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Carbon monoxide as a building block in organic synthesis

IV*. Direct preparation of amines from alkenes by aminomethylation catalysed by dinuclear rhodium complexes

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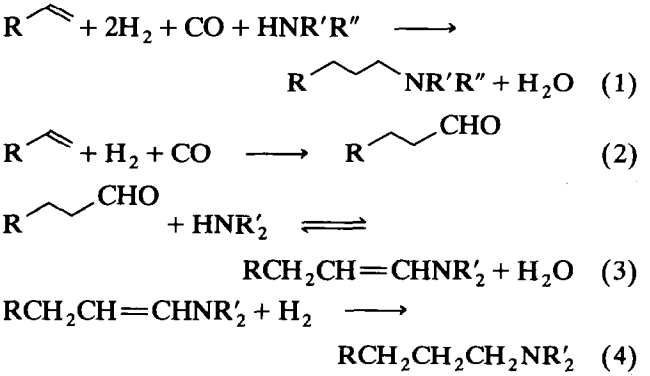
Abstract

The one-pot aminomethylation reaction has been performed under low pressures of carbon monoxide and hydrogen in the presence of the complex $[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(PPh_3)_2]$. This reaction involves the successive hydroformylation of the alkene, the condensation of the aldehyde produced in the first step with the amine, and the hydrogenation of the imine or enamine thus obtained. This last hydrogenation step is rate-determining. At 1.8 MPa, oct-1-ene was transformed with 99% conversion, giving 80% diethylnonylamine, 2% of the iso-compound and 13% methyl-2-octanal, which is more resistant to the condensation with diethylamine and further hydrogenation.

1. Introduction

Amines form a widespread family of compounds, many of them being involved in industrial applications. Condensation between ammonia and alcohols is very frequently employed but is restricted to lower aliphatic amines, although recently it has been shown that long chain alcohols can react with secondary amines with homogeneous catalysis [2]. A one-step efficient and general conversion of alkenes to amines would be of fundamental interest. The catalytic amination of mono-olefins has been reviewed, and the literature shows that there are few examples of this reaction [3]. We were able to realize the synthesis of furylmorpholine starting from 2,3-dihydrofuran and morpholine but, to the best of our knowledge, this reaction cannot be generalized to every amine or alkene [4]. However, hydroformylation of alkenes [5] provides a good way to prepare aldehydes that can be condensed with a primary or secondary amine to afford an imine and an enamine respectively [6].

As early as 1949, Reppe and coworkers [7] discovered the one-step catalytic reductive alkylation of amines by alkenes, carbon monoxide and water (to generate hydrogen). This so-called aminomethylation reaction can be described by eqn. (1) where only a linear amine is represented. In fact, the reaction proceeds *via* a three-step mechanism, shown for a secondary amine by eqns. (2)–(4).



$$R\text{-}CH{=}CH_2 + 2H_2 + CO + HNR'R'' \longrightarrow R\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}NR'R'' + H_2O \quad (1)$$

$$R\text{-}CH{=}CH_2 + H_2 + CO \longrightarrow R\text{-}CH_2\text{-}CH_2\text{-}CHO \quad (2)$$

$$R\text{-}CH_2\text{-}CH_2\text{-}CHO + HNR'_2 \rightleftharpoons RCH_2CH{=}CHNR'_2 + H_2O \quad (3)$$

$$RCH_2CH{=}CHNR'_2 + H_2 \longrightarrow RCH_2CH_2CH_2NR'_2 \quad (4)$$

This aminomethylation reaction catalysed by iron pentacarbonyl requires large quantities of catalyst, long reaction times and was shown to be restricted to ethylene and propene. Moreover, the catalytic conditions were rather harsh (above 150°C and 15 MPa). The literature shows that this reaction is uncommon. Catal-

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ysis by iron pentacarbonyl, rhodium oxide, Rh_2O_3, or combinations of the two, was studied using acyclic and cyclic alkenes [8]. Although iron pentacarbonyl itself is a poor catalyst for aminomethylation, small amounts as co-catalyst strongly promote the rhodium-catalysed reaction by suppressing side reactions. Shorter reaction periods and smaller amounts of catalyst are required, and the reaction is not restricted to simple alkenes. Nevertheless, the catalytic conditions are also severe (170°C and 14 MPa).

Other mixed-metal systems such as $[Rh_6(CO)_{16}]$ or $[Ru_3(CO)_{12}]$ with $[Fe_3(CO)_{12}]$ have been studied [9]. Reactions catalysed by rhodium precursors gave better yields of aminomethylated products but higher selectivities were obtained with the iron–ruthenium system [8]. More recently [10], cobalt complexes containing diphosphine, such as $[Co_2(CO)_6(Ph_2PCH_2CH_2PPh_2)]$, were found to afford good yields but the catalytic conditions were still quite drastic (160°C and 10 MPa).

The aminomethylation reaction has been extended to tertiary polyamines either by condensation of alkenes with secondary polyamines [11] or by reaction of polyalkenes with primary or secondary amines [12,13]. Several rhodium or ruthenium precursors have been used, such as $[\{RhCl(norbornene)\}_2]$, $[Rh(norbornadiene)(PMe_2Ph)_3](PF_6)$ [11], $[HRh(CO)(PPh_3)_3]$ [12] and $[Ru_3(CO)_{12}]$ combined with a phosphonium salt [13]. Good yields of polyamines were observed.

In addition, the reductive amination of aldehydes or ketones in the presence of ammonia or amines was shown to occur with high yields using cobalt or rhodium carbonyls under pressure of H_2 and CO (10–30 MPa) [14].

It appears that the most efficient precursors are hydroformylation catalysts for the aminomethylation of alkenes by amines but high pressures and temperatures are required to obtain aminomethylated products in good yields by reducing side reactions.

We have recently described the catalytic properties of complex $[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(PPh_3)_2]$, **1**, for the low pressure (less than 1 MPa) selective hydroformylation of terminal alkenes in the presence of a slight excess of triphenylphosphine [15]. This paper deals with the extension of this hydroformylation reaction to aminomethylation under mild conditions. In a first approach, a model reaction, the aminomethylation of an unactivated alkene, oct-1-ene, by diethylamine, was studied. In a second step, this reaction was extended to various primary and secondary amines.

2. Results and discussion

Although slightly higher pressures (0.8–1.8 MPa) than those required for the hydroformylation reaction are used, complex **1** efficiently catalyses the one-pot synthesis of *N,N*-diethylnonylamine.

Table 1 shows that high conversions of oct-1-ene can be achieved at 0.8 MPa. The mass balance for the expected products or intermediates obtained is better than 95%; by-products are internal octenes and oligomers of aldehydes and enamines. The slowest step is the hydrogenation of the enamines, and for this reason a higher pressure was investigated. The results are shown on entry 2 of Table 1. A 99% conversion of alkene is maintained and the selectivity in products of interest is now 97%. Almost all the linear aldehyde and the corresponding enamine are transformed, whereas 13% of branched aldehyde are still present in the reaction medium after 15 h. In tetrahydrofuran, the rate-determining step appears to be the condensation of methyl-2-octanal with diethylamine, which is slow because of the steric hindrance of the methyl group on the α-carbon of the aldehyde.

Similarly, to improve the hydrogenation step (eqn. 4) the gaseous phase was enriched with hydrogen. The results are listed in Table 2. The experiments were performed during 3 h in order to have a better insight into the effects of an unbalanced gas phase. It appears clearly from entry 1 that too rich a hydrogen composition results in a reduced conversion, a favoured isomerisation of oct-1-ene into its internal isomers, and also a reduced production of aldehyde and enamine. In addition, 9% of heavy by-products are formed.

For a 1:2 $CO:H_2$ ratio, the conversion is higher (row 2) and more aldehydes and enamines are formed, but the balance deficiency now reaches 20%. Unexpectedly, a longer time is necessary for the hydrogenation of enamines to amines. For the hydroformylation reaction, we recently observed [15] that for complex **1** hydrogen is inhibiting. However, in this case the con-

TABLE 1. Aminomethylation of oct-1-ene by diethylamine catalysed by $[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(PPh_3)_2]$, **1**

Pressure (MPa)	Conversion (%)	Aldehydes		Enamines		Amines	
		n (%)	iso (%)	n (%)	iso (%)	n (%)	iso (%)
0.8	98	0.5	17	0.5	3	69	4
1.8	99	trace	13	trace	2	80	2

1 = 0.13 mmol; PPh_3 = 3.1 mmol (0.82 g); oct-1-ene = 38 mmol; diethylamine = 58 mmol; $CO:H_2 = 1$; $T = 80°C$; $t = 15$ h.

version is decreased and oct-2-ene and oct-3-ene are observed only for large H_2:CO ratios. This inhibition should operate even where the H_2:CO ratio corresponds to the total stoichiometry of the reaction. However, when this ratio is 1:1, 99% of oct-1-ene is converted into 96% of products of interest, and 3% internal octenes. No heavy products appear.

In addition, greater amounts of amines are formed, although the reaction is performed in an autoclave where the atmosphere becomes progressively richer in carbon monoxide as the reaction proceeds. We have shown that longer reaction times allow us to obtain the expected amines, with good selectivities. As shown in Table 3, for a 15 h reaction time, around 70% of amines are produced. As previously noted, the formation of the linear compounds is very easy.

The solvent has a dramatic influence on the course of the reaction (Table 4). Hydroformylation of terminal alkenes catalysed by **1** is favoured by polar solvents such as dichloroethane (DCE) and dimethylformamide (DMF) [15]. However, large amounts of oligomers of aldehydes and enamines are detected in dichloroethane. In this case, polymerization and side reactions are so predominant that no products of interest are obtained. In DMF, small quantities of amines are detected as well as significant amounts of the linear enamine. Presumably the hydrogenation of enamines is slower in DMF than in THF (Table 1), perhaps re-

TABLE 2. Synthesis gas composition effect on aminomethylation of oct-1-ene by diethylamine

$CO:H_2$	Conversion (%)	Internal octenes (%)	Aldehydes (%)	Enamines (%)	Amines (%)
1:4	60	8	10	30	3
1:2	95	3	29	40	3
1:1	99	3	34	49	13

1 = 0.13 mmol; PPh_3 = 3.1 mmol (0.82 g); oct-1-ene = 38 mmol; diethylamine = 58 mmol; P = 0.8 MPa; T = 80°C; t = 3 h.

TABLE 3. Influence of the reaction time on the aminomethylation of oct-1-ene by diethylamine

Reaction time (h)	Conversion (%)	Aldehydes (%)	Enamines (%)	Amines (%)
3	99	34	49	13
6	98	29	48	15
10	98	22	16	47
15	98	15	7	70

1 = 0.13 mmol; PPh_3 = 3.1 mmol (0.82 g); oct-1-ene = 38 mmol; diethylamine = 58 mmol; V_{total} = 30 ml; P = 0.8 MPa ($CO:H_2$ = 1) T = 80°C.

TABLE 4. Solvent effect on aminomethylation reaction catalysed by **1**

Solvent	Conversion (%)	Aldehydes		Enamines		Amines	
		n (%)	iso (%)	n (%)	iso (%)	n (%)	iso (%)
DCE [a]	97	Polymerization and side reactions					
DMF [b]	98	1.5	14	24	4	2	5

1 = 0.13 mmol; PPh_3 = 3.1 mmol (0.82 g); V_{total} = 30 ml; oct-1-ene = 38 mmol; diethylamine = 58 mmol; P = 0.8 MPa ($CO:H_2$ = 1); T = 80°C; t = 15 h. [a] dichloroethane; [b] *N*,*N*-dimethylformamide.

TABLE 5. Influence of a cosolvent concentration in the aminomethylation of oct-1-ene by diethylamine catalysed by **1**

EtOH (% vol)	Conversion (%)	Aldehydes		Enamines		Amines	
		n (%)	iso (%)	n (%)	iso (%)	n (%)	iso (%)
0	98	1	14	3	4	67	3
10	98	0.5	17	0.5	3	69	4
20	97.5	4	11	8	4	30	1

1 = 0.13 mmol; PPh_3 = 3.1 mmol (0.82 g); oct-1-ene = 38 mmol; diethylamine = 58 mmol; solvent = THF; V_{total} = 30 ml; P = 0.8 MPa ($CO:H_2$ = 1); T = 80°C; t = 15 h.

tarded by coordination of DMF to the rhodium hydrogenation catalyst. In addition, a lot of heavy by-products are formed in this reaction, owing to the basicity of the solvent. In an experiment in THF with triethylamine to make the system basic medium, it was similarly observed that the amounts of heavy compounds are significant.

We observed that adding ethanol to THF improves the rate of the reaction by 4–5%. Nevertheless, with more than 10% ethanol, oligomerisation of aldehydes and enamines occurs (Table 5). In this case, the reaction medium is sufficiently acid so that the classical polymerisation of aldehydes in the presence of water occurs [3]. We found that hydrogenation of enamines (produced by condensation of nonanal with diethylamine) in the presence of acetic acid gives only 5% of diethylnonylamine and a lot of heavy by-products. Thus, a cosolvent does not dramatically improve the reaction rate or the selectivity.

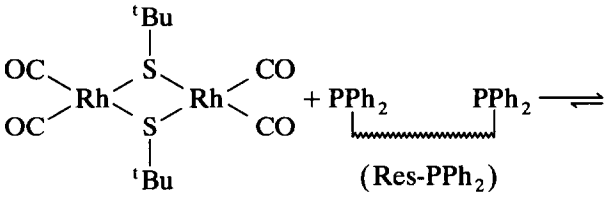
This aminomethylation reaction was extended to several other amines, in particular, bulky and basic amines. As shown on Table 6, morpholine, which is more basic and a better nucleophile than diethylamine, is characterized by a 90% total selectivity in products of interest. However, large quantities of enamines are still present after 15 h. The hydrogenation step is clearly slowed, presumably owing to strong coordination of morpholine or even enamine on rhodium. The same is true of t-butylamine, although in this case almost no terminal amine is produced (3%) and normal (71%) or branched (20%) enamines are formed (entry 2 of table 6).

Moreover, the steric hindrance of the amine was clearly established by experiment 3, where oct-1-ene is transformed almost exclusively into two C_9 aldehydes. Diethyl- and di-isopropyl-amine possess the same pKa (10.49 and 10.91 respectively). This recalls the poor reactivity of the branched aldehyde with diethylamine.

The nature of the rhodium complex was examined after catalysis. Infrared, ^1H and ^{31}P NMR spectroscopic data indicate that complex **1** was fully recovered and that no intermediate species could be detected. Moreover, after evaporation of the volatile products, about 40% of complex **1** can be precipitated, the remaining rhodium complex identified by IR as **1** mixed with heavy organic by-products. This precipitate can be recycled with no loss in activity.

As we recently showed that such a complex can be grafted onto a polymeric support to give $[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(Res\text{-}PPh_2)_2]$, **2**, which is characterized by high selectivities in linear aldehydes in hydroformylation [16], we examined the catalytic performance of **2** on the aminomethylation reaction, especially to recycle the catalyst by a simple filtration.

The supported rhodium complex was prepared according to the procedure already described [16] and summarized in eqn. (5).



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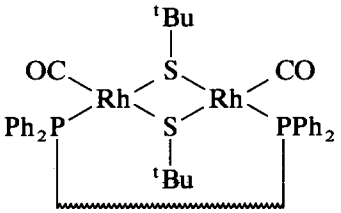

(5)

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As required for the hydroformylation reaction, the resin was exposed to complex $[Rh_2(\mu\text{-}S^tBu)_2(CO)_4]$ **3** in such a way that a molar P:Rh ratio near 10 was reached. The results of the catalytic tests carried out at 0.8 MPa are reported in Table 7. The experimental conditions were similar to those of the experiments conducted in THF. Entry 1 shows the most interesting results, because not only was there 95% conversion of alkene, but there were also high yields of enamine, especially the linear isomer. However, significant amounts of heavy compounds are responsible for the missing 25% of the mass balance. Unexpectedly,

TABLE 6. Aminomethylation of oct-1-ene by various amines

Amine	Conversion (%)	Aldehydes		Enamines		Amines	
		n (%)	iso (%)	n (%)	iso (%)	n (%)	iso (%)
Morpholine	99.5	3	6	20	6	42	13
t-butylamine	98.5	1	0.5	71 [a]	20 [a]	1	2
Di-isopropylamine	99	61	22	3	0.5	7	1

1 = 0.13 mmol; PPh_3 = 3.1 mmol (0.82 g); oct-1-ene = 38 mmol; amine = 58 mmol; V_{total} = 30 ml; solvent = 15 ml THF + 3 ml EtOH; T = 80°C; t = 15 h; P = 0.8 MPa ($CO:H_2$ = 1). [a] imines.

TABLE 7. Aminomethylation of oct-1-ene by diethylamine catalysed by $[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(Res\text{-}PPh_2)_2]$, **2**

Conversion (%)	Aldehydes		Enamines		Amines	
	n (%)	iso (%)	n (%)	iso (%)	n (%)	iso (%)
95	8	18	45	3	3	2
92 [a]	7	19	21	3.5	9	4
93 [b]	8	16.5	28	3	13	4
99.5 [c]	5	13	14	4	22	4

2 = 0.06 mmol; P/Rh = 10; oct-1-ene = 19 mmol; diethylamine = 29 mmol; solvent = THF; V_{total} = 30 ml; P = 0.8 MPa (CO : H_2 = 1); T = 80°C; t = 19 h. [a] solvent = THF (21 ml) + EtOH (3 ml); [b] **2** = 0.1 mmol, P/Rh = 5; [c] t = 63 h.

whereas for the hydroformylation reaction selectivities in linear aldehyde as high as 90% (for $P_{H_2}/P_{CO} = 1$) were easily achieved, here the reaction gives an overall 56 : 23 linear-to-branched ratio; apparently 18% branched aldehyde is present at the end of the run. This value is an overestimate because the linear products appear more quickly and the heavy products are formed mainly from the linear aldehyde. Because of the heavy-products and low linearity, we tried to improve the performance of the resins. As shown in Table 7, addition of a cosolvent, increase of the rhodium loading of the resin (thus decreasing the P : Rh ratio) and increase of the reaction time, do not change this result. From our own experience in supported homogeneous catalysis, macroporous resins that are characterized by high cross-linking release the grafted complexes very easily through the formation of the inactive species **3** under CO. In the present case of a 2% cross-linked microporous polymer, the flexibility of the polymeric chains is such that the excess of attached phosphorus groups displaces the equilibrium of eqn. 5 toward the grafted complex **2**.

We did not try to move from this, *a priori*, favourable case to macroporous resins, and we consider that this immobilisation problem remains unsolved.

3. Conclusion

We have shown that provided the reaction is performed in homogeneous solution, it is possible to transform an alkene directly into an amine by reaction with a primary or secondary amine under low pressures of carbon monoxide–hydrogen mixtures.

4. Experimental details

4.1. Equipment

^1H and ^{13}C NMR spectra were recorded on a Brüker AC 200 spectrometer and ^{31}P spectra on a Brüker WH 90 spectrometer. Gas chromatographic analyses were performed on a CARLO ERBA GC 600 gas chromatograph equipped with a flame detector fitted with a J.&W scientific 25 m DB 17 macrobore column. All the products ratios were determined by gas chromatography with anisole as internal standard (precision better than 5%). The standardization curves were made from the commercial substrates and authentic samples prepared by classical condensation of the aldehydes and amines followed by $NaBH_4$ reduction and purification.

4.2. Materials

All reagents were used as supplied by the manufacturers: oct-1-ene, diethylamine, morpholine, t-butylamine, triethylamine, tertiobutylmercaptan and triphenylphosphine were obtained from Aldrich; nonanal and diisopropylamine from Janssen; carbon monoxide and hydrogen from Prodair (purity greater than 99%).

Solvents such as tetrahydrofuran, methanol, dichloroethane and dimethyl formamide were obtained from SDS. They were distilled under dinitrogen and stored over molecular sieves.

All operations involving catalyst systems, catalytic tests and synthesis of rhodium complexes were carried out under dry dinitrogen by standard Schlenk techniques. Reagents and solvents were degassed by bubbling dinitrogen during 15 min before each use.

The complexes $[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(PPh_3)_2]$, **1**, and $[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(Res\text{-}PPh_2)_2]$, **2**, were prepared according to the literature [16,17].

4.3. General procedure for the catalytic runs

–$[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(PPh_3)_2]$, **1**, was added to a dinitrogen-saturated mixture of solvent, alkene and amine. This mixture was introduced by suction into an evacuated stainless-steel autoclave. The autoclave was heated to 80°C under 0.8 MPa or 1.8 MPa of carbon monoxide and hydrogen. After 15 h, the autoclave was cooled, then slowly depressurized. The solution was transferred to a Schlenk tube and analysed by gas chromatography.

–$[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(Res\text{-}PPh_2)_2]$, **2**, was introduced in the autoclave under dinitrogen and then a mixture of organic compounds and solvent was added by suction. The autoclave was heated to 80°C under 0.8 MPa of carbon monoxide and hydrogen. After reac-

tion, the autoclave was cooled, then slowly depressurized. After filtration under dinitrogen, the organic phase was analysed by gas chromatography.

4.4. Identification of the compounds

–$[Rh_2(\mu\text{-}S^tBu)_2(CO)_2(PPh_3)_2]$, **1**, *selected spectroscopic data*, IR (KBr), ν(CO) 1965, 1947 cm^{-1}. ^1H NMR (200 MHz, CD_2Cl_2): 0.74 (singlet) and 1.69 (singlet) ppm corresponding to the tertiobutyl groups of the *cis* isomer. ^{31}P NMR (90 MHz, CD_2Cl_2): 35.1 ppm (doublet), $J(^{31}P\text{-}^{103}Rh) = 151$ Hz.

–*N,N*-diethylnonylamine, *selected spectroscopic data*, mass spectrum (EI) *m/z* 199 (M^+), 86 ($M^+ - C_8H_7$) main pic; ^1H NMR (200 MHz; $CDCl_3$): 2.34 (2H, triplet, NCH_2 from alkyl group), 2.44 (4H, quadruplet, NCH_2 from ethyl group), 0.96 (6H, triplet, CH_3 from ethyl group) ppm.

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