Facile Nucleophilic Addition of Methyl Ketone Enolates to (η^5-Pentamethylcyclopentadienyl)rhodium η^6-*p*-Xylene Dication

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Summary: The facile nucleophilic addition of methyl ketone enolates of acetone, 2-butanone, and 2-pentanone to (η^5-pentamethylcyclopentadienyl)rhodium η^6-*p*-xylene dication ([Cp*Rh(η^6-1,4-$(CH_3)_2C_6H_4$)$^{2+}$], **1**) were studied by using 1,2,3,4-tetrahydroisoquinoline as the base at 25 °C to provide complexes **2–4**, respectively. The regio- and stereochemistry of these ketone enolate addition reactions to **1** were unequivocably established by a single-crystal X-ray structural analysis of the acetone enolate addition product, complex **2**, to reveal that the substituted arene ligand, a 6-β-keto-substituted 1,4-dimethylcyclohexadienyl group, was bonded η^5 to Cp*Rh$^+$. The acetone enolate added to the unsubstituted carbon position on the η^6-*p*-xylene ligand of complex **1** by backside nucleophilic attack (exo to the Rh metal center). The scope of the reaction was briefly studied to show that only enolates of methyl ketones, i.e., 3-pentanone failed to react, were able to undergo this nucleophilic addition reaction to **1**. Complex **2** was oxidized with Jones reagent to release the 2,5-dimethylbenzyl methyl ketone and provides a convenient synthetic method for this class of organic compounds.

Recent studies in our laboratory have focused on the bonding of mono- and polynuclear heteroaromatic nitrogen ligands to (η^5-pentamethylcyclopentadienyl)rhodium dication (Cp*Rh^{2+})[1a] and (η^5-cyclopentadienyl)ruthenium cation (CpRu$^+$).[1b] One synthetic scheme entailed an exchange reaction with the nitrogen ligand and Cp*Rh(η^6-*p*-xylene)$^{2+}$, **1**, to provide Cp*Rh(N)$_x^{2+}$ and free *p*-xylene.[1a] While attempting to study the ligand-exchange reaction of **1** with 1,2,3,4-tetrahydroisoquinoline in acetone, we instead serendipitously discovered a facile nucleophilic addition reaction of acetone enolate to the complexed η^6-*p*-xylene ligand.

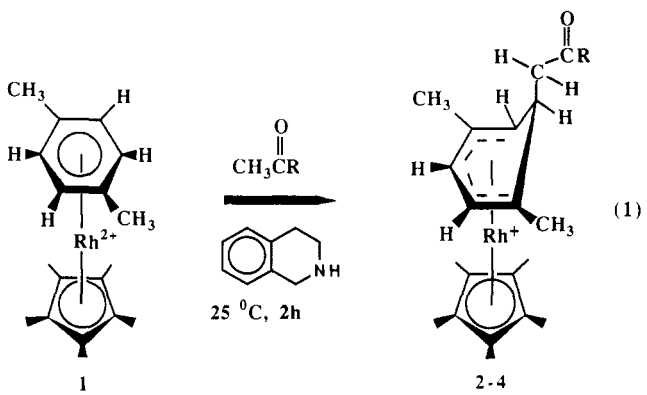
Nucleophilic additions to coordinated arenes have been extensively studied and are directly related to the electron-withdrawing ability of the metal center.[2] Since the more electrophilic arene ligands were shown to be reactive toward a variety of nucleophiles, and in particular ketone enolates,[3] it was not too surprising to find that ketone enolates readily added to a Cp*Rh(arene)$^{2+}$ complex[4] in the presence of a strong base such as 1,2,3,4-tetrahydroisoquinoline.

While no examples of the regio- or stereoselectivity of ketone enolate additions to Cp*Rh(arenes)$^{2+}$ have thus far been reported, White et al. have shown that thallium acetylacetonate added to ($C_5(CH_3)_4CH_3CH_2$)Rh(C_6H_6)(PF_6)$_2$ to provide several products and, via NMR analysis, determined that the acetylacetonyl group added to the complexes benzene ring.[5] It is also interesting to note that the strength of the base must be important, since the isomer of 1,2,3,4-tetrahydroisoquinoline, the less basic 1,2,3,4-tetrahydroquinoline, undergoes a ligand-exchange reaction with **1** in acetone to form a Cp*Rh^{2+} complex with the benzene ring (η^6) of 1,2,3,4-tetrahydroquinoline[1a] but shows no propensity to act as a base for nucleophilic enolate addition reactions.

In this paper, we demonstrate the facile addition of not only acetone enolate but also other methyl ketone enolates to **1** and establish the regio- and stereochemistry of the reaction by a single-crystal X-ray analysis of the acetone enolate addition product, **2**. We also demonstrate the synthetic utility of these nucleophilic addition reactions by using Jones reagent to release the complexed η^5-β-keto-substituted arene ligand from Cp*Rh$^+$.

Results and Discussion

The general nucleophilic addition reaction of methyl ketone enolates with complex **1** to provide complexes **2–4** is shown in eq 1. The methyl ketone enolates were formed



(1)

1 **2-4**

R = CH_3-, **2**; CH_3CH_2-, **3**; $CH_3CH_2CH_2$-, **4**

in situ by reaction with the base 1,2,3,4-tetrahydroisoquinoline and gave complexes **2–4** in yields of ~15–30% that were not optimized. The structures were determined by a combination of ^{1}H and ^{13}C NMR, elemental analysis, and in one case, complex **2**, a single-crystal X-ray analysis. The major feature of the ^{1}H NMR spectra for **2–4** (Table II, supplementary material) is the asymmetric methylene group that is adjacent to the newly generated chiral carbon center on the dimethylcyclohexadienyl ring. The 400-MHz ^{1}H NMR spectra clearly show the asymmetric methylene group as an AB portion of an ABX spin system, with a separation of each methylene proton of ~0.045 ppm. The hydrogen on the chiral carbon atom, the X portion of the ABX spin system, is also readily observed. The ^{13}C NMR spectra are also consistent with the designated structures, **2–4**, and are also tabulated in Table II (supplementary material).

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(2) (a) Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*, 2nd ed.; University Science: Mill Valley, CA, 1987; Chapter 20. (b) Davies, S. J. *Organotransition Metal Chemistry: Applications to Organic Synthesis*; Organic Chemistry Series; Pergamon Press: Oxford, England, 1982; Vol. 2, Chapter 4. (c) Semmelhack, M. F. *Pure Appl. Chem.* **1981**, *53*, 2379.

(3) Chung, Y. K.; Willard, P. G.; Sweigart, D. A. *Organometallics* **1982**, *1*, 1053.

(4) The initial nucleophilic additions to Cp*Rh(arenes)$^{2+}$ were with BH_4^-, see: White, C.; Maitlis, P. M. *J. Chem. Soc. A* **1971**, 3322.

(5) Bailey, N. A.; Blunt, E. H.; Fairhurst, G.; White, C. *J. Chem. Soc., Dalton Trans.* **1980**, 829.

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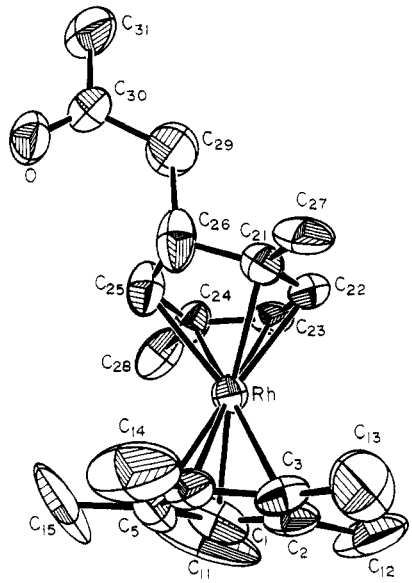


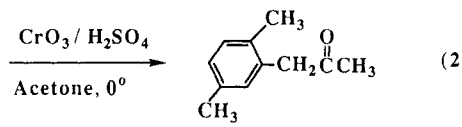
Figure 1. ORTEP diagram of $[Cp^*Rh(\eta^5\text{-}1,4\text{-}(CH_3)_2\text{-}6\text{-}(CH_2COCH_3)C_6H_4)](BF_4)$ (**2**) showing 50% probability thermal ellipsoids. Selected intramolecular bond distances are as follows: Rh(C)–Cp, 2.18 (1); C–C(C) Cp, 1.40 (2); Rh–C26, 2.63 (2); O–C30, 1.15 (2) Å. Selected intramolecular bond angles are as follows: C23–Rh–C1, 116.9 (6); C21–C26–C29, 113 (1); C30–C29–C26, 117 (1)°.

The regio- and stereochemistry of the ketone enolate addition products (eq 1) were established by an X-ray structural analysis of **2**; the ORTEP drawing of **2** is shown in Figure 1. Bond distances and angles are listed in Tables III and IV (supplementary material). The Cp* ligand is symmetrically bonded to the Rh metal atom, the Rh–C bond distance being 2.17 (2)–2.22 (1) Å. The acetonyl substituent was found to be exo to the Rh metal atom and at a position that is ortho to one of the methyl groups on an unsubstituted carbon atom, this being characteristic of other nucleophilic addition reactions.[2,3,5,6] The 1,4-dimethylcyclohexadienyl ligand is coordinated η^5 to the Rh metal center by five carbon atoms with the Rh–C bond distances being 2.15 (1)–2.32 (2) Å. The long Rh–C(26) bond distance of 2.63 (2) Å is indicative of the absence of any Rh metal bonding to the carbon atom substituted with the CH_2COCH_3 group. Similar Rh–C bond distances were observed for a $Cp^*Rh[\eta^5\text{-}C_6H_6P(O)(OMe)_2]^+$ complex containing a phosphorylated cyclohexadienyl ligand.[5]

The C(26)–C(29) bond distance of 1.65 (2) Å in complex **2** is significantly longer than a normal sp^3–sp^3 C–C single-bond distance of 1.54 Å. One possible explanation for this anomalous bond distance is indicated by the thermal ellipsoid on atom C(26). This shows that its maximum amplitude lies along the bond direction and is contrary to normal vibrational motion, which is usually greater in directions perpendicular to the bond direction (see the thermal ellipsoids for the other atoms). It is possible that the anomalously large vibrational motion of atom C(26) along the C(26)–C(29) direction could be due to a small unresolvable positional disorder of atom C(26) along that direction. Accordingly, the position of atom C(26) produced by the least-squares refinement might not represent the true atom positions and this could lead to a slightly abnormal bond length.

A brief study of the scope of the reaction indicated that only methyl ketone enolates reacted with **1** to form product, since reaction of 3-pentanone in the presence of 1,2,3,4-tetrahydroisoquinoline provided no enolate addition product. As well, methyl phenyl ketone gave a complex mixture of products, which did not provide any characterizable Cp^*Rh^+ complexes. Since the pK_a of the methylene group that is α to the carbonyl in 3-pentanone is similar to that of the α-methyl group in acetone ($\sim$20), we speculate that steric effects in the transition state prevent α-substituted ketone enolates from adding to **1**. This may possibly be a consequence of steric congestion of the ortho-methyl groups on the *p*-xylene ligand with the incoming nucleophile.

To make this a viable synthetic method for the preparation of substituted benzyl ketones, we oxidized complex **2** with Jones reagent and obtained 2,5-dimethylbenzyl methyl ketone in 60% yield (GC, eq 2).[3] The ^1H NMR and mass spectra of the isolated 2,5-dimethylbenzyl methyl ketone were in agreement with those reported in the literature.[9]



(2)

Conclusions

We have discovered a facile, regio- and stereoselective nucleophilic addition reaction of methyl ketone enolates, which were generated in situ by proton removal from the methyl ketone by 1,2,3,4-tetrahydroisoquinoline, to **1** to provide in reasonable yields the Cp^*Rh η^5-6-β-keto-substituted 1,4-dimethylcyclohexadienyl cationic complexes. The driving force for these facile addition reactions to **1** must be attributed to the electrophilicity of the complexed arene ligand, the charge on complex **1** being 2+. This nucleophilic addition method has the potential for the synthesis of a wide variety of benzyl-substituted alkyl ketones of interest to organic chemists by using an oxidation procedure with Jones reagent to release the complexed β-keto-substituted arene ligand.[2,3]

Experimental Section

Materials and Instrumentation. Complex **1**, $Cp^*Rh(p\text{-xylene})(BF_4)_2$, was prepared by the method of Maitlis et al.[7] Acetone was distilled from K_2CO_3, while methyl ethyl ketone and methyl propyl ketone were purchased from Aldrich Chemical Co. and redistilled prior to use. The diethyl ether was distilled from sodium benzophenone ketyl. The NMR spectra were recorded on a Brucker WP-400 spectrometer, and elemental analyses were performed by the Analytical Center, both located in the Department of Chemistry, University of California, Berkeley. All manipulations were performed in a two-stage Vacuum Atmospheres dry box, equipped with a −30 °C refrigerator, under an argon atmosphere.

Synthesis of $[Cp^*Rh(\eta^5\text{-}1,4\text{-}(CH_3)_2\text{-}6\text{-}(CH_3COCH_2)C_6H_4)](BF_4)$, 2. In a flask was placed 100 mg (0.193 mmol) of complex **1** in 20 mL of dry acetone along with 360 mg (2.70 mmol) of 1,2,3,4-tetrahydroisoquinoline. After this stirred for 2 h at 25 °C, 20 mL of diethyl ether was added, and the solution was then stored in the dry box refrigerator (−30 °C) overnight. The yellow solid that formed was filtered and washed with diethyl ether. Recrystallization from acetone/diethyl ether (1:1) at −30 °C

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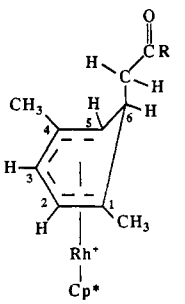
(7) White, C.; Thompson, S. J.; Maitlis, P. M. *J. Chem. Soc., Dalton Trans.* **1977**, 1654.
(8) (a) *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1975; Vol. IV. (b) *Ibid.* Table 2.3.1, pp 149–150.
(9) Hill, A. E.; Hoffman, H. M. R. *J. Am. Chem. Soc.* **1974**, *96*, 4597.

Table I. Crystal Data for Complex 2

emp formula	$RhF_4OC_{21}BH_{30}$
formula wt	488.18
cryst syst	orthorhombic
lattice params	
a, Å	15.536 (4)
b, Å	16.813 (6)
c, Å	8.409 (1)
V, Å^3	2197 (2)
space group	$P2_12_12_1$ (No. 19)
Z value	4
D_{calc}, g/cm^3	1.48
F_{000}	1000
$\mu_{Mo\,K\alpha}$, cm^{-1}	8.03
diffractometer	Rigaku AFC6
radiation	Mo Kα (λ = 0.71069 Å), graphite monochromated
temp, °C	23
$2\theta_{max}$, deg	48
no. of observations ($I > 3\sigma(I)$)	1615
no. of variables	240
residuals R, R_w	0.050, 0.058
goodness of fit indicator	1.69
max shift in final cycle	0.14
largest peak in final diff map, e$^-$/Å^3	0.80
abs corr	empirical (applied)
cryst dimens, mm	0.05 × 0.30 × 0.50
cryst faces	010,0$\bar{1}$0,100,$\bar{1}$00,11$\bar{2}$

provided 30 mg (32%) of **2**. The ^{1}H (400 MHz, $CDCl_3$, δ) and $^{13}C\{^1H\}$ NMR ($CDCl_3$, δ) data for **2** are as follows:



H(2), 5.31 (d, J_{H-H} = 5.4 Hz); H(3), 6.45 (dd, J = 5.4, 1.2 Hz); H(5), 3.55 (d, J = 6.1 Hz); H(6), 3.10 (dt, J = 4.5, 6.1 Hz); CH_2, 2.09 (d, J = 4.5 Hz), 2.14 (d, J = 4.5 Hz); 1-CH_3, 1.86 (s); 4-CH_3, 1.55 (s); R = -CH_3, 1.99 (s); Cp*(Me_5), 1.93. C(1), 72.74 (d, J_{Rh-C} = 5.3 Hz); C(2), 91.07 (d, J = 6.8 Hz); C(3), 94.04 (d, J = 6.1 Hz); C(4), 105.25 (d, J = 6.1 Hz); C(5), 56.69 (d, 8.9 Hz); C(6), 38.51 (d, J = 2.3 Hz); CH_2, 52.32 (s); 1-CH_3, 20.02 (s); 4-CH_3, 19.08 (s); CO, 206.45 (s); (C_5), 101.39 (d, J = 6.8 Hz); Me_5, 9.49 (s); R (CH_3), 30.37 (s). Anal. Calcd for $C_{21}H_{30}ORh(BF_4)$: C, 51.67; H, 6.19. Found: C, 51.82; H, 6.23.

Synthesis of [Cp*Rh(η^5-1,4-(CH_3)$_2$-6-($CH_3CH_2COCH_2$)-C_6H_4)][BF_4], 3. A similar reaction procedure as described for **2** was used to prepare **3**: 100 mg (0.193 mmol) of **1** was reacted with 360 mg (2.70 mmol) of 1,2,3,4-tetrahydroisoquinoline in 20 mL of methyl ethyl ketone. After this stirred for 2 h, 40 mL of diethyl ether was added and solution cooled to -30 °C overnight. The precipate was filtered off, an additional 40 mL of diethyl ether added, and the solution cooled again. The yellow precipate was filtered off and recrystallized from methylene chloride/diethyl ether (1:1) at -30 °C to give 15 mg (15%) of **3**. Difficulties in the separation of **3** from the BF_4^- salt of [1,2,3,4-tetrahydroisoquinolinium]$^+$ resulted in lowered yields. Anal. Calcd for $C_{22}H_{32}ORh(BF_4)$: C, 52.62; H, 6.42. Found: C, 52.84; H, 6.49.

Synthesis of [Cp*Rh(η^5-1,4-(CH_3)$_2$-6-($CH_3CH_2CH_2CO$-CH_2)C_6H_4)][BF_4], 4. A similar procedure was used for **4** as was described for **3**: 100 mg (0.193 mmol) of **1** was reacted with 360 mg (2.70 mmol) of 1,2,3,4-tetrahydroisoquinoline dissolved in 20 mL of methyl propyl ketone. After workup, 15 mg (15%) of **4** was obtained after recrystallization from methylene chloride/diethyl ether at -30 °C. Again, the yields were lowered due to separation problems of **4** from the BF_4^- salt of [1,2,3,4-tetrahydroisoquinolinium]$^+$. Anal. Calcd for $C_{23}H_{34}ORh(BF_4)$: C, 53.51; H, 6.64. Found: C, 53.09; H, 6.33.

Oxidation of 2 with Jones Reagent. A procedure similar to that published in ref 3 was used to oxidize **2**. We isolated 2,5-dimethylbenzyl methyl ketone in 60% yield and identified it by ^{1}H NMR and mass spectral analysis.[9]

Crystallographic Analysis. The yellow crystals of **2** were obtained from acetone/diethyl ether (1:1) at -30 °C. The data crystal was mounted in a thin-walled glass capillary. Diffraction measurements were made on a Rigaku AFC6 automatic diffractometer using graphite-monochromatized Mo Kα radiation. The unit cell was determined from 25 randomly selected reflections obtained by using the AFC6 automatic search center index and least-squares routines. Crystal data, data collection parameters, and results of the analysis are listed in Table I. All data processing was performed on a Digital Equipment Corp. Microvax II computer by using the TEXSAN structure-solving program library (v 2.0) obtained from Molecular Structure Corp., College Station, TX. Neutral-atom scattering factors were calculated by the standard procedures.[8a] Anomalous dispersion corrections were applied to all non-hydrogen atoms.[8b] Full-matrix least-squares refinements minimized the function

$$\sum_{hkl} w(|F_{obs}| - |F_{calc}|)^2$$

where

$$w = 1/\sigma(F)^2$$

$$\sigma(F) = \sigma(F_o^2)/2F_o$$

$$\sigma(F_o^2) = [\sigma(I_{raw})^2 + (PF_o^2)^2]^{1/2}/Lp$$

Complex **2** crystallized in the orthorhombic crystal system. The space group $P2_12_12_1$ was determined from systematic absences observed during data collection. The structure was solved by the heavy-atom method, which provides the coordinates of the rhodium atom. The coordinates of all remaining non-hydrogen atoms were obtained by difference Fourier syntheses. All non-hydrogen atoms were refined by using anisotropic thermal parameters. Hydrogen atom positions were calculated by assuming idealized geometries and employing observed positions whenever possible. The contributions of these hydrogen atoms were added to the structure factor calculations, but their positions were not refined. The BF_4^- counterion was found to exhibit a 3-fold rotational disorder, such that the boron atom and one fluorine atom were not disordered, but the remaining three fluorine atoms were disordered between two conformations, with one rotated 60° to the other.

In the final stages of analysis, a test for the anantiomorph of the structure was performed by inverting the coordinates of all the atoms and refining again. The results of this test yielded R factors that were identical with the first form. Thus, the data showed no preference for the enantiomorph, and the parameters for the original determination were retained. Error analyses were calculated from the inverse matrix obtained on the final cycle of refinement.

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Supplementary Material Available: Tables of ^{1}H and ^{13}C NMR data, bond lengths, and bond angles (7 pages); a table of observed and calculated structure factor amplitudes (11 pages). Ordering information is given on any current masthead page. Atomic coordinates have been submitted to the Cambridge Crystallographic Center.