Regioselective Allylic Substitution

$[Cp^*(\eta^2\text{-bipy})(MeCN)Ru^{II}][PF_6]$ Catalysts for Regioselective Allylic Substitution and Characterization of Dicationic $[Cp^*(\eta^2\text{-bipy})(\eta^3\text{-allyl})Ru^{IV}][PF_6]_2$ Intermediates**

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Ruthenium catalysts such as $[Cp(cod)RuCl]/NH_4PF_6$ or $[Cp^*(cod)RuCl]$ (cod = 1,5-cyclooctadiene) have gradually disclosed an increasing efficiency in assisting allylic substitution reactions.[1] In light of the advantage of the unusual regioselectivity provided by ruthenium catalysts, an efficient access to antidepressant drugs was recently reported by using

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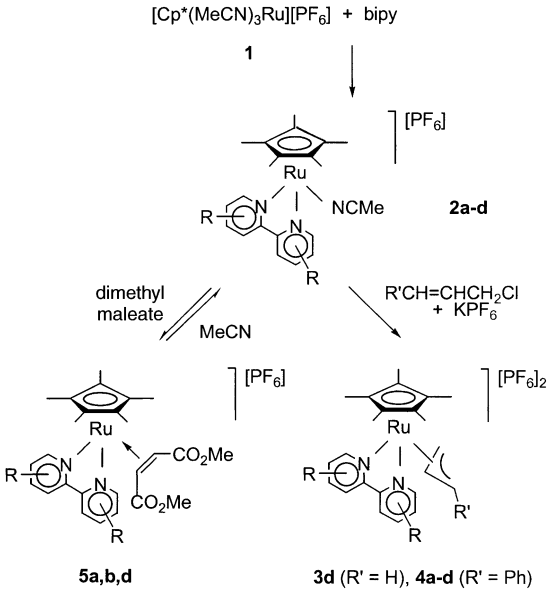
$[Cp^*(MeCN)_3Ru][PF_6]$ as the catalyst precursor.[2] Although the additional coordination of donors such as phosphanes or nitrogen ligands at the ruthenium center stabilize the (η^3-allyl)Ru^{IV} complexes, they also result in a markedly reduced catalytic activity.[1a,3] Thus, a robust cyclopentadienyl–ruthenium fragment associated solely to labile ligands such as cod or acetonitrile is apparently a required key for the design of ruthenium catalysts. However, we recently observed that coordinatively stabilized Cp*(α-diimine)Ru complexes exhibited a noteworthy catalytic activity.[4] Undoubtedly, our observation needed a better understanding because allylic substitution catalyzed by organometallic complexes represents an important tool for organic synthesis.[5] We report herein the synthesis of the new $[Cp^*(\eta^2\text{-bipy})(CH_3CN)Ru^{II}][PF_6]$ (bipy = bipyridyl derivative, see Scheme 1) complexes **2a–d**, and show their catalytic activity in allylic substitution to regioselectively form carbon–carbon or carbon–heteroatom bonds under mild conditions. Furthermore, the dicationic $[Cp^*(\eta^2\text{-bipy})(\eta^3\text{-allyl})Ru^{IV}][PF_6]_2$ derivatives **3d** and **4a–d**, were isolated and appear as key intermediates in the catalytic process.

The purple complexes, **2a–d**, were nearly quantitatively obtained by reacting $[Cp^*Ru(CH_3CN)_3Ru][PF_6]$ **1**, in solution in acetonitrile with a commercial 2,2′-bipyridine derivative (Scheme 1).

The addition of allyl chloride or cinnamyl chloride to a (highly colored) solution of **2a–d** in acetonitrile resulted in a pale-brown solution within 1 h. When the reaction was performed in the presence of KPF_6, subsequent workup afforded pale-yellow crystals of **3d** or orange–yellow crystals of **4a–d**, in 71–88% yield (Scheme 1). Complexes **2–4** are stable in air at the solid state and were characterized by ^1H and $^{13}C\{^1H\}$ NMR spectroscopy and representative elemental analysis. The NMR data collected for **3d** showed as expected a symmetrical allylic fragment as also indicated by the observation of equivalent pyridyl groups. Structural information was also provided by an X-ray study of **4d**·MeCN that showed the ruthenium atom to be coordinated by a π-bonded C_5Me_5 ring, a two σ-N-bonded phenanthroline chelate, and to an η^3-$CH_2CHCHPh$ allylic fragment that has an *endo* orientation (see Figure 1).[6]

The two Ru–N bond lengths (Ru1–N1 = 2.119(3), Ru1–N2 = 2.118(3) Å, are close to the Ru–N bond lengths (2.094 and 2.097 Å) reported for the Ru^{II} complex [Cp*(2,2′-bipyridine)(η^2-EtO_2C–CH = CH–CO_2Et)Ru][PF_6].[7] These observations emphasized the σ-donor character of the N-coordination of the rigid phenanthroline chelate. The Ru1–C11 (2.196(3) Å) and Ru1–C12 (2.197(3) Å) bond lengths are very similar. Significantly longer is the Ru1–C13 (2.398(3) Å) bond and it should be noted that the C12-C13-C14 angle, 123.9(3)°, is very close to 120°. Thus, the coordination of the allyl group in **4d** may be coarsely depicted as an intermediate between an allylic coordination and, with a minor contribution, an olefinic coordination of a formal CH_2=CH-C^+HPh ligand. Indeed, complexes **2** in dichloromethane solution easily exchange their labile acetonitrile ligand for dimethyl maleate to afford complexes **5a,b,d** (Scheme 1). Complexes **5** were characterized by ^1H NMR spectroscopy in CD_2Cl_2. The ^1H NMR spectra of solutions of **5** in CD_3CN showed a mixture of **2**, **5**, and dimethyl maleate, thus indicating a reversible reaction. Such a behavior suggests that the formation of the ruthenium(IV) complexes **3** and **4** from **2** involved a preliminary π-coordination of the allyl chloride followed by an intramolecular oxidative-addition step.

The addition of diethylamine to a yellow solution of **4** in acetonitrile immediatly resulted in an intense violet solution, thus suggesting the recovery of **2** and providing straightforward evidence for an electrophilic reactivity of complexes **4**.



Scheme 1. Synthesis of the new complexes. Bipy = a) 2,2′-bipyridine, b) 4,4′-dimethyl-2,2′-bipyridine, c) 4,4′-di-tert-butyl-2,2′-bipyridine, d) 1,10-phenanthroline.

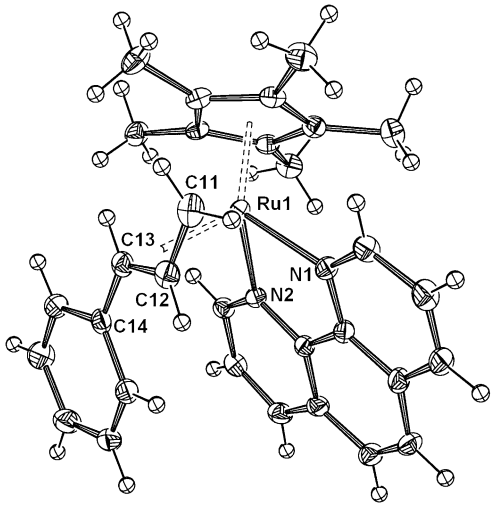
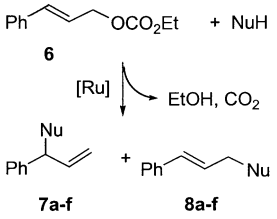


Figure 1. ORTEP view of **4d** showing thermal ellipsoids set at the 50% probability level. Selected bond distances (Å) bonds and angles (°): Ru(1)-C(11) 2.196(3), Ru(1)-C(12) 2.197(3), Ru(1)-C(13) 2.398(3), C(11)-C(12) 1.412(5), C(12)-C(13) 1.402(5), C(13)-C(14) 1.464(5), Ru(1)-N(1) 2.119(3), Ru(1)-N(2) 2.118, C(11)-Ru(1)-C(12) 37.50(13), C(12)-Ru(1)-C(13) 35.18(12), C(11)-Ru(1)-C(13) 63.29(13), C(11)-C(12)-C(13) 118.3(3), C(12)-C(13)-C(14) 123.9(3), N(1)-Ru-N(2) 77.04(10). The two PF_6 anions and the solvent molecule are omitted for clarity.

Consequently, the reactivity of complexes **2** as catalyst precursors for allylic substitution was then investigated. The catalytic activity of complexes **2** was checked by treating the cinnamyl carbonate **6** with various nucleophiles (Scheme 2) and selected experiments are listed in Table 1.



Scheme 2. Ruthenium-catalyzed nucleophilic allylic substitution. Nu = a) $CH(CO_2Me)_2$, b) $CH(COMe)_2$, c) $N(CH_2)_5$, d) NEt_2, e) $N(CH_2)_4$, f) OMe.

Table 1: Selected ruthenium-catalyzed allylic substitution reactions.

Entry[a]	Catalyst	Nucleophile	Solvent	Products	Branched/Linear[b]
1	**2b**	$NaCH[CO_2Me]_2$	THF	**7a**	
2	**2b**	$CH_2[CO_2Me]_2$	MeCN	**7a, 8a**	25:1
3	**2c**	$CH_2[CO_2Me]_2$	MeCN	**7a, 8a**	20:1
4	**2d**	$CH_2[COMe]_2$	MeCN	**7b, 8b**	55:1
5	**2c**	piperidine	MeCN	**7c, 8c**	27:1
6	**2b**	Et_2NH	MeCN	**7d, 8d**	8:1
7	**2c**	pyrrolidine	MeOH	**7e, 8e**	50:1
8	**2a**	MeOH	MeOH	**7f, 8f**	32:1
9	**2d**	MeOH	MeOH	**7f, 8f**	26:1

[a] conditions: 0.5 mmol of cinnamyl carbonate, 0.6 mmol of nucleophile, 0.015 mmol of catalyst (3 mol%), in 4 mL of solvent, 16 h, room temperature. [b] All reactions led to complete conversion of **6**, the branched/linear ratio was determined by ^1H NMR spectroscopy.

Thus, the reaction of **6** with dimethyl sodiomalonate (1.2 equiv) in the presence of 3 mol% of **2b** in THF at room temperature led to the quantitative formation of the branched isomer **7a** (entry 1). Remarkably, because rare when using a ruthenium catalyst,[8] the nucleophilic substitution by dimethyl malonate that has not been deprotonated also runs when acetonitrile is used as the solvent (entries 2,3). Similarly, acetylacetone reacted as a carbonucleophile with **6** to afford the branched isomer **7b** in more than 98% selectivity (entry 4). The amination with secondary amines showed that the regioselectivity of the reaction was strongly influenced by the nature of the amine: the branched/linear ratio obtained with diethylamine was 8:1 (entry 6), whereas piperidine offered a better regioselectivity of 27:1 (entry 5). The reaction with pyrrolidine was sluggish in acetonitrile, but occurred in methanol to afford the branched allylic amine with a high regioselectivity (entry 7). In the absence of an amine, methanol itself served as a nucleophile. The branched allylic methyl ether **7f** was obtained with a very high regioselectivity (entries 8,9), and it is especially worth mentioning that no reaction occurred when **1** was tested as the catalyst precursor.

In conclusion, the facile synthesis of complexes **2** provides novel efficient catalysts for regioselective allylic substitution from unsymmetrical allylic carbonates. The addition of a wide range of nitrogen-, oxygen-, or carbon-nucleophiles under mild conditions has been achieved with good yields and high regioselectivities in favor of the branched isomer. The characterization of allyl bipyridine–ruthenium(IV) complexes which can also be used as catalyst precursors, brings evidence of the involvement of the bipyridine ligand in the catalytic process.

Experimental Section

2a: A solution of 2,2′ bipyridine (0.69 g, 4.42 mmol) in toluene (90 mL) was added to a solution of **1** (2.20 g, 4.36 mmol) in acetonitrile (30 mL). The reaction mixture was stirred for 1 h after which the solution was slowly concentrated under vacuum to obtain dark-purple crystals that were collected then washed with diethyl ether. Yield: 2.49 g, 95%. **4d**·MeCN**:** Cinnamyl chloride (0.40 mL, 2.87 mmol) was added to a stirred mixture of **2d** (1.50 g, 2.49 mmol) and KPF_6 (0.50 g, 2.72 mmol) in acetonitrile (30 mL). After 1 h, the solvent was completely removed by evaporation. Then water (30 mL) and diethyl ether (30 mL) were added to the residue, and this mixture was stirred to obtain a yellow precipitate, which was collected by filtration. The solid was dissolved in acetonitrile (40 mL) and diethyl ether (120 mL) was added to the resulting solution to obtain orange–yellow crystals. Yield: 1.90 g, 88%. A suitable crystal was selected for the X-ray study.

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Keywords: allyl complexes · homogeneous catalysis · ligand effects · N ligands · ruthenium

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[6] Crystal data**:** $C_{33}H_{35}F_{12}N_3P_2Ru$, $M_r = 864.65$, crystal size $0.35 \times 0.32 \times 0.30$, monoclinic, space group $P2_1/c$, $Z = 4$, $a = 10.2255(1)$ Å, $b = 11.2593(1)$ Å, $c = 29.3790(4)$ Å, $\beta = 97.243(1)°$, $U = 3355.47(6)$ Å^3, $\delta_{calcd} = 1.712$ g cm^{-3}, $T = 120(1)$ K, $F(000) = 1744$, $Mo_{K\alpha}$ radiation ($\lambda = 0.71069$ Å), $\mu = 0.660$ mm^{-1}, 7583 reflexions measured in the range $2.30° \le \theta \le 27.48°$, 7583 unique, ($R_{int} = 0.038$) which were used in all calculations. The structure was refined by using full-matrix least-squares on F^2 to $R_1 = 0.047$, $wR_2 = 0.128$, $S = 0.985$, for 6559 reflections ($> 2\sigma$) and 460 refined parameters, R_1(all data) 0.055, wR_2(all data) = 0.137, goodness-of-fit on $F^2 = 1.011$. CCDC-213659 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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