Phosphane-Catalyzed Knoevenagel Condensation: A Facile Synthesis of α-Cyanoacrylates and α-Cyanoacrylonitriles

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Keywords: Aldehydes / Knoevenagel reaction / Microwave activation / Phosphanes

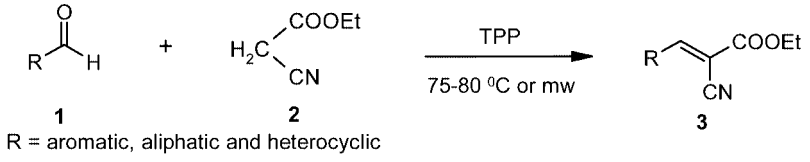
Triphenylphosphane (TPP) has been utilized as a novel and efficient catalyst for the Knoevenagel condensation of aldehydes with acidic methylene compounds such as ethyl cyanoacetate and malononitrile to afford substituted olefins. The reaction proceeds smoothly under mild and solvent-free conditions and the products are obtained in excellent yields with an *E*-geometry. This method is applicable for a wide range of aldehydes including aromatic, aliphatic and heterocyclic substrates. Microwave irradiation has been used to achieve enhanced reaction rates and improved yields.

Introduction

The Knoevenagel condensation is an important carbon-carbon bond-forming reaction in organic synthesis.[1] Ever since its discovery, the Knoevenagel reaction has been widely used in organic synthesis to prepare coumarins and their derivatives, which are important intermediates in the synthesis of cosmetics, perfumes and pharmaceuticals.[2] In recent times, there has been a growing interest in Knoevenagel products because many of them have significant biological activity, for example, tyrophostins, such as α-cyanothiocinnamide, are known to inhibit autophosphorylation of the EGF receptor, in addition to possessing antiproliferative effects on human keratinocytes.[3]

The Knoevenagel reaction is generally carried out in the presence of weak bases such as ethylenediamine, piperidine or corresponding ammonium salts, potassium fluoride, or amino acids such as glycine, β-alanine and L-proline under homogeneous conditions.[4,5] In contrast, there are only a few acid catalysts that are known to promote this reaction.[6] Recently, many efforts have been made to prepare olefinic compounds via a Knoevenagel reaction under heterogeneous conditions employing aluminium oxide, Xonotlite/*tert*-butoxide, cation-exchanged zeolites, alkali-containing MCM-41, SiO_2, calcite or fluorite and NP/KF as heterogeneous catalysts.[7–10] More recently, ionic liquids have also been employed to accomplish this reaction.[11]

In recent years, microwave-assisted reactions have received much attention because of their simplicity in operation, enhanced reaction rates and greater selectivity.[12] In particular, solvent-free reactions have gained popularity as they provide an opportunity to work with open vessels. This avoids the development of high pressure and provides a possibility of scaling-up the reaction under dry conditions. Thus, microwave irradiation, which has become a powerful synthetic tool for the rapid synthesis of a variety of biologically active compounds under solvent-free conditions, is often used to enhance the rates of classical organic reactions.[13]



Scheme 1

Results and Discussion

In this report, we wish to highlight our findings on the phosphane-catalyzed condensation of active methylene compounds, such as malononitrile and ethyl cyanoacetate,

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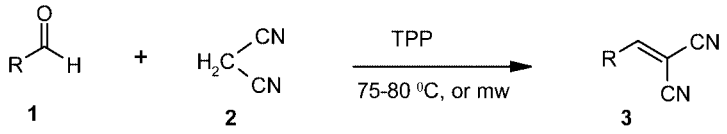
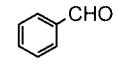
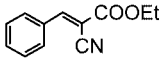
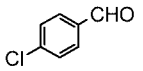
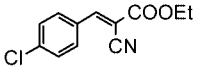
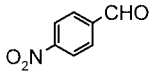
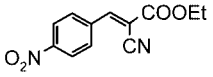
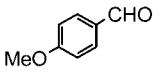
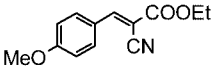
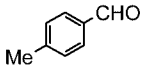
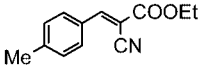
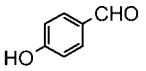
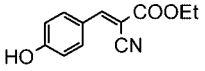
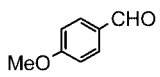
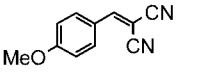
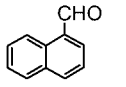
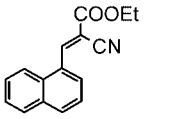
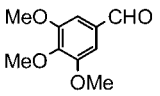
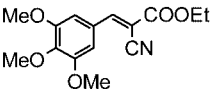
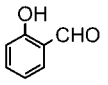
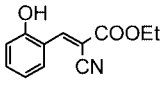
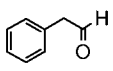
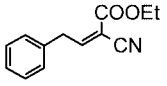
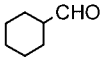
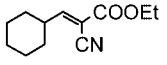
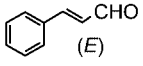
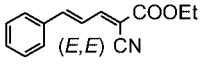
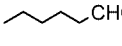
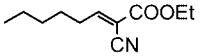
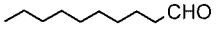
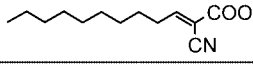


Scheme 2

Table 1. TPP-catalyzed synthesis of α-cyanoacrylonitriles

Entry	Aldehyde 1	Product[a] 3	Conversion (%)[b]	Conventional		Microwave[d]	
				Time (h)	Yield (%)[c]	Time (min)	Yield (%)[c]
a			98	4.0	85	3	90
b			99	3.0	87	3	92
c			100	2.5	90	2	95
d			95	4.5	82	4	85
e			97	3.5	85	3	91
f			96	5.0	78	4	82
g			98	4.0	83	4	86
h			100	3.5	88	3	93
i			98	5.0	79	4	82
j			97	5.5	85	5	89
k			100	4.5	82	4	85
l			95	5.0	84	4	87
m			100	4.0	80	3	83
n			96	4.0	78	4	81
o			98	4.0	83	5	85

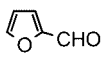
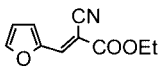
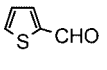
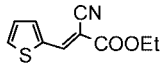
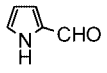
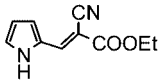
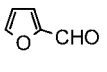
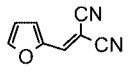
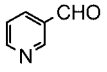
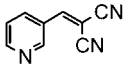
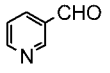
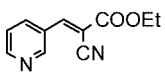
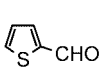
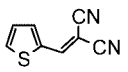
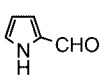
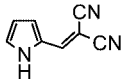
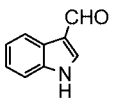
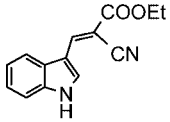
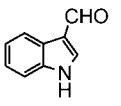
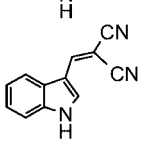
[a] All the products were reported previsiously in literature.
[b] Conversions were determined by GC analysis.
[c] Yield refers to the isolated pure products after column chromatography.
[d] Microwave irradiation was performed at 450 watts using BPL, BMO-800T microwave oven

with aromatic, heterocyclic and aliphatic aldehydes. In this study, triphenylphosphane (TPP) has been employed as a novel, mild and efficient catalyst for this condensation. Accordingly, treatment of furfural with ethyl cyanoacetate in the presence of 20 mol % of TPP at 75−80 °C resulted in the formation of ethyl 2-cyano-3-(2-furyl)-(*E*)-2-propenoate in 91% yield under solvent-free conditions. In a similar manner, a wide range of substrates including aromatic, aliphatic and heterocyclic aldehydes reacts efficiently with ethyl cycanoacetate under the same reaction conditions to give the corresponding olefins (Scheme 1).

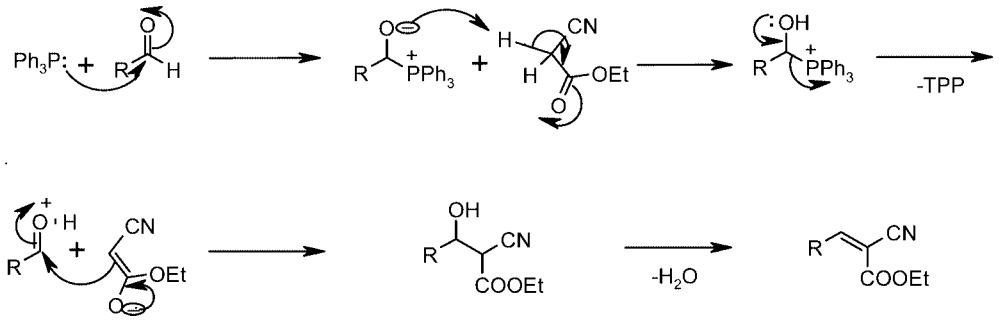
In all cases, the reaction proceeds smoothly with 20 mol % of TPP in solvent-free conditions. TPP acts as a mild Lewis base to induce the reaction. The reaction is highly stereoselective, affording α,β-ethylenic compounds in excellent yields, with an *E*-geometry. Furthermore, the treatment of aldehydes with malononitrile also gave olefinic compounds under similar reaction conditions (Scheme 2).

Both electron-rich and electron-deficient aldehydes worked well, giving high yields of products. Electron-deficient aldehydes gave relatively higher yields than their electron-rich counterparts (Table 1). Heterocyclic aldehydes, such as furfural, thiophene-2-carboxaldehde, pyrrole-2-carboxaldehyde, pyridine-3-carboxaldehyde and indole-3-carboxaldehyde, gave comparatively higher yields than aryl or aliphatic aldehydes (Table 2). However, aliphatic aldehydes afforded lower yields than aromatic aldehydes. It is noteworthy to mention that salicylaldehyde also afforded the corresponding olefin derivative in 85% yield without the formation of coumarin, which is normally observed under strongly acidic or basic conditions (entry j, Table 1). In general, the reactions are clean and free from the formation of

Table 2. TPP-catalyzed synthesis of heterocyclic α-cyanoacrylates and α-cyanoacrylonitriles

Entry	Aldehyde 1	Product[a] 4	Conversion (%)[b]	Conventional		Microwave[d]	
				Time (h)	Yield (%)[c]	Time (min)	Yield (%)[c]
a			100	2.5	91	2	95
b			99	3.5	89	3	92
c			95	4.0	85	3	90
d			100	1.5	92	2	95
e			99	3.5	86	2	89
f			98	4.5	82	3	86
g			99	3.0	93	2	95
h			100	3.5	88	3	91
i			95	5.0	83	5	86
j			97	4.0	85	3	89

[a] All the products were reported previsiously in literature
[b] Conversions (under microwaves) were determined by GC analysis
[c] Yield refers to the isolated pure products after column chromatography
[d] Microwave irradiation was carried out at 450 watts using BPL, BMO-800T domestic microwave oven



Scheme 3

the Michael adduct (for example, entry m, Table 1). In the absence of TPP, the reaction does not proceed under similar conditions even after a longer time (approximately 10 h). Furthermore, this method failed to give the desired olefinic products from aldehydes and diethyl malonate. No further improvement was observed in the reaction of benzaldehyde with diethyl malonate either by increasing the amount of TPP (stoichiometric ratio) or by raising the temperature (105−115 °C). To study the effect of the phosphorus reagent, the reaction was also carried out with *n*-tributylphosphane, triethyl phosphite and diethyl phosphite, among which inexpensive TPP was found to be the most effective catalyst. The collective details combined with the absence of a reaction with diethyl malonate and a plausible reaction mechanism are shown in Scheme 3.

In addition, the use of TPP as a catalyst helps to avoid the use of environmentally unfavorable organic solvents as reaction medium since the reaction proceeds smoothly under solvent-free conditions.[14] Microwave irradiation has been used as an alternate synthetic tool to achieve enhanced rates and improved yields. Microwave irradiation was performed at 450 W (2450 MHz) using s BPL, BMO-800T domestic microwave oven. The highest observed temperature after 3 min irradiation was 95 °C. The temperature in the microwave was controlled by pulsed irradiation (1 min with 20 s interval). Rapid reaction rates and high conversions were achieved by using microwave irradiation and the results are presented in Table 1 and 2.

Conclusion

In summary, TPP has been employed for the first time as a novel and efficient catalyst for the preparation of olefinic compounds by a Knoevenagel reaction under solvent-free conditions. This method is applicable to a wide range of aldehydes, including aromatic, aliphatic, α,β-unsaturated and heterocyclic substrates. The attractive features of this procedure are the mild reaction conditions, high conversions, cleaner reaction profiles, solvent-free reaction conditions, operational simplicity and inexpensive and readily available catalyst, all of which make it a useful and attractive strategy for the preparation of olefins.

Experimental Section

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 spectrophotometer using KBr optics. ^{1}H NMR spectra were recorded on Gemini-200 spectrometer in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 Mass spectrometer operating at 70 eV. CHN analyses were recorded on a Vario EL analyzer.

General Procedure for the Preparation of α,β-Unsaturated Compounds: A mixture of aldehyde (5 mmol), malononitrile or ethyl cyanoacetate (6.5 mmol) and triphenylphosphane (20 mol %) was stirred at 75−80 °C for a specified time as required to complete the reaction (Table 1 and 2). The progress of the reaction was monitored by TLC. After complete conversion, as indicated by TLC, the reaction mixture was diluted with water and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were concentrated in vacuo and the resulting product was directly charged onto a small silica gel column and eluted with a mixture of ethyl acetate/*n*-hexane to afford pure olefin. All the products (**3a**−**o** and **4a**−**j**) were prepared by using the same procedure. The olefinic products thus obtained were characterized by comparison of their NMR, IR, mass spectroscopic, TLC analysis and physical data with authentic samples. The spectroscopic data of all the products were identical with those reported in the literature.[11a,15]

Spectroscopic Data of Products Reported in Table 1

Ethyl (*E*)-2-Cyano-3-phenyl-2-propenoate (3a): Colorless crystalline solid, m.p. 49−50 °C. IR (KBr): $\tilde{\nu}$ = 3020, 2400, 2226, 1727, 1608, 1268, 1215, 1189, 1104, 1092, 1015, 754, 686 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.1 Hz, 3 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 7.48−7.56 (m, 3 H), 7.98 (dd, *J* = 7.9, 1.0 Hz, 2 H), 8.25 (s, 1 H) ppm. EI-MS: *m*/*z* (%) = 201 (100) [M$^+$], 200 (59), 173 (61), 172 (70), 156 (86), 129 (47), 128 (93), 127 (21), 102 (72), 101 (46), 77 (80), 76 (24), 75 (28), 51 (73), 43 (10).

Ethyl (*E*)-3-(4-Chlorophenyl)-2-cyano-2-propenoate (3b): White crystalline solid, 89−90 °C. IR (KBr): $\tilde{\nu}$ = 3100, 2850, 2220, 1730, 1610, 1590, 1490, 1270, 755, 670 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.2 Hz, 3 H), 4.40 (q, *J* = 7.2 Hz, 2 H), 7.59 (d, *J* = 8.5 Hz, 2 H), 7.95 (d, *J* = 8.5 Hz, 2 H), 8.20 (s, 1 H) ppm. EI-MS: *m*/*z* (%) = 235 (100) [M$^+$], 207 (75), 190 (87), 127 (73), 75 (77), 50 (45).

Ethyl (*E*)-2-Cyano-3-(4-nitrophenyl)-2-propenoate (3c): Colorless crystalline solid, 170−171 °C. IR (KBr): $\tilde{\nu}$ = 3278, 3020, 2400, 2230, 1730, 1660, 1530, 1265, 760, 670 cm^{-1}. ^{1}H NMR (200 MHz,

$CDCl_3$): δ = 1.40 (t, *J* = 7.0 Hz, 3 H), 4.40 (q, *J* = 7.0 Hz, 2 H), 8.12 (d, *J* = 8.5 Hz, 2 H), 8.25 (d, *J* = 8.5 Hz, 2 H), 8.35 (s, 1 H) ppm. EI-MS: *m*/*z* (%) = 246 (53) [M^+], 199 (72), 155 (68), 127 (63), 100 (54), 89 (52), 50 (85), 43 (17).

Ethyl (*E*)-2-Cyano-3-(4-methoxyphenyl)-2-propenoate (3d): Yellow crystalline solid, 79−81 °C. IR (KBr): ṽ = 3283, 3016, 2449, 2364, 1743, 1608, 1527, 1307, 1230, 771, 625 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.1 Hz, 3 H), 3.88 (s, 3 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 6.97 (d, *J* = 8.8 Hz, 2 H), 7.98 (d, *J* = 8.8 Hz, 2 H), 8.14 (s, 1 H) ppm. EI-MS: *m*/*z* (%) = 186 (50) [M^+], 159 (25), 158 (29), 157 (13), 143 (12), 116 (12), 115 (20), 114 (15), 103 (9), 89 (19), 88 (16), 77 (21), 64 (12), 63 (21), 62 (13), 51 (11), 43 (8).

Ethyl (*E*)-2-Cyano-3-(4-methylphenyl)-2-propenoate (3e): Colorless solid, 90−92 °C. IR (KBr): ṽ = 3100, 2850, 2220, 1710, 1600, 1370, 1200 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.2 Hz, 3 H), 2.40 (s, 3 H), 4.35 (q, *J* = 7.2 Hz, 2 H), 7.25−7.35 (d, *J* = 8.0 Hz, 2 H), 7.85−7.95 (d, *J* = 8.0 Hz, 2 H), 8.20 (s, 1 H) ppm. EI-MS: *m*/*z* (%) = 215 (100) [M^+], 187 (42), 170 (78), 142 (32), 115 (63), 65 (25).

Ethyl (*E*)-2-Cyano-3-(4-hydroxyphenyl)-2-propenoate (3f): Colorless solid, 169−171 °C. IR (KBr): ṽ = 3659, 3180, 3070−2900, 2230, 1710, 1590, 1510, 1440, 1370, 1260, 1200, 1185, 1100 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.1 Hz, 3 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 6.99 (d, *J* = 8.1 Hz, 2 H), 7.92 (d, *J* = 8.1 Hz, 2 H), 8.19 (s, 1 H) ppm. EI-MS: *m*/*z* (%) = 217 (100) [M^+], 189 (50), 172 (98), 144 (45), 117 (25), 189 (45), 63 (8).

2-(4-Methoxyphenylmethylene)malononitrile (3g): Yellow crystalline solid, 114−115 °C. IR (KBr): ṽ = 3110, 2850, 2230, 1600, 1550, 1460, 1370, 1280 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 3.90 (s, 3 H), 7.00 (d, *J* = 8.1 Hz, 2 H), 7.68 (s, 1 H), 7.95 (d, *J* = 8.1 Hz, 2 H) ppm. EI-MS: *m*/*z* (%) = 184 (100) [M^+], 141 (32), 114 (55), 63 (16).

Ethyl (*E*)-2-Cyano-3-(1-naphthyl)-2-propenoate (3h): Colorless solid, 73−74 °C. IR (KBr): ṽ = 3105, 2850, 2230, 1720, 1600, 1490, 1280, 1100 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.45 (t, *J* = 7.0 Hz, 3 H), 4.40 (q, *J* = 7.0 Hz, 2 H), 7.50−8.00 (m, 6 H), 8.32 (d, *J* = 7.9 Hz, 1 H), 9.12 (s, 1 H) ppm. EI-MS: *m*/*z* (%) = 251 (50) [M^+], 206, (20), 178 (100), 152 (32), 151 (33), 75 (8).

Ethyl (*E*)-2-Cyano-3-(3,4,5-trimethoxyphenyl)-2-propenoate (3i): Pale-yellow crystalline solid, 46−48 °C. IR (KBr): ṽ = 3109, 2850, 2230, 1730, 1610, 1450, 1370, 1200 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.1 Hz, 3 H), 3.90 (s, 9 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 7.25 (s, 2 H), 8.08 (s, 1 H) ppm. EI-MS: *m*/*z* (%) = 291 (40) [M^+], 246 (61), 218 (100), 125 (73), 99 (21), 74 (34).

Ethyl (*E*)-2-Cyano-3-(2-hydroxyphenyl)-2-propenoate (3j): Yellow crystalline solid, 133−135 °C. IR (KBr): ṽ = 3580, 3068, 2890, 2210, 1705, 1600, 1550, 1360, 1030, 780 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.43 (t, *J* = 7.0 Hz, 3 H), 4.40 (q, *J* = 7.0 Hz, 2 H), 7.35 (m, 2 H), 7.70 (d, *J* = 8.0 Hz, 2 H), 8.75 (s, 1 H) ppm. EI-MS: *m*/*z* (%) = 217 (40) [M^+], 172 (61), 144 (29), 118 (100), 93 (60).

Ethyl (*E*)-2-Cyano-4-phenyl-2-butenoate (3k): Colorless solid, 88−90 °C. IR (KBr): ṽ = 3433, 3090, 2259, 1727, 1642, 1215, 749, 669 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.1 Hz, 3 H), 3.88 (m, 2 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 7.18−7.33 (m, 3 H), 8.02−8.05 (m, 2 H), 8.22 (d, *J* = 10.5 Hz, 1 H) ppm. EI-MS: *m*/*z* (%) = 200 (40) [M^+], 191 (68), 190 (90, 174 (100), 164 (11), 147 (48), 146 (86), 145 (27), 126 (71), 125 (24), 120 (56), 99 (27), 95 (35), 75 (64), 69 (13), 57 (12), 43 (41).

Ethyl (*E*)-2-Cyano-3-cyclohexyl-2-propenoate (3l): Colorless solid, 88−90 °C. IR (KBr): ṽ 2987, 2257, 1730, 1609, 1465, 1257 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.20−1.38 (m, 9 H), 1.70−1.80 (m, 4 H), 2.69−2.71 (m, 1 H), 4.30 (q, *J* = 7.3 Hz, 2 H), 7.45 (d, *J* = 10.6 Hz, 1 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.7, 24.8, 25.2, 30.8, 40.9, 62.3, 107.5, 113.7, 161.6, 167.8 ppm. EI-MS: *m*/*z* (%) = 207 (30) [M^+], 179 (45),162 (90), 134 (100).

Ethyl (2*E*,4*E*)-2-Cyano-5-phenyl-2,4-pentadienoate (3m): Brown solid, m.p. 115−116 °C. IR (KBr): ṽ = 3090, 2985, 2251, 1730, 1640, 1221, 1023, 961, 857, 749, 669 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.43 (t, *J* = 7.1 Hz, 3 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 7.25−7.30 (m, 2 H), 7.35−7.45 (m, 3 H), 7.50−7.60 (m, 2 H), 8.0 (d, *J* = 10.8 Hz, 1 H) ppm. EI-MS: *m*/*z* (%) = 227 (18) [M^+], 198 (35), 154 (100), 128 (63), 103 (45), 77 (28).

Ethyl (*E*)-2-Cyano-2-octenoate (3n): Colorless liquid, IR (KBr): ṽ 2959, 2863, 2251, 1747, 1469, 1370, 1253, 1024, 854, 765 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 6.9 Hz, 3 H), 1.20−1.40 (m, 7 H), 1.50−1.60 (m, 2 H), 2.50−2.60 (m, 2 H), 4.30 (q, *J* = 7.0 Hz, 2 H), 7.65 (t, *J* = 10.7 Hz, 1 H) ppm. EI-MS: *m*/*z* (%) = 195 (10) [M^+], 151 (80), 125 (100), 96 (35), 75 (25), 69 (15), 57 (20), 40 (30).

Ethyl (*E*)-2-Cyano-2-dodecenoate (3o): Colorless liquid, IR (KBr): ṽ 2935, 2856, 2248, 1747, 1626, 1464, 1369, 1255, 1020, 857, 762 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.0 Hz, 3 H), 1.20−1.38 (m, 15 H), 1.40−1.55 (m, 2 H), 2.38−2.45 (m, 2 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 7.45 (t, *J* = 10.6 Hz, 1 H) ppm. EI-MS: *m*/*z* (%) = 251 (15) [M^+], 183 (100), 152 (10), 108 (80), 68 (55), 42 (90).

Spectroscopic Data of Products Reported in Table 2

Ethyl (*E*)-2-Cyano-3-(2-furyl)-2-propenoate (4a): Colorless solid, m.p. 89−91 °C. IR (KBr): ṽ = 3030, 2215, 1760, 1618, 1530, 1460, 1380, 1215, 1091, 756 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.1 Hz, 3 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 6.65 (dd, *J* = 1.9, 4.0 Hz, 1 H), 7.40 (d, *J* = 4.0 Hz, 1 H), 7.75 (d, *J* = 1.9 Hz, 1 H), 8.0 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 62.3, 98.3, 113.7, 115.1, 121.6, 139.2, 148.1, 148.5, 162.3 ppm. EI-MS: *m*/*z* (%) = 191 (100) [M^+], 163 (18), 146 (14), 63 (20). $C_{10}H_9NO_3$ (191.185): calcd. C 62.82, H 4.74, N 7.33; found C 62.89, H 4.79, N 7.41.

Ethyl (*E*)-2-Cyano-3-(2-thienyl)-2-propenoate (4b): Pale yellow solid, m.p. 105−108 °C. IR (KBr): ṽ = 3086, 2219, 1717, 1599, 1463, 1331, 1255, 1207, 1080, 1005, 858, 782, 735 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 6.9 Hz, 3 H), 4.38 (q, *J* = 6.9 Hz, 2 H), 7.20−7.28 (m, 1 H), 7.78 (d, *J* = 4.5 Hz, 1 H), 7.85 (d, *J* = 2.1 Hz, 1 H), 8.30 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 62.4, 99.2, 115.6, 128.5, 130.0, 135.9, 137.1, 146.6, 162.5 ppm. EI-MS: *m*/*z* (%) = 207 (100) [M^+], 179 (52), 162 (95), 134 (72), 108 (34), 90 (30), 45 (35). $C_{10}H_9NO_2S$ (207.25): calcd. C 57.96, H 4.38, N 6.76, S 15.47; found C 58.12, H 4.43, N 6.82, S, 15.41.

Ethyl (*E*)-2-Cyano-3-(1*H*-pyrrol-2-yl)-2-propenoate (4c): Light-gray solid, m.p. 135−137 °C. IR (KBr): ṽ = 3307, 2206, 1695, 1585, 1427, 1355, 1281, 1217, 1142, 1047, 750 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.0 Hz, 3 H), 4.39 (q, *J* = 7.0 Hz, 2 H), 6.40 (dd, *J* = 3.2, 2.0 Hz, 1 H), 6.90 (d, *J* = 2.0 Hz, 1 H), 7.25 (d, *J* = 3.2 Hz, 1 H), 8.0 (s, 1 H), 10.05 (br. s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1, 61.9, 91.5, 112.4, 118.2, 123.9, 126.6, 128.4, 142.6, 163.5 ppm. EI-MS: *m*/*z* (%) = 190 (100) [M^+], 162 (95), 134 (72). $C_{10}H_{10}N_2O_2$ (190.20): calcd. C 63.15, H 5.30, N 14.73; Found: calcd. C 63.21, H 5.37, N 14.82.

2-(2-Furylmethylene)malononitrile (4d): Pale-yellow solid, m.p. 67−68 °C. IR (KBr): $\tilde{\nu}$ = 3415, 3043, 2224, 1609, 1523, 1451, 1391, 1294, 1149, 1019, 935, 767, 584 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 6.75 (dd, *J* = 3.9, 1.8 Hz, 1 H), 7.40 (d, *J* = 3.9 Hz, 1 H), 7.55 (d, *J* = 1.8 Hz, 1 H), 7.8 (s,1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 77.2, 112.5, 113.7, 114.3, 123.5, 143.0, 147.9, 149.5 ppm. EI-MS: *m*/*z* (%) = 144 (100) [M^+], 141 (90), 115 (35), 89 (20), 69 (14), 62 (13), 43 (18). $C_8H_4N_2O$ (144.13): calcd. C 66.67, H 2.80, N 19.44; found C 66.61, H 2.85, N 19.51.

2-(3-Pyridylmethylene)malononitrile (4e): Brown solid, m.p. 78−80 °C. IR (KBr): $\tilde{\nu}$ = 3015, 2215, 1584, 1409, 1019, 821, 762, 691 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.45−7.58 (m, 1 H), 7.80 (s, 1 H), 8.55 (dd, *J* = 8.5, 2.0 Hz, 1 H), 8.80−8.85 (m, 2 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 85.5, 111.9, 112.8, 124.2, 126.9, 135.5, 152.2, 154.5, 156.4 ppm. EI-MS: *m*/*z* (%) = 155 (100) [M^+], 128 (26), 104 (49), 79 (19), 51 (24). $C_9H_5N_3$ (155.16): calcd. C 69.67, H 3.25, N 27.08; found C 69.61, H 3.31, N 27.15.

Ethyl (*E*)-2-Cyano-3-(3-pyridyl)-2-propenoate (4f): Light-yellow solid, m.p. 75−77 °C. IR (KBr): $\tilde{\nu}$ 2999, 2220, 1721, 1611, 1420, 1279, 1093, 1016, 820, 762, 704 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 6.9 Hz, 3 H), 4.4 (q, *J* = 6.9 Hz, 2 H), 7.40−7.50 (m, 1 H), 8.20 (s, 1 H) 8.60 (dd, *J* = 8.5, 2.1 Hz, 1 H), 8.7 (d, *J* = 8.5 Hz, 1 H), 8.90 (d, *J* = 2.1 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9, 62.9, 105.5, 114.7, 123.9, 127.3, 135.8, 151.1, 152.6, 153.2, 161.5 ppm. EI-MS: *m*/*z* (%) = 202 (2.38) [M^+], 174 (38), 159 (100), 130 (47), 103 (31), 80 (19), 76 (36), 51 (49), 50 (26). $C_{11}H_{10}N_2O_2$ (202.21): calcd. C 65.34, H 4.98, N 13.85; found C 65.39, H 4.92, N 13.91.

2-(2-Thienylmethylene)malononitrile (4g): Yellow solid, m.p. 91−92 °C. IR (KBr): $\tilde{\nu}$ = 3099, 2220, 1571, 1405, 1317, 1253, 1051, 944, 862, 736, 605 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.20−7.30 (m, 1 H), 7.80−7.90 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 77.7, 112.8, 113.6, 128.8, 135.1, 136.9, 138.3, 151.1 ppm. EI-MS: *m*/*z* (%) = 160 (100) [M^+], 133 (31), 109 (31), 69 (11), 45 (39). $C_8H_4N_2S$(160.193): calcd. C 59.98, H 2.52, N 17.49, S 20.01; found C 59.91, H 2.57, N 17.56, S, 20.11.

2-(1*H*-2-Pyrrolylmethylene)malononitrile (4h): Light gray solid, m.p. 120−122 °C. IR (KBr): $\tilde{\nu}$ = 3368, 1589, 1511, 1393, 1322, 1123, 1045, 927, 868, 769, 700, 583 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 6.40 (dd, *J* = 2.5, 3.4 Hz, 1 H), 7.20 (d, *J* = 2.5 Hz, 1 H), 7.40 (d, *J* = 3.4 Hz, 1 H), 7.65 (s, 1 H), 11.5 (br. s, 1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 69.5, 113.2, 114.5, 115.5, 125.2, 126.6, 130.2, 145.9 ppm. EI-MS: *m*/*z* (%) = 143 (100) [M^+], 116 (25), 92 (67), 39 (24), 28 (38). $C_8H_5N_3$ (143.15): calcd. C 67.13, H 3.52, N 29.35; found C 67.19, H 3.57, N 29.29.

Ethyl (*E*)-2-Cyano-3-(1*H*-indol-3-yl)-2-propenoate (4i): Yellow solid, m.p. 161−162 °C. IR (KBr): $\tilde{\nu}$ = 3325, 2212, 1697, 1565, 1505, 1363, 1263, 1136, 1012, 880, 746 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.0 Hz, 3 H), 4.40 (q, *J* = 7.0 Hz, 2 H), 7.20−7.38 (m, 2 H), 7.40−7.50 (m, 1 H), 7.78−7.85 (m, 1 H), 8.60 (s, 1 H), 8.65 (s, 1 H), 9.45 (br. s,1 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.2, 29.6, 62.0, 94.3, 111.0, 112.3, 118.2, 122.5, 124.1, 127.3, 130.8, 135.6, 146.6, 163.8 ppm. EI-MS: *m*/*z* (%) = 240 (100) [M^+], 212 (50), 195 (49), 168 (44), 140 (65), 97 (23), 83 (31), 56 (50), 28 (62). $C_{14}H_{12}N_2O_2$ (240.26): calcd. C 69.99, H 5.03, N 11.66; found C 69.93, H 5.09, N 11.73.

2-(1*H*-3-Indolylmethylene)malononitrile (4j): Brown solid, m.p. 221−223 °C. IR (KBr): $\tilde{\nu}$ = 3270, 2915, 2215, 1566, 1499, 1336, 1225, 1139, 825, 789 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ = 7.20−7.30 (m, 2 H), 7.40−7.50 (m, 1 H), 7.50−7.78 (m, 1 H), 8.10−8.20 (s, 1 H), 8.45 (s, 1 H), 12.30 (br. s, 1 H, NH) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 69.5, 110.2, 112.1, 114.9, 117.2, 121.9, 123.2, 126.0, 131.8, 135.4, 150.2 ppm. EI-MS: *m*/*z* (%) = 193 (18) [M^+]^2, 150 (13), 130 (11), 112 (11), 98 (14), 84 (25), 74 (39), 58 (78), 44 (100). $C_{14}H_7N_3$ (193.207): calcd. C 74.60, H 3.65, N 21.75; found C 74.68, H 3.70, N 21.81.

Supporting Information Available: Spectroscopic data of products reported in Tables 1 and 2.

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