

A Highly Efficient Preparation of Methacrylate Esters using Novel Solid Phase Titanium-based Transesterification Catalysts

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This paper is dedicated to Professor A. Eschenmoser

Abstract: Highly active transesterification catalysts for the synthesis of sensitive methacrylate monomers can be conveniently prepared by reacting chlorotriisopropoxy titanium with cross-linked polystyrene beads functionalised with acetyl acetone or polyethylene glycol ligands.

Key words: transesterification, methacrylate esters, polymer-bound titanium catalysts

As part of a programme of work looking at novel polymer-supported metal catalysts and their use in organic synthesis, we decided to prepare electrophilic catalysts for use in transesterification reactions.¹ We initially looked at the feasibility of supporting titanium alkoxides on functionalised cross-linked polystyrenes. The attraction of such catalysts is the ease of removal from the reaction mixture and the potential for multiple re-use.² At the commencement of this work we had an interest in the preparation of methacrylate monomers, and very little was published on the transesterification of methyl methacrylate using polymer-supported catalysts. A very recent publication by Sherrington *et al.* described a titanium catalyst supported on polymeric hydroxy-styrene³ and this paper has prompted us to report our initial results in this area.

Table: Functionalised Polystyrene Polymer catalysts

cat.	ligand	ligand (meq g ⁻¹)	rgnt.	solv.	titanium (% w/w)	titanium (meq g ⁻¹)
A	poly(4-vinylpyridine)*	9.50	A	C	6.70	1.40
B	ethylene glycol*	2.80	B	C	1.20	0.25
C	polyethylene glycol 600*	0.35	B	D	0.90	0.19
D	acetyl acetone†	4.60	B	C	3.51	0.73
E	polyethylene glycol methyl ether*	0.30	A	C	0.37	0.075

* 1-2% cross-linked, commercially available from Fluka A = Ti(OPr)₄ B = ClTi(OPr)₃

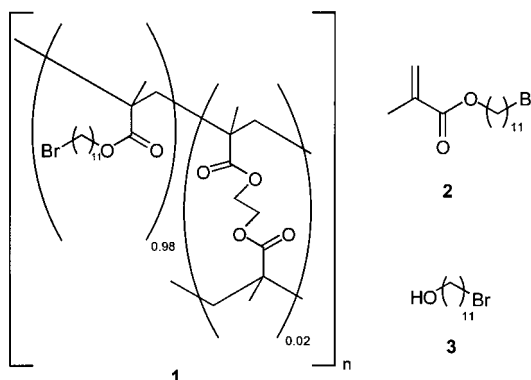
† made by method given in reference 5 C = CH₂Cl₂ D = toluene

Macroporous, cross-linked polystyrenes functionalised with a range of ligands were reacted with titanium tetraisopropoxide or chlorotriisopropoxy titanium. The result-

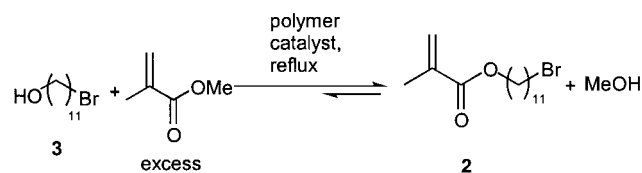
ant polymers were recovered, washed free of any excess titanium reagent and dried.^{4,5} The titanium content of the polymers prepared was determined by digestion followed by ICP analysis. Results are summarised in the Table.

From the results in the Table it can be seen that in all cases the polymers retained titanium. No attempt was made to optimise titanium incorporation, however comparison of the meq g⁻¹ of titanium with meq g⁻¹ of ligands in the Table indicated further scope for maximising titanium content. Next we sought a suitable reaction to test the activity of the polymer catalysts.

During the development of a functionalised, cross-linked methacrylate polymer **1** for use as a bile acid sequestrant⁷ we required an efficient, safe and cost effective synthesis of the monomer unit **2** under conditions where premature polymerisation did not occur. The high boiling point and thermal instability of **2** precluded purification by vacuum distillation. We had identified an efficient route to the monomer **2** in about 90% isolated yield⁸ by transesterification of methyl methacrylate with 11-bromoundecanol⁹ **3** using 5 mol% of titanium tetraisopropoxide as the transesterification catalyst. Although removal of titanium species was achieved *via* addition of water followed by filtration of the titanium sludge and removal of excess methyl methacrylate by distillation, the additional manipulations made this approach less commercially viable and increased the risk of premature polymerisation. It seemed that the polymer-supported titanium catalysts prepared would be an ideal replacement for the soluble Ti(OPr)₄ catalyst in this reaction because a simple, non-aqueous workup was envisaged.

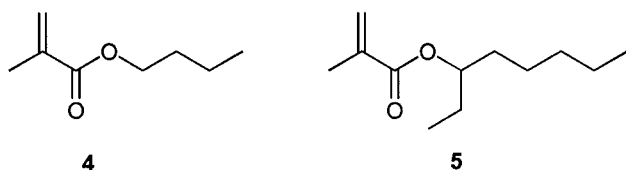


Thus the titanium containing polymers in the Table were then evaluated in the key transesterification reaction shown in the Scheme.



Scheme

Catalyst **A** was found to be totally inert as a transesterification catalyst despite containing the highest loading of titanium. Presumably the titanium species bound in the polymer is highly ligated, stopping the facile ligand exchange required for transesterification activity. Catalysts **B** and **E** were found to act as transesterification catalysts, although they were only weakly active. The most active catalysts for the preparation of **2** were catalysts **C** and **D** where transesterification was rapid (4 hours).¹⁰ In both cases high conversion to the desired methacrylate monomer **2** was obtained (92–97%). The product **2** was isolated in 87% yield and high purity (97%) simply by filtration of the catalyst and removal of excess methyl methacrylate by distillation. In addition both catalysts **C** and **D** could be re-used at least four times, although some reduction in rate of reaction was observed on re-use. It was later found that catalyst **C** was moisture sensitive and this accounted for the loss in activity since no precautions to protect the catalysts from atmospheric moisture were taken prior to re-use. Indeed a fresh batch of catalyst **C** exposed to air overnight prior to use gave only 40% conversion to **2** in 6h compared with 97% conversion in 4h for freshly made catalyst **C**. Comparing the activity of catalysts **B** to **E**, the low transesterification rate with **E** was attributed to the low level of titanium incorporation. Although catalyst **B** had an equivalent level of titanium incorporation and cross-linking to **C**, the lower activity was presumably due to the titanium being too tightly ligated (as with **A**) to enable efficient transesterification to occur.



Having discovered two active transesterification catalysts for the preparation of **2**, we briefly explored their utility using different alcohols. The acetyl acetone-based catalyst **D** was evaluated and found to be very active catalyst for n-butanol and the sterically more hindered 2-ethylhexan-1-ol giving n-butyl methacrylate **4** and 2-ethylhex-1-yl methacrylate **5** in 85% and 95% isolated yields respectively in 4–6h. Attempts to use ethylene glycol or N,N-dime-

thylamino ethanol gave no transesterification products with catalysts **C** and **D**. These substrates were found to deactivate the catalysts, presumably owing to their ability to form tight chelates with titanium.

In conclusion we have identified two highly active, insoluble polymer-based transesterification catalysts particularly useful for the formation of functionalised methacrylates. It is anticipated that these catalysts will be useful for the preparation of a range of important methacrylate monomers and other esters containing sensitive functionality. The polymers may also be useful catalysts in other titanium catalysed processes.

References and Notes

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- (4) **Typical experimental for catalyst C:** Polyethylene glycol 600 bound to cross-linked polystyrene (Fluka, 10 g) containing 0.35 m eq g⁻¹ ligand was treated with chlorotriisopropoxytitanium (1.0 g, 0.004 mol) and toluene (100ml) and heated at reflux under nitrogen for 18h. The mixture was cooled and the resulting polymer beads filtered and washed with toluene. The polymer beads were then repeatedly slurried with dichloromethane and filtered until the filtrate showed no colour change when treated with a 1% solution of hydroquinone in acetone. The resultant polymer beads were dried *in vacuo* at 75°C to give 9.6 g of catalyst **C** as white beads.
- (5) **Typical experimental for Catalyst D:** Acetyl acetone functionalised polymethylstyrene was prepared by suspension polymerisation of a mixture of 3-(3- and 4-vinylbenzyl)-pentane-2,4-dione (29.9 g, 0.15 mol) and divinylbenzene (2 ml, 0.014 mol).⁶ The monomers were suspended in a mixture of water (300ml) and polyvinylalcohol (0.2 g). Dibenzoyl peroxide (1.0 g, 0.004 mol) was added and the mixture heated at reflux for 2h. The mixture was cooled, filtered and the product washed with methanol (2x150 ml), filtered, washed with acetone and dried to give 23 g of white beads. 10g of the resulting polymer was treated with chlorotriisopropoxytitanium (30ml, 0.13 mol), Hünigs base (6.5 g, 0.05 mol) and 1,2-dichloroethane (100ml) and heated at reflux under nitrogen for 19h. The mixture was cooled and the bright orange beads filtered. The polymer beads were then repeatedly slurried with dichloromethane and filtered until the filtrate showed no colour change when treated with a solution of 1% hydroquinone in acetone. The resultant polymer beads were dried *in vacuo* at 65°C to give 11 g of polymer **D**.
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- (10) **Typical procedure for transesterification:** 11-Bromoundecanol (**3**, 5 g, 0.02 mol) was dissolved in methyl

methacrylate stabilised with 50 ppm BHT⁸ (20 mL) and the polymeric catalyst **C** or **D** (5 g) was added. The mixture was heated at reflux with a slow air bleed *via* capillary into the reaction whilst the methanol/methyl acrylate azeotrope was continuously removed *via* a Vigreux distillation column. Methyl methacrylate was added as required to maintain a constant volume. After 4h assay by gas chromatography indicated 98% conversion. The reaction mixture was cooled and the catalyst removed by filtration. The catalyst was washed with methyl methacrylate and washings were added to

the reaction filtrate. The 11-bromoundecyl methacrylate **2** was isolated by distillation of excess methyl methacrylate as an oil in 87% isolated yield.

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