

Potassium Triiodide. A New and Efficient Catalyst for Carbon–Carbon Bond Formation in Aqueous Media

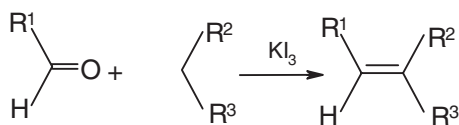
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Potassium triiodide catalyses the condensation of carbonyl compounds with active methylene compounds in aqueous media to afford *E* olefinic products in high yields.

There has been growing interest in the use of metallic elements¹ in aqueous media, as they offer significant advantages over conventional reactions using dry organic solvents. The development of such reactions is of interest because they also offer the possibility of obtaining environmentally benign reaction conditions by reducing the burden of organic solvent disposal.² The study and application of Knoevenagel condensation in water is still in its infancy. Since their century old history the full synthetic potential of such reactions is still waiting to be explored and they need to be expanded.³ In recent years there has been increasing emphasis on the use of environment friendly conditions to reduce the amount of toxic waste and by-products arising from the chemical processes. The challenge is to develop catalytic conditions leading to carbon–carbon bond formation which are widely employed in organic synthesis. The Knoevenagel condensation, have numerous applications in the elegant synthesis of fine chemicals,⁴ in hetero Diels–Alder reactions,⁵ in the synthesis of carbocycles and heterocycles⁶ and are usually catalysed by organic bases (primary, secondary and tertiary amines, ammonia and ammonium salts). With piperidine base, the by-products formed are difficult to remove.⁷ However, in recent years, new catalysts⁸ including silica gel functionalised with amine groups (Al₂O₃, AlPO₄–Al₂O₃, TiCl₄/base and doped xonontlite), solid phase resin,⁹ CdI₂ in solid⁹ state, MS 5A/ethylenediammonium diacetate¹⁰ and MW¹¹ have been employed. But these methods have their own merits as well as limitations. The main hurdle with the Knoevenagel condensation is the reactivity of ketones with the competitive Michael addition occurring in the reaction of some active methylene compounds and there is also problem with the stereocontrol in the synthesis of Knoevenagel products from unsymmetrical carbonyl compounds. Here we wish to report the first example of a new catalyst KI₃, for carbon–carbon bond formation in aqueous condition. It can perform the reaction to produce the *E* olefinic products in good purity and high yields, and eliminates the piperidine based by-products and reduces transesterification.

The results obtained with different aliphatic, aromatic and heterocyclic aldehydes and different active methylene compounds, according to scheme 1 are recorded in the table. Also it



Scheme 1.

can be seen from the table that all reactions proceeded selectively to the dehydrated products without any side reaction. The reaction between benzaldehyde and ethyl cyanoacetate in the presence of KI₃ (entry 3g) gave selectively the Knoevenagel adduct while the same reaction promoted by an alkali metal containing MCM-41 yielded a mixture of hydrated and dehydrated products.¹² The aromatic α,β -unsaturated aldehydes gave the corresponding olefinic products without the formation of any Michael-type addition products. Thus, cinnamaldehyde with malononitrile gave 1,1-dicyano-4-phenylbuta-1,3-diene (90% conversion after 20 min) exclusively. In the reaction of *o*-hydroxybenzaldehyde with active methylene compounds the first-formed Knoevenagel condensation products underwent further transformations as a result of nucleophilic attack by the phenolate ion on the cyano group, which is held in a stereochemically favourable position by the olefinic bond. Thus 2-imino-2*H*-1-benzopyran-3-carbonitrile and 2-imino-2*H*-1-benzopyran-3-carboxylate were formed exclusively in 82 and 85% yields. The reaction¹³ was carried out by mixing carbonyl compound, active methylene compound and potassium triiodide¹⁴ at room temperature and heating them at 70 °C for a specified time period, to give after usual work-up excellent yields of the corresponding Knoevenagel products. Some yields (e.g. **3a**, 98%) were much higher than reactions carried out in boiling benzene (74%). Furthermore, the rate of the

Table 1. Reaction time and yield of Knoevenagel product **3**

Prod- ucts	R ¹	R ²	R ³	Reaction time/min	Yield /%
3a	Ph	CN	CN	15	98
3b	(<i>E</i>)-PhCH=CH	CN	CN	20	88
3c	Me	CN	CN	20	80
3d	2-Furyl	CN	CN	22	80
3e	4-Quinolyl	CN	CN	21	85
3f	<i>p</i> -NO ₂ C ₆ H ₄	CN	CN	16	83
3g	Ph	CO ₂ Et	CN	15	86
3h	(<i>E</i>)-PhCH=CH	CO ₂ Et	CN	20	85
3i	<i>p</i> -NO ₂ C ₆ H ₄	CO ₂ Et	CN	16	87
3j	2-Furyl	CO ₂ Et	CN	20	82
3k	4-Quinolyl	CO ₂ Et	CN	18	83
3l	Ph	CO ₂ H	CN	16	89
3m	(<i>E</i>)-PhCH=CH	CO ₂ H	CN	15	85
3n	Ph	CONH ₂	CN	15	90
3o	(<i>E</i>)-PhCH=CH	CONH ₂	CN	20	90
3p	<i>p</i> -MeOC ₆ H ₄	CONH ₂	CN	22	90
3q	Ph	CO ₂ Et	CO ₂ Et	20	85
3r	Ph	MeCO	CO ₂ Et	22	80
3s	<i>o</i> -OHC ₆ H ₄	CN	CN	20	82
3t	<i>o</i> -OHC ₆ H ₄	CN	CO ₂ Et	22	80

reaction is quite impressive and comparable with the recently reported Knoevenagel condensation under microwave irradiation¹⁵ employing phosphorous pentoxide as dehydrating agent and chlorobenzene as an energy transfer medium for the removal of water. All the compounds obtained were characterized by spectroscopic methods and finally by comparison with authentic samples. Here the role of KI₃ is as a mild base and the reaction is probably similar to that of the reactions promoted by haomogeneous bases.¹⁶ It proceeded by the abstraction of a proton from active methylene compound, which gets stabilized by the cationic charge. This stabilized carbanion attacks the electrophilic carbonyl carbon to form an intermediate which in turn, abstracts a proton from in situ generated HI. Dehydration then takes place to form the Knoevenagel product.

In conclusion, the present investigation in aqueous condition offers a convenient and alternative method for the stereospecific preparation of *E* olefins where the reaction is rapid, the yields are excellent, the procedure is simple, the method is devoid of side reactions such as self-condensation, bis-addition, dimerisation or rearrangements and the use of nontoxic and inexpensive catalysts.

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- 13 *General procedure for the Knoevenagel condensations in the presence of potassium triiodide.* In a typical case, to a solution of potassium triiodide (0.04 gm, 0.1 mmol), benzaldehyde (0.21 g, 2 mmol) and malononitrile (0.13 g, 2 mmol) were added at room temperature. After stirring for 2 min, the resulting mixture was heated at 70 °C for 15 min (monitored vide tlc). The reaction was then cooled to room temperature, quenched with cold water, washed with sodium thiosulphate and extracted with chloroform (2 × 20 ml). The organic extract was washed with water (20 ml), dried (Na₂SO₄) and evaporated under reduced pressure to furnish a residue which was purified by column chromatography (silica gel:CHCl₃). The product benzylidene malononitrile was obtained as a crystalline solid mp 82 °C (Lit¹⁷, mp 83 °C) yield 98%. Other Knoevenagel products were (entry 2 to 18) prepared similarly and their characteristics are recorded in the table. Reaction of *o*-hydroxybenzaldehyde with active methylene compounds, carried out in the same way which gave the imino lactones in 80 to 82% yields.
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