

Niobium (V) chloride catalyzed Knoevenagel condensation: An efficient protocol for the preparation of electrophilic alkenes

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Abstract

The condensation reaction has been carryout very conveniently to obtain the corresponding substituted olefins in excellent yields and showing all the products in excellent *E*-geometry. The reaction conditions are very mild and applicable to various aldehydes as well as active methylene compounds.

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Keywords: Aldehydes; Active methylene compounds; Knoevenagel condensation; Lewis acid; Electrophilic alkenes

1. Introduction

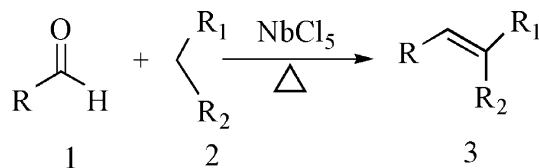
The Knoevenagel condensation has been the subject of many synthetic applications in organic chemistry, since its discovery [1]. In recent years, there has been a growing interest in Knoevenagel products, due to their use in the preparation of coumarin derivatives, cosmetics, perfumes and pharmaceuticals [2]. In general, this condensation has been carried out between carbonyl compounds and active methylene carbon in the presence of a bases such as ethylenediamine, piperidine or corresponding, ammonium salts [3], amino acids [4], dimethylaminopyridine [5] and potassium fluoride mixture [6]. There are a few number of Lewis acid catalyst [7], known to promote this reaction. Recently, many efforts have been made to prepare electrophilic alkenes under heterogeneous conditions using inorganic salts like Al_2O_3 , zeolites, calcite [8] and ionic liquids [9] also played a vital role as reaction media for this condensation. However, they have some drawbacks such as harsh reaction conditions and the lack of generality. In addition, the catalysts have to be applied in stoichiometric amounts or even large excess to effect complete conversion of the substrate. There still exists a need for the development of new and mild methods for

obtaining these products under conditions tolerated by sensitive functional groups, and using techniques involving easy workup procedures. Niobium (V) chloride is well known in the literature for various organic transformations as mild catalyst [10].

2. Results and discussions

In this communication, we wish to highlight our findings on the Niobium (V) chloride catalyzed condensation of active methylene compounds, such as ethyl cyano malonate, diethylmalonate and malonanitrile with aromatic, heterocyclic and aliphatic aldehydes. The reaction conditions are very mild and carried out in acetonitrile solvent. In view of the emerging importance of the catalytic process for replace the stoichiometric reagents, we studied the optimized reaction conditions with 10 mol%, of the catalyst. In a typical reaction, 4-methoxy benzaldehyde with diethyl malonate in the presence of NbCl_5 (10 mol%) at reflux of acetonitrile, resulted the formation of diethyl 4-methoxy benzylidene malonate (**3d**) in 92% yield within 3 h of time. In a similar manner, a wide range of aldehydes including aromatic, aliphatic and heterocyclic reacted efficiently with ethylcyanoacetate and malonanitrile under the same reaction conditions to give the corresponding substituted olefins. Heterocyclic aldehydes, such as furfural

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R = Aromatic, aliphatic and Heterocyclic
 R₁ & R₂ = CN, CO₂Et

Scheme 1.

(entry **b**) and pyridine-3-carboxaldehyde (entry **m**) gave very good yields. However, the aliphatic aldehydes (entry **e** and **i**) required little more reaction time but the yields are very good. Whereas, the conjugated aldehyde (entry **c**) converted to the olefin with high *E,E*-geometry, in short period of time, without any side products. In all cases, the reaction proceeds smoothly in acetonitrile solvent. The reactions are highly stereoselective affording α,β -ethylenic compounds in excellent yields, with an *E*-geometry. The reactions lead to completion in 2.5–4.0 h at 80–85 °C to produce the electrophilic alkenes in 82–92% yield. The reaction with the more acidic malanonitril converts very fast and giving in excellent yields where as other malonates were relatively slower or require more reaction time (Scheme 1).

Subsequently, the scope of the Knoevenagel condensation with various aldehydes like electron rich and electron different, worked well, giving high electron deficient worked well, giving high yields of products. All the products were characterized by ¹H NMR, IR mass and melting points, which were compared with literature reports. In general, the reactions are clean and free from the formation of side products.

3. Conclusion

In conclusion, we have demonstrated an efficient method for the preparation of substituted alkenes in excellent yields with high stereoselectivity of *E*-geometry. The method is applicable to a wide range of aldehydes including aromatic, aliphatic, α,β -unsaturated and heterocyclic systems. The salient features of the method are the mild reaction conditions, high conversions, cleaner reaction profiles, solvent-free conditions, readily available catalyst and operational simplicity. All the above merits make it a useful and attractive method for the preparation of olefins.

4. Experimental

4.1. General remarks

Melting points were recorded on a Buchi R-535 apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectro photometer using KBr optics. ¹H NMR spectra were recorded on Gemini-200 spectrometer in CDCl₃ using TMS as internal standard. Mass spectra were

recorded on a Finnigan MAT 1020 Mass spectrometer operating at 70 eV.

4.2. General procedure for the preparation of substituted alkenes

To a mixture of aldehyde (5.0 mmol), active methylene compound (6.0 mmol) in acetonitrile (10 ml) was added the catalyst Niobium (V) chloride (10 mol%). The resulting reaction mixture was stirred at reflux for a specified period (Table 1). The progress of the reaction was monitored by thin layer chromatography (TLC). After complete conversion, as indicated by TLC, the reaction mixture was diluted by adding ethyl acetate (50 ml) and washed with water twice and brine. The organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The obtained crude products were purified by column chromatography (using silicagel 60–120 mesh) by eluting with ethylacetate and *n*-hexane mixture in 2:8 ratio. The olefinic products thus obtained were characterized by comparison of their ¹H NMR, IR and mass spectroscopy, with authentic samples.

4.3. Spectral data for selected compounds

4.3.1. Ethyl (*E*)-2-cyano-3-(2-furyl)-2-propenoate (**3b**)

White solid, mp 91–92 °C. IR (KBr): ν 3032, 2231, 1758, 1620, 1532, 1460, 1380, 1216, 1108, 951, 834, 752 cm⁻¹. ¹H NMR (200 MHz, CDCl₃). δ 1.42 (t, 3H, *J* = 7.0 Hz), 4.38 (q, 2H, *J* = 7.0 Hz), 6.65–6.70 (m, 1H), 7.42 (d, 1H, *J* = 4.5 Hz), 7.78 (d, 1H, *J* = 2.50 Hz), 8.05 (s, 1H). EIMS *m/z* (%): 191 (m⁺ 100), 163 (29), 146 (22), 118 (64), 92 (21), 63 (32).

4.3.2. Ethyl (2*E*, 4*E*)-2-cyano-5-phenyl-2,4-pentadinoate (**3c**)

Light colored solid, mp 114–116 °C. IR (KBr): ν 3079, 2967, 2843, 2241, 1732, 1640, 1519, 1408, 1329, 1225, 1051, 963, 859, 746 cm⁻¹. ¹H NMR (200 MHz, CDCl₃). δ 1.44 (t, 3H, *J* = 7.0 Hz), 4.40 (q, 2H, *J* = 7.0 Hz), 7.26–7.32 (m, 2H), 7.36–7.46 (m, 3H), 7.55–7.65 (m, 2H), 8.10 (d, 1H, *J* = 10.0 Hz). EIMS *m/z* (%): 227 (m⁺ 32), 198 (27), 154 (100), 128 (53), 103 (67), 77 (30).

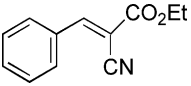
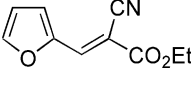
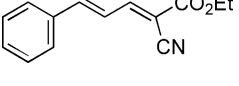
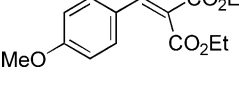
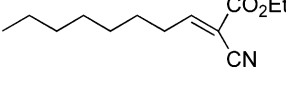
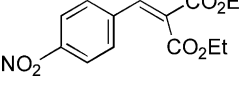
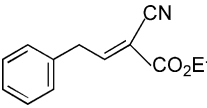
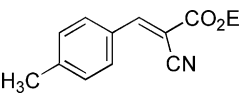
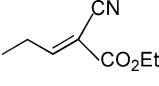
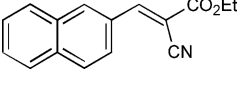
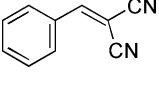
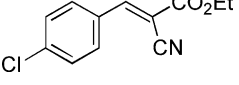
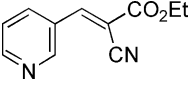
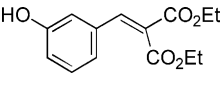
4.3.3. Ethyl (*E*)-2-cyano-2-octenoate (**3e**)

Colorless liquid. IR (neat): ν 2946, 2861, 2250, 1743, 1518, 1469, 1372, 1131, 1025, 936, 854, 765 cm⁻¹. ¹H NMR (200 MHz, CDCl₃). δ 0.90 (t, 3H, *J* = 6.5 Hz), 1.22–1.43 (m, 7H), 1.55–1.64 (m, 2H), 2.52–2.64 (m, 2H), 4.32 (q, 2H, *J* = 7.0 Hz), 7.66 (t, 1H, *J* = 10.5, Hz). EIMS *m/z* (%): 195 (m⁺ 18), 151 (73), 125 (100), 96 (54), 75 (21), 69 (32), 57 (28), 40 (31).

4.3.4. Ethyl (*E*)-2-ethylester-3-(4-nitrophenyl)-2-propenoate (**3f**)

Light yellow solid, mp 90–91 °C. IR (KBr): ν 3689, 3562, 3022, 2402, 1734, 1608, 1512, 1460, 1383, 1259, 936, 833, 762 cm⁻¹. ¹H NMR (200 MHz, CDCl₃). δ 1.32 (t, 6H,

Table 1
Niobium (V) chloride catalyzed Knoevenagel condensation

Entry	R	R ₁	R ₂	Product ^a	Time (H)	Yield ^b	Ref. ^c
a	C ₆ H ₅	CN	CO ₂ Et		2.5	90	[7d]
b	Furfural	CN	CO ₂ Et		3.0	92	–
c	C ₆ H ₅ –CH=CH	CN	CO ₂ Et		2.5	85	–
d	4-MeOC ₆ H ₄	CO ₂ Et	CO ₂ Et		3.0	92	[10a]
e	Octanal	CN	CO ₂ Et		4.0	88	–
f	4-NO ₂ –C ₆ H ₄	CO ₂ Et	CO ₂ Et		4.0	90	–
g	C ₆ H ₅ –CH ₂	CN	CO ₂ Et		3.5	87	[7d]
h	4-CH ₃ –C ₆ H ₄	CO ₂ Et	CN		3.0	90	[7b]
i	<i>n</i> -C ₃ H ₇	CN	CO ₂ Et		3.5	82	[10a]
j	2-Naphthal	CN	CO ₂ Et		3.0	89	[7d]
k	C ₆ H ₅	CN	CN		2.5	92	[10a]
l	4-Cl–C ₆ H ₄	CN	CO ₂ Et		2.5	90	[7d]
M	3-Pyridine	CN	CO ₂ Et		3.0	84	–
N	4-OH–C ₆ H ₄	CO ₂ Et	CO ₂ Et		3.5	90	[7b]

^a All the products were characterized by comparison of their MP, IR and ¹H NMR spectra with literature reports.

^b Isolated and unoptimized yields.

^c Reference for spectral data.

$J=7.0$ Hz), 4.36 (q, 4H, $J=7.0$ Hz), 8.20 (d, 2H, $J=8.5$ Hz), 8.28 (d, 2H, $J=8.5$ Hz), 8.38 (s, 1H). EIMS m/z (%): 293 (m^+ 31), 248 (68), 218 (10), 203 (100), 175 (72), 147 (28), 101 (22), 76 (34), 51 (21).

4.3.5. Ethyl (E)-2-cyano-3-(3-pyridyl)-2-propenoate (3m)

Yellow solid, mp 76–78 °C. IR (KBr): ν 2993, 2846, 2221, 1724, 1608, 1514, 1418, 1275, 1067, 1013, 952, 837, 748 cm^{-1} . ^1H NMR (200 MHz, CDCl_3). δ 1.42 (t, 3H, $J=6.6$ Hz), 4.43 (q, 2H, $J=6.8$ Hz), 7.38–7.48 (m, 1H), 8.22 (s, 1H), 8.55–8.65 (m, 1H), 8.75 (d, 1H, $J=9.0$ Hz), 8.85 (d, 1H, $J=2.0$ Hz). EIMS m/z (%): 202 (m^+ 28), 174 (47), 159 (100), 130 (33), 103 (37), 80 (20), 76 (28), 51 (44).

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