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Indium(III)-Catalyzed Knoevenagel Condensation of Aldehydes and Activated Methylenes Using Acetic Anhydride as a Promoter

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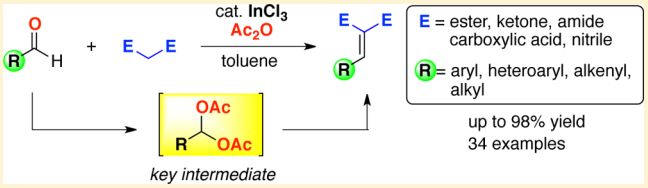
Supporting Information

ABSTRACT: The combination of a catalytic amount of $InCl_3$ and acetic anhydride remarkably promotes the Knoevenagel condensation of a variety of aldehydes and activated methylene compounds. This catalytic system accommodates aromatic aldehydes containing a variety of electron-donating and -withdrawing groups, heteroaromatic aldehydes, conjugate aldehydes, and aliphatic aldehydes. Central to successfully driving the condensation series is the formation of a geminal diacetate intermediate, which was generated in situ from an aldehyde and an acid anhydride with the assistance of an indium catalyst.



INTRODUCTION

The Knoevenagel reaction is a condensation between activated methylene and carbonyl compounds in the presence of a weak base, such as an amine; it is a powerful and practical tool for the formation of a carbon−carbon double bond.[1] Because the multisubstituted alkenes that are produced can further be used for a variety of molecular transformations, such as Michael additions and Diels−Alder reactions, a number of organic chemists have continuously improved this useful conversion.[1d] In a typical Knoevenagel condensation, a catalytic amount of primary or secondary amines along with their ammonium salts acts as an effective promoter, in which the formation of the iminium intermediate derived from the amine and a carbonyl compound plays a central role in promoting condensation.[2] During the past two decades, several Lewis acid catalysts have been used to promote Knoevenagel condensations.[3] In general, however, aldehydes with coordinating functional groups, such as methoxy, nitro, or cyano groups, and heterocyclic aldehydes are unsuitable for use as a substrate in a Lewis-acid-catalyzed Knoevenagel condensation with activated methylene that has a relatively low degree of acidity, such as dimethyl malonate (pK_a = 15.9 in DMSO).[4] This is probably due to deactivation of the acidic catalyst by coordination rather than by activation of the carbonyl compound that is used.

Indium compounds are known to display a high tolerance for functional groups.[5] We have joined several other researchers in reporting on indium-catalyzed conversions of various carbonyl compounds with a variety of functional groups.[6] On the basis of these reports, we anticipated that the indium compound that shows unique activation of typical carbonyl compounds will effectively promote a Knoevenagel condensation with a weak carbonyl compound that includes a coordinating functional group.[7] Herein, we report a novel catalytic system composed of indium chloride and acetic anhydride that effectively promotes the Knoevenagel condensation of aromatic/aliphatic/heteroaromatic aldehydes with a variety of activated methylene compounds, leading to the preparation of substituted alkene derivatives. We also describe how the condensation series proceeds via the indium-promoted formation of a geminal diacetate intermediate that is derived from an aldehyde with acetic acid anhydride.

RESULTS AND DISCUSSION

On the basis of conventional Knoevenagel reactions, we initially investigated reaction conditions using benzaldehyde (**1a**) and dimethyl malonate (**2a**) as a model substrate (Table 1). When a reaction was performed with 10 mol % of $InBr_3$ in toluene at 60 °C for 8 h, only 3% of Knoevenagel product **3aa** was detected (entry 1). Thus, to promote the initial abstraction of the activated proton, the addition of 1 equiv of several bases to the reaction mixture was examined. Consequently, when the primary amine 2-aminoethanol was added, the yield was remarkably increased to 61% (entry 2). The addition of a secondary or tertiary amine, however, was ineffective for the present condensation (entries 3 and 4). Upon further screening several additives for the condensation reaction,[8] 1 equiv of acetic anhydride showed the best additive effect to afford corresponding product **3aa** in 89% yield (entry 5). Then, a counteranion effect of the indium catalyst was investigated in the presence of Ac_2O. $InCl_3$ produced the best yield of Knoevenagel product **3aa** in 94% NMR yield (86% isolated yield) along with the formation of a small amount (4%) of geminal diacetate **4a**. Stronger Lewis acids, InI_3 and $In(OTf)_3$, showed a similar catalytic effect and provided alkene **3aa** in 79% (with 8% of diacetate **4a**) and 82% yields, respectively (entries 7 and 8); however, $In(OH)_3$ and $In(OAc)_3$ produced neither the corresponding alkene **3aa** nor diacetate

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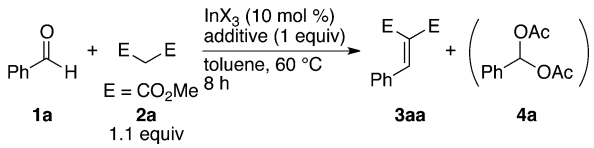
Table 1. Knoevenagel Condensation of Aromatic Aldehyde 1a with Dimethyl Malonate 2a[a]



			NMR yield (%)	
entry	InX_3	additive	3aa	4a
1	$InBr_3$		3	
2	$InBr_3$	$HOCH_2CH_2NH_2$	61	
3	$InBr_3$	piperidine	48	
4	$InBr_3$	Et_3N	6	
5	$InBr_3$	Ac_2O	89	nd[b]
6	$InCl_3$	Ac_2O	94 (86)[c]	4
7	InI_3	Ac_2O	79	8
8	$In(OTf)_3$	Ac_2O	82	nd[b]
9	$In(OH)_3$	Ac_2O	nd[b]	nd[b]
10	$In(OAc)_3$	Ac_2O	nd[b]	nd[b]
11		Ac_2O	nd[b]	nd[b]

[a]Reaction conditions: **1a** (0.60 mmol), **2a** (0.66 mmol), InX_3 (0.060 mmol), additive (0.60 mmol), toluene (0.60 mL), 60 °C, 8 h. [b]Not detected. [c]Isolated yield.

4a (entries 9 and 10). Without an indium salt, Ac_2O did not undergo the expected condensation to yield a Knoevenagel product (entry 11). When the reaction was conducted with other solvents, such as $CHCl_3$, CH_3CN, CH_3OH, and THF, remarkable improvement in the yield of **3aa** was not observed.[9]

The general application of aromatic aldehydes **1** for a Knoevenagel condensation with dimethyl malonate (**2a**) was next investigated in toluene at 60 °C for 8 h (Table 2). Aldehydes containing a strong electron-donating group, such as either Me_2N or MeO groups, on the benzene ring afforded the corresponding products **3ba**–**3ea** in good yields (entries 1–4). During the condensation series, neither the amino nor the methoxy groups, which generally deactivate a typical Lewis acid via coordination, had an effect on the activation by $InCl_3$. Similarly, 4-methyl- and 4-phenyl-substituted aromatic aldehydes also undertook the condensation to produce alkenes **3fa** and **3ga** in 80 and 84% yields, respectively, within 5–7 h (entries 5 and 6). The catalytic condensation of halogen-substituted benzaldehydes **1h**–**1l** with malonate **2a** proceeded successfully to isolate adducts **3ha**–**3la** in excellent yields (entries 7–11). Benzaldehyde derivatives bearing an electron-withdrawing group, such as a methoxycarbonyl, trifluoromethyl, cyano, or nitro group, generally showed slightly higher reactivity than benzaldehydes with an electron-donating group to give the Knoevenagel products **3ma**–**3ra** in 80–98% yields (entries 12–17). When salicylaldehyde (**1s**) was used as a substrate, the expected Knoevenagel alkene product was not detected. Instead, further *O*-acetylated product **5** and an intramolecular cyclization product, coumarin derivative **6**, were obtained in 40 and 7% yields, respectively (entry 18). For the substrates shown in Table 2, a small amount of the corresponding diacetate **4** was detected by ^1H NMR analysis.

To expand on the scope of an activated methylene derivative, we conducted an $InCl_3$-catalyzed Knoevenagel condensation of benzaldehyde (**1a**) with several methylene compounds **2** in the presence of Ac_2O (Table 3). For example, the reaction of benzaldehyde with β-ketoester methyl acetoacetate (**2b**) and ethyl benzoylacetate (**2c**) efficiently gave the Knoevenagel products **3ab** (*E*:*Z* = 42:58) and **3ac** (*E*:*Z* = 10:90).[10] β-Ketoamide **2d** afforded desired product **3ad** in a rather low yield[11] at an extended reaction time of 30 h, possibly because a decrease in the nucleophilicity of the methylene moiety by an electron-donating effect of the amino group hindered the reaction of the methylene with geminal diacetate. It was remarkable, however, that when the condensation was carried out with malonic acid (**2e**), 2-benzylidene-malonic acid (**3ae**) was obtained in 79% yield without a Doebner-type decarboxylation.[12] Also, when the reaction of malononitrile (**2f**) was carried out in toluene, only 15% (NMR yield) of the product was obtained. It was interesting that the use of *N*,*N*-dimethylformamide (DMF) as a solvent instead of toluene successfully improved the chemical yield of alkene **3af** to 86%. When the condensation of **1a** with the cyclic 1,3-diketone dimedone (**2g**) was conducted under the optimal conditions, 1:2 adduct **7** (a xanthenedione derivative) was isolated as the sole product, which otherwise would have been produced via a further Michael addition of **2g** to the first Knoevenagel adduct and a subsequent intramolecular cyclodehydration.[7g]

Further application of the indium-catalyzed condensation to a variety of aldehydes **8**, except for benzaldehyde with dimethyl malonate (**2a**), was then investigated in the presence of Ac_2O (Table 4). When 4-formylpyridine (**8a**) was used as a substrate, the corresponding alkene product **9aa** was obtained in 65% yield (entry 1). In this case, $InCl_3$ was unnecessary for the condensation based on the fact that alkene **9aa** (68% NMR yield) was obtained in the absence of $InCl_3$. When the reactions of either a pyridyl aldehyde, which have a more sterically hindered portion around the nitrogen atom, 2-bromo-6-formylpyridine (**8b**), or 2-thiophenyl aldehyde (**8c**) with malonate ester **2a** were treated with our optimal conditions, the extended π-conjugate heteroaromatic compounds **9ba** and **9ca** were obtained in good yields (entries 2 and 3). Also, the present Knoevenagel condensation could be applied to either a conjugated or an aliphatic aldehyde in addition to an aromatic aldehyde. For example, a conjugated aldehyde, (*E*)-cinnamaldehyde (**8d**), reacted with the malonate ester to afford α, β, γ, δ-unsaturated carbonyl compound **9da** in 79% yield, which retained the double-bond geometry (entry 4). The reactions of linear aliphatic aldehydes **8e** and **8f** were completed within 24 h to give the corresponding products **9ea** and **9fa** in good yields (entries 5 and 6). Moreover, when α-branched aldehydes **8g**–**8j** were reacted with malonate **2a**, the expected alkenes **9ga**–**9ja**, respectively, were produced in 68–72% yields (entries 7–10).

As control experiments, the reaction of benzaldehyde (**1a**) with 1 equiv of Ac_2O was conducted both with and without $InCl_3$ (eq 1 in Scheme 1). In the former reaction, the corresponding geminal diacetate **4a** was quickly obtained in 91% yield at room temperature, but in the latter reaction, no formation of diacetate **4a** nor any other byproducts were observed. Moreover, to find out whether geminal diacetate **4a** would be an intermediate in the Knoevenagel reaction series,[13] the reaction of **4a** with dimethyl malonate **2a** was next examined both with and without $InCl_3$. Consequently, Knoevenagel adduct **3aa** was obtained in 79% yield in the presence of a catalytic amount of $InCl_3$, but the reaction without the indium catalyst did not produce the corresponding product along with the recovery of starting diacetate **4a** (eq 2 in Scheme 1). These results indicate that geminal diacetate **4a** is one of the intermediates in the Knoevenagel condensation and proves that the indium catalyst is necessary for both stages

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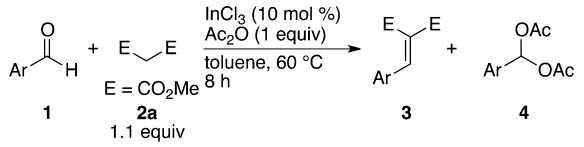
Table 2. Indium-Catalyzed Knoevenagel Condensation of Aromatic Aldehydes 1[a]



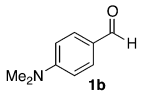
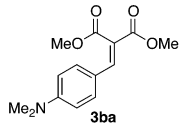
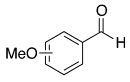
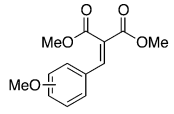
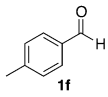
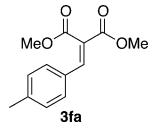
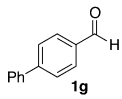
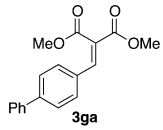
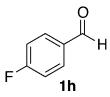
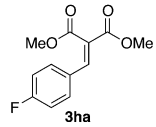
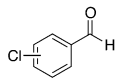
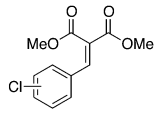
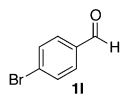
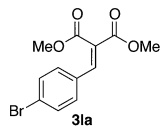
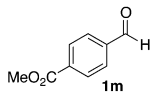
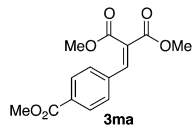
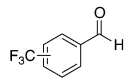
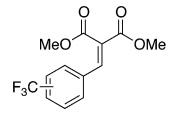
entry	substrate **1**	product **3**	yields (%)	
			3[b]	**4**[c]
1	 **1b**	 **3ba**	69	nd[d]
				
2	**1c**, 4-MeO	**3ca**	66	nd[d]
3	**1d**, 3-MeO	**3da**	59	2
4	**1e**, 2-MeO	**3ea**	71	nd[d]
5[e]	 **1f**	 **3fa**	80	8
6[f]	 **1g**	 **3ga**	84	7
7	 **1h**	 **3ha**	87	4
				
8	**1i**, 4-Cl	**3ia**	94	5
9	**1j**, 3-Cl	**3ja**	87	2
10	**1k**, 2-Cl	**3ka**	95	nd[d]
11[f]	 **1l**	 **3la**	86	10
12	 **1m**	 **3ma**	98	nd[d]
				

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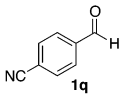
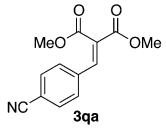
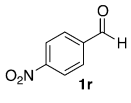
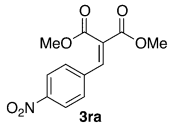
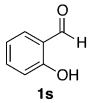
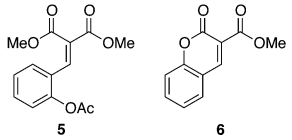
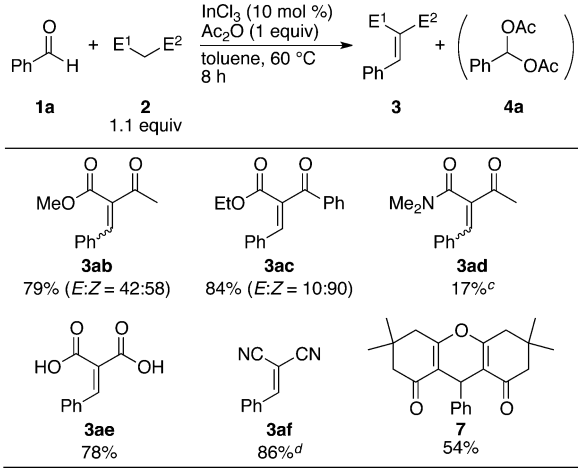
Table 2. continued

entry	substrate **1**	product **3**	yields (%)	
			3[b]	**4**[c]
13	**1n**, 4-CF_3	**3na**	88	6
14	**1o**, 3-CF_3	**3oa**	80	nd[d]
15	**1p**, 2-CF_3	**3pa**	92	nd[d]
16	 **1q**	 **3qa**	92	nd[d]
17	 **1r**	 **3ra**	92	nd[d]
18	 **1s**	 **5** **6**	40 (7)[g]	nd[d]

[a]Reaction conditions: **1** (0.6 mmol), **2a** (0.66 mmol), $InCl_3$ (0.06 mmol), Ac_2O (0.6 mmol), toluene (0.6 mL), 60 °C, 8 h. [b]Isolated yield. [c]NMR yield. [d]Not detected. [e]Reacted for 7 h. [f]Reacted for 5 h. [g]Yield of coumarin derivative **6**.

Table 3. Indium-Catalyzed Knoevenagel Condensation of Several Activated Methylenes 2[a,b]



[a]Reaction conditions: **1a** (0.6 mmol), **2** (0.66 mmol), $InCl_3$ (0.06 mmol), Ac_2O (0.6 mmol), toluene (0.6 mL), 60 °C, 8 h. [b]Isolated yield (*E*:*Z* ratio was determined by ^1H NMR). [c]Reacted for 30 h. [d]DMF was used instead of toluene.

involving the generation of **4a** from aldehyde and Ac_2O as well as a subsequent reaction of **4a** with malonate **2a**.

On the basis of the results obtained by the control experiments, a plausible reaction mechanism for the present condensation is shown in Scheme 2. When aldehyde **1** is activated by an indium catalyst, it initially reacts with Ac_2O to form geminal diacetate **4**,[14] the formation of which facilitates a subsequent nucleophilic attack of an enolizable activated methylene compound in the presence of the indium catalyst[15] to produce intermediate **A**. Finally, intramolecular elimination of acetic acid occurs to afford substituted alkene **3** along with regeneration of the indium catalyst.

CONCLUSIONS

In conclusion, we have demonstrated an indium-catalyzed Knoevenagel condensation between aldehydes with activated methylene compounds in the presence of acetic acid anhydride, leading to the preparation of polysubstituted alkenes. Also, we have clarified that to drive the Knoevenagel condensation series forward, in situ formation of a geminal diacetate intermediate derived from an aldehyde and acetic anhydride is essential. To date, several examples involving the conversion of aldehydes to geminal diacetates or the synthesis of Knoevenagel products from geminal diacetates have been reported. This novel procedure presents one-pot access to Knoevenagel products from various aldehydes via geminal diacetate as a key intermediate. Also, in conventional Lewis acid-catalyzed Knoevenagel condensations, substrates were limited to mainly either aldehydes bearing a noncoordinating functional group or activated methylenes with relatively high acidic hydrogen. With the present catalytic system in hand, therefore, the carbonyl compounds used in the Knoevenagel condensation could be extensively expanded to heteroaromatic, conjugate, and aliphatic aldehydes, including a variety of benzaldehydes. Moreover, we disclosed that the present method could be applied to various activated methylenes other than a malonate ester. The use of an indium compound with a unique and high tolerance to various functional groups allowed for extension of the substrate and a new entry for the preparation of valuable substituted alkenes. Further attempts to elucidate the reaction mechanism and extend the substrate scope are now in progress.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under a N_2 atmosphere. Toluene and *N*,*N*-dimethylformamide (DMF) were freshly distilled from CaH_2, and the aldehydes were purified via the distillation of commercially available products. Indium salts, methylene compounds, and acid anhydrides were purchased and used without

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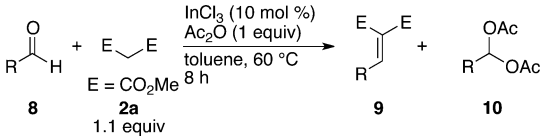
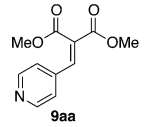
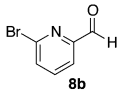
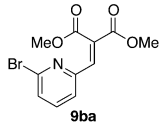
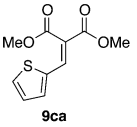
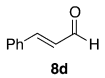
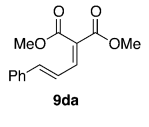
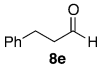
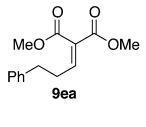
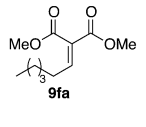
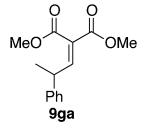
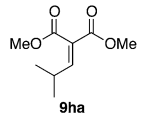
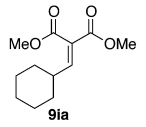
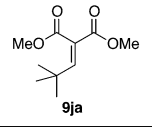
Table 4. Indium-Catalyzed Knoevenagel Condensation of Various Aldehydes 8[a]



entry	substrate **8**	product **9**	yields (%)	
			9[b]	**10**[c]
1[f]	 **8a**	 **9aa**	65 (68)[c,d]	nd[e]
2[g]	 **8b**	 **9ba**	83	nd[e]
3	 **8c**	 **9ca**	64	nd[e]
4	 **8d**	 **9da**	79[h]	nd[e]
5[i]	 **8e**	 **9ea**	60	nd[e]
6[i]	 **8f**	 **9fa**	70	8
7[i]	 **8g**	 **9ga**	71	2
8[i,j]	 **8h**	 **9ha**	71	nd[e]
9[i]	 **8i**	 **9ia**	72	3
10[i,k]	 **8j**	 **9ja**	68	nd[e]

[a]Reaction conditions: **8** (0.6 mmol), **2a** (0.66 mmol), $InCl_3$ (0.06 mmol), Ac_2O (0.6 mmol), toluene (0.6 mL), 60 °C, 8 h. [b]Isolated yield. [c]NMR yield. [d]Without $InCl_3$. [e]Not detected. [f]Reacted for 15 h. [g]Reacted for 13 h. [h]Only the (*E*)-isomer was obtained. [i]Reacted for 24 h. [j]Two equiv (1.2 mmol) of **2a** was used. [k]Two equiv (1.2 mmol) of **2a** and 20 mol % (0.12 mmol) of $InCl_3$ were used in toluene (0.3 mL) at 80 °C.

further purification. ^1H and ^{13}C NMR spectra were recorded on 500 and 300 MHz spectrometers, respectively. Chemical shifts in the ^1H and ^{13}C NMR spectra were reported in ppm relative to the internal reference for tetramethylsilane (δ 0.00 for ^1H), to the residual solvent peaks (δ 77.0 for ^{13}C) in $CDCl_3$, and to the residual solvent peaks (δ 2.50 for ^1H and δ 39.52 for ^{13}C) in DMSO-d_6. High-resolution mass spectra were measured using 3-nitrobenzylalcohol (NBA) as a matrix.

General Procedure for the $InCl_3$-Catalyzed Knoevenagel Condensation. To a screw-capped vial were added $InCl_3$ (0.0600 mmol, 13.3 mg), toluene (0.6 mL), aldehyde (**1** or **8**; 0.60 mmol),

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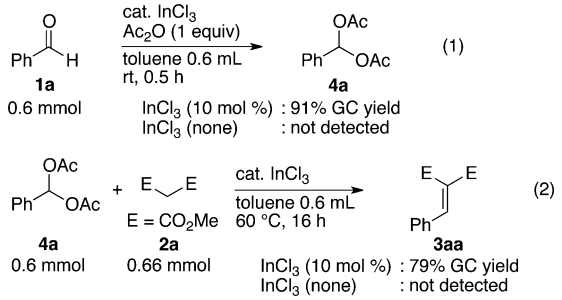
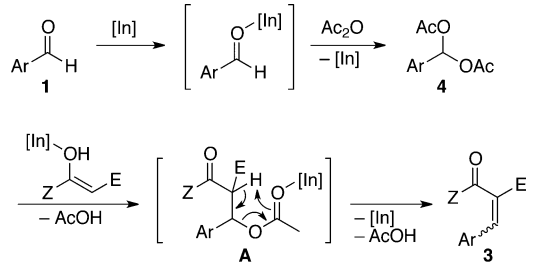
Scheme 1. Control Experiments for Clarification of the Condensation Path



Scheme 2. Possible Mechanism of an Indium-Catalyzed Knoevenagel Condensation



methylene (**2**; 0.66 mmol), and acetic anhydride (0.600 mmol, 61.3 mg) in succession. After the vial was sealed with a cap that contained a PTFE septum, the mixture was heated at 60 °C. The progress of the reaction was monitored by thin-layer chromatography (TLC) analysis, which was performed on silica gel 60 F_{254}. A saturated aqueous solution of $NaHCO_3$ was added to the resultant mixture, which was then extracted with EtOAc. The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (silica gel 60 F_{254}, 95:5 hexane/EtOAc) to give the corresponding Knoevenagel product **3** or **9** (followed by recrystallization, if necessary).

*Dimethyl 2-Benzylidenemalonate (**3aa**).* The general procedure was followed with benzaldehyde (**1a**; 63.7 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h, with the exception of performing recrystallization from hexane following column chromatography, to yield a colorless solid (**3aa**; 113.6 mg, 86%): mp 40–41 °C; ^{1}H NMR (300.5 MHz, $CDCl_3$) δ 3.84 (s, 6 H, OCH_3), 7.38–7.43 (m, 5 H, Ar*H*), 7.78 (s, 1 H, C=C*H*); ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 52.6, 125.4, 128.8, 129.3, 130.6, 132.7, 142.8, 164.4, 167.0; LRMS (FAB) *m*/*z* (% relative intensity) 221 ([M + H]$^+$, 77), 189 (100). The spectroscopic data of **3aa** were in good agreement with that reported in the literature.[16]

*Dimethyl 2-[4-(Dimethylamino)benzylidene]malonate (**3ba**).* The general procedure was followed with 4-(dimethylamino)-benzaldehyde (**1b**; 89.5 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a yellow-green solid (**3ba**; 109.0 mg, 69%): mp 86–87 °C; ^{1}H NMR (300.5 MHz, $CDCl_3$) δ 3.00 (s, 6 H, $N(CH_3)_2$), 3.80 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 6.62 (d, *J* = 8.7 Hz, 2 H, Ar*H*), 7.32 (d, *J* = 8.7 Hz, 2 H, Ar*H*), 7.66 (s, 1 H, C=C*H*); ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 39.8, 52.1, 52.4, 111.4, 118.8, 119.7, 131.7, 143.4, 151.8, 165.3, 168.3; HRMS (FAB-Magnetic Sector) calcd for [M]$^+$ ($C_{14}H_{17}NO_4$) *m*/*z* 263.1158, found 263.1166. The spectroscopic data of **3ba** were in good agreement with that reported in the literature.[17]

*Dimethyl 2-(4-Methoxybenzylidene)malonate (**3ca**).* The general procedure was followed with 4-methoxybenzaldehyde (**1c**; 81.7 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a colorless oil (**3ca**; 99.1 mg, 66%): ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 3.83 (s, 6 H, OCH_3), 3.87 (s, 3 H, OCH_3), 6.89 (d, *J* = 8.6 Hz, 2 H, Ar*H*), 7.39 (d, *J* = 8.6 Hz, 2 H, Ar*H*), 7.71 (s, 1 H, C=C*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 52.5, 52.6, 55.3, 114.3, 122.7, 125.2, 131.5, 142.6, 161.7, 164.8, 167.6; HRMS (EI-Quadrupole) calcd for [M]$^+$ ($C_{13}H_{14}O_5$) *m*/*z* 250.0841, found 250.0855. The spectroscopic data of **3ca** were in good agreement with that reported in the literature.[17]

*Dimethyl 2-(3-Methoxybenzylidene)malonate (**3da**).* The general procedure was followed with 3-methoxybenzaldehyde (**1d**; 81.7 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a pale yellow solid (**3da**; 88.6 mg, 59%): mp 81–82 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.80 (s, 3 H, OCH_3), 3.85 (s, 6 H, OCH_3), 6.94–7.00 (m, 2 H, Ar*H*), 7.01 (d, *J* = 5.0 Hz, 1 H, Ar*H*), 7.29 (t, *J* = 5.0 Hz, 1 H, Ar*H*), 7.74 (s, 1 H, C=C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.6, 52.7, 55.2, 114.2, 116.7, 121.9, 125.7, 129.9, 134.0, 142.7, 159.7, 164.4, 167.0; HRMS (EI-Quadrupole) calcd for [M]$^+$ ($C_{13}H_{14}O_5$) *m*/*z* 250.0841, found 250.0849. The spectroscopic data of **3da** were in good agreement with that reported in the literature.[17]

*Dimethyl 2-(2-Methoxybenzylidene)malonate (**3ea**).* The general procedure was followed with 2-methoxybenzaldehyde (**1e**; 81.7 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h, with the exception that recrystallization from hexane was performed after column chromatography, to yield a colorless solid (**3ea**; 106.6 mg, 71%): mp 53–54 °C; ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 3.78 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 6.92 (t, *J* = 5.0 Hz, 2 H, Ar*H*), 7.32–7.39 (m, 2 H, Ar*H*), 8.12 (s, 1 H, C=C*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 52.4, 55.4, 110.8, 120.5, 122.1, 125.2, 129.0, 132.1, 139.0, 158.0, 164.7, 167.1; HRMS (EI-Quadrupole) calcd for [M]$^+$ ($C_{13}H_{14}O_5$) *m*/*z* 250.0841, found 250.0842. The spectroscopic data of **3ea** were in good agreement with that reported in the literature.[17]

*Dimethyl 2-(4-Methylbenzylidene)malonate (**3fa**).* The general procedure was followed with 4-methylbenzaldehyde (**1f**; 72.1 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 7 h to yield a colorless oil (**3fa**; 112.4 mg, 80%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 2.37 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 7.18 (d, *J* = 8.0 Hz, 2 H, Ar*H*), 7.32 (d, *J* = 8.0 Hz, 2 H, Ar*H*), 7.74 (s, 1 H, C=C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 21.4, 52.5, 52.6, 124.3, 129.5, 129.6, 129.9, 141.3, 142.9, 164.6, 167.3; HRMS (EI-Quadrupole) calcd for [M]$^+$ ($C_{13}H_{14}O_4$) *m*/*z* 234.0892, found 234.0889. The spectroscopic data of **3fa** were in good agreement with that reported in the literature.[18]

*Dimethyl 2-(4-Phenylbenzylidene)malonate (**3ga**).* The general procedure was followed with 4-phenylbenzaldehyde (**1g**; 109.3 mg, 0.6000 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 5 h to yield a colorless solid (**3ga**; 149.3 mg, 84%): mp 75–76 °C; ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 3.86 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 7.37 (t, *J* = 8.9 Hz, 1 H, Ar*H*), 7.45 (t, *J* = 8.9 Hz, 2 H, Ar*H*), 7.50 (d, *J* = 8.9 Hz, 2 H, Ar*H*), 7.59 (d, *J* = 8.9 Hz, 2 H, Ar*H*), 7.62 (d, *J* = 8.9 Hz, 2 H, Ar*H*), 7.81 (s, 1 H, C=C*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 52.6, 52.7, 125.1, 127.0, 127.5, 128.0, 128.9, 130.0, 131.5, 139.8, 142.4, 143.4, 164.5, 167.2; IR (neat) 1731 s, 1632 w, 1434 w, 1270 m, 1223 m, 1196 m, 1070 w, 765 w cm^{-1}; HRMS (EI-Quadrupole) calcd for [M]$^+$ ($C_{18}H_{16}O_4$) *m*/*z* 296.1049, found 296.1039.

*Dimethyl 2-(4-Fluorobenzylidene)malonate (**3ha**).* The general procedure was followed with 4-fluorobenzaldehyde (**1h**; 74.5 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h, with the exception that recrystallization from hexane was performed after column chromatography, to yield a colorless solid (**3ha**; 124.3 mg, 87%): mp 38–39 °C; ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 3.85 (s, 6 H, OCH_3), 7.08 (t, *J* = 8.3 Hz, 2 H, Ar*H*), 7.42 (d, *J* = 8.3 Hz, 1 H, Ar*H*), 7.45 (d, *J* = 8.3 Hz, 1 H, Ar*H*), 7.73 (s, 1 H, C=C*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 52.6, 52.7, 116.0 (d, *J* = 22.4 Hz), 125.2, 128.9 (d, *J* = 3.7 Hz), 131.5 (d, *J* = 9.0 Hz), 141.5, 163.9 (d, *J* = 252.8 Hz), 164.3, 166.9; HRMS (EI-Quadrupole) calcd for [M]$^+$ ($C_{12}H_{11}FO_4$) *m*/*z* 238.0641, found 238.0638. The spectroscopic data of **3ha** were in good agreement with that reported in the literature.[17]

*Dimethyl 2-(4-Chlorobenzylidene)malonate (**3ia**).* The general procedure was followed with 4-chlorobenzaldehyde (**1i**; 84.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h, with the exception that recrystallization from hexane was performed after column chromatography, to yield a colorless solid (**3ia**; 143.6 mg, 94%): mp 36–37 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.85 (s, 6 H,

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OCH_3), 7.36 (s, 4 H, Ar*H*), 7.72 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.7, 125.9, 129.1, 130.5, 131.2, 136.7, 141.4, 164.2, 166.8; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{12}H_{11}ClO_4$) *m*/*z* 254.0346, found 254.0344. The spectroscopic data of **3ia** were in good agreement with that reported in the literature.[17]

*Dimethyl 2-(3-Chlorobenzylidene)malonate (**3ja**).* The general procedure was followed with 4-chlorobenzaldehyde (**1j**; 84.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a colorless solid (**3ja**; 132.9 mg, 87%): mp 65−66 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.86 (s, 6 H, OCH_3), 7.29−7.34 (m, 2 H, Ar*H*), 7.37−7.40 (m, 2 H, Ar*H*), 7.70 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.7, 52.8, 126.9, 127.3, 129.1, 130.1, 130.5, 134.5, 134.8, 141.1, 164.0, 166.5; IR (neat) 1724 s, 1624 w, 1433 m, 1373 w, 1258 m, 1200 s, 1068 w, 783 w cm^{-1}; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{12}H_{11}ClO_4$) *m*/*z* 254.0346, found 254.0328.

*Dimethyl 2-(2-Chlorobenzylidene)malonate (**3ka**).* The general procedure was followed with 4-chlorobenzaldehyde (**1k**; 84.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a colorless oil (**3ka**; 145.2 mg, 95%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.75 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 7.25 (t, *J* = 10.0 Hz, 1 H, Ar*H*), 7.33 (t, *J* = 10.0 Hz, 1 H, Ar*H*), 7.40 (d, *J* = 10.0 Hz, 1 H, Ar*H*), 7.44 (d, *J* = 10.0 Hz, 1 H, Ar*H*), 8.07 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.5, 52.7, 126.9, 127.9, 129.0, 129.9, 131.3, 131.8, 134.7, 139.9, 164.0, 166.2; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{12}H_{11}ClO_4$) *m*/*z* 254.0346, found 254.0330. The spectroscopic data of **3ka** were in good agreement with that reported in the literature.[17]

*Dimethyl 2-(4-Bromobenzylidene)malonate (**3la**).* The general procedure was followed with 4-bromobenzaldehyde (**1l**; 111 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 5 h to yield a colorless oil (**3la**; 154.3 mg, 86%): ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 3.84 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 7.28 (d, *J* = 8.3 Hz, 2 H, Ar*H*), 7.51 (d, *J* = 8.3 Hz, 2 H, Ar*H*), 7.70 (s, 1 H, C═C*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 52.7, 125.2, 126.1, 130.7, 131.6, 132.1, 141.5, 164.2, 166.8; IR (neat) 1729 s, 1630 w, 1489 w, 1437 m, 1261 s, 1221 s, 1069 m cm^{-1}; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{12}H_{11}BrO_4$) *m*/*z* 297.9841, found 297.9862.

*Dimethyl 2-[4-(Methoxycarbonyl)benzylidene]malonate (**3ma**).* The general procedure was followed with 4-(methoxycarbonyl)-benzaldehyde (**1m**; 98.5 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h, with the exception that recrystallization from hexane was performed after column chromatography, to yield a colorless solid (**3ma**; 163.6 mg, 98%): mp 114−115 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.84 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 7.48 (d, *J* = 8.0 Hz, 2 H, Ar*H*), 7.80 (s, 1 H, C═C*H*), 8.04 (d, *J* = 8.0 Hz, 2 H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.3, 52.7, 52.8, 127.5, 129.0, 129.9, 131.5, 137.0, 141.4, 164.0, 166.1, 166.5; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{14}H_{14}O_6$) *m*/*z* 278.0790, found 278.0798. The spectroscopic data of **3ma** were in good agreement with that reported in the literature.[17]

*Dimethyl 2-[4-(Trifluoromethyl)benzylidene]malonate (**3na**).* The general procedure was followed with 4-(trifluoromethyl)benzaldehyde (**1n**; 104.5 mg, 0.6000 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a colorless solid (**3na**; 152.2 mg, 88%): mp 43−44 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.85 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 7.53 (d, *J* = 8.0 Hz, 2 H, Ar*H*), 7.65 (d, *J* = 8.0 Hz, 2 H, Ar*H*), 7.79 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.8, 52.9, 123.6 (q, *J* = 272.5 Hz), 125.8 (q, *J* = 3.9 Hz), 127.9, 129.4, 132.0 (q, *J* = 32.6 Hz), 136.2, 141.0, 164.0, 166.4; IR (neat) 1732 s, 1724 s, 1721 s, 1635 w, 1439 w, 1326 s, 1265 s, 1226 m, 1166 m, 1117 s, 1067 s, 849 w cm^{-1}; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{13}H_{11}F_3O_4$) *m*/*z* 288.0609, found 288.0604.

*Dimethyl 2-[3-(Trifluoromethyl)benzylidene]malonate (**3oa**).* The general procedure was followed with 3-(trifluoromethyl)benzaldehyde (**1o**; 104.5 mg, 0.6000 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a colorless solid (**3oa**; 138.3 mg, 80%): mp 52−53 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.85 (s, 3 H, OCH_3), 3.87 (s, 6 H, OCH_3), 7.53 (t, *J* = 10.0 Hz, 1 H, Ar*H*), 7.60 (d, *J* = 10.0 Hz, 1 H, Ar*H*), 7.66 (d, *J* = 10.0 Hz, 1 H, Ar*H*), 7.68 (s, 1 H, Ar*H*), 7.79 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.7, 52.8, 123.6 (q, *J* = 272.5 Hz), 125.7 (q, *J* = 3.9 Hz), 126.9 (q, *J* = 3.9 Hz), 127.4, 129.4, 131.3 (q, *J* = 32.6 Hz), 132.3, 133.5, 140.9, 164.0, 166.4; IR (neat) 1728 s, 1635 w, 1439 w, 1366 w, 1336 m, 1253 m, 1227 m, 1196 m, 1159 w, 1117 s, 1071 m, 809 w, 698 w cm^{-1}; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{13}H_{11}F_3O_4$) *m*/*z* 288.0609, found 288.0597.

*Dimethyl 2-[2-(Trifluoromethyl)benzylidene]malonate (**3pa**).* The general procedure was followed with 2-(trifluoromethyl)benzaldehyde (**1p**; 104.5 mg, 0.6000 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a colorless oil (**3pa**; 159.1 mg, 92%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.67 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 7.44 (d, *J* = 7.5 Hz, 1 H, Ar*H*), 7.50 (t, *J* = 7.5 Hz, 1 H, Ar*H*), 7.54 (t, *J* = 7.5 Hz, 1 H, Ar*H*), 7.72 (d, *J* = 7.5 Hz, 1 H, Ar*H*), 8.10 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.5, 52.8, 123.7 (q, *J* = 273.4 Hz), 126.1 (q, *J* = 5.8 Hz), 128.7 (q, *J* = 30.7 Hz), 129.1, 129.5, 129.6, 131.8, 132.1 (q, *J* = 1.9 Hz), 140.2, 163.7, 165.8; IR (neat) 1733 s, 1438 m, 1316 s, 1306 m, 1296 m, 1263 s, 1225 m, 1168 s, 1123 s, 1067 s, 1036 m, 771 m cm^{-1}; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{13}H_{11}F_3O_4$) *m*/*z* 288.0609, found 288.0617.

*Dimethyl 2-(4-Cyanobenzylidene)malonate (**3qa**).* The general procedure was followed with 4-cyanobenzaldehyde (**1q**; 78.7 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a colorless solid (**3qa**; 135.4 mg, 92%): mp 97−98 °C; ^{1}H NMR (300.5 MHz, $CDCl_3$) δ 3.85 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 7.53 (d, *J* = 8.1 Hz, 2 H, Ar*H*), 7.69 (d, *J* = 8.1 Hz, 2 H, Ar*H*), 7.76 (s, 1 H, C═C*H*); ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 52.8, 113.6, 117.9, 128.5, 129.4, 132.4, 137.0, 140.2, 163.6, 166.0; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{13}H_{11}NO_4$) *m*/*z* 245.0688, found 245.0716. The spectroscopic data of **3qa** were in good agreement with that reported in the literature.[18]

*Dimethyl 2-(4-Nitrobenzylidene)malonate (**3ra**).* The general procedure was followed with 4-nitrobenzaldehyde (**1r**; 90.7 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a pale yellow solid (**3ra**; 146.4 mg, 92%): mp 135−136 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.86 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 7.59 (d, *J* = 9.0 Hz, 2 H, Ar*H*), 7.81 (s, 1 H, C═C*H*), 8.24 (d, *J* = 9.0 Hz, 2 H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.9, 123.9, 129.1, 129.8, 139.0, 139.8, 148.4, 163.6, 165.9; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{12}H_{11}NO_6$) *m*/*z* 265.0586, found 265.0572. The spectroscopic data of **3ra** were in good agreement with that reported in the literature.[18]

*Dimethyl 2-(2-Acetoxybenzylidene)malonate (**5**).* The general procedure was followed with 4-hydroxybenzaldehyde (**1s**; 73.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a colorless oil (**5**; 66.8 mg, 40%): ^{1}H NMR (300.5 MHz, $CDCl_3$) δ 2.33 (s, 3 H, CH_3), 3.76 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 7.15 (d, *J* = 7.8 Hz, 1 H, Ar*H*), 7.23 (t, *J* = 7.8 Hz, 1 H, Ar*H*), 7.42 (t, *J* = 7.8 Hz, 2 H, Ar*H*), 7.83(s, 1 H, C═C*H*); ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 20.8, 52.5, 52.7, 122.8, 126.06, 126.09, 127.6, 128.8, 131.4, 137.7, 149.0, 164.1, 166.3, 168.8; IR (neat) 1768 m, 1730 s, 1632 w, 1437 m, 1370 m, 1261 s, 1176 s, 1103 m, 1067 m, 910 w, 763 w cm^{-1}; HRMS (FAB-Magnetic Sector) calcd for $[M + H]^+$ ($C_{14}H_{15}O_6$) *m*/*z* 279.0869, found 279.0872.

*3-(Methoxycarbonyl)coumarin (**6**).* The general procedure was followed with 4-hydroxybenzaldehyde (**1s**; 73.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a colorless solid (**6**; 8.6 mg, 7%): mp 115−116 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.96 (s, 3 H, OCH_3), 7.35 (t, *J* = 7.5 Hz, 1 H, Ar*H*), 7.37 (d, *J* = 7.5 Hz, 1 H, Ar*H*), 7.63 (d, *J* = 7.5 Hz, 1 H, Ar*H*), 7.67 (t, *J* = 7.5 Hz, 1 H, Ar*H*), 8.58 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.9, 116.7, 117.8, 117.9, 124.9, 129.5, 134.4, 149.1, 155.2, 156.7, 163.7; HRMS (EI-Quadrupole) calcd for $[M]^+$ ($C_{11}H_8O_4$) *m*/*z* 204.0423, found 204.0404. The spectroscopic data of **6** were in good agreement with that reported in the literature.[19]

*Methyl 2-Benzylidene-3-oxobutanoate (**3ab**).* The general procedure was followed with benzaldehyde (**1a**; 63.7 mg, 0.600 mmol) and methyl acetoacetate (**2b**; 76.6 mg, 0.660 mmol) for 8 h to yield a pale yellow oil ((*Z*)-**3ab**; 56.4 mg, 46%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 2.42 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 7.39−7.44 (m, 5 H, Ar*H*), 7.58 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$)

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δ 26.4, 52.5, 128.9, 129.4, 130.8, 132.8, 134.2, 141.6, 168.2, 194.6; LRMS (FAB) *m/z* (% relative intensity) 205 ([M + H]$^+$, 49%), 173 (100), 131 (52), 73 (54). The spectroscopic data of (*Z*)-**3ab** were in good agreement with that reported in the literature.[20]

Also generated was a pale yellow-green oil ((*E*)-**3ab**; 40.4 mg, 33%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 2.35 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 7.39 (s, 5 H, Ar*H*), 7.70 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 31.2, 52.5, 128.9, 129.6, 130.5, 132.8, 133.6, 140.8, 164.9, 203.4; LRMS (FAB) *m/z* (% relative intensity) 205 ([M + H]$^+$, 100), 173 (35), 147 (25), 73 (38). The spectroscopic data of (*E*)-**3ab** were in good agreement with that reported in the literature.[20]

*Ethyl 2-Benzoyl-3-phenyl Acrylate (**3ac**).* The general procedure was followed with benzaldehyde (**1a**; 63.7 mg, 0.600 mmol) and ethyl benzoylacetate (**2c**; 126.9 mg, 0.6600 mmol) for 8 h to yield a colorless solid (**3ac**; 141.3 mg, 84%, *E*:*Z* = 10:90): mp 94−95 °C; ^{1}H NMR (297.6 MHz, $CDCl_3$, *Z* isomer) δ 1.17 (t, 3 H, CH_3), 4.21 (q, 2 H, OCH_2), 7.20−7.27 (m, 3 H, Ar*H*), 7.35 (d, *J* = 7.4 Hz, 2 H, Ar*H*), 7.42 (t, *J* = 7.4 Hz, 2 H, Ar*H*), 7.55 (t, *J* = 7.4 Hz, 1 H, Ar*H*), 7.94−7.97 (m, 3 H, C═C*H*, Ar*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$ *Z* isomer) δ 13.9, 61.5, 128.7, 128.8, 129.0, 130.1, 130.3, 131.2, 132.7, 133.8, 136.0, 142.5, 164.9, 195.6; LRMS (EI) *m/z* (% relative intensity) 280 (M$^+$, 100), 251 (18), 235 (20), 178 (42), 105 (100). The spectroscopic data of **3ac** were in good agreement with that reported in the literature.[21]

*2-Benzylidene-N,N-dimethyl-3-oxobutanamide (**3ad**).* The general procedure was followed with benzaldehyde (**1a**; 63.7 mg, 0.600 mmol) and *N*,*N*-dimethylacetoacetamide (**2d**; 85.2 mg, 0.660 mmol) for 30 h to yield a pale yellow-green oil (**3ad**; 22.2 mg, 17%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 2.44 (s, 3 H, CH_3), 2.77 (s, 3 H, NCH_3), 3.09 (s, 3 H, NCH_3), 7.39−7.40 (m, 3 H, Ar*H*), 7.48−7.50 (m, 2 H, Ar*H*), 7.51 (s, 1 H, C═C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 26.5, 34.5, 37.4, 129.0, 129.6, 130.6, 133.1, 136.1, 139.3, 168.4, 195.7; IR (neat) 1662 m, 1620 s, 1497 w, 1407 w, 1242 w, 1210 w, 1155 w, 763 w cm^{-1}; LRMS (FAB) *m/z* (% relative intensity) 218 ([M + H]$^+$, 100), 173 (59), 131 (36), 73 (22).

*2-Benzylidenemalonic Acid (**3ae**).* The general procedure was followed with benzaldehyde (**1a**; 63.7 mg, 0.600 mmol) and malonic acid (**2e**; 68.7 mg, 0.660 mmol) for 8 h, with the exception of using H_2O instead of aq. $NaHCO_3$ for the reaction workup, which was followed by isolation via recrystallization from $CHCl_3$ to yield a colorless solid (**3ae**; 89.9 mg, 78%): mp 193−194 °C; ^{1}H NMR (297.6 MHz, DMSO-d_6) δ 7.43 (t, *J* = 8.0 Hz, 3 H, Ar*H*), 7.54 (s, 1 H, C═C*H*), 7.56 (d, *J* = 3.3 Hz, 1 H, Ar*H*), 7.58 (d, *J* = 3.3 Hz, 1 H, Ar*H*), 13.2 (s, 2 H, COO*H*); ^{13}C NMR (74.8 MHz, DMSO-d_6) δ 128.5, 129.0, 129.3, 130.5, 132.9, 138.7, 165.3, 168.1; HRMS (FAB-Magnetic Sector) calcd for [M + H]$^+$ ($C_{10}H_9O_4$) *m/z* 193.0501, found 193.0504. The spectroscopic data of **3ae** were in good agreement with that reported in the literature.[17]

*2-Benzylidenemalononitrile (**3af**).* The general procedure was followed with benzaldehyde (**1a**; 63.7 mg, 0.600 mmol) and malononitrile (**2f**; 39.6 mg, 0.660 mmol) for 8 h, with the exception of using DMF instead of toluene, to yield a colorless solid (**3af**; 79.6 mg, 86%): mp 83−84 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.55 (t, *J* = 7.5 Hz, 2 H, Ar*H*), 7.64 (t, *J* = 7.5 Hz, 1 H, Ar*H*), 7.79 (s, 1 H, C═C*H*), 7.91 (d, *J* = 7.5 Hz, 2 H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 82.6, 112.5, 113.6, 129.5, 130.6, 130.8, 134.5, 159.9; HRMS (FAB-Magnetic Sector) calcd for [M + H]$^+$ ($C_{10}H_9O_4$) *m/z* 193.0501, found 193.0504. The spectroscopic data of **3af** were in good agreement with that reported in the literature.[3e]

*3,3,6,6-Tetramethyl-9-phenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione (**7**).* The general procedure was followed with benzaldehyde (**1a**; 63.7 mg, 0.600 mmol) and 5,5-dimethyl-1,3-cyclohexanedione (**2g**; 92.5 mg, 0.660 mmol) for 8 h to yield a colorless solid (**7**; 113.5 mg, 54%): mp 203−205 °C; ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 0.98 (s, 6 H, CH_3), 1.09 (s, 6 H, CH_3), 2.15 (d, *J* = 16.1 Hz, 2 H, CH_2), 2.23 (d, *J* = 16.1 Hz, 2 H, CH_2), 2.47 (s, 4 H, CH_2), 4.75 (s, 1 H, C*H*), 7.08 (t, *J* = 7.7 Hz, 1 H, Ar*H*), 7.20 (t, *J* = 7.7 Hz, 2 H, Ar*H*), 7.29 (d, *J* = 7.7 Hz, 2 H, Ar*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 27.2, 29.1, 31.7, 32.1, 40.7, 50.6, 115.5, 126.2, 127.9, 128.2, 144.0, 162.2, 196.3; LRMS (FAB) *m/z* (% relative intensity) 351 ([M + H]$^+$, 95), 350 (M$^+$, 40), 273 (100). The spectroscopic data of **7** were in good agreement with that reported in the literature.[22]

*Dimethyl 4-Pyridylmethylenemalonate (**9aa**).* The general procedure was followed with 4-formylpyridine (**8a**; 64.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 15 h to yield a pale brown solid (**9aa**; 86.3 mg, 65%): mp 72−73 °C; ^{1}H NMR (500.2 MHz, DMSO-d_6) δ 3.79 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 7.38 (d, *J* = 6.0 Hz, 2 H, Ar*H*), 7.78 (s, 1 H, C═C*H*) 8.66 (d, *J* = 6.0 Hz, 2 H, Ar*H*); ^{13}C NMR (125.8 MHz, DMSO-d_6) δ 52.96, 53.03, 122.7, 129.0, 139.6, 139.8, 150.5, 163.3, 165.5; IR (neat) 1722 s, 1597 w, 1441 w, 1266 m, 1221 m, 1068 w, 811 w cm^{-1}; HRMS (FAB-Magnetic Sector) calcd for [M + H]$^+$ ($C_{11}H_{12}NO_4$) *m/z* 222.0766, found 222.0796.

*Dimethyl 2-(6-Bromo)pyridylmethylenemalonate (**9ba**).* The general procedure was followed with 2-bromo-6-formylpyridine (**8b**; 111.6 mg, 0.6000 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 13 h to yield a pale brown solid (**9ba**; 149.5 mg, 83%): mp 105−106 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.87 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 7.34 (d, *J* = 5.0 Hz, 1 H, Ar*H*), 7.45 (d, *J* = 5.0 Hz, 1 H, Ar*H*), 7.55 (s, 1 H, C═C*H*), 7.58 (t, *J* = 5.0 Hz, 1 H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.7, 52.9, 125.0, 129.1, 129.6, 137.5, 139.0, 141.9, 151.7, 164.0, 166.3; IR (neat) 1726 s, 1637 w, 1438 w, 1411 w, 1376 w, 1274 m, 1248 m, 1218 m, 1207 m, 1163 w, 1063 w, 788 w cm^{-1}; HRMS (EI-Quadrupole) calcd for [M]$^+$ ($C_{11}H_{10}BrNO_4$) *m/z* 298.9793, found 298.9789.

*Dimethyl 2-(Thien-2-ylmethylene)malonate (**9ca**).* The general procedure was followed with 2-formylthiophene (**8c**; 67.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h, with the exception of performing recrystallization from hexane following column chromatography, to yield a colorless solid (**9ca**; 86.9 mg, 64%): mp 43−44 °C; ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 3.84 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 7.09 (dd, *J* = 4.5, 4.8 Hz, 1 H, Ar*H*), 7.37 (d, *J* = 4.5 Hz, 1 H, Ar*H*), 7.54 (d, *J* = 4.8 Hz, 1 H, Ar*H*), 7.90 (s, 1 H, C═C*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 52.6, 52.8, 121.5, 127.8, 131.9, 134.7, 135.5, 135.9, 164.7, 166.6; HRMS (EI-Quadrupole) calcd for [M]$^+$ ($C_{10}H_{10}O_4S$) *m/z* 226.0300, found 226.0300. The spectroscopic data of **9ca** were in good agreement with that reported in the literature.[23]

*(E)-Dimethyl 2-(3-Phenylallylidene)malonate (**9da**).* The general procedure was followed with (*E*)-cinnamaldehyde (**8d**; 79.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 8 h to yield a yellow solid (**9da**; 116.7 mg, 79%): mp 64−65 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 3.81 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 7.04 (d, *J* = 16.0 Hz, 1 H, PhC*H*), 7.27 (dd, *J* = 15.0, 15.5 Hz, 1 H, PhCH═C*H*), 7.32−7.38 (m, 3 H, Ar*H*), 7.50 (d, *J* = 6.0 Hz, 2 H, Ar*H*), 7.56 (d, *J* = 11.5 Hz, 1 H, PhCH═CH−C*H*═C); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 52.2, 52.3, 123.1, 123.9, 127.8, 128.8, 129.8, 135.4, 145.1, 146.1, 165.0, 165.6; HRMS (EI-Quadrupole) calcd for [M]$^+$ ($C_{14}H_{14}O_4$) *m/z* 246.0892, found 246.0881. The spectroscopic data of **9da** were in good agreement with that reported in the literature.[24]

*Dimethyl 2-(3-Phenylpropylidene)malonate (**9ea**).* The general procedure was followed with 3-phenylpropanal (**8e**; 80.5 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 24 h to yield a colorless oil (**9ea**; 89.4 mg, 60%): ^{1}H NMR (300.5 MHz, $CDCl_3$) δ 2.63 (q, *J* = 7.9 Hz, 2 H, CH_2CH_2CH), 2.80 (t, *J* = 7.2 Hz, 2 H, $PhCH_2$), 3.78 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 7.07 (t, *J* = 7.5 Hz, 1 H, C═C*H*), 7.17−7.19 (m, 3 H, Ar*H*), 7.26−7.30 (m, 2 H, Ar*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 31.5, 34.3, 52.2, 52.3, 126.3, 128.29, 128.32, 128.5, 140.2, 149.2, 164.3, 165.7. The spectroscopic data of **9ea** were in good agreement with that reported in the literature.[25]

*Dimethyl 2-Hexylidenemalonate (**9fa**).* The general procedure was followed with hexanal (**8f**; 60.1 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 24 h to yield a colorless oil (**9fa**; 90.0 mg, 70%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 0.89 (t, *J* = 6.6 Hz, 3 H, CH_3), 1.28−1.33 (m, 4 H, $CH_3CH_2CH_2CH_2CH_2$), 1.44−1.54 (m, 2 H, CH_3CH_2), 2.30 (q, *J* = 7.4 Hz, 2 H, $CHCH_2$), 3.78 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 7.04 (t, *J* = 7.7 Hz, 1 H, C═C*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 13.9, 22.3, 27.9, 29.8, 31.3, 52.2, 52.3, 127.8, 150.6, 164.4, 166.0; IR (neat) 2956 m, 2862 w, 1729 s, 1646 w, 1437 m, 1370 w, 1259 m, 1225 m, 1144 w, 1062 m cm^{-1}; HRMS

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(EI-Quadrupole) calcd for $[M]^+$ ($C_{11}H_{18}O_4$) m/z 214.1205, found 214.1208.

*Dimethyl 2-(2-Phenylpropylidene)malonate (**9ga**).* The general procedure was followed with 2-phenylpropionaldehyde (**8g**; 80.5 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 24 h to yield a colorless oil (**9ga**; 116 mg, 71%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 1.45 (d, J = 6.9 Hz, 3 H, CH_3), 3.76 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 3.88−3.92 (m, 1 H, ArC*H*), 7.04 (d, J = 10.8 Hz, 1 H, C=C*H*), 7.24 (d, J = 8.0 Hz, 3 H, Ar*H*), 7.32 (t, J = 7.7 Hz, 2 H, Ar*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 20.2, 39.6, 52.3, 52.4, 126.0, 127.0, 127.1, 128.8, 142.2, 152.8, 164.4, 165.8. The spectroscopic data of **9ga** were in good agreement with that reported in the literature.[26]

*Dimethyl 2-(2-Methylpropylidene)malonate (**9ha**).* The general procedure was followed with isobutyraldehyde (**8h**; 43.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 158.5 mg, 1.200 mmol) for 24 h to yield a colorless oil (**9ha**; 79 mg, 71%): ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 1.06 (d, J = 6.5 Hz, 6 H, CH_3), 2.62−2.75 (m, 1 H, CH_3CHCH_3), 3.78 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 6.81 (d, J = 10.7 Hz, 1 H, C=C*H*); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 21.8, 29.5, 52.2, 52.3, 125.7, 155.9, 164.5, 166.0. The spectroscopic data of **9ha** were in good agreement with that reported in the literature.[27]

*Dimethyl 2-(Cyclohexylmethylene)malonate (**9ia**).* The general procedure was followed with cyclohexanecarboxaldehyde (**8i**; 67.3 mg, 0.600 mmol) and dimethyl malonate (**2a**; 79.3 mg, 0.660 mmol) for 24 h to yield a colorless oil (**9ia**; 97.7 mg, 72%): ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 1.11−1.35 (m, 5H, Cy*H*), 1.70−1.73 (m, 5H, Cy*H*), 2.33−2.45 (m, 1 H, CH_2CHCH_2), 3.78 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 6.84 (d, J = 10.4 Hz, 1 H, C=C*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 25.1, 25.6, 31.6, 39.1, 52.2, 52.3, 126.0, 154.6, 164.6, 166.1. The spectroscopic data of **9ia** were in good agreement with that reported in the literature.[25]

*Dimethyl 2-(2,2-Dimethylpropylidene)malonate (**9ja**).* The general procedure was followed with pivalaldehyde (**8j**; 51.7 mg, 0.600 mmol) and dimethyl malonate (**2a**; 158.5 mg, 1.200 mmol) for 24 h to yield a colorless oil (**9ja**; 81.7 mg, 68%): ^{1}H NMR (297.6 MHz, $CDCl_3$) δ 1.14 (s, 9 H, CH_3), 3.77 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 6.92 (s, 1 H, C=C*H*); ^{13}C NMR (74.8 MHz, $CDCl_3$) δ 28.7, 34.2, 52.2, 52.4, 124.5, 155.8, 164.8, 167.3; IR (neat) 2959 m, 1734 s, 1642 w, 1436 m, 1368 w, 1251 s, 1232 s, 1197 m, 1070 m, 1002 w cm^{-1}; HRMS (EI-Quadrupole) calcd for $[M-CH_3]^+$ ($C_9H_{13}O_4$) m/z 185.0814, found 185.0814.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of the ^{1}H and ^{13}C NMR spectra of the products produced in this study. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(9) The yields of **3aa** and **4a** under the conditions in entry 6 of Table 1 are listed as follows: 95 and 0% in CH_3Cl, 68 and 6% in CH_3CN, 4 and 32% in THF, respectively, and 0% each in MeOH. Although CH_3Cl was a slightly better solvent than toluene (94 and 4%), we chose toluene as the best solvent due to its good mass balance.

(10) The *E*:*Z* geometries of the products **3ab** and **3ac** were assigned on the basis of NOESY analyses.

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