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Two mild methods for synthesis of α,β–unsaturated cyanoesters

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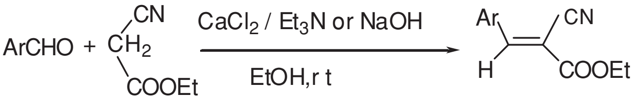
α,β–Unsaturated cyanoesters can be prepared by reaction of aldehydes and ethyl cyanoacetate catalysed by $CaCl_2$/Et_3N or NaOH at room temperature .

Keywords: α,β–unsaturated cyanoesters , catalysed reaction

α,β–Unsaturated cyanoesters which are important intermediates for the synthesis of heterocycles, are usually prepared by the condensation of cyanoacetic esters with aldehydes or ketones in the Knoevenagel reaction. Usually a base is necessary as a catalyst and the water which is formed has to be removed by azeotropic distillation.[1] The procedure is troublesome. $ZnCl_2$ was used as a catalyst for preparation of α,β–unsaturated cyanoesters,[2] but at 100°C. Ammonium acetate[3] and urotropine[4] efficiently catalysed the Knoevenagel condensation under microwave irradiation. Water is being used as a solvent in more reactions in the context of "green" chemistry. Cetyltrimethylammonium bromide (CTMAB) was found to catalyse the preparation of α,β–unsaturated cyanoesters in water,[5] but these reactions took a long time (12h), and it was difficult to filter the products due to emulsification of CTMAB. The precipitate had to stand overnight before the products could be filtered. Interestingly, α,β–unsaturated cyanoesters were prepared by the reaction of bromocyanoacetic ester with aldehydes promoted by tri-*n*-butylarsine under neutral condition.[6] This reaction must be under nitrogen, and products were separated by chromatography. Solid phase Knoevenagel catalysts were employed as heterogeneous catalysts under reflux in ethanol.[7,8] Here we report two new systems for the preparation of α,β–unsaturated cyanoesters which possess several advantages compared to literature methods: (1) They occur at room temperature, and do not need heating or microwave irradiation.[1-4,6,7,8] (2) The reactions time is short.[5,6] (3) Reagents are not sensitive to moisture or oxygen, and reactions proceed in air.[6] (4) The products do not need to be seperated by chromatography and filtration is easy.[5,6] This communication reports the results of the reaction of ethyl cyanoacetate with a variety of aromatic aldehydes in EtOH in the presence of $CaCl_2$/Et_3N or NaOH as catalyst at room temperature. Only the E isomers were produced.

We found that reaction of benzaldehyde with ethyl cyanoacetate is very easy. Reaction of equimolar benzaldehyde and ethyl cyanoacetate catalysed by 10 mol % Et_3N in ethanol at room temperature for 1/2 hour can give excellent yield (89%) of the corresponding condensation product. But p-methoxybenzaldehyde gave only a trace of the product under the same condition. In order to seek general methods for synthesis of α,β–unsaturated cyanoesters from more aromatic aldehydes, we adopt as the general reagent $CaCl_2$/Et_3N as the catalyst. The desired results were obtained according to general procedure A (Table 1).



Scheme 1 Reaction of aldehydes and ethyl cyanoacetate.

Table 1 Results for reactions catalysed by $CaCl_2$ / Et_3N

Entry	Ar (CHO)	Yield/%	M.p./°C	
			Obs.	Lit.
1	*p*-$CH_3OC_6H_4$	90	81–82	80–84[9]
2	C_6H_5	90	50–51	50–51[9]
3	*p*-$(CH_3)_2NC_6H_4$	92	124–125	124–126[12]
4	*o*-Cl C_6H_4	93	52–53	51–52[11]
5	2-furfuryl	94	92–93	92–93[9]
6	*p*-HO C_6H_4	87	172–173	171–172[10]

ArCHO (10 mmol), ethyl cyanoacetate (10 mmol), $CaCl_2$ (0.5 mmol), Et_3N(1 mmol), Ethanol 20 ml, rt, 1/2h.

Table 2 Results for reactions catalysed by NaOH

Entry	Ar	Yield(%)	M.p./°C	
			Obs.	Lit.
1	*p*-CH3OC6H4	91	80–81	80–84[9]
2	C6H5	90	50–51	50–51[9]
3	p-(CH3)2NC6H4	92	124–125	124–126[12]
4	o-Cl C6H4	92	51–52	51–52[11]
5	2-furfuryl	93	92–93	92–93[9]
6	*p*-HO C_6H_4	88	171–172	171–172[10]

ArCHO (10 mmol), ethyl cyanoacetate (10 mmol), NaOH (1 mmol), EtOH 20 ml, rt, 1/2h.

With the stronger base sodium hydroxide as a catalyst instead of triethylamine, we found reactions can proceed smoothly without $CaCl_2$, and excellent results were obtained according to general procedure B (Table 2).

Experimental

General procedure A: To a mixture of the aldehyde (10 mmol) and ethyl cyanoacetate (10 mmol) in ethanol (10 ml) (95%), $CaCl_2$ (0.5 mmol) and Et_3N (1 mmol) were added, and stirred for 1/2 h at room temperature, water (100 ml) was added, and the mixture stirred for a moment then filtered. The crude product was recrystallised from ethanol.

General procedure B: To a mixture of the aldehyde (10 mmol) and of ethyl cynaoacetate (10 mmol) in ethanol (10 ml) (95%), NaOH (1 mmol)was added, and stirred for 1/2 h at room temperature, water (100ml) was added, stirred for a moment then filtered. It was neutralised by concentrated hydrochloric acid before filtration for entry 6 in Table 2. The crude product was recrystallised from ethanol.

All the products gave mps and spectral data consistent with the reported ones. See Tables 1 and 2. [9-12]

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