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Catalyzed Knoevenagel reactions on inorganic solid supports: Application to the synthesis of coumarine compounds

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Abstract

Knoevenagel reactions involving carbonyl compounds and active methylene derivatives have been studied in the presence of alumina, KSF and K10 montmorillonites. With addition of water the ester group undergoes hydrolysis. A route is disclosed for the synthesis of coumarine compounds catalyzed by solid supports. ***To cite this article: Y. Moussaoui, R. Ben Salem, C. R. Chimie 10 (2007).***

Keywords: Knoevenagel; Alumina; Montmorillonite KSF; Montmorillonite K10; Coumarine

1. Introduction

The Knoevenagel reaction [1] represents an important route to unsaturated α,β-dicarbonyl compounds [2]. The course of the reaction depends essentially on reactants and catalysts. Aldehydes and malonic esters undergo Knoevenagel condensation in the presence of secondary amines or their salts [3]. The reaction involving ketones requires Lewis acids such as titanium tetrachloride [4], zinc chloride [5–7] or zinc acetate [8].

In the last years solid supports were increasingly used with success. Under such mild conditions the synthesis of various organic compounds can be achieved with high selectivity through oxidation [11], reduction [12], alkylation [13], condensation [14,15], and acylation [16] reactions. The Knoevenagel reaction is usually catalyzed by weak bases [1] or by suitable combinations of amines and carboxylic [17] or Lewis [18] acids under homogeneous conditions. The Knoevenagel condensation can also be carried out on clays such as montmorillonite KSF [19,20], K10 [21], K10-$ZnCl_2$ [22], bentonite [23] or other solid supports [24–27] such as alumina [28,29], silica gel [30,31], xonotlite [32,33], $AlPO_4$–Al_2O_3 [29].

The present study aims at measuring the effect of water in the Knoevenagel reaction and using the results for a synthesis of coumarines.

2. Results and discussion

2.1. Knoevenagel reaction

In the presence of solid supports the reaction between active methylene compounds and carbonyl compounds affords the Knoevenagel product (Table 1). Reactions involving ketones are weakly promoted. With aldehydes, however, the reactivity is enhanced.

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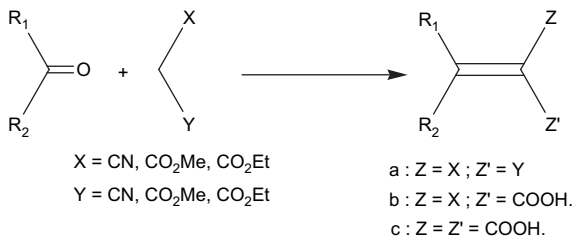
Table 1
Effect of the types of solid supports on the yield of the Knoevenagel condensation

R_1	R_2	X	Y	Yield % (product)				
				A	**B**	**C**	**D**	**E**
C_6H_5	H	CN	CN	97 (**1a**)	92 (**1a**)	97 (**1a**)	88 (**1a**)	91 (**1a**)
		CN	CO_2Me	98 (**2a**)	59 (**2a**)	70 (**2a**)	55 (**2b**)	63 (**2b**)
		CO_2Et	CO_2Et	97 (**3a**)	45 (**3a**)	56 (**3a**)	26 (**3c**)	36 (**3c**)
p-ClC_6H_4	H	CN	CN	87 (**4a**)	84 (**4a**)	81 (**4a**)	73 (**4a**)	72 (**4a**)
		CN	CO_2Me	85 (**5a**)	57 (**5a**)	66 (**5a**)	53 (**5b**)	60 (**5b**)
		CO_2Et	CO_2Et	86 (**6a**)	44 (**6a**)	55 (**6a**)	28 (**6c**)	33 (**6c**)
	H	CN	CN	95 (**7a**)	90 (**7a**)	93 (**7a**)	90 (**7a**)	91 (**7a**)
		CN	CO_2Me	98 (**8a**)	63 (**8a**)	75 (**8a**)	61 (**8b**)	69 (**8b**)
		CO_2Et	CO_2Et	94 (**9a**)	52 (**9a**)	64 (**9a**)	33 (**9c**)	44 (**9c**)
CH_3	H	CN	CN	75 (**10a**)	70 (**10a**)	71 (**10a**)	73 (**10a**)	68 (**10a**)
		CN	CO_2Me	55 (**11a**)	48 (**11a**)	56 (**11a**)	–	–
		CO_2Et	CO_2Et	59 (**12a**)	47 (**12a**)	58 (**12a**)	–	–
n-C_3H_7	H	CN	CN	66 (**13a**)	65 (**13a**)	67 (**13a**)	–	–
		CN	CO_2Me	52 (**14a**)	40 (**14a**)	48 (**14a**)	–	–
		CO_2Me	CO_2Me	51 (**15a**)	30 (**15a**)	37 (**15a**)	–	–
		CO_2Et	CO_2Et	50 (**16a**)	26 (**16a**)	33 (**16a**)	–	–
C_6H_5	CH_3	CN	CN	50 (**17a**)	30 (**17a**)	28 (**17a**)	32 (**17a**)	32 (**17a**)
		CN	CO_2Et	40 (**18a**)	31 (**18a**)	27 (**18a**)	30 (**18b**)	32 (**18b**)
		CO_2Me	CO_2Me	38 (**19a**)	27 (**19a**)	25 (**19a**)	33 (**19c**)	31 (**19c**)
		CO_2Et	CO_2Et	38 (**20a**)	27 (**20a**)	–	–	–
C_2H_5	C_2H_5	CN	CN	52 (**21a**)	33 (**21a**)	36 (**21a**)	35 (**21a**)	38 (**21a**)
		CN	CO_2Et	44 (**22a**)	34 (**22a**)	31 (**22a**)	38 (**22b**)	32 (**22b**)
		CO_2Et	CO_2Et	40 (**23a**)	27 (**23a**)	–	–	–

A: Al_2O_3 (5 mn), room temperature; **B**: KSF10, 160 °C (24 h); **C**: K10, 160 °C (24 h); **D**: KSF10, H_2O, 100 °C (24 h); **E**: K10, H_2O, 100 °C (24 h).
a: nitriles or esters; **b**: monoacids; **c**: diacids.

This is ascribed to steric and inductive (+I) effects, which in the case of aldehydes decrease the electrophilicity of the carbon atom in the CHO group and, therefore, disfavours the attack of the intermediate carbanion formed in the first step (Scheme 1). As an illustration, benzaldehyde is more reactive than *p*-chlorobenzaldehyde as the Cl atom (mesomeric effect (+M)) weakens this electrophilicity. Indeed, the presence of chloride group causes increase of the barrier for the nucleophilic attack on the carbonyl group [34].

The results are also informative about the amphoteric character of clays. KSF and K10 montmorillonites have simultaneously basic and acid sites able to capture

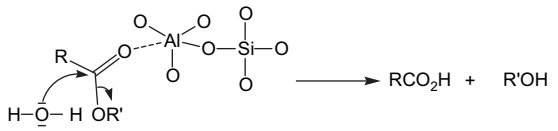


Scheme 1.

the proton of the labile hydrogen in the methylene compound. The basic sites ascribed to negative charges dispersed on the oxygen atoms [35] activate the Knoevenagel condensation. The acid sites which are due to the presence of water favour transesterification products when the active methylene compound bears an ester group, as shown by Ponde et al. [36].

As a consequence, the Knoevenagel condensation is promoted in the presence of water; however, transesterification takes place. The results may be interpreted in the sense that with water the active methylene groups come closer to the negative charges in the solid catalyst, favouring, thereby, the formation of carbanions. The Lewis acid centers of the clay activate the ester groups by coordination between the aluminum atom of the clay and the oxygen of the carbonyl group. Under such conditions the nucleophilic attack by water is favoured, leading to the formation of the corresponding acids (Scheme 2).

The results indicate that alumina is an excellent catalyst for the Knoevenagel condensation. The reaction is nearly quantitative in less than 5 min or so. The solid–liquid phase transfer process can be schematized as shown in Scheme 3.



Scheme 2.

2.2. Synthesis of coumarines

Coumarines and their derivatives are natural products which are widely used for cosmetic, agricultural, pharmaceutical purposes [37]. Several synthetic ways have been proposed [19,24,38]. Two methods emerge: the Pechmann condensation [39] and the Knoevenagel reaction between salicylaldehyde and its derivatives with functionalized ethyl acetates (Scheme 4).

The 3-carboxylic coumarines are obtained in aqueous media while without solvent there is formation of the corresponding esters (Table 2). In agreement with Bigi's papers [19], our results show that coumarines can be synthesized in high yields in the presence of KSF montmorillonite. In the presence of water, however, hydrolysis of the ester group takes place.

In this study, the preferred method uses alumina as the catalyst since under such conditions the reactivity is better than with KSF montmorillonite.

3. Conclusion

We have demonstrated a very simple and highly efficient method for the condensation of aldehydes with various active methylene compounds to give Knoevenagel products in excellent yields. We have found that coumarin-3-carboxylic esters could be synthesized in high yields by the Knoevenagel condensation in the presence of clay KSF and alumina. The reaction time is reduced to only a few minutes by using alumina as catalyst. We suggest that the present method may displace all other methods that use various organic solvents and catalysts.

4. Experimental section

4.1. General procedures

4.1.1. Procedure A

To a stirred solution of 10 mmol of aldehyde in 10 mmol of the methylene compound was added 3 g of alumina. After few minutes, the product was extracted with dichloromethane (3 × 20 mL). After removing the solvent under vacuum, the product is obtained with a good purity. The product was purified if necessary by crystallization or by flash chromatography using a mixture of hexane–ether as eluent.

4.1.2. Procedure B

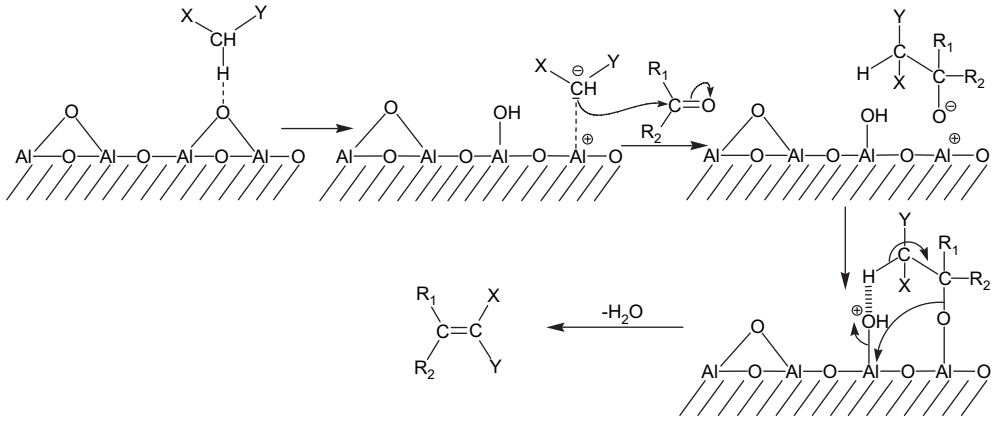
Aldehyde (10 mmol), methylene compound (15 mmol) and KSF (1 g) were heated under stirring at 160 °C for 24 h. After cooling to room temperature, methanol (50 mL) was added and heated for 5 min. The catalyst was removed by Büchner filtration and the organic phase, concentrated under vacuum, was chromatographed on silica gel using a mixture of hexane–ether as eluent.

4.1.3. Procedure C

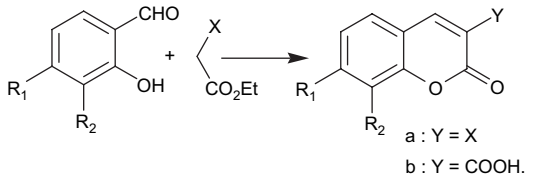
The same protocol that in procedure B, but with K10 instead of KSF.

4.1.4. Procedure D

The aldehyde (10 mmol), methylene compound (15 mmol) and KSF (1 g) in water (3.5 mL) were heated at reflux (100 °C) for 24 h. After cooling to room



Scheme 3. Mechanism of the Knoevenagel condensation in the presence of alumina.



Scheme 4.

temperature, the solid is collected by Büchner filtration and solid was heated in methanol (50 mL) for 5 min. The catalyst was removed by Büchner filtration and washed with methanol. The solvent was removed in vacuo. The product was purified by flash chromatography using a mixture of hexane–ether as eluent.

4.1.5. Procedure E

The same protocol that in procedure D, but with K10 instead of KSF.

4.1.6. Procedure F

A mixture of a hydroxyaldehyde derivative (10 mmol), ethyl acetate derivative (15 mmol) and 3 g of alumina was stirred at room temperature. At the end, the reaction mixture was extracted with an appropriate solvent (3×20 mL) than recrystallized or purified by flash chromatography to effort the corresponding coumarine.

4.1.7. Procedure G

A mixture of a hydroxyaldehyde derivative (10 mmol), ethyl acetate derivative (15 mmol) and 1 g of KSF was heated under stirring at 160 °C for 24 h. After cooling to room temperature, methanol (50 mL) was added and heated for 5 min. The catalyst was removed by Büchner filtration and the organic phase, concentrated under vacuum, was chromatographed on silica gel using a mixture of hexane–ether as eluent.

Table 2
Effect of the types of solid supports on the yield of coumarines and their derivatives

R_1	R_2	X	Yield % (product)		
			F	**G**	**H**
H	H	CN	78 (**24a**)	54 (**24a**)	55 (**24a**)
		CO_2Et	95 (**25a**)	67 (**25a**)	72 (**25b**)
H	OMe	CN	86 (**26a**)	78 (**26a**)	66 (**26a**)
		CO_2Et	93 (**27a**)	65 (**27a**)	71 (**27b**)
Cl	H	CN	84 (**28a**)	54 (**28a**)	61 (**28a**)
		CO_2Et	96 (**29a**)	67 (**29a**)	73 (**29b**)
OMe	H	CN	78 (**30a**)	51 (**30a**)	56 (**30a**)
		CO_2Et	93 (**31a**)	63 (**31a**)	66 (**31b**)

F: Al_2O_3 (5 mn), room temperature; **G**: KSF, 160 °C (24 h); **H**: KSF, H_2O, 100 °C (24 h). **a**: nitriles or esters; **b**: monoacids.

4.1.8. Procedure H

A mixture of a hydroxyaldehyde derivative (10 mmol), ethyl acetate derivative (15 mmol), water (3.5 mL) and 1 g of KSF was heated at reflux (100 °C) for 24 h. After cooling to room temperature, the solid is collected by Büchner filtration and heated in methanol (50 mL) for 5 min. The catalyst was removed by Büchner filtration and washed with methanol. The solvent removed in vacuo. The product was purified by flash chromatography using a mixture of hexane–ether as eluent.

4.2. Characterization of compounds

^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker AC300 spectrometer using tetramethylsilane as internal reference. IR spectra were recorded with a JASCO FT/IR-420 spectrophotometer. Melting points were taken on a Reichert-Heizbank apparatus.

*4.2.1. 2-(Phenylmethylene)malononitrile **1a***

Mp = 83–84 °C. IR: $\nu_{C=C} = 1590\ cm^{-1}$, $\nu_{CN} = 2224\ cm^{-1}$. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 (d, $J = 7.5$ Hz, 2H), 7.79 (s, 1H), 7.64 (t, $J = 7.2$ Hz, 1H), 7.54 (dd, $J = 7.2$, 7.5 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.08, 134.75, 130.82, 129.81, 129.71, 113.79, 112.63, 82.85.

*4.2.2. 2-Cyano-3-phenyl-acrylic acid methyl ester **2a***

Mp = 87–89 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.27 (s, 1H), 8.00 (d, $J = 7.2$ Hz, 2H), 7.49–7.60 (m, 3H), 3.94 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.20, 155.42, 133.49, 131.18, 130.14, 129.36, 117.37, 105.48, 53.47.

*4.2.3. 2-Cyano-3-phenyl-acrylic acid **2b***

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.86 (b, 1H), 8.26 (s, 1H), 7.67 (d, $J = 8.1$ Hz, 2H), 7.24–7.42 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.76, 160.51, 134.19, 129.04, 127.87, 126.32, 118.72, 101.89.

*4.2.4. 2-Benzylidene-malonic acid diethyl ester **3a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10 (s, 1H), 7.17–7.32 (m, 5H), 4.05 (q, $J = 7.2$ Hz, 4H), 1.13 (t, $J = 7.2$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.95, 142.89, 134.09, 128.98, 128.60, 127.70, 127.31, 60.85, 14.45.

*4.2.5. 2-Benzylidene-malonic acid **3c***

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.86 (b, 2H), 7.98 (s, 1H), 7.69 (d, $J = 8.1$ Hz, 2H), 7.25–7.42 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.00, 154.50, 134.39, 129.24, 127.80, 126.42, 122.05.

4.2.6. 2-[(4-Chlorophenyl)methylene]malononitrile ***4a***

Mp = 162–164 °C. IR: $\nu_{C=C} = 1585\ cm^{-1}$, $\nu_{CN} = 2226\ cm^{-1}$. ^1H NMR (300 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.69 (d, $J = 8.4$ Hz, 2H), 7.43 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.32, 141.22, 131.82, 130.16, 129.37, 113.45, 112.30, 83.45.

4.2.7. 3-(4-Chloro-phenyl)-2-cyano-acrylic acid methyl ester ***5a***

^1H NMR (300 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.68 (d, $J = 8.1$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 3.92 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.02, 157.43, 140.40, 131.92, 130.26, 129.38, 117.60, 105.80, 53.62.

4.2.8. 3-(4-Chloro-phenyl)-2-cyano-acrylic acid ***5b***

^1H NMR (300 MHz, $CDCl_3$): δ 10.85 (b, 1H), 7.73 (s, 1H), 7.58 (d, $J = 8.4$ Hz, 2H), 7.29 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.10, 158.94, 133.31, 133.02, 129.08, 127.86, 117.62, 102.05.

4.2.9. 2-[(4-Chlorophenyl)methylene]malonic acid diethyl ester ***6a***

^1H NMR (300 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.64 (d, $J = 8.4$ Hz, 2H), 7.38 (d, $J = 8.4$ Hz, 2H), 4.13 (q, $J = 7.2$ Hz, 4H), 1.16 (t, $J = 7.2$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.95, 148.90, 135.03, 134.12, 128.82, 127.72, 126.22, 60.28, 14.43, 14.46.

4.2.10. 2-(4-Chloro-benzylidene)-malonic acid ***6c***

^1H NMR (300 MHz, $CDCl_3$): δ 10.86 (b, 2H), 7.94 (s, 1H), 7.34 (d, $J = 8.1$ Hz, 2H), 7.26 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.00, 155.14, 133.52, 133.41, 129.10, 127.92, 122.05.

4.2.11. 2-Furan-2-ylmethylene-malononitrile ***7a***

^1H NMR (300 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.41 (d, $J = 1.8$ Hz, 1H), 6.27–6.35 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.20, 156.10, 146.21, 114.42, 113.92, 112.95, 111.45, 83.42.

4.2.12. 2-Cyano-3-furan-2-ylacrylic acid methyl ester ***8a***

^1H NMR (300 MHz, $CDCl_3$): δ 7.81–7.86 (m, 2H), 7.02 (d, $J = 3.3$ Hz, 1H), 6.66 (dd, $J = 1.8$, 3.3 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.03, 155.82, 155.43, 146.10, 117.22, 113.27, 112.08, 109.30, 52.61.

4.2.13. 2-Cyano-3-furan-2-ylacrylic acid ***8b***

^1H NMR (300 MHz, $CDCl_3$): δ 10.85 (b, 1H), 7.80–7.86 (m, 2H), 7.00 (d, $J = 3.3$ Hz, 1H), 6.68 (dd, $J = 1.8$, 3.3 Hz, 1H).

4.2.14. 2-Furan-2-ylmethylene-malonic acid diethyl ester ***9a***

^1H NMR (300 MHz, $CDCl_3$): δ 8.13 (s, 1H), 7.81 (d, $J = 1.8$ Hz, 1H), 7.05 (d, $J = 3.3$ Hz, 1H), 6.66 (dd, $J = 1.8$, 3.3 Hz, 1H), 4.17–4.25 (m, 4H), 1.27–1.32 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.02, 156.40, 150.10, 145.91, 129.09, 113.07, 112.01, 61.42, 13.94.

4.2.15. 2-Furan-2-ylmethylene-malonic acid ***9c***

^1H NMR (300 MHz, $CDCl_3$): δ 10.86 (b, 2H), 8.10 (s, 1H), 7.80 (d, $J = 1.8$ Hz, 1H), 7.05 (d, $J = 3.3$ Hz, 1H), 6.68 (dd, $J = 1.8$, 3.3 Hz, 1H).

4.2.16. 2-Ethylidene-malononitrile ***10a***

^1H NMR (300 MHz, $CDCl_3$): δ 6.94 (q, $J = 6.9$ Hz, 1H), 1.83 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.61, 118.12, 83.27, 12.30.

4.2.17. 2-Cyano-but-2-enoic acid methyl ester ***11a***

^1H NMR (300 MHz, $CDCl_3$): δ 6.95 (q, $J = 6.9$ Hz, 1H), 3.88 (s, 3H), 1.82 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.93, 153.24, 118.02, 106.50, 51.23, 13.19.

4.2.18. 2-Ethylidene-malonic acid diethyl ester ***12a***

^1H NMR (300 MHz, $CDCl_3$): δ 7.19 (q, $J = 6.9$ Hz, 1H), 4.22 (q, $J = 7.2$ Hz, 4H), 1.78 (d, $J = 6.9$ Hz, 3H), 1.34 (t, $J = 7.2$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.01, 147.07, 127.25, 62.06, 16.15, 14.37, 9.30.

4.2.19. 2-Butylidene-malononitrile ***13a***

IR: $\nu_{C=C} = 1607\ cm^{-1}$, $\nu_{CN} = 2238\ cm^{-1}$. ^1H NMR (300 MHz, $CDCl_3$): δ 7.33 (t, $J = 7.5$ Hz, 1H), 2.57 (q, $J = 7.5$ Hz, 3H), 1.58–1.70 (m, 2H), 1.02 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.42, 112.17, 90.28, 30.62, 21.31, 13.50.

4.2.20. 2-Cyano-hex-2-enoic acid methyl ester ***14a***

^1H NMR (300 MHz, $CDCl_3$): δ 7.27 (t, $J = 6.9$ Hz, 1H), 3.83 (s, 3H), 2.05–2.11 (m, 2H), 1.34–1.42 (m, 2H), 1.12 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.15, 156.17, 117.12, 105.40, 53.20, 27.56, 23.21, 15.14.

4.2.21. 2-Butylidene-malonic acid dimethyl ester ***15a***

^1H NMR (300 MHz, $CDCl_3$): δ 7.11 (t, $J = 6.9$ Hz, 1H), 3.82 (s, 6H), 2.05–2.11 (m, 2H), 1.35–1.42 (m, 2H), 1.07 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.21, 149.65, 128.87, 54.51, 34.01, 22.06, 15.12.

4.2.22. 2-Butylidene-malonic acid diethyl ester ***16a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.12 (t, $J = 6.9$ Hz, 1H), 4.20 (q, $J = 7.2$ Hz, 4H), 2.04–2.10 (m, 2H), 1.32–1.44 (m, 8H), 1.08 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.22, 152.56, 126.15, 60.69, 28.21, 23.01, 15.61, 14.17.

4.2.23. 2-(1-Phenylethylidene)malononitrile ***17a***

Mp = 93–95 °C. IR: $\nu_{C=C} = 1586$ cm^{-1}, $\nu_{CN} = 2228$ cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46–7.58 (m, 5H), 2.64 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.41, 135.86, 132.26, 129.15, 127.32, 112.70, 84.67, 24.20.

4.2.24. 2-Cyano-3-phenyl-but-2-enoic acid ethyl ester ***18a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47–7.60 (m, 5H), 4.24 (q, $J = 7.2$ Hz, 2H), 2.19 (s, 3H), 1.67 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.14, 165.91, 134.29, 128.94, 128.02, 126.90, 117.92, 94.76, 61.59, 24.13, 14.87.

4.2.25. 2-Cyano-3-phenyl-but-2-enoic acid ***18b***

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.86 (b, 1H), 7.38–7.58 (m, 5H), 2.14 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.77, 168.74, 135.04, 129.14, 128.07, 126.86, 117.82, 94.36, 23.17.

4.2.26. 2-(1-Phenyl-ethylidene)-malonic acid dimethyl ester ***19a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.27–7.40 (m, 5H), 3.96 (s, 6H), 2.26 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.50, 158.62, 133.94, 128.84, 127.97, 127.21, 120.21, 56.20, 19.70.

4.2.27. 2-(1-Phenyl-ethylidene)-malonic acid ***19c***

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.85 (b, 2H), 7.37–7.56 (m, 5H), 2.20 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.86, 163.84, 135.02, 129.23, 128.05, 126.73, 114.14, 20.07.

4.2.28. 2-(1-Phenyl-ethylidene)-malonic acid diethyl ester ***20a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.17–7.39 (m, 5H), 4.22 (q, $J = 7.2$ Hz, 4H), 2.16 (s, 3H), 1.41 (t, $J = 7.2$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.51, 158.62, 135.41, 129.14, 128.07, 127.12, 118.52, 62.13, 25.30, 14.37.

4.2.29. 2-(1-Ethyl-propylidene)-malononitrile ***21a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.41 (q, $J = 7.5$ Hz, 4H), 1.26 (t, $J = 7.5$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 180.62, 118.21, 78.27, 24.13, 13.05.

4.2.30. 2-Cyano-3-ethyl-pent-2-enoic acid ethyl ester ***22a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.27 (q, $J = 7.5$ Hz, 2H), 2.40 (q, $J = 7.5$ Hz, 4H), 1.37 (t, $J = 7.5$ Hz, 3H), 1.28 (t, $J = 7.5$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.52, 168.17, 117.29, 96.51, 62.19, 29.16, 17.61, 16.17, 14.10.

4.2.31. 2-Cyano-3-ethyl-pent-2-enoic acid ***22b***

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.85 (b, 1H), 2.28 (q, $J = 7.5$ Hz, 4H), 1.19 (t, $J = 7.5$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.92, 171.53, 117.20, 96.44, 24.10, 13.57.

4.2.32. 2-(1-Ethyl-propylidene)-malonic acid diethyl ester ***23a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.24 (q, $J = 7.5$ Hz, 4H), 2.38 (q, $J = 7.5$ Hz, 4H), 1.67 (t, $J = 7.5$ Hz, 6H), 1.18 (t, $J = 7.5$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.10, 166.35, 116.75, 62.96, 24.31, 15.37, 14.50.

4.2.33. 3-Cyanocoumarin ***24a***

Mp = 183–185 °C. IR: $\nu_{CO} = 1730$ cm^{-1}, $\nu_{CN} = 2230$ cm^{-1}, $\nu_{C=C} = 1600$ cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.38 (s, 1H), 7.71 (dd, $J = 9$, 3 Hz, 1H), 7.60 (td, $J = 8.4$, 3 Hz, 1H), 7.37–7.45 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.12, 156.50, 148.53, 130.41, 126.60, 120.50, 120.30, 118.90, 116.21, 102.82.

4.2.34. Ethyl-3-coumarincarboxylate ***25a***

Mp = 93–95 °C. IR: $\nu_{CO} = 1754$ cm^{-1}, $\nu_{C=C} = 1610$ cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (s, 1H), 7.64 (dd, $J = 9$, 3 Hz, 1H), 7.51 (ddd, $J = 9$, 8.4, 2.7 Hz, 1H), 7.31–7.42 (m, 2H), 4.21 (q, $J = 7.2$ Hz, 2H), 1.38 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.42, 161.76, 155.16, 148.24, 132.24, 130.10, 129.40, 124.80, 120.75, 119.97, 64.70, 16.72.

4.2.35. Coumarin-3-carboxylic acid ***25b***

Mp = 190–192 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.86 (b, 1H), 8.47 (s, 1H), 7.59–7.65 (m, 2H), 7.30–7.40 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.12, 161.41, 155.10, 148.08, 131.21, 129.14, 124.18, 120.70, 119.82, 118.94.

4.2.36. 8-Methoxy-2-oxo-2H-chromene-3-carbonitrile ***26a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.51 (s, 1H), 7.24 (dd, $J = 8.7$, 2.7 Hz, 1H), 7.17 (t, $J = 8.7$ Hz, 1H),

7.01 (dd, $J = 8.7$, 2.7 Hz, 1H), 3.93 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.26, 160.02, 155.65, 137.46, 129.14, 127.04, 119.01, 118.12, 114.03, 101.21, 61.11.

4.2.37. 8-Methoxy-2-oxo-2H-chromene-3-carboxylic acid ethyl ester ***27a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.78 (s, 1H), 7.26 (dd, $J = 8.7$, 3 Hz, 1H), 7.14 (dd, $J = 8.7$, 8.1 Hz, 1H), 7.00 (dd, $J = 8.1$, 3 Hz, 1H), 4.22 (q, $J = 7.2$ Hz, 2H), 3.92 (s, 3H), 1.35 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.80, 159.72, 155.10, 152.51, 135.21, 129.01, 126.13, 123.19, 118.72, 117.94, 63.92, 60.40, 15.67.

4.2.38. 8-Methoxy-2-oxo-2H-chromene-3-carboxylic acid ***27b***

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.84 (b, 1H), 8.67 (s, 1H), 7.56 (dd, $J = 9$, 2.7 Hz, 1H), 7.27 (dd, $J = 9$, 8.4 Hz, 1H), 7.03 (dd, $J = 8.4$, 2.7 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.20, 160.42, 155.54, 154.48, 134.39, 129.08, 127.10, 122.32, 118.70, 114.97, 60.03.

4.2.39. 7-Chloro-2-oxo-2H-chromene-3-carbonitrile ***28a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.48 (s, 1H), 7.59 (d, $J = 8.7$ Hz, 1H), 7.26 (dd, $J = 8.7$, 2.4 Hz, 1H), 7.22 (d, $J = 2.4$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.12, 159.96, 154.62, 134.19, 128.98, 126.89, 126.19, 122.76, 117.82, 102.18.

4.2.40. 7-Chloro-2-oxo-2H-chromene-3-carboxylic acid ethyl ester ***29a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.79 (s, 1H), 7.61 (d, $J = 8.7$ Hz, 1H), 7.29 (dd, $J = 8.7$, 2.1 Hz, 1H), 7.23 (d, $J = 2.1$ Hz, 1H), 4.23 (q, $J = 7.5$ Hz, 2H), 1.67 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.15, 163.10, 153.06, 152.69, 134.54, 128.91, 127.07, 126.36, 123.13, 121.97, 61.06, 15.17.

4.2.41. 7-Chloro-2-oxo-2H-chromene-3-carboxylic acid ***29b***

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.85 (b, 1H), 8.69 (s, 1H), 7.59 (d, $J = 8.7$ Hz, 1H), 7.30 (dd, $J = 8.7$, 2.1 Hz, 1H), 7.22 (d, $J = 2.1$ Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.31, 162.43, 156.04, 152.52, 134.34, 129.02, 126.12, 125.96, 122.07, 121.95.

4.2.42. 7-Methoxy-2-oxo-2H-chromene-3-carbonitrile ***30a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.46 (s, 1H), 7.53 (d, $J = 8.7$ Hz, 1H), 6.74 (dd, $J = 8.7$, 2.1 Hz, 1H), 6.69 (d, $J = 2.1$ Hz, 1H), 3.87 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.16, 160.61, 158.98, 152.81, 127.96, 121.04, 117.32, 111.42, 108.19, 100.98, 57.61.

4.2.43. 7-Methoxy-2-oxo-2H-chromene-3-carboxylic acid ethyl ester ***31a***

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.78 (s, 1H), 7.51 (d, $J = 8.7$ Hz, 1H), 6.74 (d, $J = 8.7$ Hz, 1H), 6.70 (s, 1H), 4.23 (q, $J = 7.5$ Hz, 2H), 3.81 (s, 3H), 1.63 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.31, 163.02, 161.16, 153.62, 150.86, 128.06, 123.12, 121.21, 112.81, 107.36, 62.09, 57.61, 15.37.

4.2.44. 7-Methoxy-2-oxo-2H-chromene-3-carboxylic acid ***31b***

^{1}H NMR (300 MHz, $CDCl_3$): δ 10.87 (b, 1H), 8.77 (s, 1H), 7.52 (d, $J = 8.7$ Hz, 1H), 6.74 (dd, $J = 8.7$, 2.1 Hz, 1H), 6.72 (d, $J = 2.1$ Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.02, 162.00, 160.86, 154.54, 150.58, 127.96, 122.05, 121.00, 111.18, 107.69, 57.02.

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