Michael addition to α,β-unsaturated arene ruthenium(II) cyclopentadiene complexes: *endo* nucleophilic addition

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Certain carbon and sulfur nucleophiles add to the β-terminus of the styrene system in α,β-unsaturated arene ruthenium(II) cyclopentadiene complexes, and unexpected *endo* addition occurs preferentially in some cases.

Metals in either their neutral (Cr^0, Fe^0, Mo^0) or charged state (Fe^{II}, Ru^{II}, Pd^{II}, Os^{II}, Co^{II}) activate complexed unsaturated ligands towards nucleophilic addition.[1] This behaviour is due to net inductive withdrawal of electron density from the ligand and stabilization of the anionic charge resulting from addition of the nucleophile. The addition of the nucleophile occurs on the *exo* face of the ligand, distal to the metal.[2] Within the context of this direct nucleophilic addition to the complexed ligand, one might anticipate that conjugate addition could likewise occur in α,β-unsaturated ligated systems such as styryl or 1,2-dihydronaphthalene, and indeed this has been observed; in both cases η^6-chromium(0) complexes of the aromatic ring were used. In the simplest case, tricarbonyl(η^6-styrene)chromium,[3] this type of reaction occurred in 7–30% yield, but with a discouraging mixture of side-products. Better synthetic results were obtained by Semmelhack and in the case of addition of $LiCMe_2CN$ upon tricarbonyl(η^6-1,2-dihydronaphthalene)chromium.[3b,4] The stereochemistry of the product was proposed to correspond to *exo* addition, on the basis of a ^1H NMR spectrum of the decomplexed ligand.[4a] Two other examples of conjugate addition to arene-$Cr(CO)_3$ complexes were reported.[5]

Because of our interest in nucleophilic displacement reactions upon (η^6-arene)(η^5-cyclopentadienyl)ruthenium(II) complexes,[6] we studied the Michael addition in this series with α,β-unsaturated arene ligands. The objectives were to make the reaction more synthetically useful, partly as the rate of the nucleophilic displacement, *via* addition-elimination, on aryl halides increases in the order $Cr^0(CO)_3 < Mo^0(CO)_3 \ll CpFe^+ < Mn^+(CO)_3$,[7] and also to establish the stereochemistry of the addition relative to the result observed with the $Cr(CO)_3$ group. The substrates and transformations are shown in Scheme 1.[8]

Pure *endo* forms of products **2b** and **2c**, and the *exo* form of **4** could be separated *via* fractional recrystallization from acetone–water and the X-ray structures of the major isomers could be determined.‡

The X-ray structure of the major product from reaction of **1c** with KCN is in Fig. 1. The Cl Me and C2 CN are *syn* and on the same face as the metal. This highly strained array corresponds
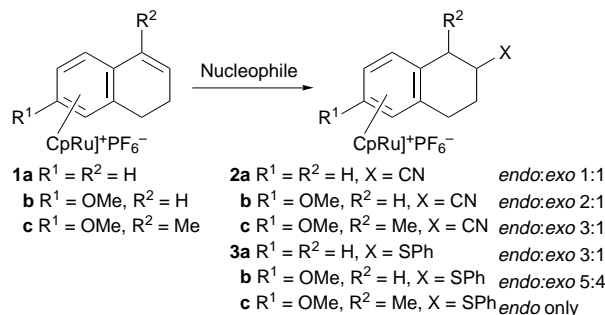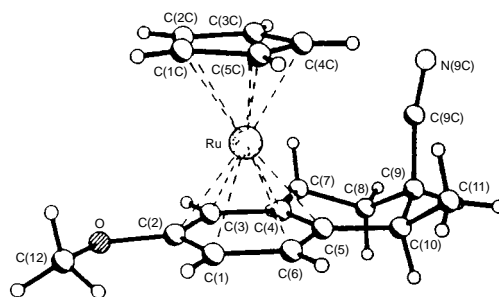

Fig. 1 X-Ray structure of compound **2c**

to *endo* addition and *exo* protonation and differs from the result observed for conjugate addition in two cases in which the stereochemistry was determined.[3b,5b] A similar preference for the *endo* addition was determined from combined NMR and X-ray studies of other products in our study (Scheme 1). An X-ray of the major component of product **2b** also shows *endo* selectivity. The major component of product **4** was the 'expected' *exo*.

How is one to explain *endo* nucleophilic addition? In a direct displacement upon a metal-complexed aromatic ring, basically an S_N2 type mechanism, the nucleophile attacks at the carbon atom undergoing displacement forming a new bond to that center (with inversion) with concomitant cleavage of a bond to the metal, *i.e.* the ligated metal is the 'leaving group'.[10] This description requires *exo* attack. Conjugate addition of the type studied here is controlled by the stereoelectronic effects of the S_N2' reaction.[11] This process occurs with *syn* stereochemistry, although it has not been recognized that the carbon–metal bond could constitute the leaving group [Fig. 2(*a*)]. Fig. 2(*b*) shows the orbital representation which reveals the LUMO of the complex and the preference for *syn* addition.

The reactions were generally slower for **1b** as compared to **1a** (rate retarding effect of OMe) and slower still for **1c** (steric effect of Cl methyl group). With KCN (5 equiv.) in DMF–H_2O in the presence of NH_4Cl (3 equiv.), the conditions required for the complete disappearance of the starting material for 70 °C overnight for **1a → 2a** and 90 °C overnight for **1b → 2b** and **1c → 2c**. The yields of *endo/exo* mixtures of isomers after chromatographic separation on silica gel (acetone–CH_2Cl_2 1 : 4) were 86 (*endo : exo* 1 : 1), 85 (*endo : exo* 2 : 1) and 82% (*endo : exo* 3 : 1) respectively. The reactions with thiophenol

Scheme 1

1a $R^1 = R^2 = H$
b $R^1 = OMe$, $R^2 = H$
c $R^1 = OMe$, $R^2 = Me$

2a $R^1 = R^2 = H$, $X = CN$ — *endo:exo* 1:1
b $R^1 = OMe$, $R^2 = H$, $X = CN$ — *endo:exo* 2:1
c $R^1 = OMe$, $R^2 = Me$, $X = CN$ — *endo:exo* 3:1
3a $R^1 = R^2 = H$, $X = SPh$ — *endo:exo* 3:1
b $R^1 = OMe$, $R^2 = H$, $X = SPh$ — *endo:exo* 5:4
c $R^1 = OMe$, $R^2 = Me$, $X = SPh$ — *endo* only

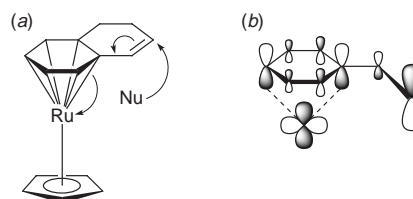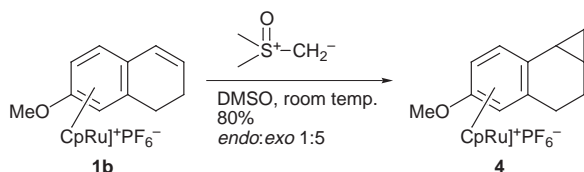**Fig. 2** (*a*) The S_N2' type mechanism illustrating *endo* conjugate nucleophilic addition to styrene-type substrates complexed to Ru^{II}. (*b*) Simple orbital diagram which represents LUMO calculated from ZINDO for the $CpRu(C_{10}H_{10})^+$ model.

Scheme 2

(1.5 equiv.) were carried out in NMR tubes in CD$_3$CN in the presence of Hunig's base (Pr$^i_2$NEt). Judging by the disappearance of the signals of the starting material in the NMR spectrum, substrate **1a** reacted completely in 30–45 min when 2 equiv. of base was used at 45 °C, and overnight with only 0.5 equiv. of Hunig's base at 25 °C. Substrate **1b** reacted completely at 45 °C overnight in the presence of Hunig's base (0.5 equiv.), and substrate **1c** reacted in only *ca.* 80% when treated with Hunig's base (0.5 equiv.) at 60 °C for 36 h. The observed *endo*:*exo* ratios were: **3a** (3:1), **3b** (5:4) and **3c** (*endo* only).

A more advanced example is the Corey–Chaykovsky cyclopropanation in which dimethyloxosulfonium methylide[9] is used in a reaction which occurs at room temp. within minutes (**1b** → **4**) (complete disappearance of the starting material, 80% isolated yield after chromatography, *endo*:*exo* 1:5, Scheme 2).

How does one reconcile *endo* addition with the observed *exo* addition of Semmelhack and others?[3b,5a] These workers used Li carbon anions and the conjugate addition in these cases is reversible.[12] Accordingly, the least hindered *exo* (*cis*-1,2) product perdominates. In contrast, our cyanide addition method involving *in situ* NH$_4$Cl/H$_2$O insures formation of the kinetic product, by immediate protonation at the benzylic position. Kinetic control is also possible in the addition of PhSH in the presence of less than 1 equiv. of base. In agreement with the interpretation, cyclopropanation (**1b** → **4**) yields the *exo* product in 5:1 ratio because of the reversibility associated with carbanion addition in the absence of a protic acid.[9,13] Semiempirical quantum calculations (ZINDO, INDO1 level basis set)[14] on a (η^5-cyclopentadienyl)(η^6-1,2-dihydronaphthalene)-Ru cation model complex, as well as its Fe substituted analog, indicate that a nucleophilic attack at the *endo* face of the conjugated π-system is slightly preferred over the *exo* face. Furthermore, the model calculations indicate that an *anti* stereochemistry of protonation to the resulting η^5-pentadienyl form of the intermediate [Fig. 2(*a*)] as the α-styryl C would be expected, consistent with the major selectivity observed in the Ru system reported here. Interpreting these predictive models in the context of the stereochemistries reported for S$_N$2′ addition[11] indicate that a general model in which attack of the nucleophile *syn* to the leaving group (Ru–C bond) in π-complexed styryl or dihydronaphthyl complexes is reasonable. Further theoretical and experimental studies are in progress to test this hypothesis.

Notes and References

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‡ *Crystal* data for **2b** (major): C$_{17}$H$_{18}$F$_6$NOPRu, *M* = 498.367, monoclinic, *P*2$_1$/*c*, *a* = 7.5734(11), *b* = 16.771(2), *c* = 14.6457(12) Å, *U* = 857.3(4) Å^3, *T* = 294(2) K, *Z* = 4, μ = 0.996 mm^{-1}, 4264 reflections measured (θ$_{max}$ = 27.50°), 3878 independent (*R*$_{int}$ = 0.0124) with 3182 observed [*I* > 2σ(*I*)]. For **2c** (major): C$_{18}$H$_{20}$F$_6$NOPRu, *M* = 512.394, orthorhombic, *P*2$_1$*P*2$_1$*P*2$_1$, *a* = 28.326(3), *b* = 7.1095(6), *c* = 9.7180(7) Å, *U* = 1957.1(3) Å^3, *T* = 294(2) K, *Z* = 4, μ = 0.946 mm^{-1}, 2917 reflections measured (θ$_{max}$ = 21.96°), 2395 independent (*R*$_{int}$ = 0.0106) with 1727 observed [*I* > 2σ(*I*)]. For **4** (major): C$_{17}$H$_{19}$F$_6$OPRu, *M* = 485.3681, monochlinc, *P*2$_1$, *a* = 8.921(3), *b* = 25.389(7), *c* = 9.037(3) Å, *U* = 1805.0(10) Å^3, *T* = 294(2) K, *Z* = 4, μ = 1.019 mm^{-1}, 2675 reflections measured (θ$_{max}$ = 23.47°), 2413 independent (*R*$_{int}$ = 0.0144) with 1921 observed [*I* > 2σ(*I*)]. CCDC 182/811.

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5 (*a*) M. Uemura, T. Minami and Y. Hayashi, *J. Chem. Soc., Chem. Commun.*, 1984, 1193. This paper reported the Michael addition of LiC(CN)MeCOCHMeOEt to tricarbonyl(5-methoxy-1,2-dihydronaphthalene)chromium. *Exo* addition was assumed. (*b*) P. Bloem, D. M. David, L. A. P. Kane-Maguire, S. G. Pyne, B. W. Skelton and A. H. White, *J. Organomet. Chem.*, 1991, **407**, C19 and references cited therein. These workers studied the addition of MeLi to tricarbonyl(*N*-benzylidene-1-methylaniline)chromium. *Exo* addition was determined by X-ray analysis.

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8 Various nitrogen nucleophiles (hydrazine, methylhydrazine, *gem*-dimethylhydrazine, 1,2-dimethylhydrazine, 1,2-ethylenediamine, ethylamine, ethanolamine) were also studied. Oxygen nucleophiles did not undergo addition to **1a**–**c** under our conditions. Since no stereochemical *endo*:*exo* assignments could be reliably made from the available data, the nitrogen nucleophiles (NMR tube experiments, [^{2}H$_6$]DMSO) were not extensively included in the present study. Still, they displayed extremely interesting reactivity patterns worth noting (data from ^{1}H NMR, ^{13}C NMR, HRMS + FAB analysis). With H$_2$NNH$_2$, H$_2$NEt and H$_2$NCH$_2$CH$_2$NH$_2$, **1**–**c** reacted completely in 30 min at rt (*ca.* 80% conversion of **1a** in the first 5 min). H$_2$NNHMe adds slower than hydrazine itself, and H$_2$NNMe$_2$, adds even slower. H$_2$NCH$_2$CH$_2$OH reacted very slowly, with <30% conversion, when heated up to 100 °C. Pr^{i}NH$_2$ and MeNHNHMe did not react even after 48 h at rt or 60 °C overnight.

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12 Semmelhack presents evidence of a mobile equilibrium between I and II. The example of ref. 5(*b*) is complicated by the α,β-unsaturation being –N=CHPh.

13 An X-ray structure of the major component of product **4** has been obtained.

14 Molecular orbital and predictive results were obtained using M. C. Zerner's ZINDO program (version 3.0) from CAChe Scientific. Atomic coordinates were first optimized using molecular mechanics (augmented CAChe MM2 force field), and orbital energies calculated directly using the INDO 1 basis set. Self-consistent field molecular orbital energies were obtained in the restricted Hartree–Fock level within 4 Å self-consistent reaction field (SCRF) cavity with the relative permittivity and refractive index of water.