Simple and Efficient Synthesis of Racemic Substituted Mandelic Acid Esters from Nonactivated Arenes and Ethyl Glyoxylate

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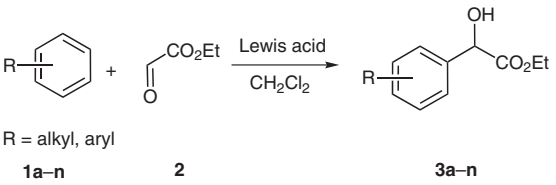
Abstract: Direct synthesis of racemic aromatic α-hydroxyacetic acid esters via Friedel–Crafts reaction of nonactivated, simple arenes with ethyl glyoxylate promoted by $SnCl_4$ or $AlCl_3$ is described. The use of $SnCl_4$ opens a fast access to various alkyl- and aryl-substituted mandelic acids esters at room temperature within two hours in good yield (>80%) and with high regioselectivity. The procedure was successfully employed also for the alkylation of compounds with condensed aromatic rings. Alternative hydroxyalkylations with $AlCl_3$ require longer reaction time and higher temperature to get a good yield.

Key words: arenes, Friedel–Crafts hydroxyalkylation, ethyl glyoxylate, α-hydroxy esters, Lewis acids, mandelic acids

Mandelic acid and its derivatives are an important class of molecules used in medicine, for example, as antibacterial and antiaging agents,[1] and as intermediates for the synthesis of target molecules (e.g., various pharmaceuticals).[2] They are usually synthesized in the racemic form via the reaction of aromatic aldehydes with hydrocyanic acid followed by acidic hydrolysis.[3] Optically pure aromatic α-hydroxy acids are usually prepared by enzymatic resolutions of racemates or in an enantioselective approach from aldehydes using chiral catalyst.[4] Another very attractive method of their synthesis is based on the Friedel–Crafts reaction[5] of aromatic or heteroaromatic compounds with 1,2-dicarbonyl compounds, especially glyoxylates, pyruvates, and trifluoropyruvates. This approach is well known both in racemic and asymmetric version;[6] however, in most cases, it is limited to highly activated aromatics, for example, phenols,[7,8] anilines, and heteroaromatics – pyrroles, indoles, and furans.[9] In fact, the examples showing the use of simple aromatic compounds without highly activating groups are rare and outdated.[10] Some other examples of the Lewis acid promoted reactions of alkyl substituted benzenes were reported for oxomalonates.[11] According to previous research, the use of the Brønsted (mineral) acids in this reaction usually leads to disubstituted products, diarylacetates.[12]

Here, we focus our attention on the neglected Friedel–Crafts reactions of simple alkyl- and aryl-substituted benzenes as well as polyaromatic systems with glyoxylates, leading directly to various mandelate analogues (Scheme 1). This approach is especially attractive since arenes are usually much more easily accessible than the corresponding aromatic aldehydes. A similar methodology was previously described for the two-step synthesis of mandelates, employing the $SnCl_4$-promoted reaction of ethyl oxomalonate with arenes followed by decarboxylation;[11d] however, the yields were usually moderate. The route to various mandelic acid derivatives, as presented here, seems to be more economic, since this easy and efficient one-step synthesis is based on the use of less expensive and readily available ethyl glyoxylate.



Scheme 1 Reaction of nonactivated arenes **1** with ethyl glyoxylate (**2**)

Our initial studies of the reaction of toluene (**1a**) with ethyl glyoxylate (**2**), in the presence of various common Lewis acids (Scheme 2, Table 1) were conducted to select the best promoter for the reaction.

Next we used two of the best performing Lewis acids in the Friedel–Crafts hydroxyalkylation, focusing our attention on the simple mono- and disubstituted alkylated derivatives of benzene, and subsequently extending our study to tri- and tetrasubstituted arenes (Scheme 1, Table 2). The positive results obtained in the reactions of simple alkylbenzenes encouraged us to further extend our study to the compounds having condensed aromatic rings (Table 3).

Table 1 shows the results obtained for the model reaction of toluene with ethyl glyoxylate, carried out in the presence of various Lewis acids as promoters (Scheme 2). The experiments were carried out at room temperature for 2–3 hours, using anhydrous dichloromethane as a solvent. In the case of $AlCl_3$, we repeated the experiment at higher temperature (reflux of CH_2Cl_2) and extend the reaction time to 20 hours, since this classic promoter is relatively less active than the rest of the tested Lewis acids (a very low yield was obtained for the reaction at r.t. for 3 h; entry 4).

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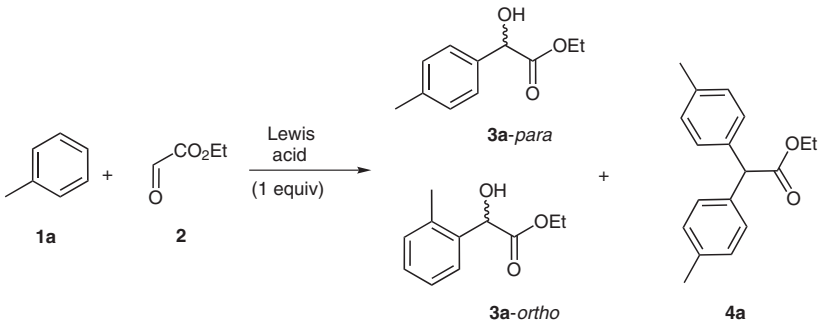


Scheme 2 The model reaction of **1a** and **2** studied to select a suitable Lewis acid

Table 1 Comparison of Common Lewis Acids in the Reaction of Toluene (**1a**) with Ethyl Glyoxylate (**2**)[a]

Entry	Lewis acid (1 equiv)	Yield (%)[b]	Regioselectivity[c] (% of *para*-product)
1	$SnCl_4$	89	96:4
2	$TiCl_4$	77	85:15
3	$ZrCl_4$	56	87:13
4	$AlCl_3$	35	87:13
5[d]	$AlCl_3$	88	90:10
6	$Yb(OTf)_3$	trace	–

[a] Reaction conditions: ethyl glyoxylate (3 mmol), CH_2Cl_2 (4 mL), toluene (2 mmol), and Lewis acid [1 equiv; 20 mol% for $Yb(OTf)_3$] at r.t.
[b] Isolated yield.
[c] Determined by ^1H NMR spectroscopy.
[d] The experiment was conducted in refluxing CH_2Cl_2 for 20 h.

The highest yield and regioselectivity were observed in the reaction promoted by $SnCl_4$ (entry 1). $AlCl_3$ was effective only at elevated temperature (entry 5); the yield reached 88%, while the regioselectivity did not change significantly, compared to the reaction carried out at room temperature. Unfortunately, neither of the two promoters was effective in the catalytic approach (10 mol% of Lewis acid). Both $TiCl_4$ and $ZrCl_4$ performed well, but the obtained regioselectivities and yields (especially for $ZrCl_4$) were worse than for $SnCl_4$. We also investigated the possibility of using other Lewis and Brønsted acids: $BF_3{\cdot}OEt_2$, $Yb(OTf)_3$ (20 mol%), $MeSO_3H$, and CF_3SO_3H. The reaction promoted by $BF_3{\cdot}OEt_2$ proceeded very slowly and led to a mixture of products. The use of $MeSO_3H$ did not lead to the expected product (Scheme 2, **3a**), while in the case of CF_3SO_3H, the product **4a** with two aryl groups was obtained. Similarly, $Yb(OTf)_3$, which had been used successfully in the reactions of ethyl glyoxylate with more active arenes,[13] gave only traces of the desired product **3a**.

Table 2 The Friedel–Crafts Alkylation of Substituted Benzenes **1** Promoted by Lewis Acid[a]

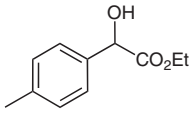
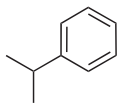
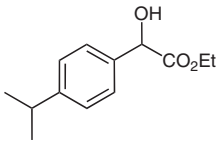
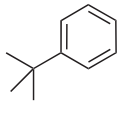
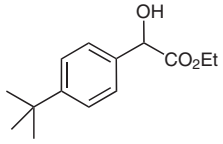
ArH	Lewis acid	Product	Yield (%)[b]	Regioselectivity[c] (% of *para*-product)
 **1a**	$SnCl_4$	 **3a**	89 84[d]	96:4 92:8[d]
	$AlCl_3$		88	90:10
 **1b**	$SnCl_4$	 **3b**	80 76[d]	98:2 98:2[d]
 **1c**	$SnCl_4$	 **3c**	84	100:0
	$AlCl_3$		73	100:0

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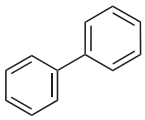
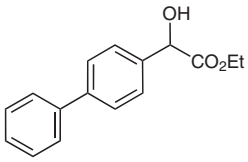
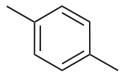
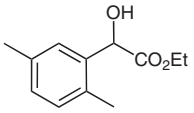
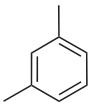
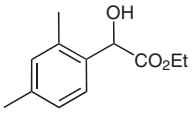
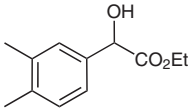
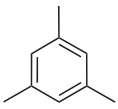
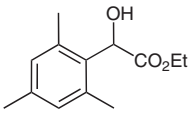
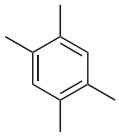
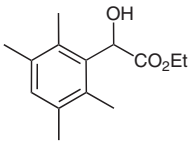
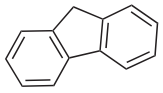
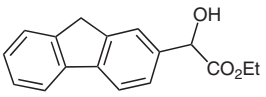
Table 2 The Friedel–Crafts Alkylation of Substituted Benzenes **1** Promoted by Lewis Acid[a] (continued)

ArH	Lewis acid	Product	Yield (%)[b]	Regioselectivity[c] (% of *para*-product)
 **1d**	$SnCl_4$	 **3d**	80	100:0
	$AlCl_3$		56	100:0
 **1e**	$SnCl_4$	 **3e**	86 73[d]	–[e]
	$AlCl_3$		86	
 **1f**	$SnCl_4$	 **3f**	92 89[d]	98:2 96:4[d]
	$AlCl_3$		90	98:2
 **1g**	$SnCl_4$	 **3g**	89 88[d]	96:4 94:6[d]
	$AlCl_3$		76	96:4
 **1h**	$SnCl_4$	 **3h**	90 74[d]	–[e]
	$AlCl_3$		75	
 **1i**	$SnCl_4$	 **3i**	90	–[e]
	$AlCl_3$		70	
 **1j**	$SnCl_4$	 **3j**	90	99:1
	$AlCl_3$[f]		72	95:5

[a] Reaction conditions: ethyl glyoxylate (3 mmol) in CH_2Cl_2 (4 mL), aromatic compound (2 mmol), and $SnCl_4$ (1 equiv) at r.t. for 2–3 h or $AlCl_3$ (1 equiv) at reflux for 20 h.
[b] Isolated yield.
[c] Determined by ^1H NMR spectroscopy.
[d] Reaction carried out under solvent-free conditions: ethyl glyoxylate (4 mmol) in aromatic compound (4 mL) and of $SnCl_4$ (1 equiv) at r.t. for 0.5 h.
[e] Only one product of monosubstitution is possible.
[f] The experiment was conducted at r.t.

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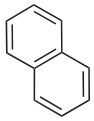
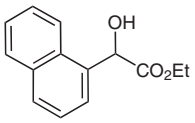
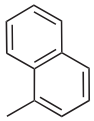
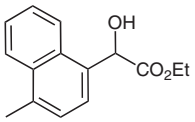
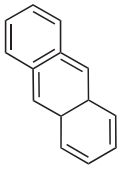
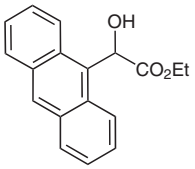
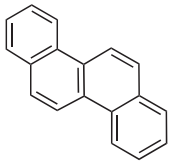
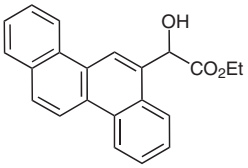
Table 3 The Friedel–Crafts Alkylation of Compounds with Condensed Aromatic Rings[a]

ArH	Lewis acid	Product	Yield (%)[b]
 **1k**	$SnCl_4$	 **3k**	91 (α:β = 3:1)[c]
	$AlCl_3$[d]		76 (α:β = 1:1)[c]
 **1l**	$SnCl_4$	 **3l**	62 (one product)
 **1m**	$SnCl_4$	 **3m**	54 78 (one product)[f]
	$AlCl_3$		75 (one product)[f]
 **1n**	$SnCl_4$	 **3n**	90 (one product)[e]

[a] Reaction conditions: ethyl glyoxylate (3 mmol), CH_2Cl_2 (4 mL), aromatic compound (2 mmol), and $SnCl_4$ (1 equiv) at r.t. for 2–3 h or $AlCl_3$ (1 equiv) at reflux for 20 h.
[b] Isolated yield.
[c] Determined by ^1H NMR spectroscopy.
[d] The experiment was conducted in refluxing CH_2Cl_2 for 20 h.
[e] The substitution position was not confirmed, but a monosubstituted product was obtained.
[f] The reaction was carried out in Et_2O (r.t.) over 5 h ($SnCl_4$) or 20 h ($AlCl_3$).

The Alkylation of Simple Arenes Promoted by $SnCl_4$ or $AlCl_3$

For the Friedel–Crafts alkylation reactions of monosubstituted benzenes, the product of *para*-substitution dominated over the product of *ortho*-substitution. The $SnCl_4$-promoted reactions were carried out at room temperature for two hours, while cheaper and less toxic $AlCl_3$ require higher temperature and longer reaction time. The results of the reactions of various alkylbenzenes with ethyl glyoxylate promoted either by $SnCl_4$ or by $AlCl_3$ are shown in the Table 2. Reactions of monosubstituted arenes (products: **3a**–**d**), promoted by $SnCl_4$ perform very well in the terms of yield (80–89%) and regioselectivity (>95% of *para*-product) obtained. A similarly high efficacy was observed in the reactions of disubstituted arenes **1e**–**g** as well as mesitylene (**1h**), durene (**1i**), and fluorene (**1j**). The regioselectivities obtained were excellent: 96–99%, along with good to very good yields of 86–92%. Additionally, we investigated the possibility of carrying out the $SnCl_4$-promoted reactions under the solvent-free conditions using liquid aromatic compounds in an amount larger than stoichiometric. In most cases, the drop in yields and regioselectivities is less than 6% compared to the reactions performed in the presence of CH_2Cl_2 (except for *p*-xylene and mesitylene, where the yield decreased by 15–17%).

With respect to the $AlCl_3$-promoted reactions of monosubstituted benzenes, the yields obtained are more dependent on the nature of the substituent (e.g., 88% of **3a** for $PhCH_3$, 73% of **3c** for *t*-BuPh, and 56% of **3d** for biphenyl, respectively). The correlation of regioselectivity is reversed: only one product is obtained for *t*-BuPh and biphenyl, while the ratio of the *para*-substitution product to the *ortho*-substitution product is 9:1 for toluene. For the alkylation of disubstituted benzenes, that is, xylenes **1f** and **1g** and fluorine (**1j**), the regioselectivities were found

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to be equally high as in case of the monosubstituted arenes (95–98%). The reaction yields for disubstituted benzenes **1e–g**, **j** as well as for mesitylene (**1h**) and durene (**1i**) were also very good (70–90%).

The Alkylation of Compounds with Condensed Aromatic Rings Promoted by $SnCl_4$ or $AlCl_3$

The reactions of polycyclic aromatic hydrocarbons with ethyl glyoxylate (Table 3) were carried out employing the same method as the reactions of simple arenes.

The yields obtained in the reactions promoted by $SnCl_4$ were very good for naphthalene (91%, **3k**) and chrysene (90%, **3n**), while the yield was lower for α-methylnaphthalene (62%, **3l**). With respect to anthracene, the relatively low yield (54%, **3m**) was attributable to partial decomposition of the product. In view of that, we found that the reaction carried out in another solvent, Et_2O, proceeded slower (completion time: 5 h), but the amount of decomposition products dramatically decreased, resulting in an increase of the reaction yield to 78%. Only one regioisomer was obtained in all $SnCl_4$-promoted reactions, except for naphthalene (75% of the α-substitution product, **3k**). Using the other Lewis acid, $AlCl_3$, we obtained a 1:1 mixture of kinetic and thermodynamic products for naphthalene, and a mixture of few products for anthracene (probably due to subsequent decomposition of the product). Once again, however, the use of Et_2O as a solvent gave exclusively the desired product in 75% yield (the reaction was carried out at r.t. for 20 h).

In summary, we have found an easy and general procedure for the efficient synthesis of mandelic acid derivatives, employing the $SnCl_4$- or $AlCl_3$-promoted Friedel–Crafts alkylation of simple arenes without highly activating substituents. Products of $SnCl_4$-promoted alkylation of arenes were obtained in very good yields exceeding 80% as well as with excellent regioselectivities exceeding 95% (the reaction clearly proceeded at ambient temperature over a short period of time). Furthermore, the $SnCl_4$-promoted reaction of liquid alkylbenzenes could be carried out without the need of using additional solvent. The promoter was effective also in the reactions of polycyclic aromatic hydrocarbons. This significantly broadens the scope of the potential products. Despite the need to increase the reaction time and temperature, the classic Friedel–Crafts reaction using $AlCl_3$ performs very well also in the alkylation of simple arenes, affording the products in good yields (≥70%) and high regioselectivities (≥90%).

The NMR spectra were recorded in $CDCl_3$ using a Varian Gemini 400 MHz or 200 MHz spectrometer while the NOE and COSY experiments were performed on a Bruker 500 MHz spectrometer. Chemical shifts of ^1H NMR and ^{13}C NMR are reported as δ values relative to TMS (0.00) and $CDCl_3$ (77.0), respectively. The high-resolution mass spectra (HRMS) were recorded on a Mariner PE Biosystems unit using the ESI technique. The IR spectra were taken on an FT-IR PerkinElmer Spectrum 2000. Analytical TLC was carried out on commercial plates coated with 0.25 mm of Merck Kieselgel 60. Preparative flash silica chromatography was performed using Merck Kieselgel 60 (230–400 mesh).

Ethyl glyoxylate (commercially available in 1:1 toluene solution) was separated from toluene through distillation in vacuo (36–40 °C/10 mmHg). Then the distillation was repeated in order to obtain pure substance with no traces of toluene.

The substitution position in fluorene was determined employing advanced NMR techniques: COSY and NOE experiments. In the ^1H NOE experiment, the activation of the C-1 carbon protons (3.87 ppm) resulted in obtaining a signal (singlet) from the C-10 hydrogen atom (7.59 ppm).

$SnCl_4$-Promoted Friedel–Crafts Alkylation of Arenes 1 with Ethyl Glyoxylate (2) in CH_2Cl_2 or Et_2O; General Procedure

To a stirred solution of ethyl glyoxylate (**2**; 0.306 g, 3.0 mmol) in CH_2Cl_2 (4 mL) or Et_2O (4 mL, used in the alkylation of anthracene) was added the appropriate aromatic compound **1a–n** (2.0 mmol). Then, $SnCl_4$ (0.625 g, 2.4 mmol) was slowly added (portionwise) at r.t. and the stirring was continued for 2 h. After that time, aq 2 M HCl (5 mL) was added to the vigorously stirred reaction mixture. After ca. 10 min, the organic layer was separated and the aqueous layer was extracted with Et_2O (2 × 10 mL). The organic layers were then combined and quenched with aq sat. $NaHCO_3$ (15 mL). After separating the organic layer, the aqueous layer was extracted with Et_2O (15 mL). The separated organic layers were combined, dried ($MgSO_4$), concentrated in vacuo, and subjected to flash chromatography using hexane–EtOAc (9:1) as an eluent.

Solvent-Free $SnCl_4$-Promoted Friedel–Crafts Alkylation of Arenes 1 with Ethyl Glyoxylate (2); General Procedure

Ethyl glyoxylate (**2**; 0.408 g, 4.0 mmol) was added to the stirred appropriate aromatic compound **1a–n** (4 mL). Then $SnCl_4$ (1.146 g, 4.4 mmol) was slowly added (portionwise) at r.t. and the stirring was continued for 0.5 h. Et_2O (5 mL) was added to the stirred suspension, followed by aq 2 M HCl (10 mL). After ca. 10 min, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 15 mL). The organic layers were then combined and quenched with aq sat. $NaHCO_3$ (15 mL). After separation of the organic layer, the aqueous layer was extracted with CH_2Cl_2 (15 mL). The separated organic layers were combined, dried ($MgSO_4$), concentrated in vacuo, and subjected to flash chromatography using hexane–EtOAc (9:1) as an eluent.

$AlCl_3$-Promoted Friedel–Crafts Alkylation of Arenes 1 with Ethyl Glyoxylate (2) in CH_2Cl_2 or Et_2O; General Procedure

To a stirred solution of ethyl glyoxylate (**2**; 0.460 g, 4.5 mmol) in CH_2Cl_2 (3 mL) or Et_2O (3 mL, used in the alkylation of anthracene) was added $AlCl_3$ (0.600 g, 4.5 mmol) at r.t. and the stirring was continued for ca. 10 min. After the $AlCl_3$ had dissolved, the appropriate aromatic compound **1a–n** (3.0 mmol) was added and the stirring was continued for 20 h under reflux (50 °C, oil bath). Aq 2 M HCl (5 mL) was slowly added to the stirred suspension cooled to r.t. After ca. 10 min, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were combined and quenched with aq sat $NaHCO_3$ (15 mL) After separating the organic layer, the aqueous layer was extracted with CH_2Cl_2 (15 mL). The separated organic layers were combined, dried ($MgSO_4$), concentrated in vacuo, and subjected to flash chromatography using hexane–EtOAc (9:1) as an eluent.

Ethyl Hydroxy(4-methylphenyl)acetate (3a)[14]

Yield: 345 mg (89%); mp 70–71 °C (Lit.[15] mp 72 °C).

IR (KBr): 3463, 2995, 2978, 2953, 2900, 1726, 1611, 1514, 1309, 1224, 1183, 1081, 1018, 834, 763 cm^{-1}.

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.30 (m, 2 H), 7.18–7.17 (m, 2 H), 5.12 (d, *J* = 5.6 Hz, 1 H), 4.30–4.12 (m, 2 H), 3.44 (d, *J* = 5.6 Hz, 1 H), 2.35 (s, 3 H), 1.23 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 Hz, $CDCl_3$): δ = 173.8, 138.2, 135.5, 129.2, 126.4, 72.7, 62.1, 21.1, 14.0.

Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.95; H, 7.12.

Ethyl Hydroxy(4-isopropylphenyl)acetate (3b)[16]
Yield: 355 mg (80%); mp 37–39 °C (Lit.[17] mp 39–41 °C).

IR (KBr): 3483, 2962, 2934, 2872, 1733, 1513, 1465, 1258, 1213, 1191, 1083, 1019, 832 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.31 (m, 2 H), 7.23–7.20 (m, 2 H), 5.12 (s, 1 H), 4.31–4.12 (m, 2 H), 3.40 (s, 1 H), 2.95–2.85 (m, 1 H), 1.24 (d, *J* = 6.8 Hz, 6 H), 1.24 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.8, 149.1, 135.8, 126.6, 126.5, 72.7, 62.1, 33.8, 23.88, 23.86 14.0.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.22; H, 8.15.

Ethyl 4-*tert*-Butylphenyl(hydroxy)acetate (3c)
Yield: 396 mg (84%); oil.

IR (KBr): 3475, 2964, 2906, 2870, 1733, 1513, 1464, 1268, 1199, 1183, 1084, 1018 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.32 (m, 4 H), 5.13 (s, 1 H), 4.32–4.12 (m, 2 H), 3.43 (s, 1 H) 1.31 (s, 9 H), 1.24 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.7, 151.3, 135.4, 126.2, 125.5, 72.7, 62.1, 34.5, 31.3, 14.0.

Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.04; H, 8.45.

Ethyl Biphenyl-4-yl(hydroxy)acetate (3d)
Yield: 410 mg (80%); mp 109–111 °C.

IR (KBr): 3440, 3063, 3036, 2981, 2912, 1735, 1489, 1477, 1199, 1184, 1074, 1024, 837, 755, 733, 686 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.57 (m, 4 H), 7.50–7.48 (m, 2 H), 7.45–7.41 (m, 2 H), 7.37–7.32 (m, 1 H), 5.21 (d, *J* = 5.6 Hz, 1 H), 4.33–4.15 (m, 2 H), 3.52 (d, *J* = 5.6 Hz, 1 H), 1.25 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.6, 141.3, 140.6, 137.4, 128.8, 127.4, 127.3, 127.1, 126.9, 72.6, 62.3, 14.0.

Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.99; H, 6.24.

Ethyl (2,5-Dimethylphenyl)(hydroxy)acetate (3e)
Yield: 358 mg (86%); oil.

IR (KBr): 3474, 2981, 2926, 1732, 1504, 1446, 1254, 1217, 1119, 1072, 1022, 812 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11 (s, 1 H), 7.07–7.01 (m, 2 H), 5.32 (s, 1 H), 4.32–4.12 (m, 2 H), 3.41 (s, 1 H), 2.38 (s, 3 H), 2.30 (s, 3 H), 1.23 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.3, 136.4, 135.7, 133.1, 130.6, 129.1, 127.3, 70.3, 62.1, 20.9, 18.8, 14.0.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.03; H, 7.68.

Ethyl (2,4-Dimethylphenyl)(hydroxy)acetate (3f)
Yield: 383 mg (92%); oil.

IR (KBr): 3474, 2981, 2926, 1735, 1615, 1503, 1446, 1219, 1194, 1120, 1074, 1022, 818 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.16 (m, 1 H), 7.01–6.99 (m, 2 H), 5.31 (s, 1 H), 4.30–4.11 (m, 2 H), 3.31 (s, 1 H), 2.39 (s, 3 H), 2.30 (s, 3 H), 1.21 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.3, 138.1, 136.2, 133.8, 131.5, 126.9, 126.7, 70.2, 62.0, 21.0, 19.1, 14.0.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.25; H, 7.78.

Ethyl (3,4-Dimethylphenyl)(hydroxy)acetate (3g)
Yield: 370 mg (89%); oil.

IR (KBr): 3475, 2980, 2939, 1734, 1503, 1453, 1258, 1237, 1197, 1091, 1022, 807, 737 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (s, 1 H), 7.14–7.10 (m, 2 H), 5.08 (s, 1 H), 4.31–4.11 (m, 2 H), 3.38 (s, 1 H), 2.26 (s, 3 H), 2.25 (s, 3 H), 1.23 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.9, 136.8, 135.9, 129.8, 127.7, 124.0, 72.8, 62.1, 19.7, 19.5, 14.0.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.18; H, 7.70.

Ethyl Hydroxy(mesityl)acetate (3h)
Yield: 400 mg (90%); mp 51–52 °C (Lit.[18] mp 54 °C).

IR (KBr): 3427, 2961, 2923, 1739, 1608, 1486, 1463, 1213, 1078, 1013, 856 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.84 (s, 2 H), 5.52 (s, 1 H), 4.32–4.15 (m, 2 H), 3.25 (s, 1 H), 2.33 (s, 6 H), 2.26 (s, 3 H), 1.22 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.9, 137.8, 137.1, 131.4, 129.8, 69.1, 62.2, 20.9, 19.9, 14.1.

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.30; H, 8.24.

Ethyl Hydroxy(2,3,5,6-tetramethylphenyl)acetate (3i)
Yield: 425 mg (90%); mp 110–111 °C.

IR (KBr): 3396, 2982, 2962, 2917, 2864, 1750, 1474, 1232, 1097, 1061, 1008, 869 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 (s, 1 H), 5.63 (s, 1 H), 4.33–4.17 (m, 2 H), 3.16 (s, 1 H), 2.22 (s, 12 H), 1.23 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.4, 134.3, 134.2, 133.3, 132.1, 69.6, 62.1, 20.5, 15.6, 14.1.

Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.16; H, 8.54.

Ethyl 9*H*-Fluoren-2-yl(hydroxy)acetate (3j)
Yield: 482 mg (90%); mp 128–129 °C.

IR (KBr): 3463, 2979, 2942, 2912, 1731, 1476, 1191, 1081, 1023, 762, 736 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78–7.74 (m, 2 H), 7.59 (s, 1 H), 7.53 (d, *J* = 7.3 Hz, 1 H), 7.42–7.28 (m, 3 H), 5.22 (s, 1 H), 4.32–4.13 (m, 2 H), 3.88 (s, 2 H), 3.56 (s, 1 H), 1.22 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.8, 143.6, 143.4, 142.0, 141.1, 136.9, 126.9, 126.8, 125.4, 125.0, 123.1, 120.0, 119.9, 73.1, 62.2, 36.8, 14.0.

Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.00; H, 6.12.

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Ethyl Hydroxy(naphthalen-1-yl)acetate (3k)[19]
Yield: 419 mg (91%); oil.

IR (KBr): 3463, 3052, 2982, 1732, 1599, 1511, 1368, 1214, 1096, 1020, 800, 791, 777 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 8,3 Hz, 1 H), 7.90–7.83 (m, 2 H), 7.56–7.43 (m, 4 H), 5.79 (s, 1 H), 4.30–4.10 (m, 2 H), 3.60 (s, 1 H), 1.14 (t, *J* = 7.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.2, 134.1, 134.0, 131.0, 129.3, 128.7, 126.5, 125.8, 125.7, 125.2, 123.7, 71.4, 62.3, 13.9.

Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 73.03; H, 6.22.

Ethyl Hydroxy(4-methyl-naphthalen-1-yl)acetate (3l)
Yield: 303 mg (62%); oil.

IR (KBr): 3463, 3073, 2981, 2939, 2904, 1734, 1598, 1516, 1443, 1214, 1085, 1024, 824, 760 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20–8.15 (m, 1 H), 8.05–8.01 (m, 1 H), 7.56–7.51 (m, 2 H), 7.38 (d, *J* = 7.2 Hz, 1 H), 7.30–7.27 (m, 1 H), 5.76 (s, 1 H), 4.30–4.10 (m, 2 H), 3.51 (s, 1 H), 2.68 (s, 3 H), 1.14 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.3, 135.7, 133.1, 132.4, 131.1, 126.1, 126.0, 125.7, 125.5, 124.8, 124.2, 71.5, 62.2, 19.6, 14.0.

Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.93; H, 6.77.

Ethyl 1,4-Dihydroanthracen-9-yl(hydroxy)acetate[20]
Yield: 437 mg (78%); mp 104–105 °C (Lit.[21] mp 107 °C).

IR (KBr): 3464, 3054, 2993, 2905, 1716, 1524, 1474, 1221, 1093, 1013, 889, 729 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.48 (s, 1 H), 8.33–8.31 (m, 2 H), 8.03–8.00 (m, 2 H), 7.54–7.44 (m, 4 H), 6.57 (s, 1 H), 4.21–4.08 (m, 2 H), 3.66 (s, 1 H), 0.99 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 131.5, 130.4, 129.3, 129.2, 128.4, 126.6, 124.9, 123.7, 68.1, 62.3, 13.9.

Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 76.94; H, 5.61.

Ethyl Chrysen-6-yl(hydroxy)acetate (3n)
Yield: 594 mg (90%); mp 145–146 °C.

IR (KBr): 3529, 3081, 2994, 2857, 1722, 1513, 1477, 1244, 1077, 1019, 821, 762 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.82–8.74 (m, 3 H), 8.67 (d, *J* = 9.0 Hz, 1 H), 8.31–8.29 (m, 1 H), 8.01–7.96 (m, 2 H), 7.23–7.60 (m, 4 H), 5.96 (d, *J* = 4.3 Hz, 1 H), 4.31–4.14 (m, 2 H), 3.77 (d, *J* = 4.3 Hz, 1 H), 1.12 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.3, 132.8, 132.1, 131.2, 130.4, 129.8, 128.7, 128.6, 128.1, 127.3, 126.8, 126.64, 126.61, 126.5, 124.5, 123.7, 123.0, 121.8, 120.9, 72.4, 62.4, 14.0.

Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.98; H, 5.49. Found: C, 79.38; H, 5.54.

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