Pergamon

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Tetrahedron Letters 44 (2003) 1631–1634

TETRAHEDRON LETTERS

Montmorillonite K10 as a suitable co-catalyst for atom economy in chelation-assisted intermolecular hydroacylation

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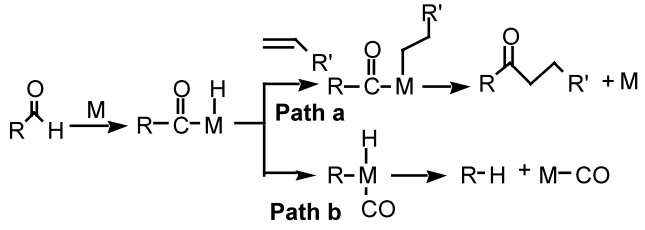
Received 25 November 2002; accepted 20 December 2002

Abstract—The clay montmorillonite K10 is an efficient acidic solid that can act as a reusable co-catalyst in the condensation reaction of aldehydes and amines to provide the imine intermediate which is then transformed into the ketone through the hydroiminoacylation reaction, in the presence of rhodium complexes.

Carbon–hydrogen bond activation through catalysed hydroacylation reaction is a useful tool to convert aldehydes into ketones. A key step in this reaction is the C–H bond activation in the aldehyde by a metal complex to generate an acyl–hydride intermediate.[1] However, these intermediates can take two different pathways: hydrometalation of an olefin to give acyl–metal–alkyl complexes which eventually provide the expected ketone through reductive elimination[2] (Scheme 1, path a), or decarbonylation to give an alkane and a metal–carbonyl[3] (Scheme 1, path b).

Decarbonylation is not competitive in the intramolecular hydroacylation,[4] but becomes an important limitation in the intermolecular version. In order to stabilise the acyl–metal–hydride intermediate, the addition of an excess of ethylene, or carbon monoxide, or vinylsilanes with Co(I) catalysts, have been used as suitable strategies.[2] However, chelation by cyclometalation of the substrate has efficiently suppressed decarbonylation.[5] The chelation-assisted intermolecular hydroacylation is based on the conceptual transformation of chelated carboxaldimines (usually pyridyl–carboxaldimine) into carboxketimines through catalytic hydroiminoacylation.[6] In this context a general synthetic method has been recently developed to obtain, in one step, ketones from aldehydes in the presence of chelating amines as additives.[7] However, the in situ condensation of aldehydes and amines seems to be one of the rate-determining steps of the global process. The alternatives to enhance the reactivity in this step involve the formation of a previous imine compound **1** from aniline and benzaldehyde (Scheme 2, path b), followed by transimination with 2-amino-3-picoline towards the carboxaldimine **2** (Scheme 2, path b).[7] A carboxylic acid must also be added to catalyse both condensation and transimination steps. The success of this reaction, therefore, depends on a large number of additives and co-catalysts.



Scheme 1.

All this prompted us to search for a way of facilitating the formation of **2**, avoiding additives. As part of our research[8] concerning the use of acidic solids as catalysts[9] to reduce the hazardous materials involved in chemical processes, we have investigated the hydroacylation through hydroiminoacylation of aldimines in presence of montmorillonite K10 (MK10) clay as acidic co-catalyst (Scheme 2, path a). We started by examining the catalytic hydroacylation of benzaldehyde with 1-hexene to give heptanophenone, in the presence of 2 mol% of $[Rh(PPh_3)_3Cl]$ and 2-amino-3-picoline as the chelating amine reagent. It must be pointed out, as it has been reported previously,[7] that working at the

Keywords: aldehydes; ketones; clays; intermolecular hydroacylation.
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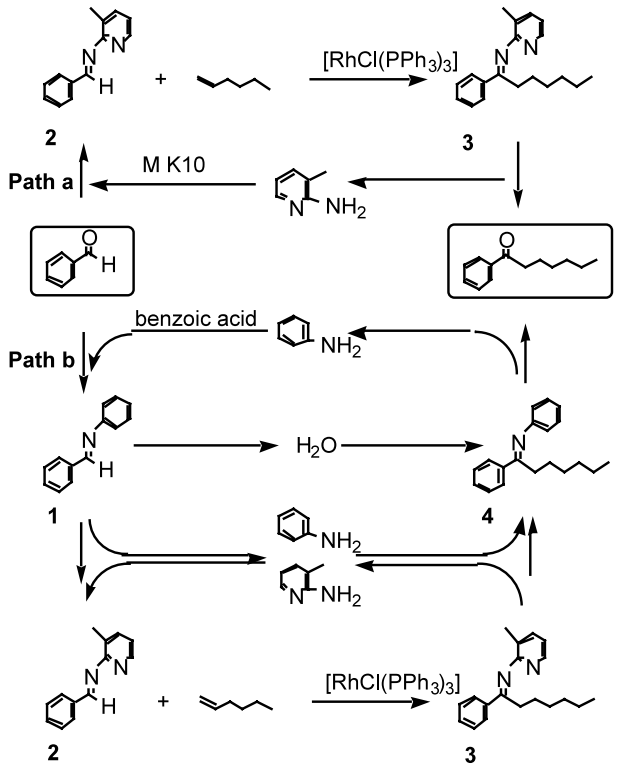
0040-4039/03/$ - see front matter
PII: S0040-4039(03)00026-1



Scheme 2.

reaction temperature of 130°C for 1 h, only 9% of yield on heptanophenone was observed (Table 1, entry 1). The use of organic acids as co-catalysts in this reaction increased the percentage of heptanophenone, although it seems to be dependent of the strength and amount of the Brønsted acid. The stronger the acidity of the co-catalyst, the lower conversion and selectivity on heptanophenone were observed (Table 1, entry 2 and 3). It seems that *p*-toluen-sulphonic acid could react with 2-amino-3-picoline diminishing the amount of the base required in the hydroacylation reaction. Even the addition of a larger quantity of benzoic acid does not contribute to a major conversion of benzaldehyde into heptanophenone (Table 1, entry 4). On the other hand, the addition of MK10 provides values of conversion and percentage of heptanophenone comparable to the reaction with benzoic acid, (Table 1, entry 5). Montmorillonite K10 is characteristic of a high surface area (BET area = 221 m^2/g) and Brønsted acidity centres (1.4×10^{-4} meq H^+/m^2). MK10 efficiently catalyses the condensation of benzaldehyde and 2-aminopicoline due to its acidic properties and to the shift of the equilibrium towards the formation of **2** by removing water from the reaction media.[10] The subsequent rhodium catalysed hydroiminoacylation converted aldimine **2** into ketimine **3**, which was partially hydrolysed in situ towards the corresponding hydroacylated product, heptanophenone (42%) (Table 1, entry 5). Because of its acidic properties, MK10 can catalyse aldimine formation but also ketimine hydrolysis. This methodology has avoided using aniline and benzoic acid, as well as forming intermediates **1** and **4**.[7] Taking into account how the number of Brønsted acid centres affects to the

Table 1. Influence of the amines in the hydroacylation of benzaldehyde with 1-hexene catalysed by $[RhCl(PPh_3)_3]$ and MK10[a]

Entry	Acidic co-catalyst	Amine	Conv. [%][b]	**2** [%][b]	**3** [%][b]	Heptanophenone [%][b]
1	---					9[c]
2	PTS[d] (6%)	"	38	39	27	34
3	Benz. ac (6%)	"	86	2	42	56
4	Benz. ac (12%)	"	74	16	10	74
5	MK10	"	80	2	56	42
6	$^+$H-MK10	"	64	0	59	41
7	MK10		39	60	33	7
8	MK10		43	38	53	9
9	MK10		35	94	6	0

[a]Standard conditions: benzaldehyde (2.5 mmol), 1-hexene (12.5 mmol), amine (0.75 mmol), $[RhCl(PPh_3)_3]$ (0.05 mmol), MK10: Montmorillonite K10 (83 mg). Solvent: toluene (0.5 mL). T: 110°C. Time: 2h. [b]Percentages determined by G.C. [c]Ref 7. [d]PTS = *p*-toluen-sulphonic acid.

catalytic process, we prepared a more acidic clay than montmorillonite K-10, by acidification of MK10 with HNO_3 to provide $^+$H-MK10 with 7.7×10^{-4} meq H^+/m^2. However, the conversion significantly decreases, probably due to the interaction of $^+$H-MK10 with the reactant picoline (Table 1, entry 6).

Different types of 2-aminopyridine derivatives were examined to determine how the amine influenced both aldimine formation through the NH_2 functional group and the chelating ability with the rhodium complex through the nitrogen atom in the pyridinyl group. Of all the 2-aminopyridine derivatives studied, 2-amino-3-picoline contributed to the highest catalytic activity, followed by 2-amino-5-picoline (Table 1, entries 5 and 8). However those amine derivatives having a methyl group in *meta* position with respect to the NH_2 functional group provided the lowest conversion (Table 1, entries 7 and 9). These results contrast with those observed in a previously reported work,[11] where 2-amino-4-picoline showed the highest catalytic activity. In addition, it should be pointed out that 2-amino-6-picoline did not contribute to the hydroiminoacylation, probably because of the steric hindrance provided by the 6-methyl group, which disfavoured the formation of the six-membered ring metallacyclic complex.[11]

Another interesting advantage of the use of MK10 as acidic co-catalyst is that it can be easily separated from the products by a simple filtration. The addition of two

Table 2. Hydroacylation of benzaldehyde with 1-hexene catalysed by $[RhCl(PPh_3)_3]$ and MK10[a]

Entry	MK10 (mg)	2-Amino-3-picoline (mmol)	T (°C)	t (h)	Conv. (%)[b]	Aldimine **2** (%)[b]	Heptano-phenone (%)[b,c]
1	83	0.75	110	2	80	2	98
2	83	0.75	130	2	72	12	88
3	83	0.75	130	4	76	12	88
4	166	0.75	110	2	67	21	79
5	333	0.75	110	2	41	22	78
6	83	0.25	110	2	33	0	100
7	83	1.25	110	2	81	7	93

[a] Standard conditions: benzaldehyde (2.5 mmol), 1-hexene (12.5 mmol), $[RhCl(PPh_3)_3]$ (0.05 mmol), MK10: MK10 (83 mg). Solvent: toluene (0.5 mL). T: 110°C. Time: 2 h.
[b] Percentages determined by GC.
[c] With the addition of two drops of HCl (1N) to the filtrates.

drops of HCl (1N) to the filtrates favoured the total hydrolysis of ketimine **3** towards heptanophenone (Table 2, entry 1). Similar results are obtained when the filtrates are purified by column chromatography (SiO_2, *n*-hexane/ethyl acetate 4/1), to yield pure heptanophenone. The literature reports the use of the last procedure (purification in acidic silica), to guarantee the ketimine hydrolysis towards the ketone.[7]

The search of best reaction conditions is summarised in Table 2. The suitable amounts of MK10 and 2-amino-3-picoline are 83 mg (Table 2, entry 1, 4 and 5) and 0.75 mmol (Table 2, entries 1, 6 and 7), respectively. Temperature has also been optimised at 110°C, (Table 2, entries 1 and 2), and the reaction time at 2 h, because longer reaction times do not improve significantly the conversion of the reaction (Table 2, entries 2 and 3). Under these conditions the conversion achieved is about 80% and the selectivity for heptanophenone is 98%. When the reaction was scaled up to 7.5 mmol of benzaldehyde and 37.5 mmol of 1-hexene, (in the presence of 250 mg of MK10 and 0.15 mmol of $[Rh(PPh_3)_3Cl]$), similar values were obtained for conversion and selectivity, 80% and 97% respectively.

When the concentration of 1-hexene was changed from 12.5 mmol (5 equiv.) to 2.5 mmol (1 equiv.), based upon benzaldehyde, the conversion and percentage on heptanophenone dramatically decreased (Fig. 1). Thus an excess of 1-hexene seems to be required.

We extended the study to explore several other olefins and aldehydes as substrates in order to determine the scope of the intermolecular hydroacylation co-catalysed by MK10 and $[Rh(PPh_3)_3Cl]$. All terminal olefins were hydroacylated in fairly good yields within 2 h (Table 3, entries 1 and 2). A lower conversion and lower selectivity towards the corresponding ketone have been found for the internal olefin cyclohexene (Table 3, entry 3), which can be related to its higher steric hindrance. It is worth saying that cyclohexene failed to undergo hydroacylation in the literature reported.[7a] Also satisfactory results in terms of selectivity were obtained by using as well electron-releasing or electron-withdrawing aryl substituents on the aldehyde substrate (Table 3, entries 4 and 5).

Finally, one other advantage of this new methodology is the recycling capacity of MK10 after it is separated from the products and washed with toluene and CH_2Cl_2. As is shown in Figure 2, MK10 can be reused,

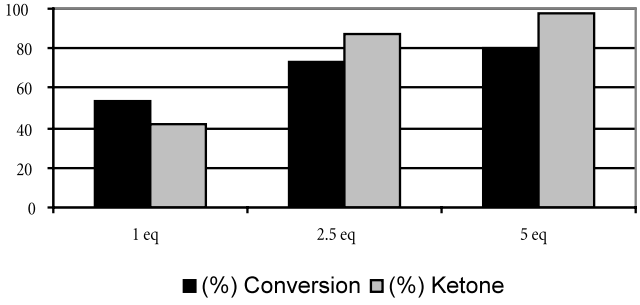
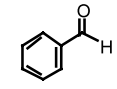
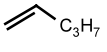
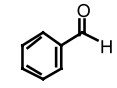
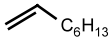
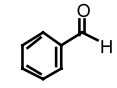
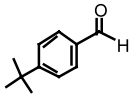
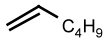
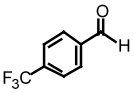
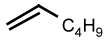


Figure 1.

Table 3. Scope of the hydroacylation reaction catalysed by $[RhCl(PPh_3)_3]$ and MK-10[a]

Entry	Aldehyde	Olefin	Conv. (%)[b]	Ketone (%)[b,c]
1			90	90
2			74	96
3			35	22
4			68	96
5			61	97

[a]Standard conditions: aldehyde (2.5 mmol), olefin (12.5 mmol), $[RhCl(PPh_3)_3]$ (0.05 mmol), MK10: Montmorillonite K10 (83 mg). Solvent: toluene (0.5 mL). T: 110°C. Time: 2h. [b]Percentages determined by G.C. [c]With the addition of 2 drops of HCl (1N) to the filtrates.

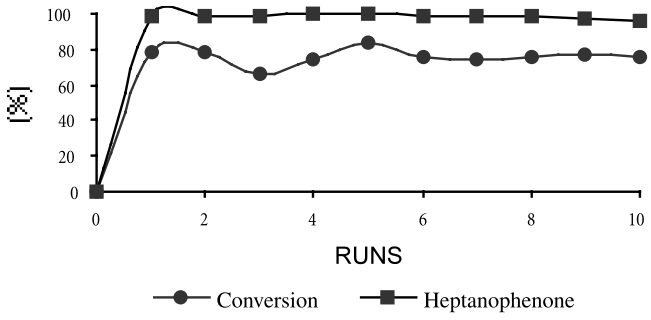


Figure 2.

with re-addition of the rhodium complex, for at least ten consecutive runs without a significant loss in activity. The easy separation of MK10 from the reaction products and its reutilization, becomes an additional advantage to the use of organic acids as co-catalysts.

The results show that intermolecular hydroacylation is efficiently carried out using MK10 as acidic co-catalyst. This reduces the number of reactants required and the intermediates formed, improving the atom economy of the process. In addition, the co-catalyst can be easily separated from the products and reused for a significant number of consecutive runs, without affecting the activity. Further work on the extension of this methodology towards other aldehydes and olefins (including not aromatic aldehydes) is in progress.

Acknowledgements

This work was supported by Ministerio de Ciencia y Tecnologia (BQU2001-0656). We thank the University of Pamplona (Colombia) for leave (to X.Y.).

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