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An efficient synthesis of alkyl α-(hydroxymethyl)acrylates induced by DABCO in an aqueous medium

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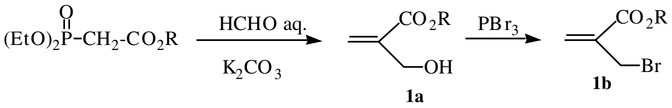
Abstract—Alkyl α-(hydroxymethyl)acrylates are prepared in high yields on a synthetic scale by hydroxymethylation of the corresponding acrylates using 30% aqueous formaldehyde in THF or DME as solvent and DABCO as the catalyst.

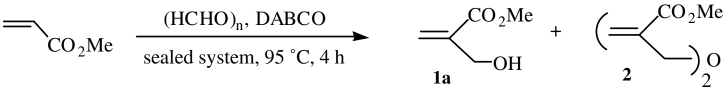
Since its first preparation on a large scale via the Wittig–Horner reaction, alkyl α-(hydroxymethyl)acrylate **1a**[1a–c] has proved to be a key intermediate for the preparation of alkyl α-(bromomethyl)acrylate **1b**[1d] (Scheme 1), a precursor of α-methylene-γ-butyrolactones[2] and lactams[3] via organozinc chemistry.

The Baylis–Hillman reaction using DABCO as a catalyst for the α-hydroxyalkylation of acrylates,[4] acrylonitrile[5] and vinyl ketones[6] would have been a shorter route to **1a** from formaldehyde but it seems that it has to be performed in an aprotic medium. Compound **1a** can also be made in 30% yield from paraformadehyde, methyl acrylate and DABCO in a sealed system at 95 °C for 4 h. However, this reaction gives rise to a mixture of **1a** and the difunctional methacrylate ether **2**[7] (60%) (Scheme 2).

Our interest in **1a** and also in the Baylis–Hillman reaction[8] led us to undertake the synthesis using formaldehyde as a 30% aqueous solution. Triethylamine and DABCO were examined as catalysts (25 mmol %), but only the latter was consistent with mild reaction conditions. The report that water as solvent accelerated the DABCO-catalyzed coupling of aromatic aldehydes with activated alkenes[9,10] prompted us to look at the effect of water on the Baylis–Hillman coupling of formaldehyde and some alkyl acrylates. Surprisingly, we found that



Scheme 1.



Scheme 2.

Keywords: Wittig–Horner reaction; Baylis–Hillman; Triethyl phosphonoacetate; Acrylates; Hydroxymethylation.
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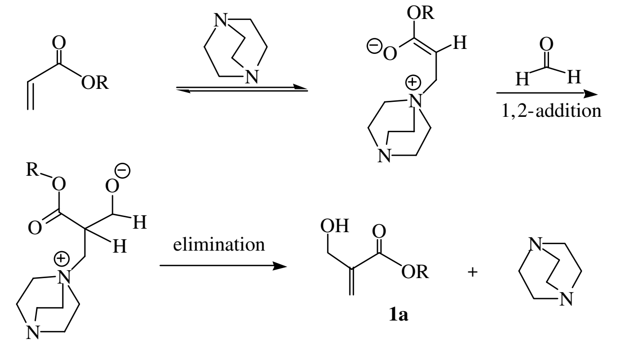
Table 1. DABCO-catalyzed coupling of acrylates with (30%) aqueous formaldehyde

Entry	R	Solvent	Time (h)	Yield (%)[a]
1	C_2H_5	1,4-Dioxane	12	74
2	CH_3	1,4-Dioxane	10	81
3	C_2H_5	DME	16	60
4	CH_3	DME	16	57
5	C_2H_5	MeOH	16	71
6	$^{t}C_4H_9$	DME	16	50
7	C_2H_5	THF	12	70
8	CH_3	THF	16	62
9	$^{t}C_4H_9$	THF	20	72
10	C_2H_5	PEG 400	12	50

[a] Isolated yields. Products were characterized by ^1H NMR and mass spectrometry.



Scheme 3.

the best yields of **1a** were obtained when the reaction takes place in a two-phase liquid–liquid system in the presence of an ethereal solvent (DME, THF, 1,4-dioxane) or in methanol.[1b] Generally the reaction was achieved overnight at the reflux temperature of the organic solvent and gave rise to α-(hydroxymethyl)acrylates (R = Me, Et, ^{t}Bu) as pure, distilled products. It could be performed on a preparative scale (2 mol). As listed in Table 1, the best yield (81%, R = Me) we obtained was in a binary medium consisting of 1,4-dioxane and water. However, the toxicity of this solvent made us prefer DME and especially THF (70% on 2-M run for R = Et). Polyethylene glycol PEG 400[11] can also be used as the solvent in place of 1,4-dioxane (Scheme 3).

We must mention that side reactions occurring via *trans*-esterification by the methanol or arising from methacrylate ethers and acetals resulting from the reaction of two molecules of **1a** with monomeric and oligomeric formaldehyde,[12] were avoided when 30% aqueous formaldehyde solution was prepared by acidic depolymerization of paraformaldehyde (10 mol), in water at reflux in the presence of 25 mL 1 N H_3PO_4 for 2 h. These side reactions were always observed when **1a** was prepared using commercially available formaldehyde solutions, which contain up to 10% methanol as stabilizer.

In conclusion, this communication reports an efficient and practical methodology for the synthesis of alkyl α-(hydroxymethyl)acrylates of type **1a** using DABCO as the catalyst in an aqueous medium.

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