Formation of Coordinatively Unsaturated Cp*Ir–Amino Acid Complexes and Their Highly Diastereoselective Complexation Reactions

D. B. Grotjahn* and T. L. Groy†

Department of Chemistry and Biochemistry
Arizona State University, Tempe, Arizona 85287-1604

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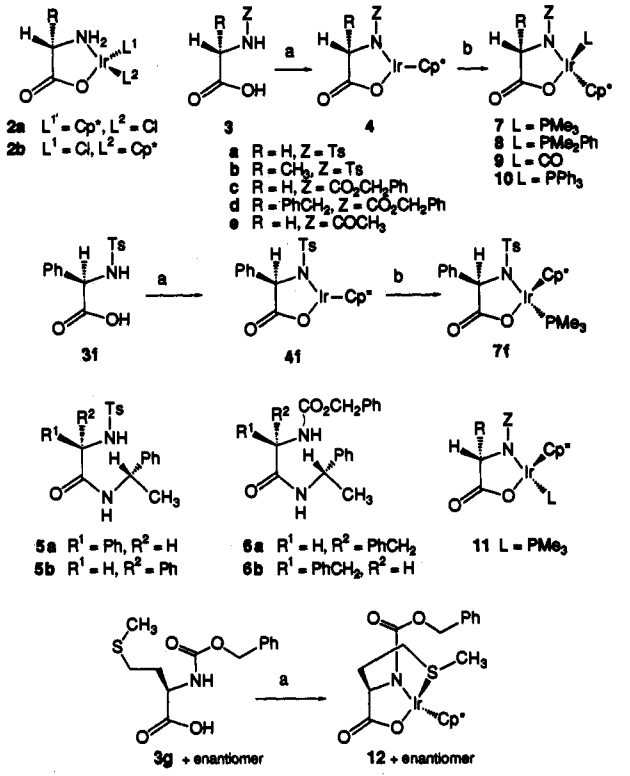
Amino acid–metal complexes have been the subject of innumerable studies,[1] prompted by the roles of metals in biochemistry[2] and amino acids in producing chiral catalysts.[3] With very few exceptions,[4] amino acid–metal complexes are coordinatively* saturated. For example, interaction of *N*-unsubstituted amino acid salts with $[Cp^*IrCl(\mu\text{-}Cl)]_2$ **1** leads to 18-electron complexes **2**, the stereogenic element of the amino acid producing mixtures modestly enriched in diastereomer **2a** (from 50:50 up to 92:8).[5] Here we report that under modified conditions, amino acid derivatives **3** bearing electron-withdrawing groups Z on N afford air-stable 16-electron species **4**, two members of which are characterized by X-ray diffraction. Furthermore, unlike ligand substitutions on **2** and related species, ligand *addition* reactions of chiral **4** proceed with high (≥25:1) stereoselectivity.

Typically, a mixture of **3**,[6] dimer **1**,[7] and anhydrous K_2CO_3 (molar ratio 1.00:0.50:2.0–3.0) was diluted with THF or CH_3CN until the concentration of **3** was 0.01–0.04 M. Nitrogen was bubbled through the mixture for 5–10 min, and the orange (THF) or yellow (CH_3CN) mixture was stirred for 4–36 h, until the color deepened to red. The residue remaining after rotary evaporation was diluted with CH_2Cl_2 and filtered through Celite, and the filtrate was concentrated to afford air-stable brick-red to burgundy-red **4** in ≥90% yields.[8] Surprisingly, elemental analysis, IR, and NMR data[9] pointed to absence of coordination by THF, CH_3CN, or N_2 in the isolated products. The ^1H NMR data for glycine derivative **4a** in CD_2Cl_2 were particularly revealing, a sharp two-proton singlet being seen at δ 3.20 ppm for the methylene group even at −90 °C, consistent with either an achiral structure or rapidly interconverting, enantiomeric, octahedral structures. X-ray crystallographic analysis on **4a**[10] confirmed the former suggestion: the centroid of Cp* lies 0.022 Å away from the mean plane defined by the five atoms of the chelate ring, and no atom of the chelate lies more than 0.029 Å away from that plane. Compared with 18-electron, **2**,[5] the Ir–N and Ir–O bonds are ca. 0.15 and 0.06 Å shorter, respectively, suggesting stabilization of the formally 16-electron metal by lone pairs on N and O;[11] additional evidence for this insight follows.

Scheme 1[a]



[a] (a) K_2CO_3, $[Cp^*IrCl(\mu\text{-}Cl)]_2$, THF or CH_3CN, room temperature, 4–36 h; (b) ligand, $CDCl_3$ or C_6D_6, room temperature, ≤15 s.

Enantiomeric purity of complexes **4f** and **4d** was determined to be at least 95%;[12] derivatization[9,13] gave mixtures of amides **5a/5b** and **6a/6b**,[14] respectively, in ratios of at least 20:1.

The deep red color of solutions of **4** fades to yellow within seconds after addition of a phosphine ligand or CO,[15] apparently a diagnostic color change for coordinative saturation in these systems. The resulting glycine-derived complexes **7a**, **8a**, and **9a** display ^1H NMR signals[9] ascribable to two mutually coupled diastereotopic methylene protons, as expected for chiral species

* Author to whom correspondence should be addressed.
† X-ray crystal structures.

(1) Laurie, S. H. Amino Acids, Peptides and Proteins. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Ed.; Pergamon: Oxford, 1987; Vol. 2, pp 739–776. Ioganson, A. A. *Russ. Chem. Rev.* **1985**, *54*, 277–292.

(2) Metalloproteins: Structural Aspects. *Adv. Protein Chem.* **1991**, *42*. Ibers, J. A.; Holm, R. H. *Science* **1980**, *209*, 223–235.

(3) Brunner, H. *Top. Stereochem.* **1988**, *18*, 129–247.

(4) (a) To our knowledge, the only coordinatively unsaturated amino acid complexes reported are $(CO)_2Rh^I$(aminoacidato) complexes, which undergo CO substitution by PR_3 and AsR_3: Dowerah, D.; Singh, M. M. *J. Ind. Chem. Soc.* **1980**, *57*, 368–371. Dowerah, D.; Singh, M. M. *J. Chem. Res. (S)* **1979**, 38. Dowerah, D.; Singh, M. M. *Trans. Met. Chem.* **1976**, *1*, 294–5. (b) A dimeric Cp*Rh–glycine *amide* complex was recently suspected on the basis of ^1H NMR evidence of undergoing partial monomerization in solution to a species related to **4** (but formulated as rapidly epimerizing at Rh): Krämer, R.; Polborn, K.; Robl, C.; Beck, W. *Inorg. Chim. Acta* **1992**, *198–200*, 415–420.

(5) (a) Krämer, R.; Polborn, K.; Wanjek, H.; Zahn, I.; Beck, W. *Chem. Ber.* **1990**, *123*, 767–778. (b) Carmona, D.; Mendoza, A.; Lahoz, F. J.; Oro, L. A.; Lamata, M. P.; San Jose, E. *J. Organomet. Chem.* **1990**, *396*, C17–21.

(6) Compounds **3** were commercially available or made by standard procedures.

(7) White, C.; Yates, A.; Maitlis, P. M. *Inorg. Synth.* **1992**, *29*, 228.

(8) The synthesis of **4e** (in THF) occasionally required addition of drying agent Na_2SO_4 to achieve red color.

(9) See supplementary material.

(10) Crystallization occurred from hot toluene (**4a**) or xylenes (**4f**) by vapor diffusion with petroleum ether. Single crystals were analyzed at 20 °C. **4a**: monoclinic, space group $P2_1/n$–C^5_{2h} (No. 14), with a = 7.290(1) Å, b = 12.137(2) Å, c = 22.119(4) Å, β = 91.88(3)°, V = 1955.9(10) Å³, Z = 4, d_{calcd} = 1.884 g cm⁻³, and μ(Mo Kα) = 6.956 mm⁻¹. **4f**: monoclinic, space group $P2_1$–C^2_2 (No. 4), with a = 8.221(3) Å, b = 9.435(3) Å, c = 15.896(5) Å, β = 91.03(3)°, V = 1232.8(7) Å³, Z = 2, d_{calcd} = 1.699 g cm⁻³, and μ(Mo Kα) = 5.530 mm⁻¹. After Patterson synthesis and refinement (SHELXTL/PC), standard discrepancy indices were R = 3.48 and R_w = 3.56 for 2516 reflections with $F > 4\sigma(F)$ in the case of **4a**; for **4f**, R = 3.25 and R_w = 4.15 for 2289 reflections with $F > 4\sigma(F)$. Anisotropic thermal parameters were refined for all non-hydrogen atoms, and fixed thermal parameters were used for the included hydrogens. The configuration of **4f** was confirmed by Rogers η parameter refinement to 1.09(5). Rogers, D. *Acta Crystallogr., Sect. A* **1981**, *37*, 734–741.

(11) We thank Professor Bergman for pointing out this explanation: Glueck, D. S.; Wu, J.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1991**, *113*, 2041–2054.

(12) The purity of **4f** is considered to be an especially stringent test: Carpino, L. *J. Org. Chem.* **1988**, *53*, 875–878.

(13) Treatment of **4** with HCl followed by DCC-mediated coupling of the **3** so liberated with (*S*)-α-methylbenzylamine afforded the amides. Chiral shift reagents merely broadened peaks for **4**. (*S*)-α-Methylbenzylamine binds to **4**, but this complexation appears to be rapidly reversible on the NMR time scale, so far precluding determination of the enantiomeric purity of **4**.

(14) (a) **5** is mentioned, but without detail: Clark, C. R.; Bouhadir, K.; Mayfield, C. A.; DeRuiter, J. *J. Chromatogr. Sci.* **1990**, *28*, 407–412. (b) **6**: Herlinger, H.; Kleinmann, H.; Ugi, I. *Justus Liebigs Ann. Chem.* **1967**, *706*, 37–46.

(15) Kölle, U.; Kossakowski, J.; Raabe, G. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 773–774.

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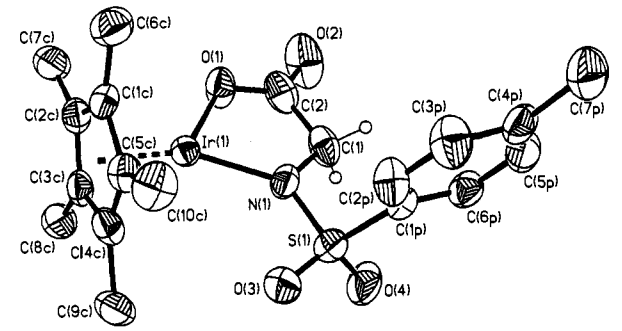

Figure 1. Molecular structure of **4a**, shown with 50% thermal ellipsoids. Hydrogen atoms other than those shown (assumed positions) are omitted for clarity. Selected bond distances (Å) and angles (deg): Ir(1)–N(1) = 1.981(7), Ir(1)–O(1) = 2.030(6), O(1)–C(2) = 1.281(11), C(2)–O(2) = 1.222(12), N(1)–S(1) = 1.629(7), N(1)–Ir(1)–O(1) = 80.3(3).

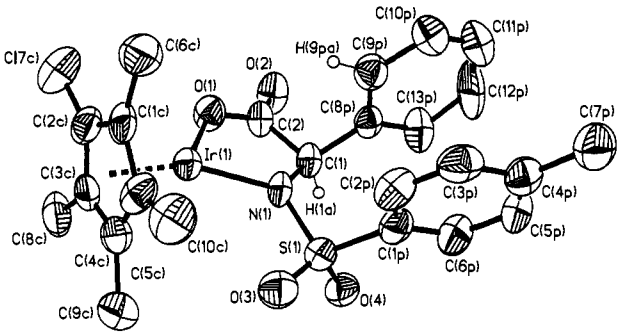

Figure 2. Molecular structure of **4f**, shown with 35% thermal ellipsoids. Hydrogen atoms other than those shown (assumed positions) are omitted for clarity. Selected bond distances (Å) and angles (deg): Ir(1)–N(1) = 1.977(9), Ir(1)–O(1) = 2.043(16), O(1)–C(2) = 1.222(20), C(2)–O(2) = 1.220(16), N(1)–S(1) = 1.646(9), N(1)–Ir(1)–O(1) = 78.8(5).

7–10. Comparison of ν_{CO} = 1684 cm^{-1} for **4a** and ν_{CO} = 1650 cm^{-1} for **7a** suggests reduced donation of electron density from O to Ir upon coordinative saturation. Further, whereas **4c** (ν_{CO} = 1672 cm^{-1}, br) shows a single set of resonances in its NMR spectrum at ambient temperatures, **7c** (ν_{CO} = 1645 cm^{-1}, br) shows *two* sets of absorptions which coalesce at elevated temperatures (ca. 90 °C at 400 MHz) and whose ratio changes with solvent. These data point to the presence of rotameric forms of *N*-Cbz-substituted complexes which interconvert rapidly on the NMR time scale at ambient temperatures in the case of **4** because the unsaturated Ir competes successfully with the carbonyl group for electron density from N. Racemic **3g** and **1** afford yellow (±)-**12** (98% yield, two rotamers, configuration at S undetermined) directly, showing the possibility of side-chain coordination.

Evaporation of a red solution of **4e** in CH_2Cl_2 (ν_{CO} = 1642, 1659 cm^{-1}) leaves a yellow solid (in KBr, ν_{CO} = 1553, 1570, 1653 cm^{-1}) which redissolves rapidly to give a red solution in noncoordinating solvents, properties ascribed to interconversion of red **4e** in solution and a yellow dimer in the solid.[4b,16]

Significantly, addition of ligand PMe_3, PMe_2Ph, or CO to chiral **4** proceeds within seconds with high diastereoselectivity (≥50:1 for **4d** and **4f**,[17] ≥25:1 for **4b**, yields ≥89%) to produce the isomer in which R and Cp* are syn,[18] results ascribed to preferred attack of the ligand from the side of the metallacycle unhindered by R.[19] The possibility that an aryl substituted played a special role (entering into C–H agostic[20,21] or η^2-coordination[22]) was discounted by (a) normal NMR chemical shifts for aryl protons[9] and (b) examination of the structure of **4f**:[10] the Ir atom is only 0.19 Å away from the mean plane of the C_6H_5 ring, but the distance between Ir and H(9pa), and nearest hydrogen of the C_6H_5 ring, is ca. 3.6 Å. As in **4a**, the chelate ring is nearly planar (all five atoms are less than 0.022 Å from the mean chelate plane), although some distortion is suggested by the distances of the Cp* centroid and S (0.099 and 0.378 Å, respectively) from that plane. The syn arrangement of C_6H_5 and $CH_3C_6H_4$ substituents (angle between mean planes, 19°) is an interesting contrast to the anti arrangement proposed for structurally uncharacterized boron-derived Lewis acids based on **3** and related species.[23]

Complexes **4** are unique coordinatively unsaturated derivatives of amino acids which enter into highly diastereoselective, rapid complexation reactions directed by steric interactions with nonpolar side chains, findings which we feel have relevance to the design of both chiral transition metal[3] and group 13[23] catalysts. Studies of the addition of other ligands to **4**, the regioselectivity of complex formation from peptides, and the use of other metal fragments are underway.

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Supplementary Material Available: Spectral data and preparations of 20 compounds and crystallographic data and refinement information for **4a** and **4f** (64 pages); listing of observed and calculated structure factors for **4a** and **4f** (14 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm edition of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(16) We cannot exclude the possibility of oligomerization, but see: Brown, L. D.; Itoh, K.; Suzuki, H.; Hirai, K.; Ibers, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 8232–8238.

(17) Reaction of $Cp^*IrPMe_3Cl_2$, **3d**, and K_2CO_3 in CH_3CN gave a mixture of **7d** and its presumed diastereomer **11d** (1:4), from which **11d** was isolated (67%). In toluene-d_8 at 110 °C, **7d** was unchanged after 17 h (^{1}H NMR) but had decomposed significantly after 85 h, although signals for **11d** were not detected. Attempts to synthesize **11b** and **11f** so far have not been successful.

(18) NOE experiments indicated syn orientation of Cp* and R (**7b**, **7f**, **9b**) and of PMe_3 and methine H (**7b**, **7f**), ref 9. Addition of PMe_3 to **4d** and of PMe_2Ph to **4b** is presumed to proceed in the same fashion.

(19) Addition of PPh_3 to **4b** appears to (a) produce a mixture (6:1) of adducts of unassigned configuration (presumably **10b** and its diastereomer) and (b) be readily reversible at room temperature.

(20) A related Cp*Ir–phenylglycine complex shows an agostic interaction: Grotjahn, D., unpublished results.

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(22) Harman, W. D.; Sekine, M.; Taube, H. *J. Am. Chem. Soc.* **1988**, *110*, 5725–5731.

(23) Deloux, L.; Srebnik, M. *Chem. Rev.* **1993**, *93*, 763–784 and references therein.