pinacolone, was the least selective and the least active, with an ee and conversion of 7 and 43, respectively. This is likely due to the steric constraints from both the small ring system and the benzyl group conflict with the highly hindered nature of the 2,2-dimethyl-1-phenylpropan-1-one (see Table 7).

The chirality of the product is determined primarily by the chirality of the nitrogen. For example, in the case of pinacolone, the *L*-prolinate and *L*-azetidine-2-carboxylate based systems possess S_N, leading to an *R* product. The larger *L*-piperidine-2-carboxylate systems possess an R_N, which leads to an *S* product. This implies a transition state where the sterically bulky *t*-butyl portion of pinacolone is directed away from the bulky Cp^* portion of the complexes. In the reduction of acetophenone, selectivity again corresponds to the chirality of the nitrogen, however, the bulky portion of acetophenone is directed up toward the Cp^* portion of the molecule, which coincides with the CH–π interaction described

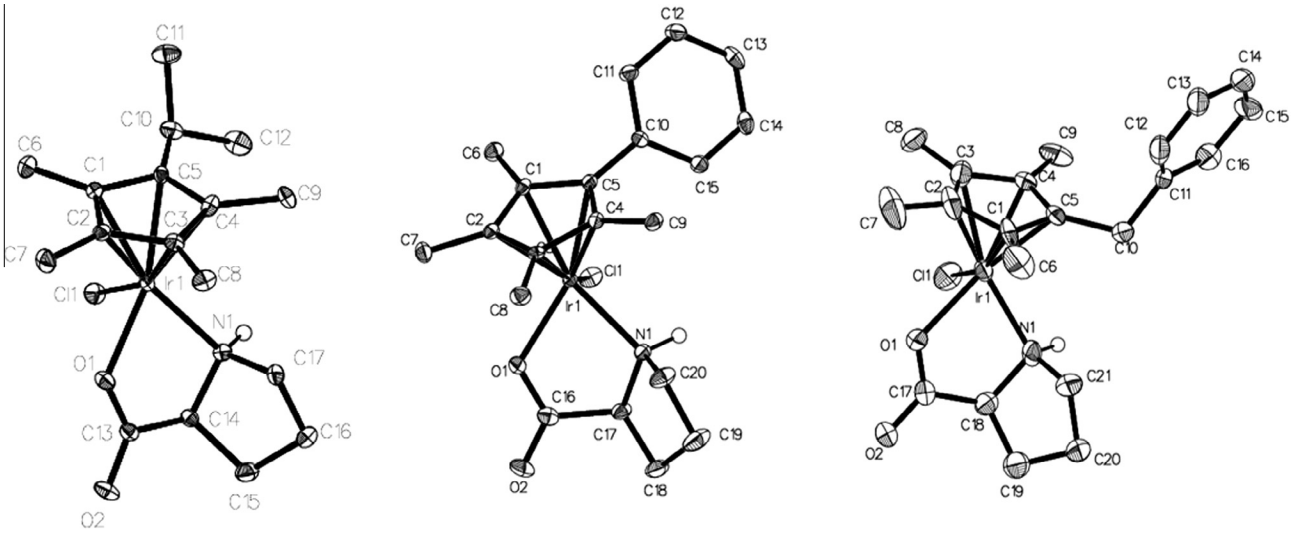


Fig. 7. Crystal structures of **18**, **8** and **11**. All hydrogens except the amine hydrogen are omitted. Ellipsoids shown at 50% probability.

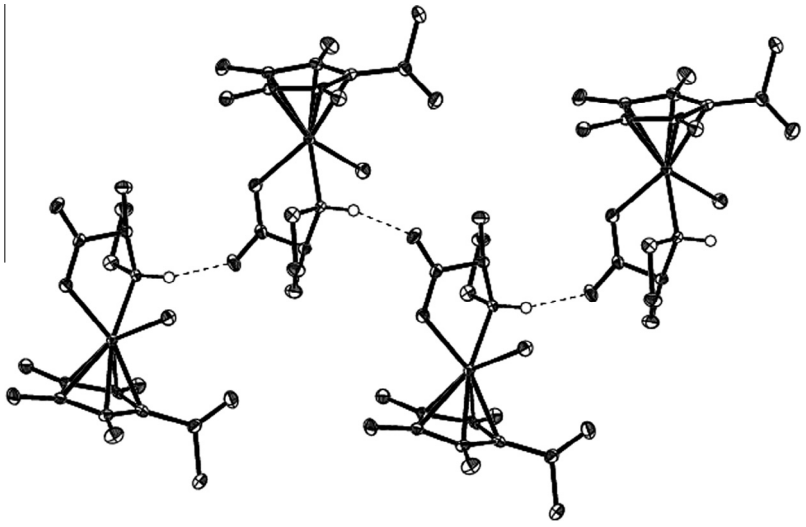


Fig. 8. Extended lattice showing the intermolecular hydrogen-bonding network of complex **18**.

by Noyori and co-workers [25] The loss of selectivity with complexes **8**(Cp^{*Ph}), **11**(Cp^{*Bn}), and **23**(Cp^{*Cy}) can be explained by a disruption of this effect, as compared to complex **18**(Cp^{*iPr}). Interestingly, in the reduction of 2,2-dimethyl-1-phenylpropan-1-one, the CH–π interaction overrides the steric class between the *t*-butyl group and the Cp^* moiety. The observed products are consistent with their acetophenone counterparts, though rate of conversion is reduced. The solvent effects observed are the most surprising, though rate enhancement in aqueous media has been reported before, such substantial loss of selectivity has not been observed with the related mono-tosylated DPEN ligands.

4. Conclusions

This study shows that modification to the chemically inert pentamethylcyclopentadienyl moiety impacts the catalytic activity of half-sandwich Ir amino acid complexes. While not changing the configuration or ratios of the diastereomers, the steric bulk introduced can drastically impact both rate of reduction and selectivity in the asymmetric transfer hydrogenation of ketones. When comparing the *L*-prolinate based systems in the reduction of the aromatic substrates of acetophenone and 2,2-dimethyl-1-phenylpropan-1-one, the 2-propyl based systems achieved the highest selectivity. This is due to the larger systems (Cp^{*Ph}, Cp^{*Bn}, and Cp^{*Cy}) greater steric bulk and possible disruption of the stabilizing CH–π interaction.

This work displays the first reported examples of half-sandwich Cp^{*Bn}, Cp^{*iPr}, and Cp^{*Cy} containing iridium complexes, either dimer type complexes, or reacted half-sandwich complexes. The structures of [(η^5-$C_5Me_4CH_2C_6H_5$)Ir(*L*-prolinate)Cl], [(η^5-$C_5Me_4CH_2C_6H_5$)Ir(*L*-azetidine-2-carboxylate)Cl], [(η^5-$C_5Me_4CH_2C_6H_5$)Ir(*L*-piperidine-2-carboxylate)Cl], and [(η^5-C_5Me_4*iPr*)Ir(*L*-prolinate)Cl] are the first structures of iridium complexes containing Cp^{*Bn} and Cp^{*iPr}.

The solvent effects displayed in this work are striking. While it has been shown that water will accelerate the ATH of ketones, the selectivity differences are substantial. This leads to the conclusion that a concerted pathway is not the mechanism of reduction, but a step-wise pathway. The reduction of acetophenone by the fully N-methylated [(η^5-C_5Me_4*iPr*)Ir(*N*,*N*-dimethyl-glycinate)Cl] gives experimental credence to the theoretical mechanisms presented by Ikariya [47] and Meijer, and are in agreement with results previously presented by Xiao and co-workers [9,47,48].

Acknowledgments

The authors would like to thank Dr. Carla Slebodnick for her assistance with resolving several crystal structures. We thank the National Science Foundation for funds (CHE-01311288) for the purchase of the Oxford Diffraction XCalibur2 single-crystal diffractometer. We thank the Virginia Tech Department of Chemistry for funds for supplies and the Hamilton Company for a generous grant of syringes.

Appendix A. Supplementary data

CCDC 996090–996097 contain the supplementary crystallographic data for complexes **2**, **3**, **4**, **8**, **11**, **12**, **13** and **18**. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.poly.2014.06.053. These data include MOL files and InChiKeys of the most important compounds described in this article.

References

[1] T.J. Kealy, P.L. Pauson, Nature 168 (1951) 1039, http://dx.doi.org/10.1038/1681039b0.
[2] G.B. Kauffman, J. Chem. Educ. 60 (1983) 185, http://dx.doi.org/10.1021/ed060p185.
[3] H. Werner, Angew. Chem. 51 (2012) 6052, http://dx.doi.org/10.1002/anie.201201598.
[4] G. Wilkinson, J. Organomet. Chem. 100 (1975) 273, http://dx.doi.org/10.1016/S0022-328X(00)88947-0.
[5] D. Slocum, C. Ernst, Adv. Organomet. Chem. 10 (1972) 79, http://dx.doi.org/10.1016/S0065-3055(08)60338-X.
[6] J.E. Bercaw, R.H. Marvich, L.G. Bell, H.H. Brintzinger, J. Am. Chem. Soc. 94 (1972) 1219, http://dx.doi.org/10.1021/ja00759a032.
[7] J.W. Kang, K. Moseley, P.M. Maitlis, J. Am. Chem. Soc. 91 (1969) 5970, http://dx.doi.org/10.1021/ja01050a008.
[8] Y. Wei, C. Wang, X. Jiang, D. Xue, J. Li, J. Xiao, Chem. Commun. 49 (2013) 5408, http://dx.doi.org/10.1039/C3CC41661E.
[9] X.F. Wu, J.K. Liu, D. Di Tommaso, J.A. Iggo, C.R.A. Catlow, J. Bacsa, J.L. Xiao, Chem. Eur. J. 14 (2008) 7699, http://dx.doi.org/10.1002/chem.200800559.
[10] X. Wu, X. Li, M. McConville, O. Saidi, J. Xiao, J. Mol. Catal. A: Chem. 247 (2006) 153, http://dx.doi.org/10.1016/j.molcata.2005.11.040.
[11] J.H. Li, Y.F. Tang, Q.W. Wang, X.F. Li, L.F. Cun, X.M. Zhang, J. Zhu, L.C. Li, J.G. Deng, J. Am. Chem. Soc. 134 (2012) 18522, http://dx.doi.org/10.1021/ja308357y.
[12] J.D. Blakemore, N.D. Schley, D. Balcells, J.F. Hull, G.W. Olack, C.D. Incarvito, O. Eisenstein, G.W. Brudvig, R.H. Crabtree, J. Am. Chem. Soc. 132 (2010) 16017, http://dx.doi.org/10.1021/ja104775j.
[13] N.D. McDaniel, F.J. Coughlin, L.L. Tinker, S. Bernhard, J. Am. Chem. Soc. 130 (2008) 210, http://dx.doi.org/10.1021/ja074478f.
[14] Z. Codolà, J.M.S. Cardoso, B. Royo, M. Costas, J. Lloret-Fillol, Chem. Eur. J. 19 (2013) 7203, http://dx.doi.org/10.1002/chem.201204568.
[15] S. Gençaslan, W.S. Sheldrick, Eur. J. Inorg. Chem. 2005 (2005) 3840, http://dx.doi.org/10.1002/ejic.20050022.
[16] Z. Liu, A. Habtemariam, A.M. Pizarro, G.J. Clarkson, P.J. Sadler, Organometallics 30 (2011) 4702, http://dx.doi.org/10.1021/om2005468.
[17] G.W. Karpin, J.S. Merola, J.O. Falkinham, Antimicrob. Agents Chemother. 57 (2013) 3434, http://dx.doi.org/10.1128/AAC.00452-13.
[18] R.S. Threlkel, J.E. Bercaw, J. Organomet. Chem. 136 (1977) 1, http://dx.doi.org/10.1016/S0022-328X(00)87959-0.
[19] H. Brintzinger, J.E. Bercaw, J. Am. Chem. Soc. 93 (1971) 2045, http://dx.doi.org/10.1021/ja00737a033.
[20] P.T. Wolczanski, J.E. Bercaw, Organometallics 1 (1982) 793, http://dx.doi.org/10.1021/om00066a006.
[21] R. Noyori, Angew. Chem., Int. Ed. 41 (2002) 2008. http://dx.doi.org/10.1002/1521-3773(20020617)41:12%3C2008::AID-ANIE2008%3E3.0.CO;2-4.
[22] D. Carmona, F.J. Lahoz, P. Garcia-Orduna, L.A. Oro, M.P. Lamata, F. Viguri, Organometallics 31 (2012) 3333, http://dx.doi.org/10.1021/om3001394.
[23] D. Carmona, F. Viguri, M. Pilar Lamata, J. Ferrer, E. Bardaji, F.J. Lahoz, P. Garcia-Orduna, L.A. Oro, Dalton Trans. 41 (2012) 10298, http://dx.doi.org/10.1039/c2dt30976a.
[24] A. Fujii, S. Hashiguchi, N. Uematsu, T. Ikariya, R. Noyori, J. Am. Chem. Soc. 118 (1996) 2521, http://dx.doi.org/10.1021/ja954126l.
[25] M. Yamakawa, I. Yamada, R. Noyori, Angew. Chem., Int. Ed. 40 (2001) 2818. http://dx.doi.org/10.1002/1521-3773(20010803)40:15%3C2818::aid-anie2818%3E3.0.co;2-y.
[26] F. Hanasaka, K.-I. Fujita, R. Yamaguchi, Organometallics 25 (2006) 4643, http://dx.doi.org/10.1021/om060475k.
[27] M. Ito, Y. Endo, N. Tejima, T. Ikariya, Organometallics 29 (2010) 2397, http://dx.doi.org/10.1021/om1001809.
[28] G. Kohl, H. Pritzkow, M. Enders, Eur. J. Inorg. Chem. 2008 (2008) 4230, http://dx.doi.org/10.1002/ejic.200800217.
[29] D.S. Matharu, J.E.D. Martins, M. Wills, Chem. Asian J. 3 (2008) 1374, http://dx.doi.org/10.1002/asia.200800189.
[30] D.M. Bensley Jr., E.A. Mintz, J. Organomet. Chem. 353 (1988) 93, http://dx.doi.org/10.1016/0022-328X(88)80303-6.
[31] Z. Liu, A. Habtemariam, A.M. Pizarro, S.A. Fletcher, A. Kisova, O. Vrana, L. Salassa, P.C. Bruijnincx, G.J. Clarkson, V. Brabec, P.J. Sadler, J. Med. Chem. 54 (2011) 3011, http://dx.doi.org/10.1021/jm2000932.
[32] D.S. Matharu, D.J. Morris, A.M. Kawamoto, G.J. Clarkson, M. Wills, Org. Lett. 7 (2005) 5489, http://dx.doi.org/10.1021/ol052559f.
[33] CrysAlisPro Software System, Agilent Technologies, Oxford, UK, 2013.
[34] G.M. Sheldrick, Acta Crystallogr., Sect. A 64 (2007) 112, http://dx.doi.org/10.1107/S0108767307043930.
[35] O.V. Dolomanov, L.J. Bourhis, R.J. Gildea, J.A. Howard, H. Puschmann, J. Appl. Crystallogr. 42 (2009) 339, http://dx.doi.org/10.1107/S0021889808042726.
[36] D. Carmona, M. Pilar Lamata, F. Viguri, E. San José, A. Mendoza, F.J. Lahoz, P. García-Orduña, R. Atencio, L.A. Oro, J. Organomet. Chem. 717 (2012) 152, http://dx.doi.org/10.1016/j.jorganchem.2012.07.022.
[37] W.S. Sheldrick, E. Hauck, S. Korn, J. Organomet. Chem. 467 (1994) 283, http://dx.doi.org/10.1016/0022-328X(94)80014-6.

[38] D. Grotjahn, T. Groy, J. Am. Chem. Soc. 116 (1994) 6969, http://dx.doi.org/10.1021/ja00094a075.
[39] D. Carmona, F.J. Lahoz, R. Atencio, L.A. Oro, M. Pilar Lamata, E. San José, Tetrahedron 4 (1993), http://dx.doi.org/10.1016/S0957-4166(00)80331-6.
[40] D. Carmona, A. Mendoza, F.J. Lahoz, L.A. Oro, M.P. Lamata, E. San Jose, J. Organomet. Chem. 396 (1990) C17, http://dx.doi.org/10.1016/0022-328X(90)85204-C.
[41] R. Krämer, K. Polborn, H. Wanjek, I. Zahn, W. Beck, Chem. Ber. 123 (1990) 767, http://dx.doi.org/10.1002/cber.19901230420.
[42] N. Makihara, S. Ogo, Y. Watanabe, Organometallics 20 (2001) 497, http://dx.doi.org/10.1021/om0008676.
[43] S. Ogo, N. Makihara, Y. Kaneko, Y. Watanabe, Organometallics 20 (2001) 4903, http://dx.doi.org/10.1021/om010523v.
[44] D. Carmona, M.P. Lamata, F. Viguri, I. Dobrinovich, F.J. Lahoz, L.A. Oro, Adv. Synth. Catal. 344 (2002) 499. http://dx.doi.org/10.1002/1615-4169(200207)344:5%3C499::AID-ADSC499%3E3.0.CO;2-R.
[45] Á. Kathó, D. Carmona, F. Viguri, C.D. Remacha, J. Kovács, F. Joó, L.A. Oro, J. Organomet. Chem. 593 (2000) 299, http://dx.doi.org/10.1016/S0022-328X(99)00433-7.
[46] X. Wu, X. Li, W. Hems, F. King, J. Xiao, Org. Biomol. Chem. 2 (2004) 1818, http://dx.doi.org/10.1039/B403627A.
[47] P.A. Dub, T. Ikariya, J. Am. Chem. Soc. 135 (2013) 2604, http://dx.doi.org/10.1021/ja3097674.
[48] A. Pavlova, E.J. Meijer, ChemPhysChem 13 (2012) 3492, http://dx.doi.org/10.1002/cphc.201200454.