Diastereoselectivity in Enolate Coordination in a New Class of Chiral Ruthenium Enolate Complexes

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*Summary: The new chiral, carbon-bound enolate complexes Cp(CO)Ru(η^2(P,C)-$Ph_2PC_6H_4$-o-C(O)CHR), where R = H (**5a**) or CH_3 (**5b**), are formed via deprotonation of the corresponding cationic ketone complex precursors with $LiN(^iPr)_2$. The latter species is formed diastereoselectively, and the major diastereomer (S_{Ru},R_C/R_{Ru},S_C) has been structurally characterized by X-ray crystallography. Deprotonation of the ethyl ketone complex with KO^{t}Bu affords the O-bound analog (**6**), which converts to the C-bound form (**5b**) in the presence of $LiOSO_2CF_3$. Reaction of **5a** with $CH_3OSO_2CF_3$ forms the methyl enol ether complex by selective O-alkylation.*

Carbon−carbon bond-forming reactions of nucleophilic enolate anions play a major role in the selective synthesis of complex organic molecules.[2] Considering the pronounced ability of transition metals to influence the reactivity of organic fragments within their coordination spheres,[3] it is not surprising that enolate complexes of transition metals have received considerable attention in recent years.[4] Several d-block metal complexes with either oxygen- or carbon-bound enolate ligands have been isolated and structurally characterized, in one case with C-bound and O-bound forms existing in equilibrium.[5] In some cases, these complexes undergo C−C bond-forming reactions with electrophiles.[4c,d,g] Additionally, several catalytic or stoichiometric reactions are proposed to proceed via pathways involving enolate complexes as reactive intermediates.[6] While a few of the known enolate complexes are chiral (with either metal- or ligand-based stereogenicity),[4e,f,6k] we are unaware of any systematic studies of the influence of chirality on the stereochemistry of bond formation in the preparation or reactions of late-transition-metal enolate complexes. In this communication, we present our initial observations on the synthesis and structure of a new class of chiral (cyclopentadienyl)ruthenium enolate complexes, in which we observe the first reported example of regio- and stereoselectivity in coordination of the enolate moiety to a stereogenic metal center.[7]

Scheme 1 outlines the preparation of chelating enolate complexes of the $Cp(CO)(PAr_3)Ru$ fragment.[8] Treatment of $Cp(CO)_2RuCl$ (**1**) with 1 equiv of the (2-acylphenyl)diphenylphosphine ligand **2a** or **2b**[9,10] in refluxing toluene affords the chloro(cyclopentadienyl)(phosphine)ruthenium complexes Cp(CO)Ru(η^1(*P*)-$Ph_2PC_6H_4$-*o*-$COCH_2R$)Cl (**3a**, 47%, R = H; **3b**, 66%, R = CH_3) via CO displacement. Chloride abstraction ($AgOSO_2CF_3$, CH_2Cl_2) produces the cationic, chelating keto−phosphine complexes [Cp(CO)Ru(η^2(*P*,*O*)-$Ph_2PC_6H_4$-*o*-$C(O)CH_2R$)]OSO_2CF_3 (**4a**, 53%, R = H; **4b**, 79%, R = CH_3).[11,12] Addition of Et_4NCl to **4a** and **4b**

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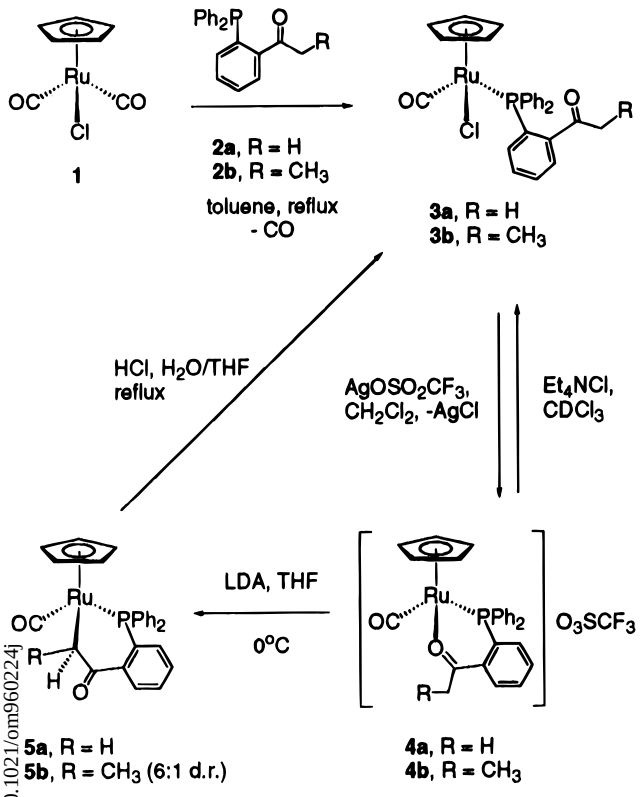
(11) Complete spectroscopic and analytical data for all new compounds are provided in the Supporting Information.

(12) The X-ray crystal structure of complex **4b** has been determined and clearly shows η^1 coordination of the oxygen in a six-membered chelate ring: Dickman, M. H., Rasley, B. T. Unpublished results, 1995. Preliminary crystal data for **4b**: $C_{29}H_{26}Cl_2F_3O_5PRuS$ (CH_2Cl_2 solvate), monoclinic, $P2_1/c$, crystal size 0.37 × 0.35 × 0.05 mm, a = 10.0426(9) Å, b = 11.3610(9) Å, c = 25.221(6) Å, $\alpha = \gamma = 90.00°$, β = 91.50(2)°, V = 2876.6(8) Å^3, Z = 4, D(calcd) = 1.592 g/cm^3, absorption coefficient 0.734 mm^{-1}, T = 293(2) K, λ = 0.710 73 Å, R = 0.0636 for 6598 reflections with $I > 2\sigma(I)$.

S0276-7333(96)00224-5 CCC: $12.00

Scheme 1



($CDCl_3$, Scheme 1) regenerates the chloro compounds **3a** and **3b** in quantitative yields, by ^{1}H NMR.

Deprotonation of the cationic methyl ketone complex **4a** (LDA, THF, 0 °C) affords the enolate complex Cp(CO)Ru(η^2(*P*,*C*)-$Ph_2PC_6H_4$-*o*-$C(O)CH_2$) (**5a**, 85%). The ^{1}H and ^{13}C NMR spectra suggest coordination via carbon: the diastereotopic methylene protons resonate at δ 2.72 (dd, J = 5.1, 5.3 Hz) and δ 2.62 (dd, J = 5.1, 8.8 Hz), and the metalated carbon resonates at δ 7.4 (d, J = 8.8 Hz). The low chemical shifts, and the substantial geminal H−H and C−P and vicinal H−P couplings, are more consistent with a Ru−CH_2C(=O)R linkage isomer than a Ru−OC(=CH_2)R species.[5] All of the other spectroscopic properties are consistent with the structure depicted in Scheme 1.

Deprotonation of the cationic ethyl ketone complex **4b** under the same conditions leads to the formation of the enolate complex Cp(CO)Ru(η^2(*P*,*C*)-$Ph_2PC_6H_4$-*o*-$C(O)CHCH_3$) (**5b**, 70%), which exists as a 6:1 mixture of carbon-bound diastereomers.[13] Diffraction-quality crystals of **5b** were obtained by slow diffusion of pentane into a toluene solution at 5 °C. The X-ray crystal structure of **5b** is depicted in Figure 1[14] and clearly demonstrates that the enolate moiety is carbon-bound. The diastereomer that crystallized exists in the (±)-(S_{Ru},R_C/R_{Ru},S_C) configuration, with the methyl group lying syn to the cyclopentadienyl ligand in the six-membered chelate ring. We propose that this species is the major diastereomer observed in solution, on the basis of the observation that the diastereomer ratio increases from 6:1 immediately after isolation by rapid precipitation, to >20:1 after slow crystallization. The mother liquor is enriched in the minor diastereomer, suggesting that the major diastereomer is isolated because it is less soluble, not because thermal equilibration occurs. In a separate experiment, heating a solution of **5b** in $CDCl_3$ (60 °C, 4 days) caused no observed interconversion of diastereomeric enolate complexes (determined by integration vs an internal standard). On the basis of this result and of the observation that different preparations of **5b** result in differing diastereomer ratios (ranging from 3:1 to 9:1), we suggest that the diastereoselectivity observed in the formation of enolate complex **5b** is kinetic rather than thermodynamic, with a high barrier to diastereomer interconversion.

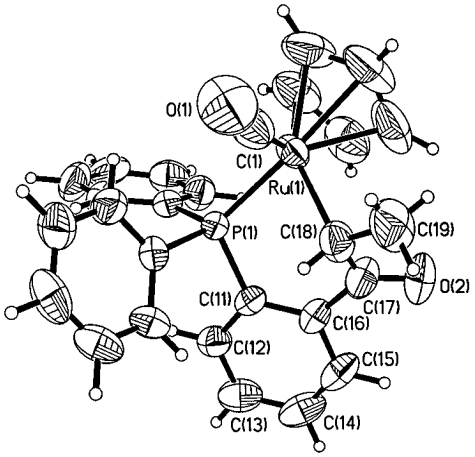
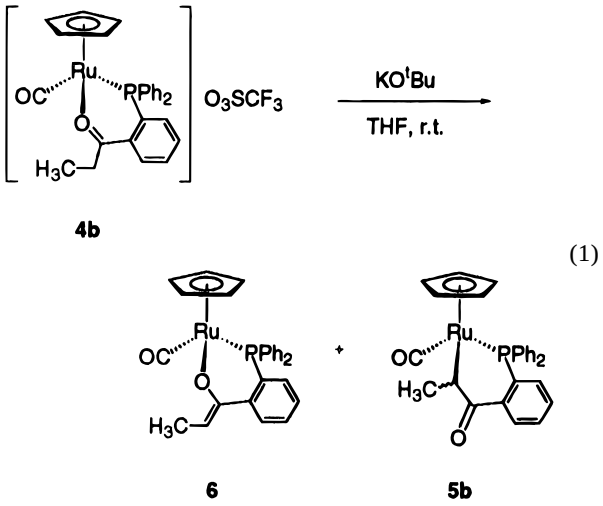


Figure 1. Thermal ellipsoid (50% probability) diagram for the molecular structure of **5b**. Selected bond distances (Å): Ru−C(18), 2.220(7); Ru−P(1), 2.277(2); Ru−C(1), 1.845(8); C(17)−C(18), 1.494(10); C(18)−C(19), 1.491(4); C(17)−O(2), 1.197(8); C(16)−C(17), 1.508(9); C(1)−O(1), 1.131(9); P(1)−C(11), 1.822(5); C(11)−C(16), 1.395(7). Selected bond angles (deg): C(1)−Ru−P(1), 94.9(2); C(1)−Ru−C(18), 87.4(3); C(18)−Ru−P(1), 82.5(2); C(17)−C(18)−Ru, 101.1(4); Ru−C(18)−C(19), 113.9(5); C(17)−C(18)−C(19), 114.6(6); C(18)−C(17)−O(2), 121.1(8); C(16)−C(17)−C(18), 118.9(6); C(16)−C(17)−O(2), 119.9(7); Ru−C(1)−O(1), 174.0(7).

The coordination mode of the enolato moiety is strongly influenced by the conditions under which the ketone complex precursor is deprotonated. Thus, deprotonation of **4b** with KO^{t}Bu in THF affords a mixture of enolate complexes (86% isolated yield), the major component of which shows an entirely new set of ligand resonances: δ 1.63 (d, J = 6.7 Hz, CH_3) and 5.35 (q, J = 6.7 Hz, CH). The downfield chemical shift of the methine proton and the absence of coupling to ^{31}P are consistent with coordination of the enolate via oxygen (**6**; eq 1). In addition, the ^{1}H NMR spectrum also shows resonances arising from the two diastereomers of **5b**, with a 20.8:2.7:1 ratio of **6**:**5b** (major):**5b** (minor). Enolate complex **6** apparently exists as a single double-bond isomer; although the precise stereochemistry has not yet been definitively established, we suggest that the *Z* isomer is more likely, on the basis of preliminary spectroscopic studies of a derivative.[15] The O-bound enolate complex **6** is not sufficiently stable to isolate;

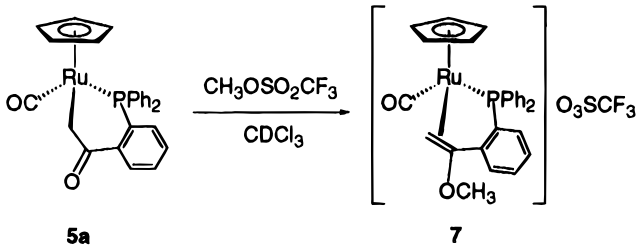
(13) The diastereomers of **5b** show ligand resonances at δ 1.55 (dd, J = 1.0, 6.2 Hz, CH_3) and δ 2.88 (dq, J = 4.2, 6.2 Hz, CH) for the major diastereomer and δ 1.57 (dd, J = 0.8, 5.9 Hz, CH_3) and δ 3.39 (dq, J = 4.0, 5.9 Hz, CH) for the minor diastereomer.

(14) Crystal data for **5b**: $C_{27}H_{23}O_2PRu$, triclinic, $P\bar{1}$, crystal size 0.40 × 0.35 × 0.05 mm, a = 9.1230(10) Å, b = 9.3190(10) Å, c = 14.2720(10) Å, α = 73.06°, β = 78.11°, γ = 82.66°, V = 1132.8(2) Å^3, Z = 2, D(calcd) = 1.500 g/cm^3, absorption coefficient 0.784 mm^{-1}, T = 293(2) K, λ = 0.710 73 Å, R = 0.0626 for 5155 reflections with $I > 2\sigma(I)$. See the Supporting Information for details on data collection and structure determination.



attempted crystallization resulted in decomposition to intractable materials. The origin of the dependence of coordination mode on the base employed remains unclear, although it may be related to the greater oxophilicity or "hardness" of Li^+ compared to K^+, which is expected to lead to tighter binding to the enolate oxygen; this effect has been invoked to explain differences in the regioselectivity of alkylation of the corresponding enolates.[16] Supporting this hypothesis is our observation that $LiOSO_2CF_3$ catalyzes the conversion of **6** to **5b**,[17] demonstrating that the nature of the countercation influences the enolate coordination mode and that the carbon-bound form is more thermodynamically stable than the oxygen-bound form. In contrast, Hartwig et al. have shown that the acetone enolate complex of $(PMe_3)_4Ru(Me)^+$ exists as an equilibrium mixture of O-bound and C-bound forms.[5] Treatment of ethyl ketone complex **4b** with other bases (e.g., $NaOH/H_2O$/THF) also yields mixtures of **5b** and **6**; however, in no case have we obtained pure **6**, nor have we observed evidence for the formation of an O-bound isomer of methylene complex **5a** via deprotonation of methyl ketone complex **4a** with KO^{t}Bu in THF. Studies designed to elucidate the precise mechanism of the kinetic formation of the O-bound enolate are in progress.

In preliminary investigations of the reactivity of these new enolate complexes, we find that reaction of **5a** and **5b** with 1 M HCl (ca. 2 equiv, THF, reflux; Scheme 1) affords the chloro complexes **3a** (86%) and **3b** (89%), presumably via protonation of the enolate, followed by displacement of the carbonyl group by chloride. Alkylation of enolate complex **5a** with 1 equiv of methyl triflate ($CDCl_3$, room temperature; eq 2) results in clean



formation of the *O*-methyl enol ether complex $[Cp(CO)Ru(Ph_2PC_6H_4$-*o*-$C(OCH_3)=CH_2)]OSO_2CF_3$ (**7**; 83% by NMR). The O-alkylation product was identified by its characteristic ^{1}H NMR and IR spectra.[18] None of the possible C-alkylation product (i.e., the chelating ketone complex **4b**) was formed, nor was alkylation observed ($CDCl_3$, 50 °C) with CH_3I or allyl bromide.

To summarize, we have demonstrated that (1) a new class of chiral, chelating, carbon-bound ruthenium enolate complexes can be prepared rationally via deprotonation of well-characterized ketone complex precursors, (2) metal-centered chirality can influence the relative configuration of a stereogenic carbon bound to the metal, and (3) while the C-bound form is intrinsically preferred over the O-bound form, the kinetic coordination mode of the enolate ligand can be controlled by varying the base used to generate the enolate complex. We suggest that the synthetic strategy described above may be general for the preparation of a variety of types of enolate complexes. These observations also raise the question of whether the stereogenicity of the metal center in a chiral enolate complex can influence the selectivity of reactions occurring within its coordination sphere, a possibility we are continuing to investigate.

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Supporting Information Available: Text giving complete synthetic procedures and characterization data for all new compounds and tables containing complete crystal and data collection parameters for **5b**, atomic coordinates and equivalent isotropic displacement parameters, bond distances and angles, anisotropic displacement factors, and hydrogen coordinates (13 pages). Ordering information is given on any current masthead page.

OM960224J

(15) Alkylation of **6** ($CH_3OSO_2CF_3$, $CDCl_3$) affords a methyl enol ether complex which exists in the *Z* configuration, by NOE difference spectroscopy; the O-alkylation is presumed to occur with retention of double-bond geometry: Rasley, B. T. Unpublished results, 1996.

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(17) Treatment of a 0.05 M C_6D_6 solution of a mixture of **6** and **5b** (9.3:1 isomer ratio) with $LiOSO_2CF_3$ (10 mol %) resulted in complete conversion to **5b** ($t_{1/2} \approx 35$ h at ambient temperature; mass balance >95%) by ^{1}H NMR, as determined by integration vs an internal standard. The conversion of **6** to **5b** also occurred in the absence of lithium triflate but was considerably slower ($t_{1/2} \approx 130$ h).

(18) Characterization data for **7**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.90−7.20 (m, 14H), 5.46 (d, $J = 0.3$ Hz, 5H), 4.38 (dd, $J = 3.5$, 2.7 Hz, 1H), 3.77 (s, 3H), 2.38 (dd, $J = 3.5$, 4.9 Hz, 1H). IR (film) 1984 (vs), 1436 (m), 1276 (vs), 1225 (m), 1157 (s), 1097 (m), 1031 (s), 705 (m), 637 (m) cm^{-1}. For examples of enol ether complexes, see: Cutler, A. R.; Raghu, S.; Rosenblum, M. *J. Organomet. Chem.* **1974**, *77*, 381−391 and references therein.