A practical Knoevenagel condensation catalysed by imidazole

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The Knoevenagel condensation of aldehydes with active methylene compounds is easily carried out in dichloromethane using imidazole as an inexpensive catalyst. The olefinic products were obtained in high to excellent yields.

Keywords: Knoevenagel condensation, imidazole, active methylene compounds, olefinic compounds

The Knoevenagel reaction is well known for the synthesis of electrophilic olefins from active methylene and carbonyl compounds.[1] There are a number of catalysts for this transformation and affording variable yields of olefins. The reaction is catalysed by weak bases such as primary, secondary and tertiary amines, and ammonium salts under homogenous conditions.[1-3] When aldehydes are used the reaction is regioselective yielding the E-isomer.[4] In continuation of our interest in catalytic reactions[5] and Knoevenagel reaction,[6] we report a convenient method for the synthesis of olefin derivatives utilising imidazole as catalyst (Scheme 1). Arylidene cyanoacetates and arylidene malononitriles were obtained from the Knoevenagel condensation of several aldehydes with ethyl cyanoacetate and malononitrile respectively under mild reaction conditions using imidazole as a catalyst at room temperature or under reflex.

The aromatic aldehydes readily condensed with malononitrile, while with ethyl cyanoacetate, the reaction is slower. This may be attributed to the fact that abstraction of a proton from the active methylene group of ethyl cyanoacetate is most difficult. It can be seen from Table 1 that all reactions proceeded selectively to the dehydrated products without any side reaction. No products of self-condensation, Cannizaro reactions or hydrated products of the Knoevenagel adducts were obtained. No reactions occurred with aliphatic aldehydes under the conditions in which aromatic aldehydes gave almost quantitative conversions.

Aldehydes were shown to be more reactive than ketones under the same reaction condition. The condensation of malononitrile was not successful with ketones at room temperature, and a longer reaction time was required to obtain a moderate yield of the product under reflux condition(entries **3g**, **3h**). In the reaction of aromatic α,β-unsaturated carbonyl compounds (entries **3i**, **3p**), the Knoevenagel condensation products were obtained in 98% yields after 15 and 40 minutes with 10 and 25 mol% of catalyst respectively. The resulting olefins, the reaction conditions and yields are shown in Table 1. In all cases, the products were identified as the E-isomers by the comparison of the IR, ^{1}H NMR spectra and melting points of authentic samples.

Aromatic aldehydes bearing electron-donating or electron-withdrawing groups both reacted with active methylene compounds in the presence of catalytic amount of imidazole in very good yield. These reactions went to completion in 5–120 minutes at room temperature or under reflux to produce the olefinic compounds (Table 1). The reaction with the more acidic malononitrile proceeds at 25°C with 10 mol% of catalyst. In contrast, ethyl cyanoacetate requires elevated temperature and a larger amount of catalyst (25-30 mol%).

The Knoevenagel condensation for ketones in the presence of imidazole catalyst, required a large amount of catalyst and afforded moderate yields of adducts after a longer reaction time. The use of imidazole as catalyst in this reaction allowed us to perform the condensation under mild conditions with excellent yields. Important features of this reaction are the following. The catalyst is non-toxic, inexpensive and readily available. Imidazole is water soluble and can be readily removed by aqueous extraction.

In summary, we have developed a simple and easy procedure, for the stereoselective preparation of E-olefin compounds.

Experimental

Melting points were measured by using the capillary tube method with an Electrothermal 9100 apparatus. ^{1}H NMR spectra were recorded on Bruker DRX-90 AVANCE using TMS as an internal standard ($CDCl_3$ solution). IR spectra were recorded as KBr disk on the FT-IR Bruker Tensor 27. All products were known compounds and identified by comparison of their spectra and physical data with the literature.[7,9,14,10,12,8,13]

Preparation of olefinic compounds

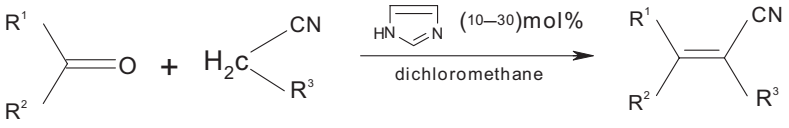
General procedure

Imidazole (10–30 mol%) was treated with an appropriate carbonyl compound (1 mmol) and active methylene compound (1 mmol) in dichloromethane (2 ml) at room temperature. When ethyl cyanoacetate was used as active methylene compound the mixture was refluxed. The progress of reaction was monitored by TLC. On completion to the reaction mixture water (5 ml) was added and extracted with dichloromethane (2 × 3 ml) and dried over $MgSO_4$. Evaporation of the solvent afforded the pure desired olefinic products with excellent yields (Table 1). In two cases (entries **3g**, **3h**), the pure products were obtained after recrystallising from ethanol.

1,1-Dicyano-2 phenylethylene **(3a):** M.p. = 83–84°C (83[7]°C). ^{1}H NMR($CDCl_3$, δ ppm): 7.90 (s, 1H), 7.50–8.15 (m, 5H). IR (KBr, cm^{-1}): 3020, 2250, 1590.

1,1- Dicyano-2- (4- chlorophenyl) ethylene **(3b):** M.p. = 167–168°C (164[8]°C). ^{1}H NMR ($CDCL_3$,δ ppm): 7.75 (s, 1H),7.56 (d, 2H J = 9.0 Hz), 7.88 (d, 2H, J = 9.0 Hz). IR (KBr, cm^{-1}): 2205, 1560, 1110.

1,1- Dicyano-2-(4-nitrophenyl) ethylene **(3c):** M.p. = 161–162°C (159-160[7]°C). ^{1}H NMR ($CDCL_3$, δ ppm): 8.39 (d, 2H, J = 7.2 Hz), 8.1 (d, 2H, J = 7.2 Hz), 7.88 (s, 1H). IR(KBr,cm^{-1}): 3010, 2250, 1600, 1530, 1350.



1 **2** **3a**

Scheme 1

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Table 1 Knoevenagel condensation catalysed by Imidazole

Entry	R^1	R^2	R^3	Catalyst/mol%	Time/min	Condition	Yield/%[a]	M.p.(°C)	
								Found	Reported[lit]
3a	C_6H_5	H	CN	10	5	Room temperature	98	83–84	83[7]
3b	4–Cl–C_6H_4	H	CN	10	5	Room temperature	98	167–168	164[8]
3c	4–NO_2–C_6H_4	H	CN	10	5	Room temperature	98	161–162	159–160[7]
3d	3–NO_2– C_6H_4	H	CN	10	5	Room temperature	97	100–101	104–105[9]
3e	4–CH_3– C_6H_4	H	CN	10	5	Room temperature	98	137–138	135[10]
3f	4–CH_3O– C_6H_4	H	CN	10	5	Room temperature	98	113–114	115[7]
3g	C_6H_5	C_6H_5	CN	30	60	Reflux	50	138	138[11]
3h	C_6H_5	CH_3	CN	30	60	Room temperature	40	92	90–91[7]
3i	HC =CH–C_6H_5	H	CN	10	15	Room temperature	98	126	128[12]
3j	C_6H_5	H	COOEt	25	40	Reflux	97	50–51	52[7]
3k	4–Cl– C_6H_4	H	COOEt	25	75	Reflux	97	87–89	87[8]
3l	2–NO_2– C_6H_4	H	COOEt	25	30	Reflux	98	102	96[13]
3m	4–CH_3– C_6H_4	H	COOEt	25	120	Reflux	97	93–94	92[7]
3n	4–CH_3O– C_6H_4	H	COOEt	25	30	Reflux	98	85	80–84[7]
3o	4–HO– C_6H_4	H	COOEt	25	30	Reflux	98	169	170[8]
3p	HC=CH–C_6H_5	H	COOEt	25	40	Reflux	98	109–110.5	116[14]

[a]Yields refer to the isolated products.

1,1- Dicyano-2- (3-nitrophenyl) ethylene **(3d):** M.p. = 100–101°C (104–105[9]°C). ^{1}H NMR ($CDCL_3$, δ ppm): 8.60 (t, 1H, J = 1.8 Hz), 8.3-8.4 (dd, 1H, J = 0.8, J = 9 Hz), 8.3 (d, 1H), 7.85 (s, 1H), 7.7 (t, 1H, J = 8 Hz). IR (KBr,cm^{-1}): 3010, 2225, 1590, 1530, 1350.

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