

Catalytic activity of polymerizable metal β -ketoesterato complexes towards Michael addition reactions

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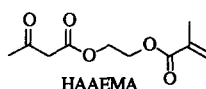
Abstract

The addition of β -dioxigenato compounds to methyl vinyl ketone was catalysed by nickel(II) and cobalt(II) complexes with the polymerizable β -ketoesterato 2-(acetoacetoxy)ethyl methacrylate (AAEMA⁻) under homogeneous and heterogeneous phases. The homogeneous reactions were carried out using the soluble Ni(AAEMA)₂ and Co(AAEMA)₂ complexes whereas the heterogeneous catalytic tests were carried out using the copolymers obtained by reaction of M(AAEMA)₂ (M = Ni or Co) with suitable acrylamides.

Keywords: Cobalt; Michael addition; Ketoesterate; Nickel; Polymer support; Supported catalysts

1. Introduction

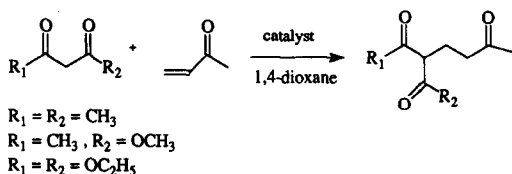
The formation of C–C bond through metal-catalysed Michael addition has recently received much attention, especially in view of the advantages in terms of chemoselectivity and activity that can be achieved by substituting the classical basic catalysts [1] with a transition metal complex. The first example reported in the literature is the copper isocyanide catalysed addition of active hydrogen compounds to α,β -unsaturated substrates [2]. Since then, many catalytic systems [3], most of which comprise a metal acetylacetonate or acetate, have been employed successfully for this reaction and asymmetric catalysis has also been achieved [4].



In the course of the investigation on the catalytic activity [5] of AAEMA⁻ transition metal complexes [6] (AAEMA⁻ = deprotonated form of 2-(acetoacetoxy)ethyl methacrylate, vide supra) and their heterogeneous analogues, we have focused our attention to the metal catalysed Michael addition of β -dioxigenato compounds such as acetylacetone, methyl acetoacetate and diethyl malonate to methyl vinyl ketone (Scheme 1).

The tests in homogeneous phase were carried out using the soluble Ni(AAEMA)₂ or Co(AAEMA)₂ complexes. The heterogeneous reactions were carried out with insoluble polymer-bound complexes obtained, as described by us

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Scheme 1. Catalytic Michael additions of dioxygenated donors to methyl vinyl ketone.

[7], by thermal copolymerization of $\text{Ni}(\text{AAEMA})_2$ or $\text{Co}(\text{AAEMA})_2$ with *N,N*-dimethylacrylamide (DMAA) and *N,N'*-methylenebisacrylamide (MBAA).

2. Results and discussion

Table 1 summarizes the results obtained when a Michael donor such as acetylacetone, methyl acetoacetate or diethyl malonate was reacted with methyl vinyl ketone at various conditions. It is apparent that in the absence of metal catalyst the reaction does not proceed (entry 1), and that $\text{Fe}(\text{AAEMA})_3$ is a poor catalyst for this reaction (entry 2). On the other hand, by stirring at 75°C

Table 1
Michael additions of dioxygenated donors (2.5 mmol) to methyl vinyl ketone (2.9 mmol) in dioxane (2 ml) in homogeneous phase catalysed by AAEMA^- (0.025 mmol)

Entry	Michael donor	Catalyst	Temp °C	Time (h)	Yield %
1		none	75	19	<3
2	"	$\text{Fe}(\text{AAEMA})_3$	75	19	5
3	"	$\text{Ni}(\text{AAEMA})_2$	RT	78	4
4	"	$\text{Ni}(\text{AAEMA})_2$	75	19	95
5		$\text{Ni}(\text{AAEMA})_2$	RT	64	62
6	"	$\text{Ni}(\text{AAEMA})_2$	75	19	90
7		$\text{Ni}(\text{AAEMA})_2$	RT	140	15
8	"	$\text{Ni}(\text{AAEMA})_2$	75	36	99
9		$\text{Co}(\text{AAEMA})_2$	RT	78	15
10	"	$\text{Co}(\text{AAEMA})_2$	75	19	99
11		$\text{Co}(\text{AAEMA})_2$	RT	54	80
12	"	$\text{Co}(\text{AAEMA})_2$	75	19	99
13		$\text{Co}(\text{AAEMA})_2$	RT	140	30
14	"	$\text{Co}(\text{AAEMA})_2$	75	36	99

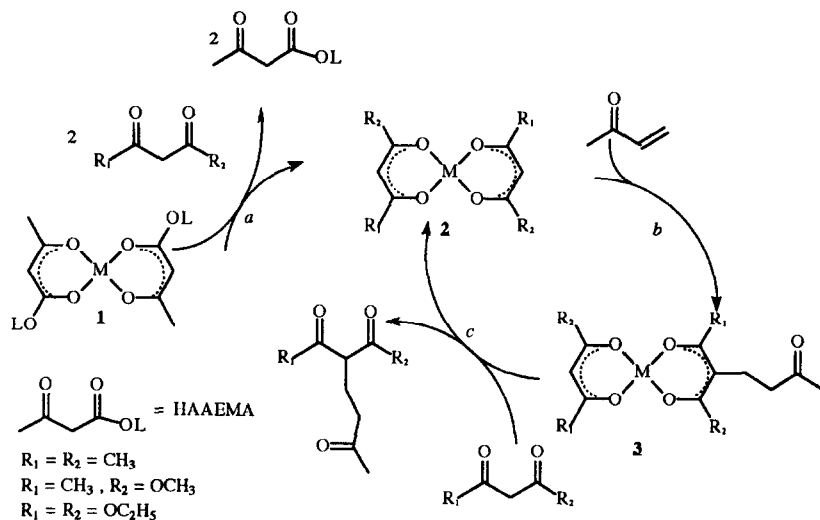
a mixture of the Michael donor and methyl vinyl ketone in dioxane in the presence of 1.0% nickel(II) or cobalt(II) catalyst, high yields of the relevant adducts were achieved (entries 4, 6, 8, 10, 12, 14). For all reactions the observed selectivity was good (>98%).

When the Michael additions were carried out at room temperature (RT) methyl acetoacetate was found to be the most reactive substrate (62% after 64 h with $\text{Ni}(\text{AAEMA})_2$, entry 5; 80% after 54 h with $\text{Co}(\text{AAEMA})_2$, entry 11), whereas acetylacetone reacted sluggishly either with Ni(II)- and with Co(II)-based catalysts (entries 3 and 9, respectively). Furthermore, the reaction observed with diethylmalonate as the Michael donor was slow, but significant (15% after 140 h with $\text{Ni}(\text{AAEMA})_2$, entry 7; 30% after 140 h with $\text{Co}(\text{AAEMA})_2$, entry 13).

The comparison between entries 3–8 and 9–14 shows a higher activity of the Co(II)-based catalyst with respect to Ni(II)-based one. The same activity order was already found in the $\text{Ni}(\text{acac})_2$ or $\text{Co}(\text{acac})_2$ catalysed addition of acetylacetone to 3-thienyldenemalonaldhyde [3](h). The different activity of Ni(II) and Co(II) can be explained if we consider the commonly accepted catalytic cycle for the addition reaction (Scheme 2).

It is likely that step *a*, leading to species **2**, is completely driven to the right if acetylacetone or methyl acetoacetate are present as Michael donors. This is due to the higher formation constant of the metal acetylacetonates with respect to the β -ketoesterates [8], in the case of acetylacetone, and to the mass action of the one hundred-fold excess of the substrate with respect to the starting complex, in the case of methyl acetoacetate. For diethyl malonate a compromise between the two effects (that is the lower strength of the diesterate as a ligand and its one hundred-fold excess in the reaction solutions) should lead to the establishment of an equilibrium between **1** and **2**.

The higher electron density is present on the activated methyne carbon in species **2**, the higher reactivity is expected in the subsequent nucleo-



Scheme 2. Catalytic cycle.

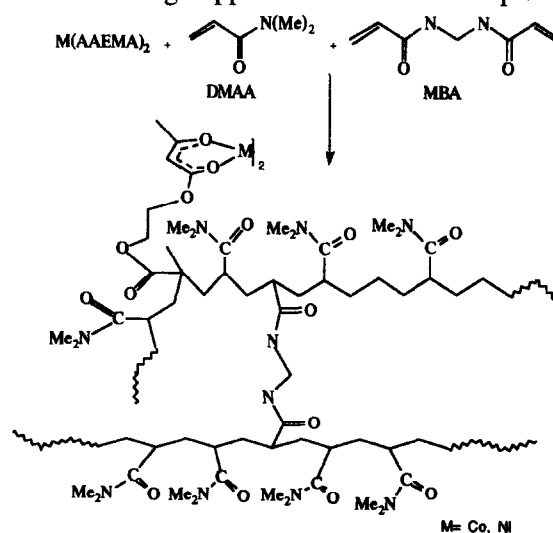
philic attack to methyl vinyl ketone (step *b* in Scheme 2). The stability of a high oxidation-state metal chelate (where electron back-donation is not operative) is related to the degree of electron density transfer from the ligand to the metal centre. Nickel(II) forms more stable complexes with β -dioxigenato ligands with respect to Co(II) [9] and therefore a higher degree of electron density is transferred from the acetylacetonate anion to the metal. This results in a lower nucleophilicity of species 2 in nickel(II) catalysis and therefore accounts for the higher reactivity of Co(II)- compared to Ni(II)-based systems.

The combined effect of nucleophilicity of the methyne carbon of intermediate 2 and the relative strength of the Michael donors as ligands, could also account for the observed reactivity order at room temperature among the three Michael donors, e.g. acetylacetonate < methyl acetoacetate > diethyl malonate.

By correlating the number of resonance structures in which the methyne carbon bears a negative charge with the nucleophilicity of the species 2, it is apparent that the nucleophilicity follows the order diethyl malonate > methyl acetoacetate > acetylacetonate. The more effective addition of methyl acetoacetate respect to acetylacetonate at room temperature for both Ni(II) and Co(II) catalysts, hence, can be rationalized in terms of the enhanced electron density at the methyne carbon

of the coordinated β -ketoesterate with respect to the β -diketonate, due to mesomeric effects. When diethylmalonate is reacted with methyl vinyl ketone at room temperature, the ligand exchange with AAEMA^- is less efficient than in the two previous cases. If the intermediate 2 is not efficiently formed then the donor cannot be expected to perform any attack to the α,β -unsaturated ketone. This could be the reason for the slower reactivity of the system diethyl malonate–methyl vinyl ketone respect to the expectations based on the mere nucleophilicity of the intermediate 2.

In order to test if hybrid catalysis could be achieved using supported AAEMA^- complexes

Scheme 3. Synthesis of supported AAEMA^- complexes.

we copolymerized $\text{Ni}(\text{AAEMA})_2$ and $\text{Co}(\text{AAEMA})_2$ using *N,N*-dimethyl acrylamide (DMAA) as comonomer and *N,N'*-methylene bisacrylamide (MBAA) as cross-linker (Scheme 3).

The two resins obtained, bearing the metal- β -ketoesterate moiety, were used in some tests of supported metal-catalysed Michael addition.

Of the only two examples of hybrid catalysis reported in the literature, the first one [10] studies the activity of β -nitro styrenes as Michael acceptors, whereas the second [3](g) reports that $\text{Ni}(\text{acac})\text{dppe}^+$ supported on an isonitrilic resin

catalyses the reaction between acetylacetone and methyl vinyl ketone yielding 56% of the adduct after 24 h at 60°C. Moreover, Laszlo has reported on Michael reactions catalysed by a combination of clay-supported nickel bromide and ferric chloride [11].

The results obtained by us in heterogeneous catalytic Michael additions are summarized in Table 2. Also with supported catalysts, acetylacetone gave almost negligible reaction at room temperature (entries 1, 10) and good conversions at 75°C (entries 2, 11). The recycles carried out after runs 2 and 11 show that the catalytic activity

Table 2

Michael additions of dioxygenated donors (2.5 mmol) to methyl vinyl ketone (2.9 mmol) in dioxane (2 ml) in heterogeneous phase catalysed by AAEMA^- (0.025 mmol of metal)

Entry	Michael donor	Supported metal	Temp °C	Time (h)	Yield %	% of metal in the recycled resin*
1		nickel	RT	190	7	
2	"	"	75	46	66	
3a	"	"	75	70	18	13
4		"	RT	78	66	
5a	"	"	RT	48	35	60
6	"	"	75	19	92	
7a	"	"	75	24	76	80
8		"	75	92	34	
9a	"	"	75	72	10	90
10		Cobalt	RT	96	8	
11	"	"	75	19	88	
12a	"	"	75	19	10	4
13		"	RT	60	70	
14a	"	"	RT	40	42	21
15	"	"	75	19	97	
16a	"	"	75	19	93	35
17		"	75	39	68	
18a	"	"	75	41	53	68

* With respect to the initial amount.

^a Recycle of the previous run.

of the resin is considerably lowered (entries 3, 12). Moreover the analysis of the metal content in the resins after two cycles showed metal loss which is more severe in the case of cobalt.

For all the investigated substrates the Co(II) catalysts were more active than Ni(II) ones also in heterogeneous phase. It is apparent that the resistance of the resins to the metal leaching depends on the Michael donor used in the reaction. This is rationalizable upon considering metal leaching as a consequence of the competition between the Michael donor and the supported ligand in the coordination to the metal centre. It is not surprising that the reactions with acetylacetonate exhibit the higher loss of metal, followed by those with methyl acetoacetate and diethyl malonate. On the other hand the reactions with diethyl malonate, which are expected to show the highest metal retention are also the less effective (entries 8, 9, 17, 18).

Methyl acetoacetate represents the best compromise between activity in the first run and the recycle, and metal leaching. In this case the best results obtained in the heterogeneous reactions were those relative to Ni(II)-catalysis at 75°C. These reactions yielded 92% of the relevant adduct after 19 h reaction in the first cycle, and 76% after 24 h in the recycle. The retention of metal was satisfactory, the percentage of nickel in the recovered resin after two cycles being 80% with respect to the initial amount. The analogous reactions carried out with supported cobalt were very satisfactory from the point of view of the activity and recyclability (97% yield after 19 h in the first cycle, entry 13, and 93% after 19 h in the recycle, entry 14) but the loss of metal after two cycles was significant (65% of the initial amount).

3. Experimental

3.1. Materials and apparatus

Ni(AAEMA)₂, Co(AAEMA)₂ and Fe(AAEMA)₃ were prepared as described in the

literature [6] by adding to an ethanol solution of the relevant metal nitrate, the solution obtained by dissolving in ethanol HAAEMA and a base such as KOH or triethylamine (metal:HAAEMA:base = 0.5:1:1). Polymer-bound M(AAEMA)₂ (M = Ni or Co) were obtained [7] by reacting under vigorous stirring DMF solutions of M(AAEMA)₂ with DMF solutions of *N,N*-dimethyl acrylamide and *N,N'*-methylene bisacrylamide at 50°C when M = Co and 120°C when M = Ni. The content of metal in the resins was 1.62% when M = Ni and 2.98% when M = Co.

The catalytic tests were carried out using freshly distilled and oxygen-free dioxane. Gas chromatographic analyses were carried out by a Varian Vista 6000 instrument equipped with a 30 m Carbowax 20M capillary column (He carrier). IR spectra were recorded on a Perkin Elmer 883 spectrometer. NMR spectra were recorded on a Bruker AM500 instrument. GC-MS analyses were performed using a HP 5890 chromatograph (30 m SE30 column) coupled with a mass selective detector HP 5970B, 70 eV. Methyl vinyl ketone was distilled under nitrogen prior to use. The yields were calculated as mmoles of adduct per mmoles of initial Michael donor by the internal standard method. The adducts were isolated by column chromatography (silica gel, suitable mixtures of ethyl acetate and petroleum ether as eluents) after evaporation of the solvent. The isolated yields were 15–20% less than those calculated by GLC.

Catalytic runs: homogeneous phase

A Schlenk tube wrapped with an aluminium foil was charged under nitrogen with the Michael donor (2.5 mmol), methyl vinyl ketone (2.9 mmol), the relevant metal catalyst (0.025 mmol) and 1,4-dioxane (2 ml) and stirred at the desired temperature till completion of the reaction, as monitored by GLC.

Catalytic runs: heterogeneous phase

A Schlenk tube wrapped with an aluminium foil was charged under nitrogen with the Michael donor (2.5 mmol), methyl vinyl ketone (2.9

mmol), the relevant metal supported catalyst (0.025 mmol of metal) and stirred at the desired temperature till completion of the reaction, as monitored by GLC. After the first cycle the reaction solution was added of light petroleum ether and the resulting suspension was filtered to separate the used resins. The resins, washed with acetone and diethyl ether and dried under vacuum, were recycled in a new run, then isolated again and analysed for the residual metal content.

3-Acetyl heptane-2,6-dione

^1H NMR (ppm, CDCl_3): keto form: 2.08 (q, $J=7.0$ Hz, 2-H), 2.13 (s, 3-H), 2.20 (s, 6-H), 2.46 (t, $J=7.0$ Hz, 2-H), 3.69 (t, $J=7.0$ Hz, 1-H); enol form: 13.69 (s); ^{13}C NMR (CDCl_3 , ppm), keto form: 21.5, 29.3, 29.9, 40.5, 67.0, 204.1, 207.5; enol form: 22.9, 29.9, 40.5, 44.0, 109.0, 191.1, 207.5. IR (liquid film): 3408, 2928, 1713, 1423, 1360, 1154, 720 cm^{-1} . MS (70 eV): m/e (relative intensity): 170 (1, M^+), 128 (14), 127 (4), 110 (7), 95 (10), 71 (28), 58 (11), 43 (100).

2-Acetyl-5-oxo methyl hexanoate

^1H NMR (ppm, CDCl_3): 2.08 (m, 2-H), 2.13 (s, 3-H), 2.24 (s, 3-H), 2.50 (td; $J_1=7.1$ Hz, $J_2=2.6$ Hz, 2-H), 3.52 (t, $J=7.24$ Hz, 1-H), 3.73 (s, 3-H); enol form: 12.58 (s); ^{13}C NMR (CDCl_3 , ppm): 21.8, 29.0, 29.9, 40.5, 52.4, 58.1, 170.0, 202.7, 207.4. IR (liquid film): 3421, 2959, 1740, 1716, 1435, 1360, 1246, 1157, 1056, 856 cm^{-1} . MS (70 eV): m/e (relative intensity): 186 (1, M^+), 144 (18), 116 (8), 112 (11), 111 (11), 87 (14), 85 (6), 84 (16), 58 (7), 55 (14), 43 (100).

(3-Oxobutyl)-diethylmalonate

^1H NMR (ppm, CDCl_3): 1.27 (t, $J=7.13$ Hz, 6-H), 2.16 (m, 5-H), 2.55 (t, $J=7.26$ Hz, 2-H), 3.39 (t, $J=7.35$ Hz, 1-H), 4.19 (m, 4-H) enol form: 12.20 (s); ^{13}C NMR (CDCl_3 , ppm), 14.1, 22.5, 29.9, 40.5, 50.7, 61.5, 169.2, 207.2. IR (liquid film): 3455, 2988, 1750, 1738, 1446, 1370, 1255, 1156, 1028, 860 cm^{-1} . MS (70 eV): m/e (relative intensity): 230 (2, M^+), 185 (29), 173 (13), 169 (12), 160 (56), 139 (58), 133 (20),

127 (16), 111 (15), 88 (9), 86 (14), 69 (9), 55 (24), 43 (100).

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