Synthesis and Reactions of Enantiopure (Neomenthylcyclopentadienyl)iridium(III) Halides with Silver Salts. A Dramatic Steric Effect on the Competition between Inter- and Intramolecular C–H Activation

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Summary: Reactions of enantiomerically pure (NMCp)M(PMe$_3$)(Me)X complexes (NMCp = neomenthylcyclopentadienyl; M = Rh, Ir) have revealed that the 16-electron (NMCp)M(PMe$_3$)(Me)$^+$ intermediates are achiral (planar) at the metal centers on the time average. Generation of the presumed intermediate (NMCp)Ir(PMe$_3$) by photolysis of (NMCp)Ir(PMe$_3$)(H)$_2$ in the presence of hydrocarbons results in intermolecular C–H activation. In contrast, the presumed intermediate (NMCp)M(PMe$_3$)(Me)$^+$ exhibits only intramolecular C–H activation involving the neomenthyl group. One of these cyclometalation products has been structurally characterized. The different outcomes of these two systems are attributed to energy differences in the transition states based on molecular mechanics calculations.

Enantiomerically resolved organometallic complexes have become increasingly useful in mechanistic studies[1–4] and in applications to organic synthesis.[5–11] To look for ways to extend chiral chemistry to C–H activation, we have begun to explore the development of pseudotetrahedral iridium- and rhodium-based C–H activating systems containing enantiomerically resolved ligands. Our initial goals are the development of useful methods for preparing such systems and determining the configurational stability of the chiral metal centers. In the first of these results, reported here, we have found a surprising intramolecular C–H activation/dehydrogenation reaction that results in significant amplification of enantiomeric excess at the chiral Ir center in the product mixture.

For our initial experiments we chose to investigate the reactivity of the chiral systems (NMCp)(L)M(R)X (M = Ir, Rh) containing the enantiomerically pure neomenthylcyclopentadienyl ligand (NMCp) as both an NMR and resolution handle. The preparations of the Ir compounds have been based on their Cp analogs without significant modification.[12] The synthesis of [NMCpRhCl$_2$]$_2$ was previously reported,[13] and preparations of the subsequent derivatives are similar to those of the Ir analogs.

The recent discovery in our group of an exceptionally reactive racemic complex[14] Cp*Ir(Me)(PMe$_3$)(OTf) (OTf = OSO$_2$CF$_3$) that activates nonfunctionalized hydrocarbons under ambient conditions prompted us to investigate the possibility of stereoselective C–H activation using its optically resolved analogs. In an attempt to replace the iodide in **1a** and **1b**, its diastereomer having the opposite stereochemical configuration at Ir,[15] with the more weakly coordinating OTf$^-$ ligand, we treated each complex with 1 equiv of AgOTf in CD_2Cl_2 at room temperature. In both cases, immediate gas evolution was noted and ^{1}H NMR spectra indicated the formation of methane and two iridium hydride species. When **1a** was treated with AgSbF$_6$ at room temperature, four products (**2a–2d**) were formed in a 5:1:1:5 ratio, all exhibiting coupling of their hydride ligands to phosphorus.[16] Over a period of 24 h at 20 °C, the two minor isomers in this kinetic product mixture disappeared and an equilibrium ratio of 9:1 was noted for the two remaining isomers. Only isomer **2a**, arising from overall loss of halide and CH_4 (Scheme 1), was isolated in crystalline form. In CD_2Cl_2 solution its proton NMR spectrum matched that of the major thermodynamic isomer, whose stereochemistry was designated as $R_{Ir}R_C$ on the basis of a single crystal X-ray diffraction study.[17,18] An ORTEP diagram of this complex is illustrated in Figure 1. The minor thermodynamic isomer, **2d**, was assigned the stereochemistry $S_{Ir}S_C$ on the basis of evidence from ^{1}H NMR NOE experiments which demonstrate that the hydride ligand is located syn to the vinyl methyl group, as shown in Scheme 1. The two minor isomers observed in the initial reaction mixture are presumably the corresponding epimers of the two major species and have

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(15) Diastereomer **1a** can be enriched (de >95%) by fractional crystallization from diethyl ether solution. It is assigned as the diastereomer with an *R* configuration at the Ir center on the basis of 2D-NOESY and 1D NOE NMR experiments. The detailed characterization and assignments will be published elsewhere.
(16) An equal molar amount of AgSbF6 was added to the solution of **1** in CD_2Cl_2 at 20 °C. The reaction mixture was immediately filtered, and the filtrate was examined by proton NMR spectroscopy. These measurements were usually taken within 5 min of the initial mixing.
(17) Anal. Calcd for **2a**, $C_{22}H_{39}OPF_6IrSb$: C, 33.94; H, 5.05. Found: C, 33.47; H, 4.97. ^{1}H NMR (400 MHz, CD_2Cl_2, 25 °C): δ 6.26 (m, 1H, NMCp*H*), 5.82 (m, 1H, NMCp*H*), 5.79 (m, 1H, NMCp*H*), 5.66 (m, 1H, NMCp*H*), 4.08 (s, 1H, MeC=C*H*H, trans to Me), 2.22 (d, 1H, MeC=C*H*H, $^3J_{P-H}$ = 12.2 Hz, cis to Me), 2.07 (s, 3H, *Me*C=CH$_2$), 1.78 (d, 9H, P*Me*$_3$, $^3J_{P-H}$ = 11.3 Hz), 0.90 (d, 3H, H$_3$C(15), $^3J_{H-H}$ = 6.1 Hz), −16.95 (d, 1H, IrH, $^3J_{P-H}$ = 33.1 Hz). Assignment of the rest of the aliphatic protons was not attempted due to their complexity. ^{13}C{^{1}H} NMR (101 MHz, CD_2Cl_2, 25 °C): δ(C) 120.3, 83.2; δ(CH) 95.6, 95.2, 82.3, 79.1; δ(CH$_2$) 35.6, 33.72, 31.20, 28.1; δ(CH$_3$) 28.5, 22.2, 21.8 ($^2J_{P-C}$ = 42 Hz). ^{31}P{^{1}H} NMR (162 MHz, CD_2Cl_2, 25 °C): δ −37.8.

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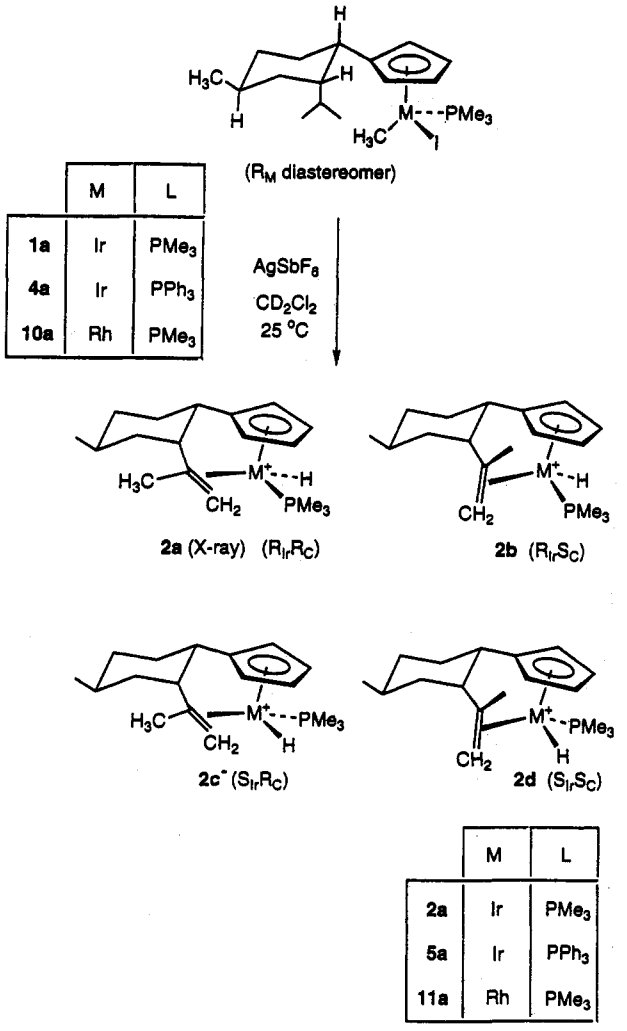
Scheme 1



been assigned by inference as **2b** and **2c**, respectively. We believe that their thermodynamic instability relative to that of **2a** and **2d** is due to an unfavorable steric interaction between the PMe_3 group and the proximal methyl group on the coordinated double bond.

As nearly as we can determine by ^1H NMR monitoring of the reaction at low temperature, the kinetic ratio of alkene hydride products appears to be independent of the stereochemistry of the starting halide when the reaction is run either at room temperature or at −77 °C, indicating that an intermediate achiral at Ir (at least on the average), such as complex **3** in Scheme 2, precedes the cyclometalation step. For each diastereomer the kinetic product distribution does, however, depend strongly on the reaction temperature. When the reaction was carried out at −77 °C, the initial product ratio **2a:2b:2c:2d** was approximately 1:1:1:5, in contrast to the ratio 5:1:1:5 measured in the room temperature reaction, as discussed above. Interestingly, **2d**, the less stable isomer in the final equilibrium, was the kinetically favored product at low temperature.

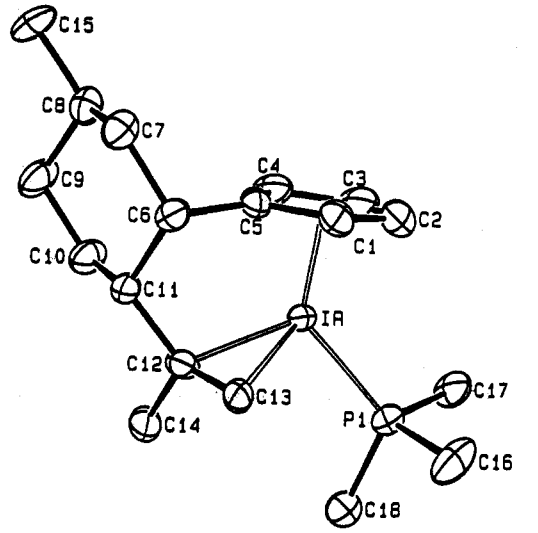
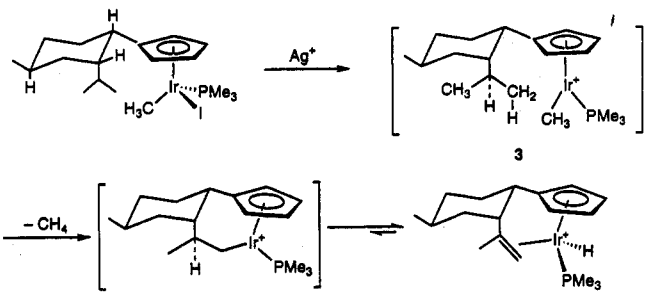


Figure 1. ORTEP drawing of **2a**. Selected bond distances (Å) and angles (deg): Ir–Cp, 1.868; Ir–P_1, 2.277(2); Ir–C_{12}, 2.119(9); Ir–C_{13}, 2.182(9); C_{12}–C_{13}, 1.378(12); Cp–Ir–P_1, 130.4; Cp–Ir–C_{13}, 118.1; C_{12}–Ir–P_1, 111.00(22); C_{13}–Ir–P_1, 90.11(25); C_{13}–Ir–C_{12}, 36.7(3).

Scheme 2



When the triphenylphosphine analog of **1**, (NMCp)IrMe(PPh_3)I, **4**, was treated with $AgSbF_6$, similar cyclometalation of the neomenthyl group resulted to give **5**,[19] the PPh_3 substituted complex analogous to **2**. There was no evidence for attack on the phenyl group of the phosphine ligand, which is normally an easy target for orthometalation.[20] The Ir–Ph bond in NMCpIrPh(PMe_3)I, **6**, undoubtedly a substantially stronger bond than Ir–Me,[21] also underwent replacement by cyclometalation to give benzene and **2** when treated with $AgSbF_6$. We believe that this reaction is reversible, however, because deuterium was incorporated extensively into the coordinated isopropenyl group of **2** when the compound was heated at 90 °C in benzene-d_6.

To investigate whether the formation of **2** proceeds by initial intermolecular activation of solvent followed by metathesis with the neomenthyl C–H bond, we examined the labeling pattern in the extruded methane when the cyclometalation reaction was carried out in C_6D_6. No CDH_3 was detected in the product mixture. We conclude that the reaction proceeds exclusively via direct intramolecular C–H activation. To compare the reactivity of this system with the well-known C–H activation behavior of the corresponding iridium dihydride,[20] we prepared

(18) A crystal of **2**($R_{Ir}R_{C12}$)·THF ($IrSbPF_6C_{22}H_{39}$, FW 778.5) covered by Paratone N hydrocarbon oil was enclosed in a glass capillary and mounted on an Enraf-Nonius CAD-4 diffractometer. Cell parameters: monoclinic space group $P2_1$ ($Z = 2$); $\beta = 98.0°$, $a = 8.2944(13)$ Å, $b = 18.4223(24)$ Å, $c = 8.8151(12)$ Å, and $V = 1333.8(6)$ Å^3. A total of 3304 unique reflections were measured, of which 2726 with $F^2 > 3\sigma(F^2)$ were used in the refinement (289 variables), with $R = 0.0228$, $R_w = 0.0237$, and GOF = 0.77. The R value for all 3304 data was 0.0322. Full details of data collection and refinement are included in the supplementary material. The hydride attached to the Ir was not located directly by the structure analysis, but its presence is clearly evident from NMR and the geometry around the Ir atom.

(19) The characterization of **4** is provided as supplementary material. There are also two isomers of **5** in the final equilibrium mixture in a ratio of 17:83, similar to the reaction involving compound **2**. The spectroscopic characterization of the major isomer (**5a**) is included as supplementary material.

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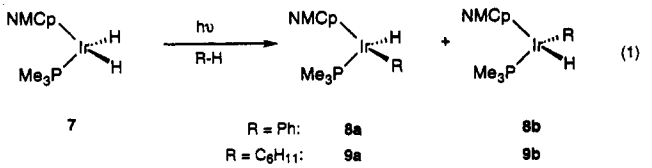
(NMCp)Ir(H)$_2$(PMe$_3$), **7**, and subjected it to ultraviolet irradiation in benzene and cyclohexane. In contrast to the behavior of **1**, only the products of *intermolecular* C–H activation of solvent were formed (eq 1). Further-



7 R = Ph: **8a** **8b**; R = C_6H_{11}: **9a** **9b**

more, diastereoselectivity in the dihydride photolysis is insignificant; the ratio of the two diastereomeric hydrido(phenyl)iridium products, **8a** and **8b**, formed in benzene solvent is 48:52,[22] and it is also approximately 1:1 in the cyclohexane case.

The Rh analog of **1**, (NMCp)RhI(Me)(PMe$_3$), **10**, exhibits similar reactivity toward AgSbF$_6$. The reaction goes to completion instantaneously at room temperature to give four isomers of **11**, which are analogous to those of **2** (Scheme 1). However, the reactivity of the Ir and Rh complexes toward AgOTf is somewhat different. The rate of reaction is much slower for the Rh system, allowing an intermediate triflate complex, NMCpRh(PMe$_3$)(Me)(OTf), to be detected by NMR spectroscopy. Over the course of a few hours, this triflate-bound intermediate releases methane followed by β-hydride elimination to give the cyclometalated product at room temperature, whereas the Ir triflate apparently undergoes such rapid cyclometalation under the same conditions that it cannot be observed by conventional spectroscopic techniques.

When the reaction between **1** and AgSbF$_6$ was carried out in acetonitrile, intramolecular C–H activation was no longer observed. Instead, simple replacement of halide by acetonitrile occurs, giving the salts [NMCpM(PMe$_3$)(NCCH$_3$)Me]SbF$_6$. Once again, however, the stereochemistry of this reaction results in complete scrambling at the Ir center: when a sample of **1a** (R_{Ir} isomer) was used in this reaction in CD$_3$CN, a 1:1 ratio of the acetonitrile-bound diastereomers was observed by NMR spectroscopy within 10 min of the initial mixing. Exchange of CH$_3$CN into these products has a half-life of 1 h, suggesting that epimerization at the Ir center precedes the coordination of an acetonitrile molecule.

A suggested mechanism for the cyclometalation/β-hydride elimination reaction is illustrated in Scheme 2. The high reactivity of AgSbF$_6$ compared to AgOTf, as well as the fact that the rhodium triflate reacts more slowly than the iridium triflate, suggests that a cationic intermediate having an available coordination site at the metal center (e.g., complex **3** in Scheme 2) is required for the cyclometalation. The fact that the kinetic ratio of cyclometalation/β-hydride elimination products is independent of the stereochemistry of starting material **1** suggests that the 16-electron cationic iridium complex **3** (or a solvate of this material) is planar at iridium at least on the time average. Running the cyclometalation/β-hydride elimination at −77 °C, or carrying out the reaction of **1** with Ag$^+$ in acetonitrile (which results in trapping the cationic Ir center before it can attack the neomenthyl group), still does not lead to stereoselective conversion of the diastereomers of **1**. The fact that the cationic intermediate loses its stereochemistry faster than it combines with CH$_3$CN contrasts with the more configurationally stable behavior of the 16-electron pyramidal CpRe(NO)(PPh$_3$)$^+$ systems extensively studied by Gladysz et al.[11]

There has been some discussion in the literature of the relative rates and thermodynamics of intra- vs intermolecular C–H activation.[23-25] A delicate balance of steric and electronic influences on the inter- and intramolecular pathways is clearly demonstrated in the present work. The difference between the two 16-electron species, (NMCp)Ir(PMe$_3$)(Me)$^+$ and (NMCp)Ir(PMe$_3$), is the presence of the Me$^+$ moiety. The former intermediate undergoes only intramolecular C–H activation whereas the latter exclusively activates C–H bonds intermolecularly. In order to examine the steric differences between these related systems, we have carried out molecular mechanics calculations on C–H activation with the following four systems, with the indicated results (potential energies in kcal/mol):[26] (Cp)(PMe$_3$)Ir to (Cp)(PMe$_3$)Ir(Ph)(H), 10.2; (NMCp)(PMe$_3$)Ir to (NMCp)(PMe$_3$)Ir(Ph)(H), 9.8; (Cp)(PMe$_3$)Ir(Me)$^+$ to (Cp)(PMe$_3$)Ir(Me)(Ph)(H)$^+$, 26.2; (NMCp)(PMe$_3$)Ir(Me)$^+$ to (NMCp)(PMe$_3$)Ir(Me)(Ph)(H)$^+$, 31.1. We draw two conclusions from these calculations: (1) the rather obvious idea that charge-neutral CpIrL and (NMCp)IrL centers are substantially less crowded than the methyl-containing CpLIrMe$^+$ and NMCpLIrMe$^+$ centers, and therefore experience less resistance overall to R–H oxidative addition; (2) *the more subtle insight that the neomenthyl group attached to the Cp ring in the (NMCp)Ir–Me$^+$ intermediate causes 4.9 kcal/mol more steric resistance to R–H oxidative addition than the amount calculated for the non-neomenthyl-containing CpIr–Me$^+$ system.* Addition of a neomenthyl group to the Cp ring of the CpIrL system produces a much smaller energetic differential (0.4 kcal/mol). The result of this difference is that both CpIrL and NMCpIrL can undergo easy intermolecular C–H activation. However, in the (NMCp)IrMe$^+$ system, a much higher activation energy for the intermolecular C–H activation results in a more favorable energy for cyclometalation and this pathway becomes predominant.

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Supplementary Material Available: Textual presentation of analytical and spectral data of the compounds prepared in this study, an ORTEP diagram, and tables of crystallographic data, positional and anisotropic thermal parameters, and bond distances and angles for the structural analysis of compound **2a** (11 pages). This is provided with the archival edition of the journal, available in many libraries. Alternatively, ordering information is given on any current masthead page.

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(22) The phenyl(hydrido)iridium species was converted to its iodo analogue NMCpIr(I)(phenyl)(PMe$_3$), **6**, by treatment with CHI$_3$. The S_{Ir} isomer (**6b**) has been resolved, and its analysis and spectroscopic data are included as supplementary material.

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