Ruthenium-Bisimine: A New Catalytic Precursor for Regioselective Allylic Alkylation

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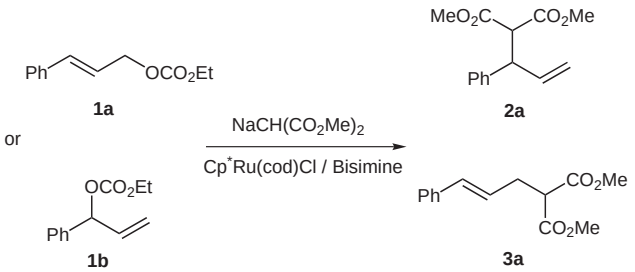
Abstract: New complexes [Cp*Ru(bisimine)Cl] are active catalysts for the regioselective alkylation of allylic carbonates by soft carbonucleophiles, in favour of the branched isomers. The catalysts can be conveniently prepared in situ from [Cp*Ru(cod)Cl] and a bulky aromatic bisimine.

Keywords: regioselective allylic alkylation, ruthenium(bisimine) complex catalysed, coupling reactions

Transition metal catalysed allylic substitution is a useful process in organic synthesis.[1] Good results have been obtained with symmetrically disubstituted substrates,[2] but there is still a challenge to achieve high control of the regioselectivity with unsymmetrical allyl substrates. Although a few ligands have been reported to favour the formation of the branched isomer,[3] monosubstituted allylic acetates with palladium catalysts mainly provide the linear internal olefin. Attempts to prepare the terminal olefin have been achieved by employing other transition metal complexes[4] including ruthenium derivatives.[5] In our ongoing studies of new carbon-carbon bond coupling reactions catalysed by [Cp*Ru] complexes,[6] we were interested in developing a new catalytic system to produce branched products from unsymmetrical carbonates. We report here the first use of Cp*Ru(bisimine)Cl complexes in catalysis, and show that these new precursors favour the regioselective alkylation of allylic carbonates corresponding to nucleophilic addition of malonate to the most substituted allylic terminus.



Scheme 1

The discovery of the efficiency of the in situ generated catalytic systems based on Cp*Ru(cod)Cl/bisimine complexes resulted from our investigations on the allylic substitution of the unsymmetrical ethyl cinnamyl carbonate **1a** with sodium dimethyl malonate according to Scheme 1. Remarkably in contrast to palladium chemistry,[7] the allylic substitution with soft carbonucleophiles starting from carbonates does not proceed under neutral conditions with ruthenium catalysts but requires the preparation of the nucleophilic species. Even if pure triethylamine is used as solvent and base, we observed no alkylation. Thus, the reaction of 0.6 mmol of sodium dimethyl malonate separately prepared from dimethyl malonate and sodium hydride, with 0.5 mmol of carbonate **1a** in the presence of 3 mol% of Cp*Ru(cod)Cl as ruthenium source and 3 mol% of bis(phenyl)ethylenediimine $\mathbf{L_1}$, in 4 mL of THF at room temperature for 16 h led to complete conversion of **1a** and a 9:1 ratio of **2a**:**3a** (Table 1).

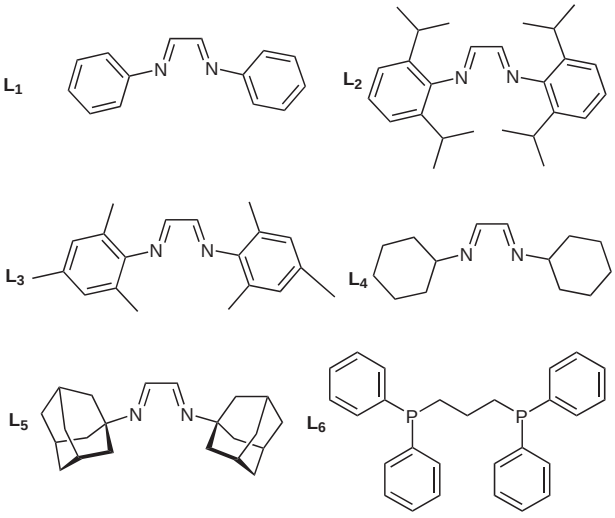


Figure 1 Various bidentate bisimine and diphosphine ligands

The aromatic bisimine ligands $\mathbf{L_1}$, $\mathbf{L_2}$, and $\mathbf{L_3}$ were more efficient in terms of regioselectivity than the aliphatic bisimines $\mathbf{L_4}$ and $\mathbf{L_5}$ derived from cyclohexyl and adamantyl amines (Figure 1). The presence of catalysed $\mathbf{L_4}$ and $\mathbf{L_5}$ does not improve the regioselectivity of the reaction catalysed by Cp*Ru(cod)Cl alone (Table 1, entries 1, 5, 6). The best ligand was the bulky bis(mesityl)ethylenediimine $\mathbf{L_3}$, which led to a 15:1 ratio of **2a**:**3a** (Table 1, entry 4). It is noteworthy that the chelating 1,3-bis(diphenylphosphino)propane ligand $\mathbf{L_6}$ is not appropriate for this reaction as

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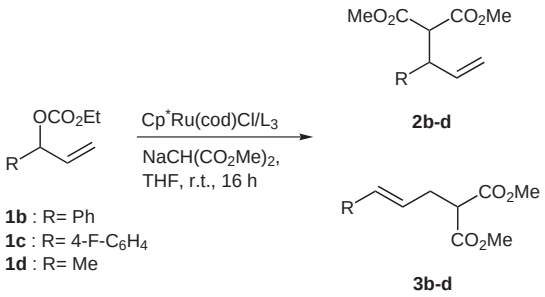
Table 1 Effect of the Bidentate Ligand $\mathbf{L_n}$ on the Regioselectivity of the Alkylation[a]

Entry	Ligand $\mathbf{L_n}$	Yield (%)[b]	Selectivity (**2a**:**3a**)[c]
1	none	100	8:1
2	$\mathbf{L_1}$	100	9:1
3	$\mathbf{L_2}$	100	11:1
4	$\mathbf{L_3}$	100	15:1
5	$\mathbf{L_4}$	77	2.5:1
6	$\mathbf{L_5}$	100	3.5:1
7	$\mathbf{L_6}$	N.R.	

[a] Conditions: 0.6 mmol of dimethyl malonate, 0.6 mmol of NaH, 0.5 mmol of carbonate **1a**, 0.015 mmol of [Cp*Ru(cod)Cl] (3 mol%), 0.015 mmol of ligand L (3 mol%), in 4 mL of THF, 16 h.
[b] Isolated yield.
[c] Based on NMR data.
[d] N.R.: no reaction.

no conversion occurs at all (Table 1, entry 7). On the basis of these results, we prepared and isolated the complex [Cp*Ru($\mathbf{L_3}$)Cl] upon treatment of [Cp*Ru(cod)Cl] with one equivalent of bis(mesityl)ethylenediimine $\mathbf{L_3}$ in CH_2Cl_2 at room temperature.[8] The alkylation of carbonate **1a**, with sodium dimethyl malonate in the presence of 3 mol% of this bisimine ruthenium complex under the previous reaction conditions described in Table 1, led to a 19:1 ratio of **2a**:**3a**, very close to the value obtained from the system generated system in situ. We have also shown that the nature of the catalyst precursor was crucial for the regioselectivity, as the reaction carried out in the presence of $[CpRu(CH_3CN)_3]PF_6$/$\mathbf{L_3}$ under the conditions of Table 1 also led to complete conversion but reversed the **2a**:**3a** ratio to 1:2 in favour of the linear compound. Moreover, the isolated cationic complex [Cp*Ru($\mathbf{L_3}$)$(CH_3CN)]PF_6$ was not as efficient as the catalyst generated in situ from [Cp*Ru(cod)Cl] and $\mathbf{L_3}$, as under the same reaction conditions it led to a **2a**:**3a** ratio of only 6:1 in favour of the branched isomer. These results clearly exhibit the role of the ancillary ligand (Cp or Cp*) and the ionic or neutral nature of the ruthenium catalyst, which modifies the reactivity of the allylic moiety.

To extend the scope of this reaction, the alkylation of different allylic carbonates was investigated in THF with NaH as malonate generator (Scheme 2, Table 2) in the presence of the catalytic system easily and conveniently generated from Cp*Ru(cod)Cl and $\mathbf{L_3}$. For carbonates bearing an aromatic ring on the allyl moiety, the selectivity was mainly in favour of the branched isomer and the best result was obtained from **1b** (Table 2, entry 1). Furthermore, it is interesting to note that an electron withdrawing group has little influence on the selectivity. Thus, with carbonate **1c**, the branched alkylated product was isolated in a 15:1 ratio. Nevertheless, the aliphatic allylic carbonate **1d** led to a **2d**:**3d** ratio of 2:1 in contrast with carbonates **1a**–**c**. The behaviour of these carbonates might be explained by the different polarization of the allylic termini. Indeed, the reactivities of the allylic termini generated from **1d** are quite similar, the nucleophile can then attack both sites and the regioselectivity decreases.



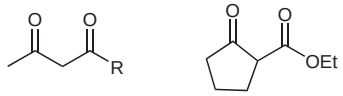
Scheme 2

Table 2 Alkylation of Allylic Carbonates **1b**–**d** with $NaCH(CO_2Me)_2$ in the Presence of Cp*Ru(cod)Cl and $\mathbf{L_3}$[a]

Entry	Carbonate	Yield (%)[b]	Selectivity (**2**:**3**)[c]
1	**1b**	100	18:1 (**2b**:**3b**)
2	**1c**	100	15:1 (**2c**:**3c**)
3	**1d**	100	2:1 (**2d**:**3d**)

[a] Conditions: 0.6 mmol of dimethyl malonate, 0.6 mmol of NaH, 0.5 mmol of carbonate **1a**, 0.015 mmol of [Cp*Ru(cod)Cl] (3 mol%), 0.015 mmol of ligand L_3 (3 mol%), in 4 mL of THF, 16 h.
[b] Isolated yield.
[c] Based on NMR data.

The extension of this reaction to other soft carbonucleophiles was also studied (Figure 2, Table 3). With acetylacetone **4** and the carbonate **1b**, the selectivity in favour of the branched isomer is significantly increased to 25:1. With β-ketoesters **5-7**, the regioselectivity was still good and the branched:linear ratio was located in the range of 4:1 to 18:1. The products were isolated in a diastereomeric ratio of 1:1 and no double allylation was detected as it is often the case in the presence of palladium catalysts. Moreover, it has to be pointed out that the regioselectivity increases with the bulkiness of the ester group (from 9:1 to 18:1, Table 3, entry 3 and 4).



4 = Me
6 = OMe
7 = O*t*-Bu

5

Figure 2

In conclusion, we have shown that the new complex [Cp*Ru($\mathbf{L_3}$)Cl] is an active catalyst for the regioselective alkylation of allylic carbonates by soft carbonucleophiles, and demonstrated that this new family of efficient catalysts could be conveniently prepared in situ from

Table 3 Addition of Soft Nucleophiles in the Presence of $Cp^*Ru(cod)Cl$ and $\mathbf{L_3}$[a]

Entry	Ligand	Yield (%)[b]	Selectivity (**2**:**3**)[c]
1	**4**:**1b**	100	25:1
2	**5**:**1a**	100	4:1 (2 diastereomers 1:1)
3	**6**:**1b**	96	9:1 (2 diastereomers 1:1)
4	**7**:**1b**	97	18:1 (2 diastereomers 1:1)

[a] Conditions: 0.6 mmol of dimethyl malonate, 0.6 mmol of NaH, 0.5 mmol of carbonate **1a**, 0.015 mmol of [$Cp^*Ru(cod)Cl$] (3 mol%), 0.015 mmol of ligand $\mathbf{L_3}$ (3 mol%), in 4 mL of THF, 16 h.
[b] Isolated yield.
[c] Based on NMR data.

[$Cp^*Ru(cod)Cl$] and a bulky aromatic bisimine. Whatever the starting carbonate **1** with the bis(mesityl)ethylene-diimine as ligand, the branched product is preferentially formed.

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(8) $(C_5Me_5)RuCl(MesN{=}CH{-}CH{=}NMes)$: selected ^1H NMR data (200 MHz): δ (ppm) 1.07 (s, 15 H, C_5Me_5), 1.87 (s, 6 H, 2 Me), 2.30 (s, 6 H, 2 Me), 2.38 (s, 6 H, 2 Me), 6.82 (s, 2 H, 2 HAr), 6.92 (s, 2 H, 2 HAr), 8.68 (s, 2 H, 2 CH=N).