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Hydroaminomethylation of olefins using a rhodium carbene catalyst

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Abstract—Hydroaminomethylation of terminal as well as internal aliphatic and aromatic olefins with various amines is described in the presence of [Rh(cod)(Imes)Cl] as a catalyst. In general good to excellent yields and high chemoselectivity were obtained in THF at 85–105°C using 0.1 mol% of catalyst. © 2003 Published by Elsevier Science Ltd.

Aliphatic amines are important products for bulk as well as fine chemicals and pharmaceutical industries. General methods for their synthesis include alkylation of organic halides with ammonia, reductive amination of carbonyl compounds and hydrocyanation of alkenes followed by reduction. From both economic and environmental points of view, developing new versatile and more direct preparation routes to amines from inexpensive feedstock is most desirable. In this respect the hydroamination[1] and the hydroaminomethylation[2] of aliphatic olefins to amines represent elegant, atom-economic and efficient synthesis methods. While the direct hydroamination of olefins still remains one of the important challenges in catalysis, the hydroaminomethylation is closer to application. As shown in Figure 1, this domino reaction consists of initial hydroformylation of the olefin to an aldehyde and subsequent formation of an enamine (or imine) followed by hydrogenation. In spite of the advantages of this one-pot reaction, for example easy availability of starting materials and atom efficiency, comparatively few preparative applications are known.[2]

Known hydroaminomethylation procedures often suffer from the limited chemo- and regioselectivities. In addition, state-of-the-art hydroformylation catalysts (rhodium phosphine catalysts with excess of ligand) often do not show sufficient hydrogenation activity for aliphatic enamines or imines.[3] Hence, in order to make this method more attractive for organic synthesis there is a need for improved catalysts.

Some time ago, we reported the first selective hydroaminomethylation reaction of aliphatic olefins using ammonia.[4] Recently, we developed a new rhodium phosphine catalyst system for hydroaminomethylation reactions of internal aliphatic olefins to linear amines.[5] In the present paper, we describe for the first time the use of a rhodium carbene complex for various hydroaminomethylation reactions. While carbene ligands have become popular for palladium-catalyzed coupling reactions,[6] only very few applications of rhodium carbene complexes have been reported so far.[7]

We thought that the use of a defined rhodium monocarbene complex might solve the problem of the low hydrogenation activity of known catalyst systems in which an excess of strongly coordinating phosphine ligands slows down the hydrogenation of the imine or enamine.

Based on our previous synthesis of monocarbenepalladiumdiolefin complexes[8] the new rhodium complex

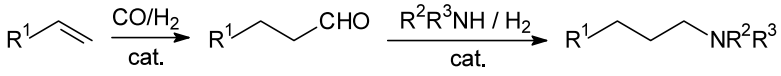

Figure 1. Hydroaminomethylation of olefins.

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Rh(cod)(Imes)Cl (Imes = 1,3-dimesitylimidazol-2-ylidene, cod = cyclooctadiene) was prepared straightforwardly from $[Rh(cod)Cl]_2$.[9]

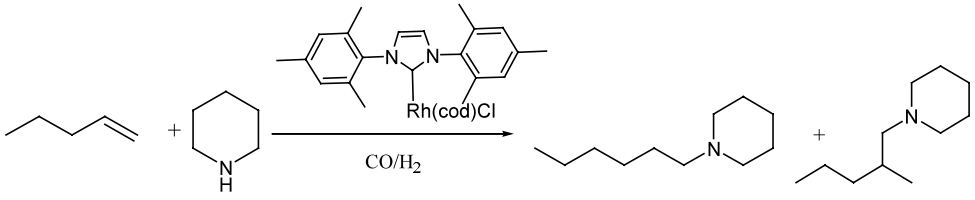
The reaction of 1-pentene with piperidine in the presence of Rh(cod)(Imes)Cl was chosen as a model system in order to study the influence of different reaction parameters (solvent, temperature, partial pressure of carbon monoxide and hydrogen).[10] As shown in Table 1, the conversion of 1-pentene proceeded smoothly in toluene, THF and methanol. In general, hydrogenation of the in situ produced enamine is the rate-determining step of the reaction sequence (Table 1; compare entries 1–5). Hence, THF was used for most of the experiments owing to higher hydrogenation activity compared to that in toluene. Moreover, the chemoselectivity in THF is higher than that in methanol. After 12 h a high amine selectivity (93%) is obtained in THF using 0.1 mol% of rhodium catalyst. However, the n/iso selectivity (65:35) is only of mediocre quality, which is in agreement with hydroformylation reactions in the presence of rhodium complexes and imidazolium salts.[11] While the partial pressure of hydrogen has no significant influence on the outcome of the reaction (Table 1, entries 5, 8, 9), the concentration of CO plays an important role (Table 1, entry 5). Increase in the CO pressure leads to a gradual decrease in the hydrogenation activity of the catalyst and becomes predominant at higher partial pressures. Also, the reaction temperature affects strongly the hydrogenation of the enamine. At 65°C hardly any hydrogenation takes place, offering a possibility to obtain enamines directly from olefins. At 95°C the reaction is complete within 6–12 hours giving an excellent yield (96–98%) and chemoselectivity (99%) of *n*-hexylpiperidine and (2-methyl-1-pentyl)piperidine (Table 1, entry 10).

In order to compare the rhodium carbene complex with a 'ligand free' system, the reaction of 1-pentene was also performed with $[Rh(cod)Cl]_2$ as the catalyst precursor. Though the catalytic activity was found to be higher compared to the Rh–carbene complex, lower selectivity to total amines enamines as well as a slightly lower n:iso ratio were observed (Table 1; compare entries 2 and 3). Noteworthy, the ligand free system is also less stable as seen from the formation of metal particles by decomposition of the active Rh species.[12]

Next, we studied the hydroaminomethylation reaction of different terminal aliphatic and aromatic olefins as well as some cyclic olefins. Apart from 1-pentene, various olefins such as 1-octene, cyclohexene, cyclooctene, styrene, α-methylstyrene, and 1,1′-diphenylethene were used as substrates (Table 2). Piperidine, morpholine, dimethylamine and *n*-hexylamine were employed as amines. In all cases excellent conversion (>95%) and chemoselectivity (87–>99) towards the corresponding amines are observed in THF at 95°C in the presence of 0.1 mol% of Rh(cod)(Imes)Cl.

In most cases the reaction proceeds with an extremely high degree of selectivity towards the amine. Only small amounts of the corresponding enamines or imines are produced, if the reaction is run for 12–16 h. Among the different reactions studied, the hydroaminomethylation of morpholine has the slowest rate, probably due to the

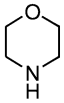
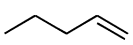
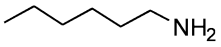
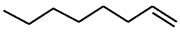
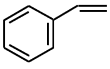
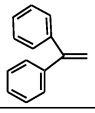
Table 1. Hydroaminomethylation of 1-pentene[a]



Entry	P_{CO} (bar)	P_{H_2} (bar)	Solvent	Temp. (°C)	Time (h)	Conversion[b] (%)	Selectivity (%)[b]		n:iso	
							Amine	Enamine	Amine	Enamine
1	10	50	Toluene	85	20	99	95	nd	63:37	nd
2	10	50	Toluene	85	12	95	65	18	83:17	15:85
3[c]	10	50	Toluene	85	12	99	85	nd	56:44	nd
4	30	30	Toluene	85	12	87	27	63	79:21	65:35
5	10	50	THF	85	12	92	93	5	65:35	0:100
6	15	50	THF	85	12	92	10	90	61:39	72:28
7	7	50	THF	85	12	99	99	nd	60:40	nd
8	10	70	THF	85	12	94	60	32	72:28	47:53
9	10	30	THF	85	12	87	70	30	74:24	60:40
10	10	50	THF	95	12	99	99	nd	62:38	nd
11	10	50	THF	65	12	19	nd	87	nd	51:49
12	10	50	MeOH	85	12	89	82	nd	70:30	nd

[a] Reaction conditions: 1-pentene (15 mmol), piperidine (15 mmol), solvent (30 ml), 0.1 mol% Rh(Imes)(cod)Cl.
[b] Conversions and selectivities were determined by GC using internal standard bis(methoxyethyl)ether.
[c] $[Rh(cod)Cl]_2$ as the catalyst precursor.

Table 2. Hydroaminomethylation of various olefins[a]

Entry	Olefin	Amine	Conversion (%)	Selectivity (%)	n:iso
1			99	99	62:38
2			95	34	82:18
3			100	99	60:40
4			99	87	51:49
5			>99 [b]	85	68:32
6			>99 [b]	>99	-
7			85 [b]	>99	-
8			99 [b,c]	95	21:79
9			99 [b,c]	96	>99:1
10			55 [b, c]	99	>99:1

[a] Reaction conditions: olefin (15 mmol), amine (15 mmol), THF (30 ml), 0.1 mol% Rh(Imes)(cod)Cl, CO (10 bar), H_2 (50 bar), temperature (95 °C), time (12 h). [b] Time (16 h). [c] Temperature (105 °C).

chelating coordination mode of morpholine.[13] Here, longer reaction times or higher reaction temperatures are needed for complete hydrogenation.

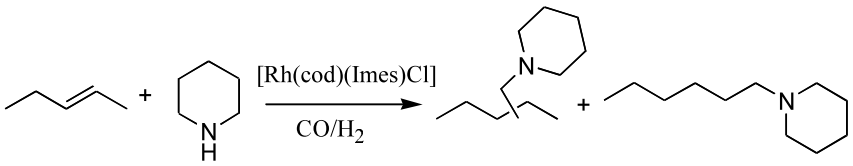
Unfortunately, the n/iso selectivity of the reaction of terminal aliphatic olefins, which is determined at the hydroformylation step, is similar or marginally higher compared to those reactions with non- or low-ligated rhodium phosphine complexes. Further improvements are desirable and might be possible by using carbene ligands having increased steric properties. In agreement with hydroformylation catalysis,[14] the hydroaminomethylation of styrene gave preferentially the branched product. Very high linear selectivities are obtained with α-substituted styrenes as shown in Table 2.

The selective functionalization of internal aliphatic olefins towards linear products is an important goal for industrial catalysis. This type of reaction requires a fast isomerization of the internal to the terminal olefin and subsequent regioselective hydroformylation.[15] Therefore, we were also interested in the hydroaminomethylation of internal olefins, e.g. 2-pentene, using Rh(cod)(Imes)Cl as the catalyst.

Some preliminary studies demonstrate the possibility of hydroaminomethylations of these substrates, too. However, olefin isomerization is observed only to a small extend in toluene as a solvent and no isomerization was observed in THF as a solvent. As shown in Table 3, the reaction of 2-pentene and piperidine proceeded in the presence of 0.1 mol% of Rh(cod)(Imes)Cl at 95°C in toluene at 60 bar pressure ($CO:H_2$, 1:5) with good conversion (95%) and chemoselectivity (89%) with an n:iso ratio of 1:9.

In summary, we have shown for the first time that hydroaminomethylation reactions can be performed by using monocarbenerhodium complexes as catalysts. Good to excellent activity and chemoselectivity to amines are achieved under comparatively mild reaction

Table 3. Hydroaminomethylation of 2-pentene[a]



Entry	Solvent	Conv. %	Amine Sel.,%	n:iso	Enamine Sel.,%	n:iso
1	Toluene	95	89	10:90	8	0:100
2	THF	43	29	0:100	49	0:100

[a] Reaction conditions: 2-pentene (15 mmol), piperidine (15 mmol), THF (30 ml), 0.1 mol%, Rh(Imes)(cod)Cl, CO (10 bar), H_2 (50 bar), temperature (85°C), time (12 h).

conditions. A high degree of regioselectivity (n/iso selectivity) is obtained in the case of substituted styrenes. Terminal aliphatic olefins gave mixtures of linear and branched products. The procedure is environmentally friendly (i.e. water is the only by-product) and the starting materials are both inexpensive and readily available.

Acknowledgements

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9. To a solution of $[Rh(cod)Cl]_2$ (0.5 mmol) in THF (20 ml) was added slowly a THF solution (10 ml) of 1,3-dimesitylimidazol-2-ylidene (1.0 mmol) at room temperature. The clear solution was stirred for 2 h and the solvent was evaporated. The residue was triturated with pentane. The yellow solid obtained was analytically pure. It can be recrystallized from CH_2Cl_2/pentane. Yield = 450 mg, 82%. ^1H NMR ($CDCl_3$): 1.54 (m, 4H), 1.83 (m, 4H), 2.10 (s, 6H), 2.34 (s, 6H), 2.38 (s, 6H), 3.30 (s, 2H), 4.40 (s, 2H), 6.96 (s, 2H), 7.03 (s, 4H); ^{13}C NMR ($CDCl_3$): 18.5, 20.0, 21.4, 28.9, 33.2, 68.7 (d, $^1J_{RhC} = 14.3$ Hz), 96.3 (d, $^1J_{RhC} = 7.6$ Hz), 124.3, 128.8, 129.8, 135.1, 137.0, 137.9, 139.2, 183.5 (d, $^1J_{RhC} = 52.5$ Hz); MS (EI): 550 (M^+, 13), 404 (21), 303 (100); Anal. calcd for $C_{29}H_{36}ClN_2Rh$ (550.98): C, 63.22; H, 6.58; N, 5.08; Found: C, 63.08; H, 6.34; N, 5.05.
10. **General procedure:** In a typical experiment (Table 1, entry 9), 1-pentene (15 mmol), piperidine (15 mmol), Rh(cod)(Imes)Cl (0.1 mol%) and freshly distilled THF (30 ml) were charged under argon atmosphere into a 100 ml stainless steel autoclave provided with an overhead stirrer and temperature controlled heating. The autoclave was closed and pressurized to 60 bar ($CO/H_2 = 1:5$) and the reaction was carried out for 12 h at a temperature of 95°C (total pressure at 95°C was ca. 66 bar). After the reaction, the autoclave was cooled slowly to 0–5°C and slowly depressurized. The reaction mixture was analyzed by gas chromatography with bis(methoxyethyl)ether as an internal standard. *N*-Hexylpiperidine and (2-methyl-1-pentyl)piperidine were identified by comparison with authentic samples by GC (HP5890 series; column: HP5 (Crosslinked 5% PH ME Siloxane) 30 m, 0.25 mm, 0.25 μm). The products were also confirmed by GC MS and NMR.
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