Methyl Salicylate as a Selective Methylation Agent for the Esterification of Carboxylic Acids

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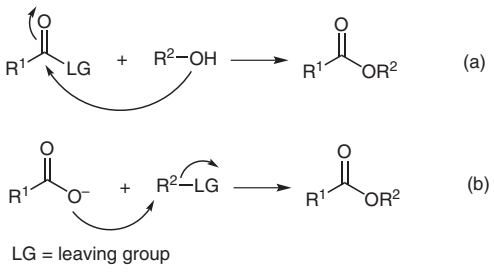
Abstract: Methyl salicylate is a selective and inexpensive methylating agent for the esterification of carboxylic acids with a wide range of functional group tolerance. The intramolecular hydrogen bonds between the carboxylate and hydroxyl groups in methyl salicylate are essential for the transformation. Allyl, benzyl, methallyl, and propargyl salicylates can also be used as alkylating agents for the preparation of the corresponding alkyl carboxylates.

Key words: carboxylic acid, esterification, esters, alkylation, methyl salicylate

The esterification of carboxylic acids is an important transformation in organic chemistry and it has been widely used in organic synthesis for the preparation of drugs, fine chemicals, materials, and the protection of carboxylic acids.[1] Numerous methods for the conversion of carboxylic acids into esters can be envisioned in two general schemes (Scheme 1). The first is nucleophilic attack on the carbonyl carbon of the carboxylic acid or acid derivative by an alcohol [Scheme 1 (a)]; this direct esterification proceeds at a reasonable rate only in the presence of an acid catalyst (LG = OH).[1] The reversibility of this acid-catalyzed esterification often requires the removal of water and/or the use of a large excess of alcohol to drive the reaction to completion. Difficulties are also encountered with acid-sensitive compounds and sterically hindered carboxylic acids. The conversion of a carboxylic acid to its acyl halide or anhydride results in an additional preparative step.



Scheme 1 Major methods for the esterification of carboxylic acids

Another method is the alkylation of the carboxyl oxygen atom of a carboxylate anion by an appropriate alkylating agent [Scheme 1 (b)]. This method does not suffer from problems associated with reversibility and steric hindrance.[2] In the preparation of methyl carboxylates, methylation reactions are frequently effected with methyl iodide,[3] dimethyl sulfate,[4] diazomethane,[5] methyl *p*-tolyltriazene,[6] and others.[7] However, these methods have limitations. In many cases, the methylating reagents are environmentally hazardous, difficult to handle, not readily available, or costly. For example, both methyl iodide[8] and dimethyl sulfate[9] are highly toxic. Methyl iodide is a suspected carcinogen, and its low boiling point (40 °C) may cause air emission problems. Diazomethane[10] and methyl *p*-tolyltriazene[6] are toxic and dangerous (explosive decomposition). Dimethyl carbonate is considered as a green methylating reagent. However, methylation of a carboxylic acid to an ester by dimethyl carbonate requires high temperatures and an autoclave,[7f,g] or use of one equivalent of expensive base (DBU) and a large excess of dimethyl carbonate as the solvent.[7h]

Methyl salicylate, commonly called oil of wintergreen, is an organic ester naturally produced by many species of plants. It may be found in creams, ointments, lotions, liniments, and medicated oils intended for topical application to relieve musculoskeletal aches and pains.[11] It is added to toothpaste, candy, and soft drinks as an alternative to other flavors, and it is used as a fragrance additive in shampoos and decorative cosmetics.[12] Structural studies show that two strong intramolecular hydrogen bonds exist in methyl salicylate. One is between the hydroxyl hydrogen and the carbonyl oxygen, and another is between the hydroxyl hydrogen and the methoxy oxygen (Scheme 2).[13] In both structures, the methyl group is positioned out of the plane of the benzene ring in order to minimize steric repulsions for free rotation.[14] Methyl salicylate has been used as a methylating reagent for tertiary amines.[15] We surmise that with the activation of the strong intramolecular hydrogen bonds and the orientation of the methyl group, methyl salicylate may be exploited as a good methylating reagent for the conversion of carboxylic acids into esters (Scheme 2). In addition, salicylic acid as a byproduct may be easily recovered from the aqueous phase by simple filtration. Herein we report the esterification of carboxylic acids by the use of commercially available, inexpensive, and less toxic methyl salicylate as the methylating agent. The reaction tolerates a wide range of functional groups and salicylic acid is readily recovered.

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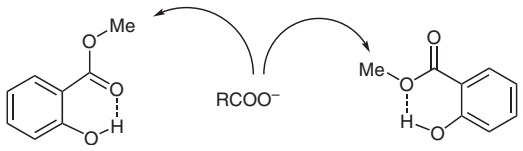
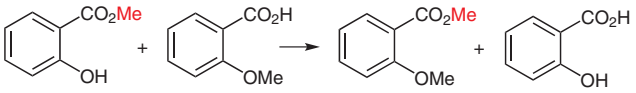


Scheme 2 Intramolecular hydrogen bonds in methyl salicylate facilitate nucleophilic substitution

Initially, the reaction of methyl salicylate (**1a**) with 2-methoxybenzoic acid (**2a**) was chosen as a model reaction to optimize the reaction conditions (Table 1). The reaction was conducted in air and monitored by TLC. To ensure the intramolecular hydrogen bonds in methyl salicylate are retained, and to increase the nucleophilicity of the carboxylic acids, the base was firstly allowed to react with the carboxylic acid to generate a carboxylate anion. Varying solvents, bases, temperatures, and mole ratios of substrate, reagent, and base were investigated. As shown in Table 1, solvent screening revealed that *N*,*N*-dimethylacetamide (DMA) is the best of choice for this reaction (entry 8), though the reaction proceeded well in other nonprotic polar solvents such as *N*,*N*-dimethylformamide, dimethyl sulfoxide and *N*-methylpyrrolidin-2-one (entries 1–3). In water, the hydrolysis of methyl salicylate was observed and no product was produced (entry 4). When glycol was used as the solvent, methyl salicylate was transformed into 2-hydroxylethyl salicylate due to an ester exchange reaction (entry 5). No reaction occurred in 1,2-dichloroethane and toluene (entries 6 and 7). Next, the reaction was investigated in the presence of different bases. It was found that potassium carbonate gave the best product yield (entry 8), while sodium carbonate and some organic bases were less effective (entries 9–12). Further exploration showed that 0.6 equivalents of potassium carbonate were sufficient to generate the product in excellent yields (entries 8, 13, and 14), and the mole ratio of methyl salicylate to 2-methoxybenzoic acid should not be less than 1.5:1 (entries 8, 15, and 16). In addition, the reaction gave lower yields at lower temperatures (entry 18). Thus, the optimized reaction conditions for the esterification of carboxylic acids with methyl salicylate used potassium carbonate (0.6 equiv) and methyl salicylate (1.5 equiv) in *N*,*N*-dimethylacetamide at 110 °C.

Having defined the optimum reaction conditions, we investigated the scope of the esterification reaction with respect to carboxylic acids. As shown in Table 2, the present method is generally applicable to aromatic, aliphatic, and heterocyclic acids. In general, carboxylic acids with a variety of substituted groups afforded the products in good to excellent yields under the optimum reaction conditions. In addition to 2-methoxybenzoic acid (**2a**), other substituted aromatic acids containing electron-rich groups showed good reactivity (entries 1–8). The reaction of methyl salicylate with aromatic acids bearing 4-methoxy, 4-hydroxy, 3-methyl, 2-amino, 3-amino, 4-amino, and 3-acetamido groups gave the desired products **3b**–**h** in 75–94% yields (entries 2–8). For 4-hydroxybenzoic acid and

Table 1 Esterification of 2-Methoxybenzoic Acid with Methyl Salicylate: Optimization of the Reaction Conditions[a]



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

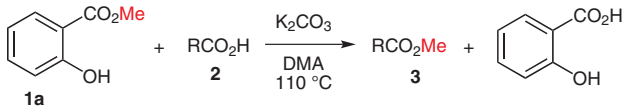
Entry	Solvent	Base	Mole ratio (**1a**/**2a**/base)	Yield[b] (%) of **3a**
1	NMP	K_2CO_3	1.5:1:0.6	89
2	DMF	K_2CO_3	1.5:1:0.6	86
3	DMSO	K_2CO_3	1.5:1:0.6	76
4	H_2O	K_2CO_3	1.5:1:0.6	–[c]
5	glycol	K_2CO_3	1.5:1:0.6	–[d]
6	DCE	K_2CO_3	1.5:1:0.6	–
7	toluene	K_2CO_3	1.5:1:0.6	–
8	DMA	K_2CO_3	1.5:1:0.6	92
9	DMA	Na_2CO_3	1.5:1:0.6	79
10	DMA	pyridine	1.5:1:1	26
11	DMA	DBU	1.5:1:1	78
12	DMA	DIPEA	1.5:1:1	60
13	DMA	K_2CO_3	1.5:1:0.5	90
14	DMA	K_2CO_3	1.5:1:1	93
15	DMA	K_2CO_3	1:1:0.6	84
16	DMA	K_2CO_3	2:1:0.6	92
17[e]	DMA	K_2CO_3	1.5:1:0.6	93
18[f]	DMA	K_2CO_3	1.5:1:0.6	65

[a] All reactions were performed in air at 110 °C for 24 h.
[b] Isolated yield.
[c] Hydrolysis of methyl salicylate occurred.
[d] 2-Hydroxyethyl salicylate was produced.
[e] 130 °C.
[f] 90 °C.

4-aminobenzoic acid, less than 1% of methyl 4-methoxybenzoate and 3% of methyl *N*-(methylamino)benzoate were observed, demonstrating good selectivity (entries 3, 5–7). We next examined the methylation reaction of aromatic acids bearing electron-deficient groups. The methylation of 3-nitro-, 4-nitro-, 2-chloro-, 2-bromo-, 4-formyl-, and 4-(ethoxycarbonyl)benzoic acid proceeded smoothly to give the corresponding products **3i**–**n** in 88–93% yields (entries 9–14). Alkylcarboxylic acids underwent the esterification as well as aromatic acids (entries 15–20). The protocol was also applied to the esterification of methacrylic acid and cinnamic acid, giving the desired methyl methacrylate (**3u**) and methyl cinnamate (**3v**) in 72% and 79% yield respectively (entries 21 and 22). Finally, the methylation of carboxylic acids with a heteroarene, 1*H*-indol-3-ylacetic acid, pyridine-3-carboxylic

acid, and thiophene-2-carboxylic acid, gave the corresponding esters **3w**, **3x**, and **3y** in 79%, 81%, and 83% yields, respectively, under the same reaction conditions (entries 23–25). Notably, when the reaction was completed, salicylic acid was readily recovered as a white precipitate after hydrolysis of the excess of methyl salicylate, extraction of the reaction mixture, and acidification of the aqueous phase with hydrochloric acid.

Table 2 Esterification of Various Carboxylic Acids with Methyl Salicylate[a]

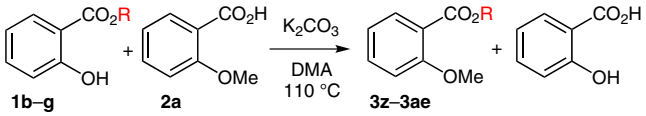


Entry	R	Product	Yield[b] (%)
1	2-$MeOC_6H_4$	**3a**	92
2	4-$MeOC_6H_4$	**3b**	93
3[c]	4-HOC_6H_4	**3c**	75
4	3-MeC_6H_4	**3d**	94
5[d]	2-$H_2NC_6H_4$	**3e**	84
6[d]	3-$H_2NC_6H_4$	**3f**	81
7[d]	4-$H_2NC_6H_4$	**3g**	79
8	3-$AcHNC_6H_4$	**3h**	86
9	4-$O_2NC_6H_4$	**3i**	92
10	3-$O_2NC_6H_4$	**3j**	93
11	2-ClC_6H_4	**3k**	90
12	2-BrC_6H_4	**3l**	91
13	4-OHC_6H_4	**3m**	89
14	4-$EtO_2CC_6H_4$	**3n**	88
15	*t*-Bu	**3o**	80
16	Cy	**3p**	88
17	$(CH_2)_{12}Me$	**3q**	95
18	$(CH_2)_2Ph$	**3r**	86
19	1-naphthylmethyl	**3s**	95
20	CH(OH)Ph	**3t**	74
21	$CMe{=}CH_2$	**3u**	72
22	(E)-CH=CHPh	**3v**	79
23	1*H*-indol-3-ylmethyl	**3w**	79
24	3-pyridyl	**3x**	81
25	2-thienyl	**3y**	83

[a] Reaction conditions: carboxylic acid **2** (25 mmol), K_2CO_3 (15 mmol), methyl salicylate (**1a**, 37.5 mmol), DMA (50 mL), 110 °C, air.
[b] Isolated yield.
[c] About 1% of methyl 4-methoxybenzoate was observed.
[d] About 3% of methyl *N*-(methylamino)benzoate was detected.

Esterification of carboxylic acids with other alkyl salicylates was also explored. As shown in Table 3, the reaction of 2-methoxybenzoic acid (**2a**) with allyl, benzyl, methallyl, and propargyl salicylates **1b–e** produced the corresponding allyl, benzyl, methallyl, and propargyl 2-methoxybenzoate **3z–ac** in 80–92% yields (entries 1–4). The reactions of less active ethyl salicylate (**1f**) and isopropyl salicylate (**1g**) with 2-methoxybenzoic acid (**2a**) were carried out at higher temperatures. While ethyl salicylate (**1f**) gave ethyl 2-methoxybenzoate (**3ad**) in 70% yield at 130 °C (entry 5), isopropyl salicylate (**1g**) generated only traces of product (entry 6), suggesting that the steric hindrance of the alkyl group in this alkyl salicylate significantly retarded the reaction.

Table 3 Esterification of 2-Methoxybenzoic Acid with Alkyl Salicylates[a]

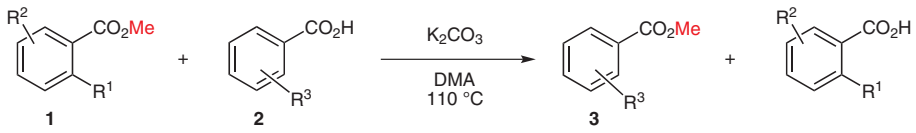


Entry	**1**	R	Product	Yield[b] (%)
1	**1b**	$CH_2CH{=}CH_2$	**3z**	92
2	**1c**	Bn	**3aa**	87
3	**1d**	$CH_2CMe{=}CH_2$	**3ab**	86
4	**1e**	$CH_2C{\equiv}CH$	**3ac**	80
5[c]	**1f**	Et	**3ad**	70
6[c]	**1g**	*i*-Pr	**3ae**	trace

[a] Reaction conditions: 2-methoxybenzoic acid (**2a**, 25 mmol), K_2CO_3 (15 mmol), alkyl salicylate **1** (37.5 mmol), DMA (50 mL), 110 °C, air.
[b] Isolated yield.
[c] At 130 °C.

To elucidate the importance of intramolecular hydrogen bonds in methyl salicylate for the esterification of carboxylic acids, the reaction of 2-methoxybenzoic acid (**2a**) and 4-nitrobenzoic acid (**2i**) with some other methyl benzoates under the same conditions were investigated. The results are summarized in Table 4 and they clearly showed that activation of the methyl carboxylate group by intramolecular hydrogen bonds in methyl salicylate is essential for the esterification reaction. As expected, methyl 5-nitrosalicylate (**1h**) underwent reaction with 2-methoxybenzoic acid (**2a**) and 4-nitrobenzoic acid (**2i**) as efficiently as methyl salicylate (**1a**) (entries 1, 2 and 6, 7) under the optimized conditions. At lower temperatures, however, the reactions of methyl 5-nitrosalicylate (**1h**) and methyl 4-nitrosalicylate (**1l**) with 4-nitrobenzoic acid (**2i**) gave lower product yields (entries 8 and 9). This indicates that the introduction of the electron-withdrawing group on the salicylate aromatic ring did not reduce the reaction temperature. Methyl benzoate (**1i**), methyl 4-hydroxybenzoate (**1j**), methyl 2-methoxybenzoate (**1m**), and methyl 4-nitrobenzoate (**1k**), in which there is no intramolecular

Table 4 Reaction of Substituted Methyl Benzoates with Substituted Benzoic Acids[a]



Entry	1	R^1	R^2	2	R^3	Product	Yield[b] (%)
1	**1a**	OH	H	**2a**	2-OMe	**3a**	92
2	**1h**	OH	5-NO_2	**2a**	2-OMe	**3a**	93
3	**1i**	H	H	**2a**	2-OMe	–	–
4	**1j**	H	4-OH	**2a**	2-OMe	–	–
5	**1k**	H	4-NO_2	**2a**	2-OMe	–	–
6	**1a**	OH	H	**2i**	4-NO_2	**3i**	93
7	**1h**	OH	5-NO_2	**2i**	4-NO_2	**3i**	95
8[c]	**1h**	OH	5-NO_2	**2i**	4-NO_2	**3i**	45
9[c]	**1l**	OH	4-NO_2	**2i**	4-NO_2	**3i**	32
10	**1i**	H	H	**2i**	4-NO_2	–	–
11	**1j**	H	4-OH	**2i**	4-NO_2	–	–
12	**1m**	OMe	H	**2i**	4-NO_2	–	–

[a] Reaction conditions: substituted benzoic acid **2** (25 mmol), K_2CO_3 (15 mmol), substituted methyl benzoate **1** (37.5 mmol), DMA (50 mL), 110 °C, in air.
[b] Isolated yield.
[c] At 90 °C.

hydrogen bond, did not react with 2-methoxybenzoic acid (**2a**) and 4-nitrobenzoic acid (**2i**) (entries 3–5 and 10–12).

In summary, we have discovered that commercially available, inexpensive, and less toxic methyl salicylate can be used as a selective methylating agent for the esterification of carboxylic acids with a wide range of functional group tolerance. Allyl, benzyl, methallyl, and propargyl salicylates can also be employed for the preparation of the corresponding alkyl carboxylates in good to excellent yields. Intramolecular hydrogen bonds in methyl salicylate are found to be the key to the successful esterification of carboxylic acids.

All reagents and solvents were purchased from commercial suppliers and used without further purification. TLC was carried out using silica gel GF254 plates. Melting points are uncorrected. ^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ using TMS as internal standard. GC-MS were made on a GC-MS spectrometer. HRMS analyses were made on a mass spectrometer using ESI ionization with TOF mass analyzer.

Except for methallyl 2-methoxybenzoate (**3ab**), all other products are known and they were identified by comparing their ^{1}H NMR spectra with those reported in the literature.

Methyl 2-Methoxybenzoate (3a); Typical Procedure
A mixture of 2-methoxybenzoic acid (3.8 g, 25 mmol) and K_2CO_3 (2.07 g, 15 mmol) in DMA (50 mL) was stirred at 110 °C for 0.5 h. Methyl salicylate (5.70 g, 37.5 mmol) was added and the resulting mixture was stirred for 24 h. The solvent was then removed in vacuo. After cooling to r.t., K_2CO_3 (2.42 g, 17.5 mmol) and water (50 mL) were added to hydrolyze the excess methyl salicylate. The resulting mixture was heated at 60 °C until methyl salicylate disappeared on TLC. Then, the solution was extracted with EtOAc (3 × 20 mL). The organic layer was washed with water, sat. aq NaCl solution, and dried (anhyd $MgSO_4$). Evaporation of solvent in vacuo afforded methyl 2-methoxybenzoate (3.82 g, 92%). More than 90% of salicylic acid was recovered as a white precipitate by acidifying the aqueous phase with 1 M HCl.

Methyl 2-Methoxybenzoate (3a)[16]
Colorless oil; yield: 3.82 g (92%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.80 (dd, *J* = 1.8, 7.8 Hz, 1 H), 7.46–7.49 (m, 1 H), 6.98–7.00 (m, 2 H), 3.92 (s, 3 H), 3.90 (s, 3 H).

Methyl 4-Methoxybenzoate (3b)[16]
White solid; yield: 3.86 g (93%); mp 47–48 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.4 Hz, 2 H), 6.93 (d, *J* = 8.4 Hz, 2 H), 3.89 (s, 3 H), 3.86 (s, 3 H).

Methyl 4-Hydroxybenzoate (3c)[4b]
White solid; yield: 2.85 g (75%); mp 127–128 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.8 Hz, 2 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 5.96 (br, 1 H), 3.90 (s, 3 H).

Methyl 3-Methylbenzoate (3d)[17]
Colorless oil; yield: 3.53 g (94%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (s, 1 H), 7.83 (d, *J* = 11.2 Hz, 1 H), 7.31–7.36 (m, 2 H), 3.91 (s, 3 H), 2.40 (s, 3 H).

Methyl 2-Aminobenzoate (3e)[16]
Colorless oil; yield: 3.17 g (84%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 8.0 Hz, 1 H), 7.30 (d, *J* = 7.6 Hz, 1 H), 6.66–6.72 (m, 2 H), 5.71 (br, 2 H), 3.87 (s, 3 H).

Methyl 3-Aminobenzoate (3f)[16]
Colorless oil; yield: 3.06 g (81%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 7.6 Hz, 1 H), 7.36 (s, 1 H), 7.23 (t, *J* = 8.0 Hz, 1 H), 6.88 (d, *J* = 8.0 Hz, 1 H), 3.89 (s, 3 H), 3.59 (br, 2 H).

Methyl 4-Aminobenzoate (3g)[16]
White solid; yield: 2.98 g (79%); mp 110–112 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.8 Hz, 2 H), 6.65 (d, *J* = 8.8 Hz, 2 H), 4.04 (br, 2 H), 3.85 (s, 3 H).

Methyl 3-Acetamidobenzoate (3h)[7i]
White solid; yield: 4.15 g (86%); mp 135–136 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (s, 1 H), 7.91 (d, *J* = 8.4 Hz, 1 H), 7.78 (d, *J* = 7.6 Hz, 1 H), 7.68 (br, 1 H), 7.41 (t, *J* = 8.0 Hz, 1 H), 3.90 (s, 3 H), 2.21 (s, 3 H).

Methyl 4-Nitrobenzoate (3i)[7i]
Pale yellow solid; yield: 4.16 g (92%); mp 95–96 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 9.2 Hz, 2 H), 8.23 (d, *J* = 8.4 Hz, 2 H), 3.99 (s, 3 H).

Methyl 3-Nitrobenzoate (3j)[7h]
Pale yellow solid; yield: 4.21 g (93%); mp 77–78 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.88 (s, 1 H), 8.43 (d, *J* = 8.0 Hz, 1 H), 8.38 (d, *J* = 8.0 Hz, 1 H), 7.69 (t, *J* = 8.0 Hz, 1 H), 4.00 (s, 3 H).

Methyl 2-Chlorobenzoate (3k)[18]
Colorless oil; yield: 3.83 g (90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 7.6 Hz, 1 H), 7.40–7.47 (m, 2 H), 7.34 (t, *J* = 7.6 Hz, 1 H), 3.94 (s, 3 H).

Methyl 2-Bromobenzoate (3l)[17]
Colorless oil; yield: 4.87 g (91%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 6.8 Hz, 1 H), 7.67 (d, *J* = 7.6 Hz, 1 H), 7.39 (m, 2 H), 3.94 (s, 3 H).

Methyl 4-Formylbenzoate (3m)[19]
White solid; yield: 3.65 g (89%); mp 61–62 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.11 (s, 1 H), 8.22 (d, *J* = 8.4 Hz, 2 H), 7.97 (d, *J* = 8.4 Hz, 2 H), 3.97 (s, 3 H).

Ethyl Methyl Terephthalate (3n)[20]
White solid; yield: 4.58 g (88%); mp 34–35 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (s, 4 H), 4.43 (q, *J* = 7.2 Hz, 2 H), 3.95 (s, 3 H), 1.43 (t, *J* = 7.2 Hz, 3 H).

Methyl Trimethylacetate(3o)[7i]
Colorless oil; yield: 2.33 g (80%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.67 (s, 3 H), 1.20 (s, 9 H).

Methyl Cyclohexanecarboxylate (3p)[21]
Colorless oil; yield: 3.55 g (88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.65 (s, 3 H), 2.34–2.26 (m, 1 H), 1.92–1.88 (m, 2 H), 1.77–1.72 (m, 2 H), 1.66–1.62 (m, 1 H), 1.48–1.39 (m, 2 H), 1.30–1.22 (m, 3 H).

Methyl Tetradecanoate (3q)[22]
Colorless oil; yield: 5.75 g (95%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.67 (s, 3 H), 2.32 (t, *J* = 7.6 Hz, 2 H), 1.25–1.28 (m, 22 H), 0.90 (t, *J* = 6.0 Hz, 3 H).

Methyl 3-Phenylpropanoate (3r)[7i]
Colorless oil; yield: 3.53 g (86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.31 (m, 3 H), 7.20 (d, *J* = 7.6 Hz, 2 H), 3.67 (s, 3 H), 2.97 (t, *J* = 8.0 Hz, 2 H), 2.66 (t, *J* = 8.0Hz, 2 H).

Methyl Naphthalene-1-acetate (3s)[7h]
Colorless oil; yield: 4.75 g (95%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.0 Hz, 1 H), 7.87 (d, *J* = 7.6 Hz, 1 H), 7.80 (d, *J* = 7.2 Hz, 1 H), 7.40–7.56 (m, 4 H), 4.08 (s, 2 H), 3.67 (s, 3 H).

Methyl Mandelate (3t)[23]
White solid; yield: 3.07 g (74%); mp 53–54 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.43 (m, 5 H), 5.18 (s, 1 H), 3.76 (s, 3 H), 3.66 (br, 1 H).

Methyl Methacrylate (3u)[24]
Colorless oil; yield: 1.80 g (72%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.11 (m, 1 H), 5.57 (m, 1 H), 3.76 (s, 3 H), 1.95 (t, *J* = 1.2 Hz, 3 H).

Methyl Cinnamate (3v)[7i]
Colorless oil; yield: 3.2 g (79%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 16.0 Hz, 1 H), 7.52 (s, 2 H), 7.39 (s, 3 H), 6.47 (d, *J* = 16.0 Hz, 1 H), 3.81 (s, 3 H).

Methyl 1*H*-Indol-3-ylacetate (3w)[7i]
White solid; yield: 3.73 g (79%); mp 49–50 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (br, 1 H), 7.63 (d, *J* = 7.6 Hz, 1 H), 7.36 (d, *J* = 8.0 Hz, 1 H), 7.12–7.22 (m, 3 H), 3.79 (s, 2 H), 3.70 (s, 3 H).

Methyl Nicotinate (3x)[18]
White solid; yield: 2.77 g (81%); mp 38–39 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.24 (s, 1 H), 8.80 (d, *J* = 4.4 Hz, 1 H), 8.34 (d, *J* = 8.0 Hz, 1 H), 7.43 (dd, *J* = 8.0, 4.8 Hz, 1 H), 3.97 (s, 3 H).

Methyl Thiophene-2-carboxylate (3y)[4b]
Colorless oil; yield: 2.95 g (83%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 3.2 Hz, 1 H), 7.56 (d, *J* = 4.8 Hz, 1 H), 7.10 (t, *J* = 4.4 Hz, 1 H), 3.89 (s, 3 H).

Allyl 2-Methoxybenzoate (3z)[25]
Colorless oil; yield: 4.42 g (92%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 7.6 Hz, 1 H), 7.47 (t, *J* = 8.4 Hz, 1 H), 6.96–6.99 (m, 2 H), 5.99–6.08 (m, 1 H), 5.45 (d, *J* = 17.2 Hz, 1 H), 5.29 (d, *J* = 10.4 Hz, 1 H), 4.81 (d, *J* = 5.6 Hz, 2 H), 3.91 (s, 3 H).

Benzyl 2-Methoxybenzoate (3aa)[26]
Colorless oil; yield: 5.27 g (87%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 7.6 Hz, 1 H), 7.49–7.45 (m, 3 H), 7.40–7.31 (m, 3 H), 6.99–6.90 (m, 2 H), 5.35 (s, 2 H), 3.91 (s, 3 H).

Methallyl 2-Methoxybenzoate (3ab)
Colorless oil; yield: 4.43 g (86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.0 Hz, 1 H), 7.47 (t, *J* = 7.6 Hz, 1 H), 6.97–7.00 (m, 2 H), 5.00 (d, *J* = 12 Hz, 2 H), 4.73 (s, 2 H), 3.91 (s, 3 H), 1.84 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$, TMS): δ = 163.4, 156.8, 137.6, 131.1, 129.2, 117.6, 117.5, 110.3, 109.5, 65.5, 53.4, 17.1.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{14}O_3Na$: 229.0841, found: 229.0835.

Prop-2-ynyl 2-Methoxybenzoate (3ac)[27]
Colorless oil; yield: 3.8 g (80%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (d, *J* = 7.6 Hz, 1 H), 7.51 (t, *J* = 7.6 Hz, 1 H), 6.97–6.99 (m, 2 H), 4.90 (s, 2 H), 3.91 (s, 3 H), 2.50 (s, 1 H).

Ethyl 2-Methoxybenzoate (3ad)[26]
Colorless oil; yield: 3.15 g (70%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.0 Hz, 1 H), 7.46 (t, *J* = 8.0 Hz, 1 H), 6.97–6.99 (m, 2 H), 4.36 (q, *J* = 7.2 Hz, 2 H), 3.90 (s, 3 H), 1.38 (t, *J* = 7.2 Hz, 3 H).

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