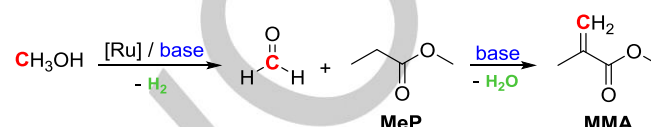


Upon the α -methylenation of methyl propanoate via catalytic dehydrogenation of methanol

Patrizia Lorusso,^[a] Jacorien Coetzee,^[a] Graham R. Eastham^[b] and David J. Cole-Hamilton*^[a]

Abstract: A one-pot system for the conversion of methyl propanoate (MeP) to methyl methacrylate (MMA) has been investigated. In particular, this study is focused on the possibility of performing catalytic dehydrogenation of methanol for the *in situ* production of anhydrous formaldehyde, which is then consumed in a one-pot base-catalysed condensation with MeP to afford methyl 3-hydroxy-2-methylpropanoate, which spontaneously dehydrogenates to MMA, some of which is subsequently hydrogenated to methyl 2-methylpropanoate (MiBu).

afford methyl 3-hydroxy-2-methylpropanoate as an intermediate, which, in turn, would dehydrate to MMA (Scheme 1).



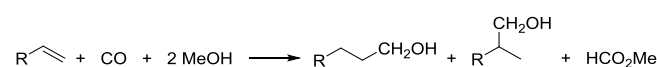
Scheme 1. Proposed one-pot formation of methyl methacrylate (MMA) from methyl propanoate (MeP) and methanol

Introduction

Formaldehyde is a chemical used widely in several industrial processes including the manufacture of building materials. A remarkable example in this area is represented by the innovative two-step Alpha technology developed by Lucite for the large scale production of methyl methacrylate (MMA), the essential building block of all acrylic-based products.^[1] This successful technology involves methoxycarbonylation of ethene to methyl propanoate (MeP), in the presence of a palladium based complex,^[2] followed by condensation with gaseous formaldehyde on a fixed bed catalyst (caesium oxide on silica), affording MMA as the final product.^[1b, 3] The formaldehyde involved in this second stage is initially produced as formalin in a separate process and then dehydrated to afford anhydrous formaldehyde, which is essential for ensuring high selectivity to MMA. Another drawback of this procedure is represented by the easy polymerisation of paraformaldehyde giving insoluble polyoxymethylenes which can lead to severe fouling of transfer lines.^[3] The development of an alternative process where anhydrous formaldehyde is produced *in situ* would provide a simplification over the current process. As an alternative second step, the possibility of performing the one-pot α -methylenation of methyl propanoate has not been investigated so far. In an ideal system, anhydrous formaldehyde would be generated *in situ* by catalytic dehydrogenation of methanol and would subsequently undergo base-catalysed condensation with methyl propanoate to

Alpha methylenation of simple esters can be achieved in low yield using condensation of the ester with formaldehyde catalysed by caesium oxide on silica at high temperature^[3], or by a complex series of reactions using Meldrum's acid Eschemoser's iodide salt (dimethylmethyleimmonium iodide).^[4] We are not aware that it has been achieved using metal complex catalysed reactions. However, the reactions involved (Scheme 1) are very similar to those involved in hydrogen borrowing reactions,^[5] acceptorless dehydrogenation^[6] and hydrogen autotransfer.^[7] Generally, the hydrogen from the dehydrogenation of the alcohol is transferred back into the product leading to alkylation rather than alkylation. In addition, the substrates that are alkylated are exclusively ketones rather than esters.

Methanol has only rarely been used as an *in situ* source of formaldehyde. Formaldehyde is presumably formed in the thermal^[8] or photochemical^[9] production of hydrogen from methanol, and subsequent reactions of the formed formaldehyde can lead for example to dimethoxymethane,^[9b, 10] to CO and H₂,^[9a] to CO₂ or carbonate in the presence of hydroxide bases,^[8b] to formylamines on reaction with primary or secondary amines,^[11] or it can be added to a metal allyl formed from an allene to give 3-hydroxyethyl-1-alkenes in a reaction which is formally the addition of a C-H of methanol across a double bond.^[12] In early work, some of us showed that, using methanol as the hydrogen source in hydrocarbonylation reactions of 1-hexene to heptanol catalysed by Rh/PEt₃ complexes, the formed formaldehyde was converted into methyl formate (Scheme 2). Interestingly, in these reactions, methanol proved to be a better source of hydrogen than ethanol, 1-butanol or 2-propanol.^[13]



Scheme 2. The use of methanol as a source of hydrogen in the hydrocarbonylation of 1-hexene (R = C₄H₉). Methyl heptanoate, methyl 2-methylhexanoate and hexylhexanoate are also significant products. Methyl formate is formed from methanol.^[13]

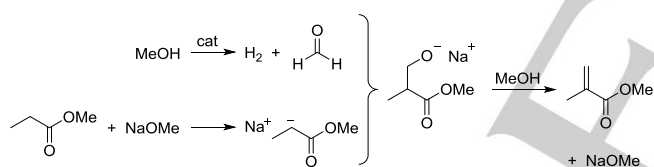
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Results and Discussion

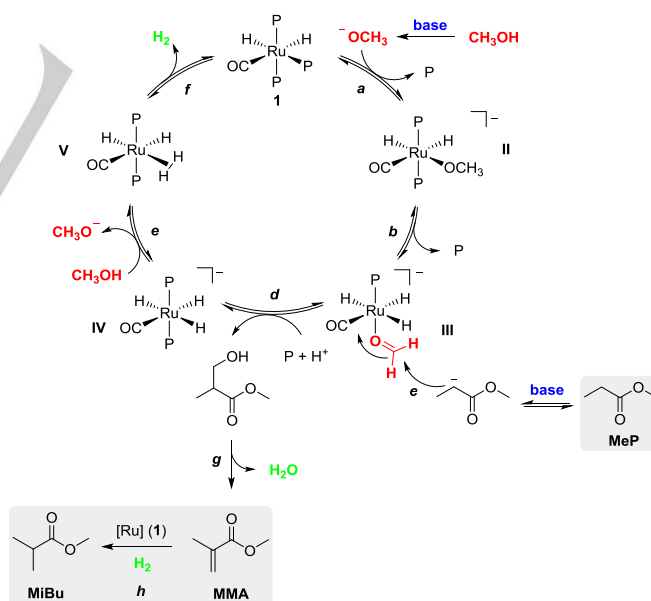
Minor amounts of MMA were detected after heating MeP together with Na_2CO_3 at 170 °C in a stainless steel batch autoclave in the absence of any added formaldehyde. In addition to MMA, the GC-MS spectrum of the crude product revealed the presence of the hydrogenated product, methyl 2-methylpropanoate (MiBu) along with 3-pentanone and significant amounts of methanol, suggesting that a carbon alkylating agent and hydrogen source must have been present at some stage during the reaction. Methanol, possibly from hydrolysis of methyl propanoate was believed to be the most likely source of the methylene group in MMA (see Scheme 3). Based on this observation, the *in situ* generation of anhydrous formaldehyde and hydrogen gas by metal-catalysed dehydrogenation of methanol has been investigated. The role of the base in this system is twofold. It is involved in the deprotonation of methanol affording the alkoxide ion, which is the active species in methanol dehydrogenation, and it is essential for the α -deprotonation of MeP which can then undergo condensation with the newly formed formaldehyde affording an intermediate species, methyl 3-hydroxy-2-methylpropanoate. The latter provides the desired product, MMA, *via* spontaneous water elimination (Scheme 3). Since H_2 is produced in the reaction system and we wish not to hydrogenate MMA, suitable catalysts should be chemoselective for the dehydrogenation of methanol leading to formaldehyde without promoting the hydrogenation of the C=C bond in MMA to give methyl 2-methylpropanoate (MiBu).



Scheme 3. Route to methyl methacrylate involving attack of deprotonated MeP on formaldehyde formed by the *in situ* dehydrogenation of methanol.

Some of us reported in the late 80's that catalytic dehydrogenation of alcohols can be achieved from a wide range of alcoholic substrates using Rh and Ru catalysts.^[14] Among these catalysts, one of the best was $[\text{RuH}_2(\text{CO})(\text{PPh}_3)_3]$ (**1**). Similar complexes, such as $[\text{RuHCl}(\text{CO})(\text{PPh}_3)_3]$ have been reported to give some preference for hydrogenation of C=O over C=C bonds, e. g. in cinnamaldehyde.^[15] Therefore, based on the principle of microscopic reversibility, it was examined as a suitable dehydrogenation catalyst in these preliminary studies together with other hydrogenating catalysts. The initial catalyst screening involved four Ru species which exhibited only minor activity, Shvo's catalyst^[16] (**2**), $[\text{RuCl}(\text{CO})_2(\eta^5\text{-Ph}_5\text{C}_5)]$ ^[17] (**3**), $[\text{Ru}(\text{OAc})_2(\text{TriPhos})]$ ^[18] (**4**), $[\text{RuH}_2(\text{CO})(\text{TriPhos})]$ ^[19] (**5**), and a Rh catalyst $[\text{RhH}(\text{CO})(\text{PEt}_3)_3]$ ^[20] (**6**) which showed some activity but no selectivity to MMA (MMA yield 0%; MiBu yield 6 %).

Preliminary studies in which methanol, methyl propanoate and sodium methoxide were heated in the presence of catalyst **1** showed the presence of small amounts of both MMA and MiBu. Scheme 4 depicts a plausible mechanism for the formation of MMA based on a published mechanism for the dehydrogenation of methanol, ethanol or propan-2-ol catalysed by related ruthenium complexes.^[21] In the initial stage a methoxide ion is generated by deprotonation of methanol in the presence of the added base. This species is then believed to enter the cycle by displacing PPh_3 from $[\text{RuH}_2(\text{CO})(\text{PPh}_3)_3]$ (**1**, **I**), generating an anionic methoxy intermediate **II**; (**b**) loss of PPh_3 followed by β -hydrogen abstraction allows the formation of coordinated formaldehyde, **III**, onto which (**c**) deprotonated MeP attacks; (**d**) protonation and displacement of methyl 3-hydroxy-2-methylpropanoate by PPh_3 produces the anionic trihydrido carbonyl complex **IV**; (**e**) the trihydrido complex, by abstracting a proton from a molecule of methanol, could regenerate the methoxide ion and afford molecular hydrogen (which remains associated with the metal complex as a coordinated dihydrogen molecule) **IV**; (**f**) the liberation of molecular hydrogen in the final step regenerates the catalyst **I**; (**g**) the methyl 3-hydroxy-2-methylpropanoate produced in stage **d** spontaneously dehydrates to give MMA as the final product; (**h**) MiBu is then undesirably formed by catalytic hydrogenation of MMA. The nucleophilic attack of deprotonated MeP is shown as occurring to coordinated formaldehyde (**c**) on the basis of a precedent of attack of an amine^[11] and because coordinated formaldehyde will be a better electrophile. It could also occur onto free formaldehyde.



Scheme 4. Proposed mechanism for ruthenium catalysed dehydrogenation of MeOH leading to the *in situ* production of anhydrous formaldehyde and subsequent condensation with MeP to afford MMA via water elimination and MiBu by hydrogenation of MMA. (P = PPh_3)

The low yields of MMA and MiBu could arise because of poor deprotonation of MeP or low rates of formation of formaldehyde. Hence, a set of deuterium labelling experiments was conducted with the aim of determining the extent to which a variety of bases affect the α -deprotonation of MeP. Three parallel reactions were performed in the presence of MeP, in methanol- d_4 as solvent and deuterating agent and three different bases, K_2CO_3 , NaOH or Cs_2CO_3 . Upon heating the mixtures at 170 °C for 2 hours the formation of non-, mono- and bis-deuterated MeP was observed by $^{13}C\{^1H\}$ DEPT analysis of the recovered liquid phases. The methyl group of non deuterated MeP generates a singlet at δ 9.5 ppm, which results in β -shifted resonances at δ 9.4 and 9.3 ppm in the mono- and bis-deuterated species respectively. Similarly, the methylene groups give rise to a singlet at δ 28.1 (-CH₂-), a triplet at δ 27.8 (-CHD-) and a quintet at δ 27.5 ppm (-CD₂-). The methyl resonances were used to calculate the ratio of the non-, mono- and bis-deuterated MeP, giving evidence that Cs_2CO_3 is the most effective (fastest) base for the α -deprotonation with a ratio (CH₂ : CHD : CD₂) of 10 : 41 : 49 %, followed by K_2CO_3 with a corresponding ratio of 47 : 42 : 11 %, while NaOH was the slowest giving a ratio of 61%: 33%: 6%. During these experiments, significant amounts of non, mono and bis-deuterated metal propanoate salts were also formed, despite attempts to exclude all water. We return to this observation later on.

Based on these results, simple base catalysed condensation experiments of formaldehyde with MeP were conducted to identify the most efficient base, prior to use in the one-pot system. Since none of the attempts with K_2CO_3 and NaOH was successful, attention was moved to the strong non-nucleophilic organic base, 1,8-diazobicyclo[5.4.0]undec-7-ene (DBU). Even in this case, NMR analysis of the final mixtures revealed the presence of only trace amounts of MMA.^[22]

Given that none of the previous experiments gave significant quantities of MMA, methanol dehydrogenation to formaldehyde and subsequent condensation with MeP affording MMA was performed in the presence of simple carbonates, Cs_2CO_3 and Na_2CO_3 . The latter has been reported by Renken and co-workers to catalyse methanol dehydrogenation.^[23]

At the end of reactions of MeP with formaldehyde in the presence of Cs_2CO_3 or Na_2CO_3 , a large amount of solid material was recovered from the batch reactor. This material was again identified as propanoate salts (1H NMR spectroscopy). Our initial conclusion was that these salts might arise from hydrolysis of MeP. The two potential sources of water in this system are the condensation step to form MMA (not observed in this case) and as an impurity in the metal carbonates, which are hygroscopic and usually stored in air. In an attempt to minimise the amount of water and the subsequent ester bond hydrolysis, NaOMe (1.46 g, 27 mmol) was employed as the base (MeP: 10 mL, 103.9 mmol). In this case traces of MiBu (0.67 %) and MMA (<0.5 %) were observed, but 1H NMR analysis of the solid phase at the end of the reaction showed mainly sodium propanoate. This solid product was isolated (2.53 g, 26 mmol), indicating that all of the sodium methoxide had been converted in to sodium propanoate.

Similarly, upon heating a mixture of MeP, methanol, NaOMe and 0.13% of **1** in toluene, in a Hastelloy™ autoclave at 170 °C for 3 hours, MMA was produced together with the hydrogenated by-product MiBu, but once again, a substantial amount of methyl propanoate was formed. It is clear from these experiments that the major reaction occurring is the formation of sodium propanoate from MeP and NaOMe.

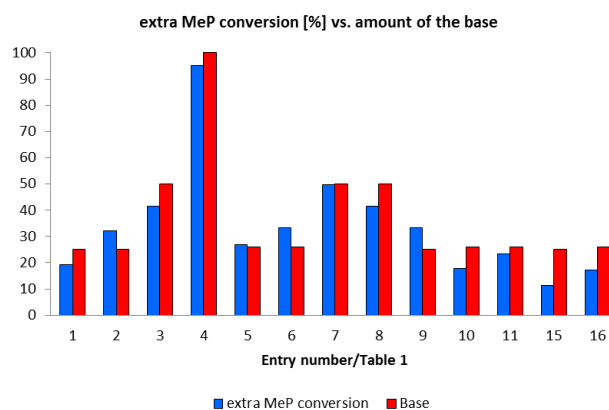
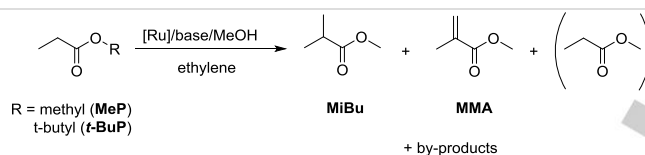


Figure 1. [MeP conversion – (MMA + MiBu)] compared with the proportion of base employed. [%] Values (relative to MeP) are taken from Table 1 which summarises the general reaction conditions.

Further confirmation that NaOMe is almost all consumed in the formation of sodium propanoate comes from an analysis of Table 1 and Figure 1, which show the results of a number of experiments carried out under different conditions. In all cases, the total of MMA and MiBu (the major soluble organic products) formed was much less than the conversion of MeP and substantial amounts of propanoate salts were formed. Comparing the [MeP converted – (MMA+MiBu)] with the amount of base added (Figure 1), it becomes clear that they are correlated, and confirms that the major problem with the reaction is an interaction between the base and MeP consuming the base and forming sodium propanoate.

This reaction, which also occurs in the absence of added methanol, is very surprising as one would expect two possible reactions between a propanoate ester and a sodium alkoxide. The first would be transesterification, which, in the case of MeP and NaOMe would not give different products and the second would be the desired α -deprotonation of MeP (see Scheme 5a). Sodium propanoate might be formed by an S_N2 attack of methoxide ion on the OMe group of MeP to form dimethyl ether with propanoate acting as a leaving group. Although quantitative analysis of Me₂O is difficult, qualitative GC analysis shows significant quantities of Me₂O in both the gas and liquid fractions after reactions involving MeP and NaOMe with or without methanol, suggesting that this unusual etherification reaction is occurring (see Scheme 5b).

Table 1. Optimisation of the conditions for MeP (**Table 1a**) and *t*-BuP (**Table 1b**) conversions [%] to MMA and MiBu, employing nucleophilic and non-nucleophilic strong bases at different concentrations

Entry Table 1a	Substrate	Cat.	Base	t [h]	MeP Conv.	MMA Yield	MiBu Yield	MMA+ MiBu	Extra MeP Conv.†
1	MeP	1	NaOMe(25%)	1	25.6	2.7	3.5	6.2	19.4
2	MeP	1	NaOMe (25%)	3	41.1	3.8	5.1	8.9	32.2
3	MeP	1	NaOMe (50%)	3	52.1	1.9	8.8	10.7	41.4
4	MeP	1	NaOMe (100%)	3	96.4	0.3	1.2	1.5	95
5	MeP	1	<i>t</i> -BuONa (26%)	3	35.6	3.5	6.1	9.6	26
6	MeP	1	<i>t</i> -BuONa (26%)	15	42.7	3.6	5.9	9.5	33.2
7	MeP	1	<i>t</i> -BuONa (50%)	3	62.2	3	9.5	12.5	49.7
8	MeP	1 ^d	<i>t</i> -BuONa (50%)	3	47.9	3.3	3.2	6.5	41.4
9	MeP	1	<i>t</i> -BuOK (25%)	3	38.2	2.3	2.7	5	33.2
10	MeP	7	<i>t</i> -BuONa (26%)	3	28	3.9	6.4	10.3	17.7
11	MeP	7	<i>t</i> -BuONa (26%)	15	32.6	2.8	6.3	9.1	23.5
12	MeP	1	NaP (25 %)	15	-	-	-	-	-
13 [§]	MeP	1	NaP (25 %)	15	-	-	-	-	-
14 [§]	MeP	8	NaP (30 %)	15	NQ	DNQ	DNQ	-	-
15	MeP	8	NaOCH ₃ (25%)	15	17.7	1.8	4.4	6.2	11.5
16	MeP ^[a]	1	<i>t</i> -BuONa (26%)	3	28.5	4.1	7.1	11.2	17.3

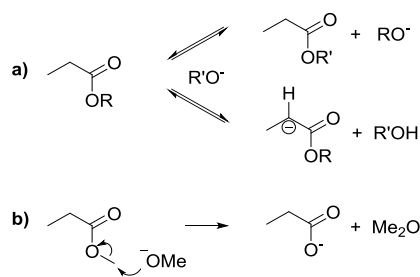
Entry Table 1b	Substrate	Cat.	Base	t [h]	<i>t</i> -BuP Conv.	MeP Yield	MMA yield	MiBu Yield	MMA+MiBu
17	<i>t</i> -BuP	1	NaOMe (25%)	3	98	63	4.4	6.6	11
18	<i>t</i> -BuP	1	<i>t</i> -BuONa (26%)	3	98.5	71	3.3	7.3	10.6
19	<i>t</i> -BuP ^[a]	1	<i>t</i> -BuONa (26%)	3	97.2	64.5	4	7.5	11.5
20	<i>t</i> -BuP ^[b]	1	<i>t</i> -BuONa (26%)	3	98.3	55.8	3.7	6.4	10
21	<i>t</i> -BuP ^[c]	1	<i>t</i> -BuONa (26%)	3	99	78	4.5	7.6	12
22	<i>t</i> -BuP	7	<i>t</i> -BuONa (26%)	3	99.6	58.5	2.7	3	5.7

General reaction condition: MeP (10 mL, 103.85 mmol); *t*-BuP (15.65 mL, 103.9 mmol); substrate/MeOH 1:1.8 unless stated otherwise (Entry 14 MeP/MeOH 1:1); catalyst loading: 0.13 mol % relative to the substrate; solvent: toluene (10 mL); Hastelloy™ autoclave; 170 °C under an atmosphere of ethene (6 bar). § reaction temperature: 200 °C.

Conversions [%] were determined by GC-FID analysis using decane as internal standard (IS). NQ (not quantified), DNQ (detected, not quantified).

†Mainly NaP.

*In the presence of *t*-BuOH: [a] MeOH/*t*-BuOH 2:1; [b] MeOH/*t*-BuOH 1:1; [c] MeP/MeOH 1:2.7 and MeOH/*t*-BuOH 3:1; the ratios were adjusted by simply adding *t*-BuOH to the standard system; [d] a stoichiometric amount of xantphos was added.^[24]



Scheme 5. a) Expected reactions between an alkoxide and a propanoate ester; b) Observed reaction between methyl propanoate and sodium methoxide

Table 1 also shows that both MMA and MiBu are formed from systems where methyl propanoate and methanol are reacted with NaOMe in the presence of catalyst **1** (Entries 1-3). Increasing the concentration of base from 26 % relative to MeP to 50 % almost doubles the total conversion to these products, but a higher amount of base reduces the yield of these products dramatically.

MMA is the desired product in these reactions so in order to try to reduce the hydrogenation of MMA to MiBu, we investigated potential sacrificial hydrogen acceptors. Although crotononitrile has been described as a good hydrogen acceptor in ruthenium-catalysed hydrogen transfer reactions,^[24a, 25] it completely suppressed formation of the desired products when introduced in the one-pot system. Two more attempts were conducted in the presence of benzophenone and methyl acrylate (with the idea of forming more MeP), respectively, but both experiments gave a decrease in terms of MeP conversion. Ethene proved to be a more effective hydrogen acceptor under moderate pressures. Figure 2 displays optimisation of ethene pressure for the α -methylenation of MeP, showing an optimum at 6 bar, although MMA was never the major product. All reactions described in Table 1 were carried out under ethene (6 bar). The high reaction temperature required and the low boiling points of methanol and MeP meant that the reaction could not be carried out in an open system allowing venting of H₂.

In order to try to prevent (or slow down) the nucleophilic attack of the methoxide on MeP, we investigated the use of *t*-BuONa in place of methoxide and/or *t*-butylpropanoate (*t*-BuP) in place of MeP. *t*-BuP was chosen since we anticipated that the lower stability of the *t*-BuO⁻ ion relative to MeO⁻ should reduce the transesterification of *t*-BuP by methanol/methoxide, whilst the steric bulk of the *t*-Bu group should reduce the rate of nucleophilic attack by MeO⁻ to produce MeO-*t*-Bu (MTBE). Using *t*-BuO⁻ in place of MeO⁻, we anticipated that the higher basicity and larger steric bulk might favour α -deprotonation of MeP over nucleophilic attack on the methoxy C atom.

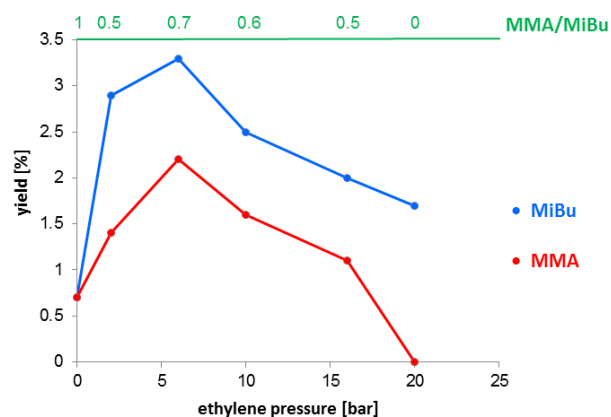


Figure 2. Effect of ethene pressure on the yield of MMA and MiBu. Reaction conditions: MeP/MeOH 1:1.2; cat **1**: 0.13 mol % relative to MeP; base: NaOCH₃ (25 % relative to MeP); solvent: toluene (10 ml); Hastelloy™ autoclave, 170 °C, 16 hours. MeP conversions [%] were determined by calibrated GC-FID analysis using toluene as internal standard (IS). Numbers along the top of the Figure are MMA/MiBu ratio.

In general, using *t*-BuONa allowed a modest increase in MeP conversion to the desired MMA and MiBu (Compare Table 1, Entries 2 with 5 and 3 with 7). Addition of xantphos (1:1 with Ru), which has been shown to disfavour C=C hydrogenation when used with [RuH₂(CO)(PPh₃)₃],^[24a] partially inhibited the reaction (Table 1, Entry 8), while the stronger base *t*-BuOK appeared to be less effective (Table 1, Entry 9). Very little *t*-BuP or MTBE was produced in these reactions. Changing the catalyst precursor from **1** to **7**, which is expected to react with NaOMe to give **1**,^[26] had little effect on the formation of the desired products (Table 1, Entries 10 and 11).

Minor improvements in the yield of MMA and MiBu were obtained using *t*-BuP in place of MeP (Table 1, Entries 2 and 17 when using NaOMe as the base; Entries 5 and 18 using *t*-BuONa). Complex **7** was not as effective under these conditions as **1** (Table 1, Entry 22). Even in these experiments using *t*-BuP as substrate almost no *t*-BuP was left at the end of the experiments. It had undergone complete transesterification to MeP. *tert*-Butanol (*t*-BuOH) was added to the reaction mixture in an attempt to move the equilibrium back towards *t*-BuP (Table 1, entries 19-22) but this had little effect on the yield of MMA and MiBu. It also did not stop the transesterification reaction. Addition of *t*-BuOH to a reaction using MeP and *t*-BuONa did improve the yield somewhat (Table 1, Entry 16).

As indicated above, the major problem with obtaining high yields of methylenation products of MeP is the unexpected S_N2 attack of methoxide ion onto methyl propanoate to give dimethyl ether and propanoate anion. Since methanol is required for the formation of formaldehyde in this system and base is required both for the dehydrogenation of methanol and for the deprotonation of MeP, the only other possibility for preventing the conversion of base to propanoate would be to use sodium propanoate as the base. Initial deuterium labelling studies

showed that sodium propanoate is a strong enough base to deprotonate the α -protons of MeP. Complete H/D exchange with deuteriomethanol to the equilibrium position occurred in 5 min on heating MeP with methanol and NaP at 200 °C. However, disappointingly, no products were formed when attempting the catalytic reaction using NaP as the base under conditions of Table 1, entry 12 and 13. This could be because NaP is not a strong enough base to promote methanol dehydrogenation or because an inactive complex such as $[\text{RuH}(\text{OCOEt})(\text{CO})(\text{PPh}_3)]$ (**8**) is formed. To test the latter possibility, we have synthesised complex **8** and shown it to be an active catalyst (Table 1, Entry 15) which even gives a small amount of activity when using NaP as the base (Table 1, Entry 14).

In order to confirm our assumption that the added methylene (MMA) or methyl group (MiBu) originates from methanol, reactions were carried out using CD_3OD or $^{13}\text{CH}_3\text{OH}$ under the conditions of Table 3.2, Entry 18 using *t*-BuP as substrate and *t*-BuONa as base so that the only source of methanol/methoxide was the added methanol (see Scheme 3.2.3). For the ^{13}C experiment the ratio of $^{12}\text{CH}_3\text{OH} : ^{13}\text{CH}_3\text{OH}$ used was 8.5:1. Both MMA and MiBu products were shown by GC-MS to contain ca 8-9 % ^{13}C in the OMe group and in the methylene/methyl group. For the ^2H labelling experiment, CD_3OD (99%) was used. The MMA mainly contained 5 D atoms, whilst analysis of the $[\text{M-OMe}]^+$ fragment showed that the methylene group contained 2 (68 %) or 1 (20 %) deuterium atoms. The MiBu in this case contained 5, 6 or 7 D atoms in the ratio 29 : 49 : 22 %, whilst the $[\text{M-OMe}]^+$ fragment contained 2, 3 or 4 D atoms in a similar ratio (see Table 3.2.2). These labelling results confirm that, in the predominant pathway for the conversion of MeP to MMA and MiBu in the presence of methanol, the methylene C atom is derived from methanol. However, some H/D exchange occurs possibly with water or with the catalyst. We note that the catalyst undergoes H/D exchange into the *ortho* positions of the phenyl rings as well as into the Ru-H positions.^[27]

Conclusions

In this study a novel approach for the α -methylenation of methyl propanoate has been reported involving a one-pot system where four main reactions occur: *methanol dehydrogenation*, providing *in situ* production of anhydrous formaldehyde, *MeP deprotonation* and *condensation* with the new formed formaldehyde and partial *hydrogenation* of the MMA to MiBu. Overall the yields of the two desired products, MMA and MiBu are modest (see Figure 3). The main problem with the reaction is the formation of dimethyl ether and sodium propanoate apparently from the nucleophilic attack of methoxide on MeP with the propanoate anion acting as a leaving group. Attempts to inhibit this kind of reaction using *t*-BuP and *t*-BuONa improved the yield of the desired products but were frustrated by transesterification of the ester with methanol, inevitably present for the formation of formaldehyde. Labelling studies showed that the added methylene (MMA) or methyl group (MiBu) arose predominantly from methanol.

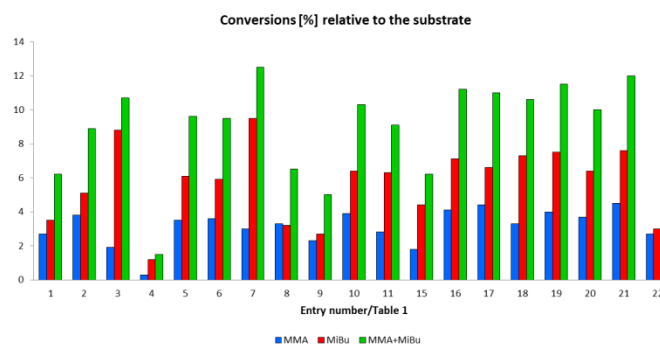


Figure 3. Yields of MMA and MiBu for the reactions shown in Table 1 (Entries 12-14 are not displayed for clarity).

Experimental Section

Full Experimental Details appear in the ESI.

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Keywords: methyl methacrylate • one-pot system • ruthenium • dehydrogenation • anhydrous formaldehyde

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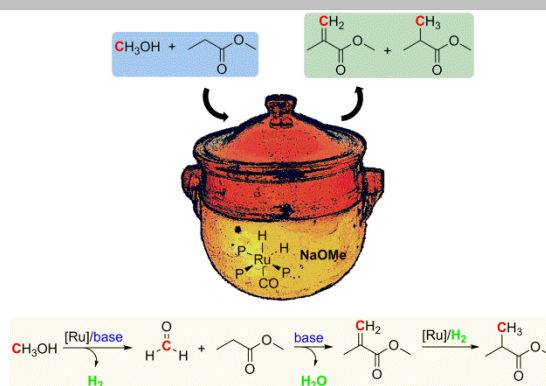
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Layout 1:

FULL PAPER

In the presence of methanol, base and $[\text{RuH}_2(\text{CO})(\text{PPh}_3)_3]$, methyl propanoate can be converted into a mixture of methyl methacrylate, methyl *iso*-butyrate and sodium propanoate. The methylene group comes from methanol.



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Graham R. Eastham^[b]
and David J. Cole-Hamilton^{[a]*}

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Upon the α -methylenation of methyl propanoate via catalytic dehydrogenation of methanol

Layout 2:

FULL PAPER

