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Baylis–Hillman reaction promoted by a recyclable protic-ionic-liquid solvent–catalyst system: DABCO–AcOH–H_2O

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ABSTRACT

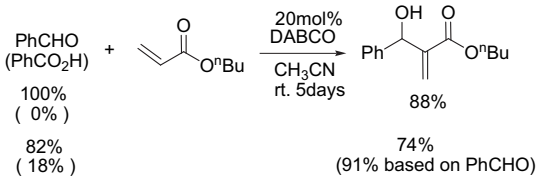
A recyclable protic-ionic-liquid solvent–catalyst system, DABCO–AcOH–H_2O, has been developed and used in the Baylis–Hillman reaction of aromatic aldehydes, aliphatic aldehydes, and cinnamaldehydes with acrylates and acrylonitrile, showing comparable performance to free DABCO in traditional solvents. The DABCO–AcOH–H_2O solvent–catalyst system could be reused for at least five times without significant loss of activity.

1. Introduction

The Baylis–Hillman reaction, a tertiary amine catalyzed carbon–carbon bond forming reaction of an aldehyde with an α,β-unsaturated carbonyl compound, is an atom-economical reaction going cleanly under very mild condition yet producing a highly functionalized adduct.[1] However, there is a major drawback, slow reaction rate, associated with this important reaction. It is often reported that days or even weeks have been required for the reaction to complete. Therefore, a number of efforts have been made to accelerate Baylis–Hillman reaction, including use of Lewisacids,[2] ionic liquids,[3] and H-bond donors,[4] application of solvent-free,[5] high pressure,[6] ultrasound,[7] and microwave[8] techniques as well as development of highly active catalysts.[9] Most of these efforts were just successful for a limited number of substrates. At present, the most general and practical technique to accelerate Baylis–Hillman reaction is the use of high loading, especially use of stoichiometric or excess amount,[10] of tertiary amine catalyst. For practical point of view, it is necessary to recycle or, at least, recover the tertiary amine catalysts when used in stoichiometric or excess amount. Although soluble polymer-supported catalysts have recently been explored in Baylis–Hillman reaction,[11] utility of recyclable ionic liquid dual solvent–catalysts[12] that serve as both solvent and catalyst looks like a more promising choice for making Baylis–Hillman reaction more practical due to the strong concentration effects of both substrates and catalysts observed in Baylis–Hillman reaction. Protic-ionic-liquids (PILs), liquid Brønsted acid–base salts that could be readily formed by simple combination of a proper Brønsted acid with a Brønsted base, have proven to be the most practical ionic liquid solvent–catalysts and have been successfully used in a wide range of Brønsted acid catalyzed organic reactions.[13] However, to the best of our knowledge, there is no report on protic-ionic-liquid promoted Baylis–Hillman reaction. Herein we describe the development of a recyclable protic-ionic-liquid solvent–catalyst system, DABCO–AcOH–H_2O, for Baylis–Hillman reaction of aromatic and aliphatic aldehydes and cinnamaldehydes with acrylates and acrylonitrile.

2. Results and discussion

During our investigation of Baylis–Hillman reaction catalyzed by 1,4-diazabicyclic [2,2,2]octane (DABCO), we noticed that the reaction with stock benzaldehyde contaminated with benzoic acid proceeded as well as that with fresh-distilled acid-free benzaldehyde (Scheme 1).



Scheme 1.

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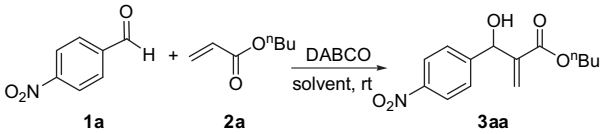
The innocence of benzoic acid in the reaction was attributed to the fact that Baylis–Hillman reaction is mainly promoted by the nucleophilicity instead of basicity of a tertiary amine. Therefore, we envision that it would be possible to develop a protic-ionic-liquid of DABCO with a proper Brønsted acid as recyclable catalyst for Baylis–Hillman reaction. It was explored at first that catalytic efficacy of Brønsted acid salts of DABCO using the reaction of *p*-nitrobenzaldehyde (**1a**) with butyl acrylate (**2a**) as model considering its easy monitoring and fast reaction rate (Table 1).

Table 1
Baylis–Hillman reaction of *p*-nitrobenzaldehyde with butyl acrylate promoted by DABCO salts of weak organic acids[a]



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

Entry	Catalyst	Solvent	Time (h)	Yield[b] (%)
1	0.2 equiv DABCO	CH_3CN	18	84
2	0.2 equiv DABCO–$PhCO_2H$	CH_3CN	18	90
3	1.0 equiv DABCO	CH_3CN	9	94
4	1.0 equiv DABCO–$PhCO_2H$	CH_3CN	9	95
5	1.0 equiv DABCO–$2PhCO_2H$	CH_3CN	18	21
6	0.2 equiv DABCO–AcOH	CH_3CN	18	88
7	1.0 equiv DABCO–AcOH	CH_3CN	9	95
8	1.0 equiv DABCO–AcOH	DMF	9	96
9	1.0 equiv DABCO–AcOH	MeOH	18	15
10	1.0 equiv DABCO–AcOH	Dioxane	18	81
11	1.0 equiv DABCO–$EtCO_2H$	CH_3CN	9	91
12	1.0 equiv DABCO–^{t}BuCO$_2$H	CH_3CN	9	93
13[c]	1.0 equiv DABCO–AcOH	CH_3CN	6	90
14[d]	1.0 equiv DABCO	CH_3CN	24	10
15[d]	1.0 equiv DABCO–AcOH	CH_3CN	24	12
16[e]	1.0 equiv DABCO–AcOH	—	12	52
17[e]	1.0 equiv DABCO	CH_3CN	12	19
18	DABCO–AcOH–$5H_2O$	CH_3CN	12	90

[a] Reaction run at 1.0 mmol scale with respect to **1a** in 2 mL solvent.
[b] Isolated yields and **1a** recovered.
[c] Run at 0–5 °C.
[d] 20 mL CH_3CN used.
[e] Run at 80 °C and **1a** decomposed in stead of being recovered.

With the almost neutral DABCO benzoic acid salt (pH≈7–8), DABCO–PhCOOH, at both catalytic (20 mol %) and stoichiometric amounts the model reaction even proceeded slightly faster than that with free DABCO at the early stage of the reaction progress (<50% conversion by TLC) although this acceleration diminished along with the increase of the conversion of aldehyde **1a**. When the salt of DABCO–$2PhCO_2H$ was used the reaction became sluggish under the otherwise identical conditions although it was reported that Baylis–Hillman reaction could proceed under aqueous acidic condition with tertiary amine catalysts[14] (Table 1, entries 1–5). The other DABCO salts of weak organic acids such as CH_3CO_2H, $EtCO_2H$, and ^{t}BuCO$_2$H showed comparable efficacy to both DABCO–PhCOOH and free DABCO (Table 1, entries 7, 11 and 12). However, the DABCO salts of stronger acids such as H_3PO_4, TsOH, and CF_3CO_2H displayed no activity. Unfortunately, no one of these DABCO salts tested is liquid at room temperature (20–25 °C), the most practical temperature range for DABCO-promoted Baylis–Hillman reaction. When the reaction was conducted at high temperature (80 °C) at which the DABCO–CH_3CO_2H salt could be used as both catalyst and medium the isolated yield of adduct **3aa** decreased significantly albeit much better than that using free DABCO in CH_3CN (Table 1, entries 16 and 17). Therefore an organic co-solvent has to be used for the reaction at room temperature. The reaction occurred very slowly using methanol as co-solvent while a fast reaction was observed using DMF and CH_3CN. It was reported that DABCO-catalyzed Baylis–Hillman reaction of aromatic aldehydes with acrylates proceeded efficiently in dioxane even at low concentration of aldehydes (0.1 M),[10a] however, the isolated yield of adduct **3aa** was lower with DABCO–AcOH salt using dioxane as co-solvent than those using CH_3CN and DMF (Table 1, entries 8–10). Similar to free DABCO, a large concentration effect was observed in the reaction using DABCO–AcOH salt. When the concentration of aldehyde **1a** was lower than 0.05 M the reaction became sluggish. Low temperature slightly benefited the reaction but to a much less degree than that reported in literature (Table 1, entry 13).[15]

There are reports that aqueous condition accelerated Baylis–Hillman reaction.[4a,10b,16] Therefore, some water (5 equiv) was deliberately added to the reaction mixture, but no remarkable difference with respect to reaction rate and product yield was observed. However, during our recovering the DABCO–AcOH salt, we noticed that the recovered DABCO–AcOH was a liquid instead of a crystalline material although no difference, expect for the peak assigned to water, could be detected between the ^{1}H NMR spectra of recovered and separately prepared samples, implying a strong freezing-point-depression by a small amount water for DABCO–AcOH salt. In fact, it has been well known that some organic salts melt at much lower temperature with a small amount of water or in the form of hydrates. In our previous work, we have developed ionic liquid media from high-melting-point organic ammonium salts by adding a small amount of water.[17] Therefore, we investigated the effects of small amount of water on melting point of the DABCO–AcOH salt. A colorless viscous liquid formed at room temperature when DABCO hydrate ($1.7H_2O$), which was prepared by crystallization from water, was mixed with 1 equiv AcOH. However, the liquid DABCO·$1.7H_2O$–AcOH was too viscous to be used as reaction medium at room temperature. When the amount of water in the DABCO–AcOH salt was increased to 3–5 equiv viscosity of the corresponding liquid, 1/1/3–5 (mol) DABCO–AcOH–H_2O, significantly decreased at room temperature. The model reaction of *p*-nitrobenzaldehyde with butyl acrylate was then investigated using this DABCO–AcOH–H_2O solvent–catalyst system (Table 2).

Table 2
Baylis–Hillman reaction of *p*-nitrobenzaldehyde with butyl acrylate promoted by DABCO–AcOH–H_2O[a]

Entry	Catalyst[b]	Co-solvent[c]	Time (h)	Yield (%)
1	DABCO–AcOH–$5H_2O$	—	12	86
2	DABCO–AcOH–$10H_2O$	—	12	55
3	DABCO·$1.7H_2O$–AcOH	0.8 mL CH_3CN	6	96
4	DABCO–AcOH–$3H_2O$	0.8 mL CH_3CN	6	94
5	DABCO–AcOH–$10H_2O$	3.5 mL CH_3CN	12	73
6	DABCO–AcOH–$3H_2O$	0.5 mL DMF	6	95
7	DABCO–AcOH–$3H_2O$	1.8 mL dioxane	6	83
8[d]	DABCO–AcOH–$3H_2O$	0.8 mL CH_3CN	4	97
9[d]	First Recycle	0.8 mL CH_3CN	4	96
10	Second Recycle	0.8 mL CH_3CN	4	95
11	Third Recycle	0.8 mL CH_3CN	4	93
12	Fourth Recycle	0.8 mL CH_3CN	4	96
13	Fifth Recycle	0.8 mL CH_3CN	4	95

[a] Reaction run at 1.0 mmol scale with respect to **1a**.
[b] 1.0 equiv used based on DABCO.
[c] The minimum amount added to form a homogeneous solution.
[d] 2.0 equiv used based on DABCO.

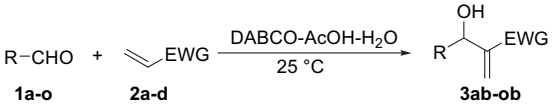
With DABCO–AcOH–$3H_2O$ as both catalyst and solvent the reaction of *p*-nitrobenzaldehyde with butyl acrylate (3 equiv) gave Baylis–Hillman adduct in 86% yield for 12 h, which is slightly slower than the reaction with free DABCO in CH_3CN (2 mL, *c*=0.5 M) due to the limited solubility of *p*-nitrobenzaldehyde in the DABCO–AcOH–$3H_2O$ solvent–catalyst system. The reaction rate decreased further in DABCO–AcOH–$10H_2O$ (Table 2, entries 1 and 2) and a biphasic mixture was observed. Therefore, some CH_3CN (0.8 mL) was added

as co-solvent to form homogeneous solution and the reaction rate restored giving the desired adduct in 94% yield in 6 h with DABCO–AcOH–3H_2O. Using DMF (0.5 mL) as co-solvent gave a comparable result to that of CH_3CN while a slower reaction was observed using dioxane (Table 2, entries 4, 6 and 7). The reaction could complete in 4 h with 2 equiv loading of DABCO–AcOH–3H_2O.

The recyclability of DABCO–AcOH–H_2O solvent–catalyst system was then investigated. After completion of the reaction, toluene (10 mL) was added to dilute the reaction mixture and dissolve the Baylis–Hillman adduct. The protic-ionic-liquid solvent–catalyst, DABCO–AcOH–H_2O, separated from the toluene phase. However, there was still some DABCO–AcOH residue in the toluene phase. Extraction of the toluene phase with water (5 mL) followed by removal of water from the aqueous phase by rotavapour led to complete recovering of the protic-ionic-liquid. Alternatively, water (5 mL) and toluene (10 mL) were added to the reaction mixture after completion of the reaction to dissolve the organics and the DABCO–AcOH salt in toluene and water, respectively. No DABCO–AcOH residue was detected in the organic phase using this work-up procedure. Removal of extra water from the aqueous phase recovered the DABCO–AcOH–H_2O solvent–catalyst system, which has been reused for five times showing no significant loss of activity (Table 2, entries 8–13).

Scope of the DABCO–AcOH–H_2O solvent–catalyst system promoted Baylis–Hillman reaction was explored (Table 3). Similar to the Baylis–Hillman reaction with free DABCO, electron-neutral aldehydes, such as benzaldehyde, *p*-methyl- and *p*-halogen-benzaldehydes, furaldehyde and electron-deficient aldehydes such as *p*-, *m*-, and *o*-nitrobenzaldehydes (Table 3, entries 4–6 and 8–11), reacted with methyl and butyl acrylates smoothly to give adducts in good to excellent yields in reasonable time while electron-rich one, *p*-methoxy benzaldehyde, reacted much slower (Table 3, entry 12).

Table 3
Scope of the DABCO–AcOH–H_2O solvent–catalyst promoted Baylis–Hillman reaction[a]



Entry	R	EWG	Time (h)	Yield (%)
1	*p*-$NO_2C_6H_4$ (**1a**)	Me (**2b**)	4	96
2	*p*-$NO_2C_6H_4$ (**1a**)	Me_3C (**2c**)	48	72
3	*p*-$NO_2C_6H_4$ (**1a**)	CN (**2d**)	4	92
4	*o*-$NO_2C_6H_4$ (**1b**)	Bu (**2a**)	6	97
5	*m*-$NO_2C_6H_4$ (**1c**)	Bu (**2a**)	12	98
6	C_6H_5 (**1d**)	Bu (**2a**)	48	82(79)[c]
7	C_6H_5 (**1d**)	CN (**2d**)	24	91[b](71)[c]
8	*p*-ClC_6H_4 (**1e**)	Me (**2b**)	48	70
9	*p*-$CH_3C_6H_4$ (**1f**)	Bu (**2a**)	48	69[c]
10	*p*-BrC_6H_4 (**1g**)	Bu (**2a**)	48	87(85)[c]
11	Furaldehyde (**1h**)	Bu (**2a**)	48	89[c]
12	*p*-$CH_3OC_6H_4$ (**1i**)	Bu (**2a**)	48	29
13	*p*-$CHOC_6H_4$ (**1j**)	Bu (**2a**)	24	69
14	*trans*-$C_6H_5CH{=}CH$ (**1k**)	Bu (**2a**)	48	63
15	*p*-$MeOC_6H_4CH{=}CH$ (**1l**)	Bu (**2a**)	56	22
16	*o*-$MeOC_6H_4CH{=}CH$ (**1m**)	Bu (**2a**)	76	38
17	$PhCH_2CH_2CHO$ (**1n**)	Me (**2b**)	48	67
18	$CH_3(CH_2)_6CHO$ (**1o**)	Me (**2b**)	48	41

[a] Reaction run at 1.0 mmol scale with respect to **1a**, using 2.0 equiv DABCO–AcOH–3H_2O based on DABCO and 0.8 mL CH_3CN as co-solvent.
[b] 1.0 mL DMF as co-solvent.
[c] No co-solvent used.

It is noteworthy to point out that for liquid aldehydes no co-solvent, such as CH_3CN or DMF is necessary. Terephthalaldehyde reacted with butyl acrylate affording mono-adduct in 69% yield while phthaldialdehyde gave a complicated mixture (Table 3, entry 13). The size of alkoxyl group of acrylates showed influences on reaction rate while a substituent on the carbon–carbon double bond blocked the reaction. For example, reaction of *p*-nitrobenzaldehyde with *tert*-butyl acrylate gave the corresponding adduct in 72% yield for 48 h, much slower than the reaction of methyl or *n*-butyl acrylates, which gave adducts in about 96–97% yields in 4 h (Table 3, entries 1 and 2). No reaction occurred for methyl crotonate under the otherwise identical conditions. Acrylonitrile reacted with *p*-nitrobenzaldehyde similarly to that of methyl and butyl acrylates (Table 3, entries 1 and 3). Interestingly, reaction of acrylonitrile with benzaldehyde proceeded significantly faster using DMF as co-solvent (Table 3, entry 7). Cinnamaldehyde and *p*- or *o*-methoxycinnamaldehydes also reacted smoothly in the DABCO–AcOH–H_2O promoted Baylis–Hillman reaction (Table 3, entries 14–16). The reaction of *p*-nitrocinnamaldehyde with butyl acrylate completed in 6 h, but the adduct was rather thermally unstable and decomposed before full characterization. Aliphatic aldehydes, such as 3-phenylpropionaldehyde and octyl aldehyde, reacted similarly to the electron-neutral aromatic aldehydes, giving the corresponding adducts in 67% and 41% yields, respectively, in 48 h (Table 3, entries 17–18). However, aldimines such as *N*-(*p*-methylbenzenesulfonyl) benzaldimine decomposed immediately to give benzaldehyde upon contacting with DABCO–AcOH–H_2O.

In summary, a recyclable protic-ionic-liquid solvent–catalyst system, DABCO–AcOH–H_2O, has been developed and used in the Baylis–Hillman reaction of aromatic aldehydes, aliphatic aldehydes, and cinnamaldehydes with acrylates and acrylonitrile. The protic-ionic-liquid could be readily prepared by simply mixing the components of DABCO, AcOH, and water at given ratios. The Baylis–Hillman reaction promoted by the protic-ionic-liquid solvent–catalyst system proceeded as well as that with free DABCO. The DABCO–AcOH–H_2O solvent–catalyst system could be recycled for at least 5 times showing no significant loss of activity.

3. Experimental

3.1. General

All manipulations were carried out in the air. All commercially available chemicals were used as-received. Products were identified by NMR spectroscopy and HRMS. ^1H NMR (500 or 400 MHz), $^{13}C\{^1H\}$ NMR (125 or 100 MHz) spectra were recorded at ambient temperatures, using $CDCl_3$ as solvent. ^1H and $^{13}C\{^1H\}$ NMR chemical shifts were reported in ppm relative to internal Me_4Si or residue of $CDCl_3$. Mass spectra were obtained at an ionization potential of 70 eV.

3.2. Preparation of 1,4-diazabicyclic [2,2,2]octane hydrate (DABCO·1.7H_2O)

Commercially available DABCO (11.2 g) (Indeed, the commercial DABCO from Alfa Aesar is partly hydrate) was dissolved in pure water (50 mL) at 80 °C. The solution was cooled to room temperature to form a colorless crystalline material, which was filtrated and dried in air. Elemental analyses showed that DABCO hydrate contained 1.7H_2O per molecule. Cacld for $C_6H_{12}N_2\cdot 1.7H_2O$: C, 50.47; H, 10.87; N, 19.62; found: C, 50.24; H, 10.65; N, 19.75.

3.3. General procedure for Baylis–Hillman reaction

To a flask (10 mL) containing 0.5 g DABCO–AcOH–H_2O (1/1/3 mol ratio) (2 mmol based on DABCO) composite were added aldehyde (1 mmol) and acrylate or acrylonitrile (3mmole) at room temperature (ca. 20 °C). A few drops (about 0.5 mL) of CH_3CN were added to the mixture to form a homogeneous solution. (For liquid aldehydes the co-solvent such as CH_3CN was not necessary provided that a homogeneous solution formed by the reaction mixture itself). The reaction mixture was stirred at room temperature monitored by TLC

until aldehyde was consumed. Then the reaction mixture was diluted with water (5 mL) and extracted with toluene (2×10 mL). The toluene extract was dried with Na_2SO_4, filtered and concentrated. The resulting residue was purified by flash column chromatography to offer the Baylis–Hillman adducts.

*3.3.1. 2-Hydroxyl-2-(4-nitrophenyl)methyl acrylic acid butyl ester (**3aa**)*[18]. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 8.22 (d, *J*=8.4 Hz, 2H, Ar), 7.59 (d, *J*=8.8 Hz, 2H, Ar), 6.41 (s, 1H), 5.87 (s, 1H), 5.63 (s, 1H, C*H*OH), 4.15 (t, *J*=6.4 Hz, 2H), 3.43 (br s, 1H, OH), 1.66–1.56 (m, 2H), 1.39–1.30 (m, 2H), 0.92 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.01, 148.79, 147.40, 141.23, 127.35, 126.97, 123.58, 72.71, 65.16, 30.44, 19.08, 13.61.

*3.3.2. 2-Hydroxyl-2-(4-nitrophenyl)methyl acrylic acid methyl ester (**3ab**)*[18]. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 8.19 (d, *J*=8.8 Hz, 2H, Ar), 7.57 (d, *J*=8.8 Hz, 2H, Ar), 6.40 (s, 1H), 5.90 (s, 1H), 5.63 (s, 1H, C*H*OH), 3.74 (s, 3H), 3.49 (br s, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.30, 148.93, 147.24, 141.14, 127.47, 127.01, 123.52, 72.12, 52.14.

*3.3.3. 2-Hydroxyl-2-(4-nitrophenyl)methyl acrylic acid tert-butyl ester (**3ac**)*[19]. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 8.20 (d, *J*=8.8 Hz, 2H, Ar), 7.57 (d, *J*=8.8 Hz, 2H, Ar), 6.31 (s, 1H), 5.76 (s, 1H), 5.57 (d, *J*=4.8 Hz, 1H, CHOH), 3.54 (br s, 1H, OH), 1.42 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 165.27, 149.08, 147.31, 142.29, 127.28, 126.54, 123.54, 82.35, 72.93, 27.95.

*3.3.4. 2-Hydroxyl-2-(4-nitrophenyl)methyl acrylonitrile (**3ad**)*[20]. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 8.23 (d, *J*=8.8 Hz, 2H, Ar), 7.60 (d, *J*=8.8 Hz, 2H, Ar), 6.19 (s, 1H), 6.10 (s, 1H), 5.45 (s, 1H, CHOH), 3.57 (br s, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 147.86, 146.35, 131.50, 127.41, 125.30, 124.02, 116.44, 73.1.

*3.3.5. 2-Hydroxyl-2-(2-nitrophenyl)methyl acrylic acid butyl ester (**3ba**)*[21]. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.97 (d, *J*=8.4 Hz, 1H, Ar), 7.75 (d, *J*=8.0 Hz, 1H, Ar), 7.66 (t, *J*=7.6 Hz, 1H, Ar), 7.48 (t, *J*=8.0 Hz, 1H, Ar), 6.40 (s, 1H), 6.19 (s, 1H), 5.77 (s, 1H, C*H*OH), 4.18–4.08 (m, 2H), 3.50 (br s, 1H, OH), 1.61–1.54 (m, 2H), 1.33–1.24 (m, 2H), 0.90 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.31, 148.57, 141.76, 136.87, 133.76, 129.25, 128.93, 125.42, 124.83, 67.50, 65.33, 30.74, 19.35, 13.95.

*3.3.6. 2-Hydroxyl-2-(3-nitrophenyl)methyl acrylic acid butyl ester (**3ca**)*[19]. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 8.27 (s, 1H, Ar), 8.17–8.15 (dd, J_1=8.4 Hz, J_2=1.6 Hz, 1H, Ar), 7.76 (d, *J*=7.6 Hz, 1H, Ar), 7.54 (t, *J*=8.0 Hz, 1H, Ar), 6.42 (s, 1H), 5.91 (s, 1H), 5.64 (d, *J*=6.4 Hz, 1H, C*H*OH), 4.15 (t, *J*=6.8 Hz, 2H), 3.42–3.40 (m, 1H, OH), 1.66–1.59 (m, 2H), 1.39–1.30 (m, 2H), 0.92 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 165.93, 148.18, 143.91, 141.41, 132.83, 129.27, 126.66, 122.61, 121.64, 72.19, 65.05, 30.38, 19.03, 13.56.

*3.3.7. 2-Hydroxyl-2-phenyl methyl acrylic acid butyl ester (**3da**)*[22]. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.39–7.27 (m, 5H, Ar), 6.35 (s, 1H), 5.84 (s, 1H), 5.56 (d, *J*=6.4 Hz, 1H, C*H*OH), 4.12 (t, *J*=6.4 Hz, 2H), 3.17 (t, *J*=6.4 Hz, 1H, OH), 1.63–1.56 (m, 2H), 1.35–1.29 (m, 2H), 0.91 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.42, 142.16, 141.36, 128.42, 127.80, 126.60, 125.92, 73.32, 64.81, 30.49, 19.10, 13.68.

*3.3.8. 2-Hydroxyl-2-(4-methylphenyl)methyl acrylic acid butyl ester (**3fa**).* ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.24 (d, *J*=8.1 Hz, 2H), 7.14 (d, *J*=7.9 Hz, 2H), 6.32 (s, 1H), 5.83 (s, 1H), 5.51 (s, 1H, C*H*OH), 4.12–4.08 (m, 2H), 3.10 (s, 1H, OH), 2.33 (s, 3H), 1.60–1.54 (m, 2H), 1.34–1.25 (m, 2H), 0.89 (t, *J*=7.40 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.38, 142.55, 138.67, 137.32, 129.03, 126.68, 125.23, 72.79, 64.67, 30.52, 21.09, 19.10, 13.66. HREI-MS *m*/*z*: calcd for $C_{15}H_{20}O_3$: 248.1412, found: 248.1414.

*3.3.9. 2-Hydroxyl-2-(4-bromophenyl)methyl acrylic acid butyl ester (**3ga**).* ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.46 (d, *J*=8.4 Hz, 2H), 7.24 (d, *J*=8.4 Hz, 2H), 6.33 (s, 1H), 5.81 (s, 1H), 5.48 (d, *J*=5.1 Hz, 1H, C*H*OH), 4.11 (t, *J*=6.6 Hz, 2H), 3.25 (d, *J*=5.6 Hz, 1H, OH), 1.74–1.56 (m, 2H), 1.35–1.28 (m, 2H), 0.90 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.14, 141.98, 140.63, 131.41, 128.48, 125.79, 121.62, 72.31, 64.87, 30.46, 19.09, 13.67. HREI-MS *m*/*z*: calcd for $C_{14}H_{17}O_3Br$ 312.0361, found: 312.0363.

*3.3.10. 2-Hydroxyl-2-(4-methoxyphenyl)methyl acrylic acid butyl ester (**3ia**).* ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.27 (d, *J*=8.7 Hz, 2H), 6.86 (d, *J*=8.6 Hz, 2H), 6.31 (s, 1H), 5.84 (s, 1H), 5.51 (s, 1H, C*H*OH), 4.14–4.07 (m, 2H), 3.78 (s, 3H), 3.09 (s, 1H, OH), 1.61–1.55 (m, 2H), 1.34–1.26 (m, 2H), 0.89 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.44, 159.16, 142.50, 133.66, 128.01, 125.20, 113.76, 72.61, 64.73, 55.21, 30.50, 19.09, 13.67. HREI-MS *m*/*z*: calcd for $C_{15}H_{20}O_4$: 264.1362, found: 264.1363.

*3.3.11. 2-Hydroxyl-2-(4-formylphenyl)methyl acrylic acid butyl ester (**3ja**).* ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 9.94 (s, 1H, CHO), 7.81 (d, *J*=8.0 Hz, 2H), 7.52 (d, *J*=7.6 Hz, 2H), 6.35 (s, 1H), 5.86 (s, 1H), 5.58 (s, 1H, C*H*OH), 4.08 (t, *J*=6.4 Hz, 2H), 3.67–3.62 (m, 1H, OH), 1.59–1.52 (m, 2H), 1.32–1.23 (m, 2H), 0.86 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 192.14, 165.95, 148.66, 141.83, 135.60, 129.78, 127.30, 126.14, 72.37, 64.84, 30.37, 19.00, 13.58. HREI-MS *m*/*z*: calcd for $C_{15}H_{18}O_4$: 262.1205, found: 262.1206.

*3.3.12. (E)-Butyl 3-hydroxy-5-phenyl-2-methylenepent-4-enoate (**3ka**).* ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.38 (d, *J*=7.4 Hz, 2H), 7.31 (t, *J*=7.4 Hz, 2H), 7.24 (t, *J*=7.4 Hz, 1H), 6.66 (d, *J*=15.9 Hz, 1H), 6.30 (dd, J_1=16.8 Hz, J_1=6.3 Hz, 2H), 5.90 (s, 1H), 5.13 (dd, J_1=J_2=6.1 Hz, 1H, C*H*OH), 4.19 (t, *J*=6.6 Hz, 2H), 3.07 (d, *J*=6.1 Hz, 1H, OH), 1.72–1.63 (m, 2H), 1.44–1.37 (m, 2H), 0.93 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.40, 141.79, 136.58, 131.30, 129.52, 128.55, 127.77, 126.61, 125.38, 71.73, 64.85, 30.60, 19.22, 13.71. HREI-MS *m*/*z*: calcd for $C_{16}H_{20}O_3$: 260.1412, found: 260.1415.

*3.3.13. (E)-Butyl 3-hydroxy-5-(4-methoxyphenyl)-2-methylene pent-4-enoate (**3la**).* ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.34 (d, *J*=8.4 Hz, 2H), 6.87 (d, *J*=8.8 Hz, 2H), 6.62 (d, *J*=16.0 Hz, 1H), 6.30 (s, 1H), 6.18 (dd, J_1=16.0 Hz, J_1=6.8 Hz, 1H), 5.91 (s, 1H), 5.12 (dd, J_1=J_1=6.4 Hz, 1H, C*H*OH), 4.21 (t, *J*=6.8 Hz, 2H), 3.82 (s, 3H), 2.97 (d, *J*=6.4 Hz, 1H, OH), 1.70–1.65 (m, 2H), 1.47–1.38 (m, 2H), 0.95 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.42, 159.33, 141.93, 130.92, 129.30, 127.77, 127.24, 125.14, 113.94, 71.90, 64.77, 55.20, 30.57, 19.18, 13.67. HREI-MS *m*/*z*: calcd for $C_{17}H_{22}O_4$: 290.1518, found: 290.1520.

*3.3.14. (E)-Butyl 3-hydroxy-5-(2-methoxyphenyl)-2-methylene pent-4-enoate (**3ma**).* ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.44 (dd, J_1=7.6 Hz, J_1=1.2 Hz, 1H), 7.24 (td, J_1=8.0 Hz, J_1=1.2 Hz, 1H), 7.00 (d, *J*=16.0 Hz, 1H), 6.92 (t, *J*=7.6 Hz, 1H), 6.87 (d, *J*=8.0 Hz, 1H), 6.34 (dd, J_1=16.0 Hz, J_1=7.6 Hz, 1H), 6.30 (s, 1H), 5.93 (s, 1H), 5.16 (dd, J_1=J_1=5.6 Hz, 1H, C*H*OH), 4.21 (t, *J*=6.4 Hz, 2H), 3.84 (s, 3H), 3.14 (br s, 1H, OH), 1.71–1.64 (m, 2H), 1.47–1.38 (m, 2H), 0.95 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.41, 156.83, 142.11, 130.11, 128.79, 126.97, 126.23, 125.53, 125.09, 120.55, 110.82, 72.00, 64.71, 55.28, 30.56, 19.19, 13.68. HREI-MS *m*/*z*: calcd for $C_{17}H_{22}O_4$: 290.1518, found: 290.1519.

*3.3.15. 2-Hydroxyl-2-phenyl methyl acrylonitrile (**3dd**)*[9a]. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.42–7.35 (m, 5H, Ar), 6.06 (s, 1H),

5.98 (s, 1H), 5.22 (s, 1H, CHOH), 3.28 (br s, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 138.16, 129.11, 127.83, 127.80, 125.52, 125.13, 116.01, 72.91.

*3.3.16. 2-Hydroxyl-2-(4-chlorophenyl)methyl acrylic acid methyl ester (**3eb**)*[21]. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.31 (s, 4H, Ar), 6.34 (s, 1H), 5.85 (s, 1H), 5.51 (s, 1H, C*H*OH), 3.72 (s, 3H), 3.33 (br s, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.63, 141.62, 139.82, 133.56, 128.58, 128.02, 126.34, 72.55, 52.07.

*3.3.17. 2-Hydroxyl-2-(furan-2-yl) methyl acrylic acid butyl ester (**3ha**)*[22]. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.38 (s, 1H), 6.39 (s, 1H), 6.34–6.33 (dd, J_1=3.2 Hz, J_2=1.8 Hz, 1H), 6.26 (d, J=3.2 Hz, 1H), 5.93 (s, 1H), 5.59 (d, J=6.6 Hz, 1H, C*H*OH), 4.19–4.14 (m, 2H), 3.19 (d, J=6.7 Hz, 1H, OH), 1.65–1.59 (m, 2H), 1.39–1.32 (m, 2H), 0.92 (t, J=7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C), δ (ppm): 165.88, 154.52, 142.00, 140.14, 125.75, 110.16, 106.94, 65.97, 64.52, 30.33, 18.87, 13.43.

*3.3.18. Methyl 3-hydroxy-2-methylene-5-phenylpentanoate (**3nb**)*[23,24]. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C), δ (ppm): 7.30–7.17 (m, 5H), 6.24 (s, 1H), 5.81 (s, 1H), 4.42 (d, J=6.0 Hz, 1H, C*H*OH), 3.77 (s, 3H), 2.83 (br s, 1H, OH), 2.73–2.67 (m, 2H), 2.02–1.95 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C), δ (ppm): 166.57, 142.51, 141.39, 128.04, 127.97, 125.44, 124.54, 69.81, 51.40, 37.51, 31.67.

*3.3.19. Methyl 3-hydroxy-2-methylenedecanoate (**3ob**)*[24]. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C), δ (ppm): 6.23 (s, 1H), 5.80 (s, 1H), 4.39 (d, J=6.26 Hz, 1H, C*H*OH), 3.78 (s, 3H), 2.62 (d, J=6.74 Hz, 1H, OH), 1.66–1.61 (m, 2H), 1.33–1.26 (m, 10H), 0.88 (t, J=6.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C), δ (ppm): 167.37, 143.60, 124.81, 71.17, 52.03, 36.82, 32.22, 29.91, 29.64, 26.14, 23.01, 14.38.

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