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A highly efficient method for the hydroaminomethylation of long-chain alkenes under aqueous, biphasic conditions

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ABSTRACT

The use of salts of secondary and primary amines with different inorganic and organic acids in hydroaminomethylation enables the quantitative conversion of 1-octene with high selectivity for saturated amines. We propose that a cationic rhodium species is formed under the acidic conditions which catalyses the hydrogenation of the enamine or imine formed subsequently. Thus the use of acids and amine salts enables the hydroaminomethylation of long-chain alkenes under aqueous, biphasic conditions with quantitative conversions and short reaction times.

1. Introduction

Hydroaminomethylation (HAM) is defined as a tandem reaction that consists of a hydroformylation reaction with an alkene to make the corresponding aldehyde, followed by an amination and a hydrogenation of the resulting enamine (Fig. 1). Eilbracht[1–4] and Beller[5–9] have investigated these reactions in single-phase systems, but few studies have examined the use of biphasic, aqueous systems.[10–12]

2. Results and discussion

Herein, we report new studies of the biphasic, aqueous hydroaminomethylation of 1-octene **1** with morpholine **2a** and various other secondary and primary amines (Fig. 2).[13a] The catalyst was formed in situ using $[Rh(cod)Cl]_2$ and the water-soluble ligand sodium-triphenylphosphinetrisulfonate (Na-TPPTS).

The effect of adding catalytic amounts of acids was described by Müller[14] and Buch et al.[5] and was found to have a positive effect on the catalytic activity but was not further examined. For the first time this approach was extended to the use of stoichiometric amounts of various salts of morpholine (Fig. 3). Table 1 shows the acids H_nX that were investigated in the hydroaminomethylation of 1-octene.

Surprisingly, the use of the corresponding amine salts in the hydroaminomethylation reaction led to significantly higher selectivities and to a further increase in catalytic activity (Table 2). All acids except **7** and **12** led to quantitative conversions (X) of 1-octene **1** in only 4 h. The overall selectivity for HAM-products (S-HAM, containing the intermediate aldehydes, enamines and the amines) increased to 99%. It is important to note that under these conditions the aldol condensation is suppressed and the enamine hydrogenation takes place quantitatively. Also, no significant quantities of octane (from the hydrogenation of 1-octene) were observed.

The use of methanesulfonic acid **13** affords amine **3a** with the best selectivity (98%) achieved in aqueous biphasic systems described to date. As confirmed by the investigations of Beller[12],

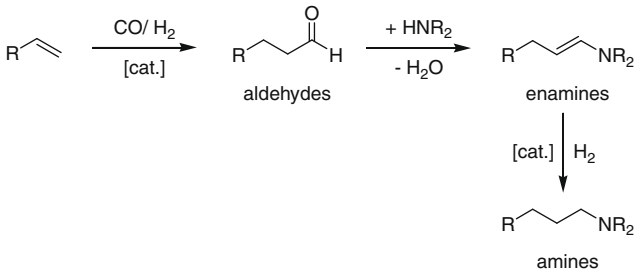

Figure 1. The hydroaminomethylation of an alkene with a secondary amine.

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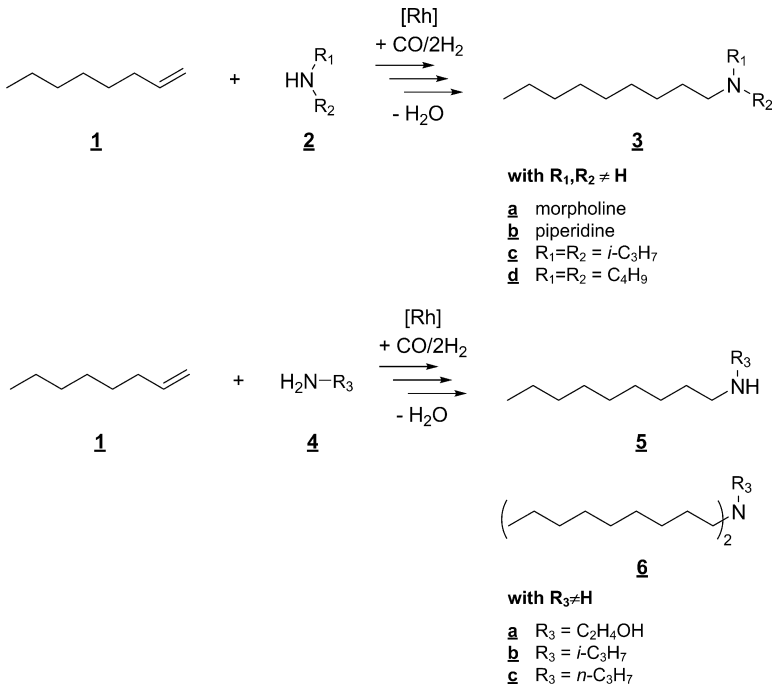


Figure 2. The hydroaminomethylation of 1-octene **1** with secondary amines **2** and primary amines **4**.

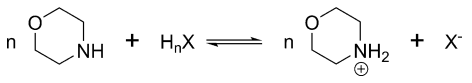


Figure 3. The general formation of morpholine salts with acids.

the hydrogenation of the intermediate enamines is the rate-determining step of the hydroaminomethylation reaction.[13a] The use of amine salts enabled a highly efficient and highly selective hydrogenation of the enamines, leading to nearly quantitative amine yields.

The influences of the different acids are not directly correlated with their pK_a values (Table 1). The reactivity cannot be explained with the strength of the acid alone, in fact soft bases seem to be essential for high conversions and selectivities.

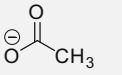
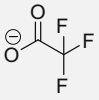
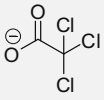
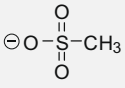
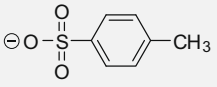
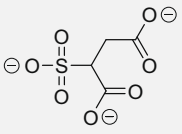
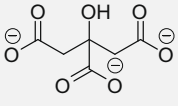
The use of various secondary (Table 3) and primary amines (Table 4) in the hydroaminomethylation reaction further emphasised the significant influence of the amine salts.

The use of piperidine **2b** and di-*n*-butylamine **2d** salts led to significantly higher conversions, and the yields and selectivities are similar to those observed with the salts of morpholine **2a**. Diisopropylamine **2c** formed the desired products only in trace amounts. However, this result is not an effect of the corresponding acid, because in its absence, only trace product was found (Table 3). Also, the reactions with primary amines, for example, *n*-propylamine **4c**, successfully provided the desired saturated amines with nearly quantitative conversions (Table 4).

The obvious influence of the acid on the hydrogenation could be explained by the formation of a new catalytically active species under the reaction conditions via protonation. The formation of cationic rhodium–phosphine and rhodium–phosphite complexes was investigated by Bitterwolf in NMR-studies.[20] The complex formed is shown in Figure 4.

The acid enables the dissociation of a carbonyl ligand, leading to the formation of a cationic rhodium hydride species, which is more active in hydrogenation (Table 3). Martin et al. have demonstrated the increased hydrogenation activity of iridium complexes in the presence of an acid. This in situ-generated cationic species showed an increased activity for the hydrogenation of imines, and in

Table 1
Acids used in the formation of morpholine salts

Acid	Anion X^-		pK_a
Hydrochloric acid		**7**	−7.0
Sulfuric acid		**8**	−3.0; 1.9
Phosphoric acid		**9**	2.1; 7.2
Acetic acid		**10**	4.8
Trifluoroacetic acid		**11**	−0.3
Trichloroacetic acid		**12**	0.7
Methanesulfonic acid		**13**	~−2 (−1.6)
p-Toluenesulfonic acid		**14**	~0.7 (−2.1)
Sulfosuccinic acid		**15**	(−1.7; 3.0; 4.6)
Citric acid		**16**	3.1; 4.8; 6.4

pK_a values were reported in the literature.[15–18]; in parentheses: pK_a values calculated with ChemAxon Marvin Calculator.[19]

Table 2
The hydroaminomethylation of 1-octene: Addition of morpholine salts with various anions

Anion X^-	X_{octene}	S(HAM)	Y(**3a**)	S(**3a**)
–	89	89	72	80
7	10	62	Trace	n.d.
8	>99	97	85	85
9	>99	>99	60	60
10	97	92	83	86
11	>99	98	93	89
12	56	70	12	22
13	>99	89	89	98
14	>99	98	93	94
15	99	97	84	88
16	>99	>99	96	96

(The conversion X, yield Y and selectivity S were determined by GC using an internal standard; 0.42 mol % $[Rh(cod)Cl]_2$, Rh/TPPTS = 1/64, 24 mmol 1-octene, amine/1-octene = 2/1, 60 bar synthesis gas (at room temperature, CO/H_2 = 1:3), stirring rate 1500 min^{-1}, 60 g water, T = 130 °C, t = 4 h).

Table 3
The hydroaminomethylation of secondary amines with 1-octene and the influence of the corresponding sulfate salt

Amine	Anion X^-	X_{Amine}	S(HAM)	Y(**3**)	S(**3**)
2a (morpholine)	–	89	89	72	80
	8	>99	97	85	85
2b (piperidine)	–	87	72	47	54
	8	>99	>99	97	97
2c (diisopropylamine)	–	79	60	<1	<1
	8	86	86	Trace	n.d.
2d (di-*n*-butylamine)	–	72	77	8.0	11
	8	>99	98	96	96

(X and Y were determined by GC using an internal standard; 0.42 mol % $[Rh(cod)Cl]_2$, Rh/TPPTS = 1/64, 24 mmol 1-octene, amine/1-octene = 2/1, 60 bar synthesis gas (at room temperature, CO/H_2 = 1:3), stirring rate 1500 min^{-1}, 60 g water, T = 130 °C, t = 4 h).

Table 4
The hydroaminomethylation of primary amines with 1-octene and the influence of the corresponding sulfate salt

Amine	Anion X^-	X_{amine}	S(HAM)	Y(**5**+**6**)	S(**5**+**6**)
4a (ethanolamine)	–	87	66	Trace	n.d.
	8	97	82	21[a]	18
4b (isopropylamine)	–	87	84	Trace	n.d.
	8	98	85	43[b]	40
4c (*n*-propylamine)	–	92	90	5[c]	5
	8	>99	95	95[d]	95

(X and Y were determined by GC using an internal standard; 0.42 mol % $[Rh(cod)Cl]_2$, Rh/TPPTS = 1/64, 24 mmol 1-octene, amine/1-octene = 2/1, 60 bar synthesis gas (at room temperature, CO/H_2 = 1:3), stirring rate 1500 min^{-1}, 60 g water, T = 130 °C, t = 4 h, ratio **5**/**6**: [a]<1/99, [b]29/71, [c]47/53, [d]16/84).

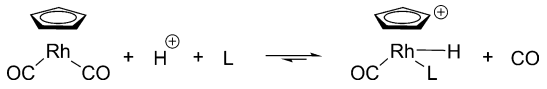


Figure 4. The influence of an acid on the formation of a cationic rhodium species.

contrast, alkenes were only hydrogenated to a slight extent.[21] Furthermore, protonated cationic ruthenium complexes are used in industrial-scale enantioselective hydrogenation reactions.[22]

The highly efficient hydrogenation of enamines and imines using a rhodium phosphine complex in acidic aqueous media has not yet been reported. The present work demonstrates the activation of a rhodium complex by the addition of an acid at pH values of <7, and the resulting complex **17** (Fig. 5) is suitable for the highly selective and efficient hydrogenation of imines and enamines.

Recent findings by Hamers et al. on the influence of protic solvent additives and pK_a on the hydroaminomethylation in non aqueous media support our results in terms of the influence on the active Rh-species.[23,24] The addition of organic and inorganic acids to rhodium complexes led to the hydroaminomethylation of 1-octene with selectivities up to 98% and with quantitative conversions. The positive influence of acids is observed for both secondary and primary amines. This cascade reaction does not require high catalyst concentrations or the addition of a second hydrogenation catalyst. Future studies will be related to the use of short-chain alkenes, dienes and the investigation of the reaction in a mini-plant jetloop reactor under improved mass-transfer conditions.[13a–d]

3. Experimental

In a typical experiment, the amine (48 mmol) is dissolved in doubly distilled water (48 g) under argon. Concentrated acid is added until the pH value reaches ca. 3.5. Then, Na-TPPTS (6.4 mmol), $[Rh(cod)Cl]_2$ (50 µmol, 0.42 mol %) and 1-octene (24 mmol) are added. The reaction is carried out in a 300 mL-Parr-autoclave at 60 bar of synthesis gas (CO/H_2 = 1:3) and 130 °C for 4 h. The mixture is analysed by gas chromatography using 1-octanol as the internal standard.

3.1. Morpholine (2a)

^{1}H NMR (DMSO, 500 MHz): δ = 2,29 (s, 1H, NH), 2.64 (t, 4H, CH_2–CH_2–NH), 3.48 (t, 4H, O–CH_2–CH_2); ^{13}C NMR (DMSO, 500 MHz): δ = 46.3; 67.6.

3.2. Morpholin-4-ium chloride (7)

^{1}H NMR (DMSO, 400 MHz): δ = 3.06 (t, 4H, CH_2–CH_2–NH_2^+), 3.81 (t, 4H, O–CH_2–CH_2), 9.74 (s, 2H, NH_2^+); ^{13}C NMR (DMSO, 100 MHz): δ = 42.5; 63.1.

3.3. Bis(morpholin-4-ium)sulfate (8)

^{1}H NMR (DMSO, 500 MHz): δ = 2.90 (t, 4H, CH_2–CH_2–NH_2^+), 3.64 (t, 4H, O–CH_2–CH_2); ^{13}C NMR (DMSO, 100 MHz): δ = 44.3; 65.2.

3.4. Bis(morpholin-4-ium)hydrogenphosphate (9)

^{1}H NMR (DMSO, 500 MHz): δ = 2.88 (t, 4H, CH_2–CH_2–NH_2^+), 3.67 (t, 4H, O–CH_2–CH_2), 5.75 (br s, 2H, NH_2^+); ^{13}C NMR (DMSO, 100 MHz): δ = 43.9; 64.9; ^{31}P NMR (DMSO, 81 MHz): δ = 1.86.

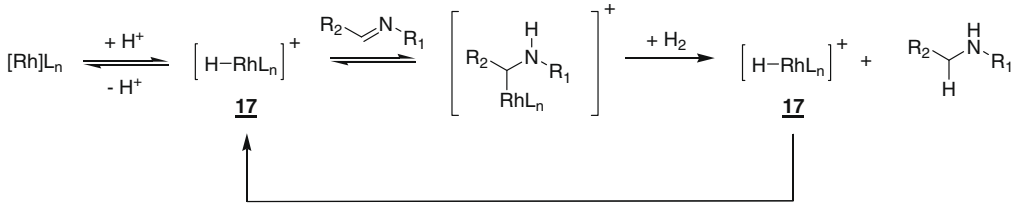


Figure 5. A proposed mechanism for the hydrogenation of an imine with a protonated rhodium complex.

3.5. Morpholin-4-ium acetate (10)

^{1}H NMR (DMSO, 400 MHz): δ = 1.84 (s, 3H, CH_3–COO^-), 2.75 (t, 4H, CH_2–CH_2–NH_2^+), 3.56 (t, 4H, O–CH_2–CH_2), 8.35 (br s, 2H, NH_2^+); ^{13}C NMR (DMSO, 100 MHz): δ = 22.2; 44.9; 66.3; 173.1.

3.6. Morpholin-4-ium trifluoroacetate (11)

^{1}H NMR (DMSO, 500 MHz): δ = 3.11 (t, 4H, CH_2–CH_2–NH_2^+), 3.76 (t, 4H, O–CH_2–CH_2), 8.99 (s, 2H, NH_2^+); ^{13}C NMR (DMSO, 100 MHz): δ = 42.8; 63.3; 115.6; 118.6; 158.5; 158.8; ^{19}F NMR (DMSO, 188 MHz): δ = −74.0.

3.7. Morpholin-4-ium trichloroacetate (12)

^{1}H NMR (DMSO, 400 MHz): δ = 3.22 (m, 4H, CH_2–CH_2–NH_2^+), 3.57 (m, 4H, O–CH_2–CH_2), 8.25 (m, 2H, NH_2^+); ^{13}C NMR (DMSO, 100 MHz): δ = 43.9; 66.0; 79.3; 157.4.

3.8. Morpholin-4-ium methansulfonate (13)

^{1}H NMR (DMSO, 400 MHz): δ = 2.39 (s, 3H, CH_3), 3.11 (t, 4H, CH_2–CH_2–NH_2^+), 3.77 (t, 4H, O–CH_2–CH_2); ^{13}C NMR (DMSO, 100 MHz): δ = 36.0; 42.9; 63.3.

3.9. Morpholin-4-ium-4-methylbenzylsulfonate (14)

^{1}H NMR (DMSO, 400 MHz): δ = 2.30 (s, 3H, C–CH_3), 3.10 (t, 4H, CH_2–CH_2–NH_2^+), 3.76 (t, 4H, O–CH_2–CH_2), 7.16 (dd, 2H, CH_3–C–CH), 7.55 (dd, 2H, CH–CH–C–SO_3^-); ^{13}C NMR (DMSO, 100 MHz): δ = 20.9; 43.0; 63.3; 125.6; 128.4; 138.4; 144.8.

3.10. Tris(morpholin-4-ium)-1,2-dicarboxyethansulfonate (15)

^{1}H NMR (DMSO, 400 MHz): δ = 2.58–2.63 (dd, 1H, CH–CHH–COO^-), 2.68–2.75 (dd, 1H, CH–CHH–COO^-), 2.95 (t, 4H, CH_2–CH_2–NH_2^+), 3.54–3.58 (dd, 1H, CH_2–CH–SO_3^-), 3.70 (t, 4H, O–CH_2–CH_2), 7.02 (br s, 2H, NH_2^+); ^{13}C NMR (DMSO, 100 MHz): δ = 35.9; 43.6; 64.4; 64.5; 172.4; 174.5.

3.11. Tris(morpholin-4-ium)-2-hydroxypropan-1,2,3-tricarboxylate (16)

^{1}H NMR (DMSO, 400 MHz): δ = 2.45 (dd, 4H, CH_2–COO^-), 2.92 (t, 4H, CH_2–CH_2–NH_2^+), 3.67 (t, 4H, O–CH_2–CH_2), 6.84 (br s, 2H, NH_2^+); ^{13}C NMR (DMSO, 100 MHz): δ = 43.8; 45.4; 64.8; 72.4; 173.6; 178.2.

Acknowledgements

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