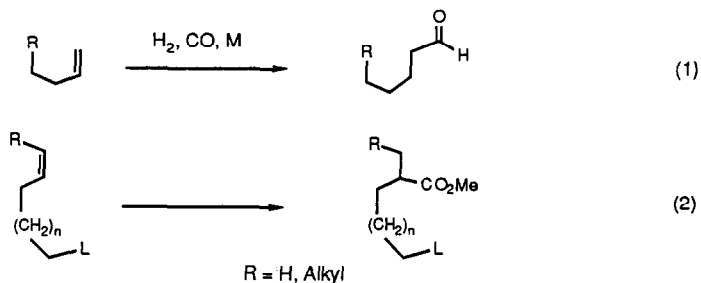


REGIOSELECTIVE HYDROCARBOXYLATIONS OF OLEFINIC AMINES: CHARACTERIZATION OF A KEY INTERMEDIATE

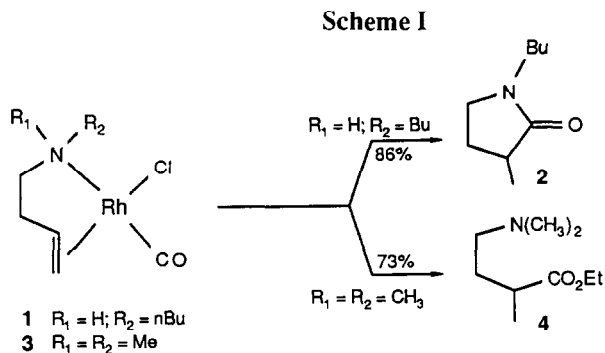
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Summary: Homoallylic and bishomoallylic amine bidentate rhodium (I) complexes undergo regioselective hydrocarboxylations and give rise to amino esters or lactams.

The functionalization of unactivated olefins is an important transformation which can be effectively carried out by the use of transition metal catalysis.¹ Both the hydroformylation and hydrocarboxylation reactions are useful industrial processes.^{1,2} Hydroformylations of terminal olefins can be regioselective (eq 1), however, with internal olefins, mixtures of regioisomers are normally obtained.^{1,2} We now report that ligands, tethered to the starting olefin, may be used to direct the regiochemical outcome of the hydrocarboxylation reaction.^{2,3} This is the first time an account of such general selectivity has been reported. The ligand not only directs the regiochemistry of the addition to an internal olefin but also reverses the regiochemical outcome of the hydrocarboxylation of terminal olefins (eq 2).⁴



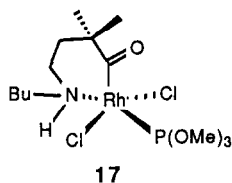
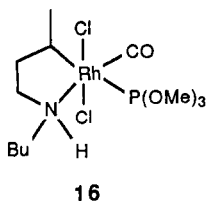
Using Rh(I) complexes, we have regioselectively hydrocarboxylated an unactivated olefin. Oxidative addition of HCl to the secondary amine-olefin Rh(I) complex **1** or the tertiary amine-olefin Rh(I) complex **3** followed by olefin insertion^{1,5} and carbonylation gave rise to lactam **2** or amino ester **4** in good yield (Scheme I). In some cases, the



hydrocarboxylation could be carried out stepwise with isolation and characterization of new, stable Rh(III) intermediates, but, generally, the conversion of the amino-olefin Rh(I) complexes to the amino esters or lactams was a one flask process.

The Rh(I) olefinic amine complexes were readily prepared from dichlorotetracarbonyldirhodium, $[(\text{CO})_2\text{RhCl}]_2$, by displacement of the labile carbon monoxide by the appropriate olefinic amine.⁶ Allylic amines did not react to form bidentate ligand complexes, however, bidentate homoallylic and bishomoallylic amine Rh(I) complexes were easily formed.⁶

In a typical experiment (entry 1 in Table), oxidation of **1** to a Rh(III) hydride was carried out by the addition of 3 equiv of an ethereal solution of anhydrous HCl to a yellow solution of complex **1** in CH_2Cl_2 . After 1 h at -78°C , 10 equiv of trimethylphosphite was added and the solution was warmed to 25°C for 12 h to produce an intermediate Rh(III) complex **16** which was generally not isolated. The trimethylphosphite was added to fill the vacant coordination site generated by insertion of the coordinated olefin into the M-H bond. Carbon monoxide insertion to form a Rh(III) acyl and subsequent methanolysis occurred after addition of excess methanol and trimethylphosphite (5 equiv, 24 h, 25°C). Lactam **2**, resulting from spontaneous cyclization of the secondary amino ester, was isolated in 86% yield after chromatography. The reaction was found to be general and the results are summarized in the Table.⁷ Both five and six-membered rings were readily formed, however, we were unable to prepare seven membered lactams due to difficulties associated with the formation of the initial bidentate Rh(I) complex.



TABLE

ENTRY	Rh(I) COMPLEX	LACTAM or AMINO ESTER	YIELD	ENTRY	Rh(I) COMPLEX	LACTAM or AMINO ESTER	YIELD
1			86%	5			62%
2			73%	6			80%
3			70%	7			85%
4			40% ⁷	8			79%

We found that some of the rhodium (III) intermediates were stable enough to be isolated and fully characterized. For example, reaction of Rh(I) complex 12 (entry 7 in Table) with HCl and trimethylphosphite, in the absence of methanol, gave rise to Rh(III) complex 17 whose IR spectrum clearly showed the existence of a rhodium acyl.

An x-ray crystallographic investigation⁸ showed the complex to adopt a 5-coordinate, square pyramidal geometry with the acyl moiety in the apical position (Figure 1). While there are still few crystallographically studied examples of 5-coordinate acylrhodium complexes, those that have been examined also exhibit this geometry,¹⁰ probably due to the strong trans influence of the acyl group.¹¹ The bond lengths associated with the rhodium are unexceptional, though the Rh-C length (1.96(2) Å) does lie nearer the short end of the observed range.^{10,12} The rhodium is displaced from the basal plane toward the acyl moiety by 0.194 Å, approximately the same amount as is observed in the anion^{10e} $[\text{Rh}(\text{COEt})(\text{PPh}_3)(\text{mnt})]^-$ and in the neutral complex^{10a} $[\text{Me}_2\text{Gapz}(\text{OCH}_2\text{CH}_2\text{NMe}_2)]\text{Rh}(\text{OMe})\text{I}$.

It is very interesting to note that complex 17 must have been formed from the corresponding tertiary alkyl complex.¹³ Subsequent reaction of 17 with trimethylphosphite in methanol gave rise to lactam 13.

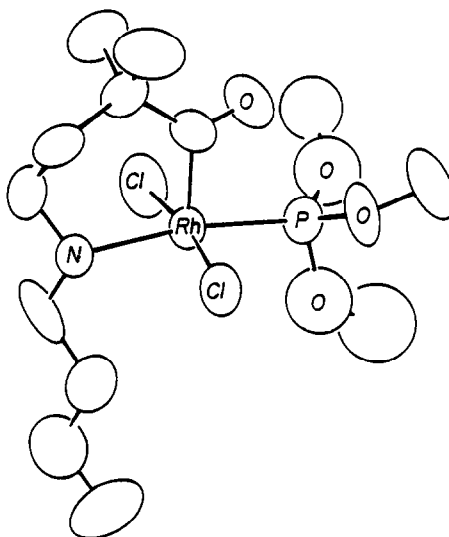


FIGURE 1. *Perspective drawing of $\text{RhCl}_2(\text{P}(\text{OMe})_3)(\text{COC}_9\text{H}_{20}\text{N})$ (17). Thermal ellipsoids have been drawn at the 50% probability level.*

The examples described in this communication represent the first cases of ligand directed olefin hydrocarboxylation. This one flask operation converts readily available⁶ Rh(I) olefin complexes to amino-esters or lactams in good yields. The problems inherent in reactions of transition metal complexes in general are 1) the instability of the intermediate metal alkyl complex toward β -elimination and isomerization from branched to normal alkyl,¹⁴ and 2) the regiochemistry of the functionalization. We have overcome both of these problems by use of a directing ligand which allows the formation of a stable bidentate ligand complex throughout the entire reaction. Further studies on the generality of the reaction and its application to the synthesis of natural products are in progress.

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- Complex 17 crystallized in space group $P2_1/c$ with cell dimensions $a = 16.441(7)$, $b = 13.148(5)$, $c = 12.392(4)$ Å, $\beta = 130.96(2)^\circ$, $X = 2023(1)$ Å³, $Z = 4$. Of the 3753 unique reflections collected on a Syntex $P2_1$ automated diffractometer at room temperature with Mo $K\alpha$ radiation ($\lambda = 0.71069$ Å) to $2\theta = 50^\circ$, the 2213 for which $I \geq 2\sigma(I)$ were used in the structure solution and refinement. The structure was solved by the Patterson method. Difficulty was encountered in the interpretation of the Fourier maps since the trimethylphosphite moiety, rather characteristically, embodied disorder,⁹ in the final model, two of the methoxy groups have been described using isotropic thermal factors. The remainder of the non-hydrogen portion of the structure was treated anisotropically. Hydrogen atoms were omitted. The final R value is 0.075 and the R_w is 0.089.
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