

Sonochemical Reformatsky Reaction Using Indium[†]

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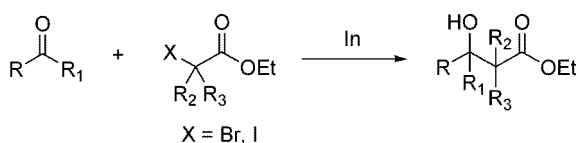
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Sonochemical Reformatsky reaction of aldehydes or ketones with ethyl bromoacetate in the presence of indium afforded β -hydroxyesters in good to excellent yields under mild conditions. 2- or 3-Hydroxybenzaldehyde that contains an acidic hydrogen reacted with ethyl bromoacetate to provide the desired compounds with the same efficiency. In the case of ethyl 2-bromopropanoate and ethyl 2-bromo-2-methylpropanoate, the desired products were obtained in good yields. Reaction of aldehyde with indium reagent in the presence of ketone group proceeded chemoselectively.

Key Words: Indium, Reformatsky reaction, β -Hydroxyester, Sonochemical reaction

Introduction

The Reformatsky reaction, which is regarded as one of the most fundamental reactions in C-C bond formations, is the reaction of a carbonyl compound with an α -haloester in the presence of zinc metal to furnish β -hydroxyesters.¹ The products are one of the most important intermediates in organic synthesis.² Recently, several modified Reformatsky reactions using other metals have been reported.³ Also, the scope of the Reformatsky reaction has been extended with special techniques for the activation of the metal (e.g. for removal of the oxide layer, and the preparation of finely dispersed metal).⁴ The activation of zinc by treatment with iodine or dibromomethane, or washing with dilute hydrochloric acid prior to use, is only moderately successful in the most known procedures. Much more effective protocol is the use of special alloys - e.g. Zn-Cu couple, or the reduction of zinc halides using potassium (the so-called Rieke procedure⁵) or potassium graphite.⁴ Although the application of ultrasound has been reported for zinc metal, promoters such as iodine and potassium iodide were needed sometimes to obtain the desired products in good yields.⁶ Our interests in extending the scope of the Reformatsky reaction and subsequent application of indium metal to modern organic synthesis⁷ have led us to investigate indium mediated Reformatsky reaction. As part of our continuing effort to expand the synthetic utility of indium, we now report a sonochemical Reformatsky reaction by the reaction of aldehydes or ketones with ethyl bromoacetate in the presence of indium (Scheme 1).⁸



Scheme 1

Results and Discussion

To find optimum conditions for sonochemical Reformatsky reaction using indium, initially benzaldehyde reacted with ethyl bromoacetate in the presence of indium in various solvents. The results are summarized in Table 1. Among the several solvents tested, THF gave the best results in terms of conversion and reaction time. The reaction of benzaldehyde with ethyl bromoacetate in the presence of indium in THF afforded ethyl 3-hydroxy-3-phenylpropanoate in 97% yield (entry 5). Sonication was carried out at room temperature in a Fisher Scientific ultrasonic cleaner bath, which delivered a 43 kHz wave, with a fixed electrical power of 435 Watts. However, the yields were decreased in other solvents under the identical conditions despite longer reaction time. Sonochemical reaction condition was superior to stirring condition. In the absence of sonic waves, the reaction occurred much more slowly (17 h) and the yield of the β -hydroxyester

Table 1. Examination of optimum condition of Reformatsky reaction

Entry	Solvent	Time (h)	Isolated yield (%) ^a
1	DMF	8	0
2	DMF	4	22 ^f
3	THF	8	58
4	THF	17	70
5	THF	2	97 ^f
6	THF	2	97 ^g
7	wet-THF ^h	4	78 ^f
8	H ₂ O	19	0
9	H ₂ O	4	0 ^f
10	THF/H ₂ O ⁱ	16	0
11	THF/H ₂ O ⁱ	9	0 ^f
12	THF/H ₂ O ⁱ	9	0 ^f
13	MeOH/HCl ^c	17	0

^aThe reaction mixture was stirred (rpm: ~900) unless otherwise noted. ^bTHF was not dried. ^cTHF : H₂O = 1 : 1. ^dTHF : H₂O = 9 : 1. ^eMeOH : HCl = 1 : 4. ^fUltrasonic irradiation. ^gEthyl iodoacetate was used.

[†]This paper is dedicated to the deceased Professor Sang Chul Shim for his outstanding achievements in organic chemistry.

Table 2. Preparation of β -hydroxyesters by In-mediated reactions of carbonyl compounds

$\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}' + \text{Br}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{OEt} \xrightarrow[\text{rt}]{\text{In / THF}} \text{R}-\overset{\text{OH}}{\underset{\text{R}'}{\text{C}}}-\text{CH}_2-\overset{\text{O}}{\parallel}{\text{C}}-\text{OEt}$				
Entry	Carbonyl compounds	Time (h)	Products	Isolated yield (%) ^a
1		3		1 95
2		3.5		2 93
3		4		3 89
4		2.5		4 91
5		2		5 92
6		2		6 97
7		2.5		7 92
8		2		8 91
9		3		9 91
10		2.5		10 90
11		2		11 90
12		2.5		12 85
13		2		13 93
14		2.5		14 92

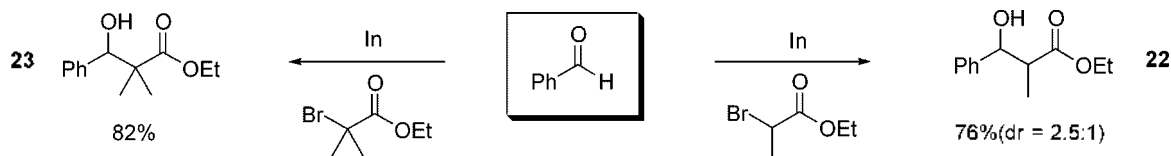
Table 2. Continued

Entry	Carbonyl compounds	Time (h)	Products	Isolated yield (%) ^a
15		2.5		15 85
16		2.5		16 90
17		2.5		17 93
18		3		18 73
19		3.5		19 82
20		3		20 90 40 ^b
21		3.5		21 88

^aSonications were carried out at room temperature in a Fisher Scientific ultrasonic cleaner bath, which delivered a 43 kHz wave, with a fixed electrical power of 435 Watts. ^bSonic wave was not used.

was only 70% (entry 4). Rate per minute (rpm) for stirring conditions was *ca.* 900. Ethyl iodoacetate gave the similar result to ethyl bromoacetate (entry 6). Also, organoindium reagent generated in situ from the reaction of 1 equiv of indium with 1.5 equiv of ethyl bromoacetate gave the best result. The use of indium less than 1 equiv and ethyl bromoacetate less than 1.5 equiv resulted in sluggish reaction and gave lower yields as well as longer reaction time.

Table 2 summarized the experimental results and illustrates the efficiency and scope of the present method. In the case of aliphatic aldehydes, the reaction afforded the desired compounds in excellent yields (entries 1–5). For the aromatic aldehydes, the presence of various substituents, *e.g.*, methyl (entry 7), chloro (entry 8), bromo (entry 9), monomethoxy (entry 10), dimethoxy (entry 11), or nitro (entry 12) on the aromatic ring showed little effects on the efficiency of the reactions. It should be mentioned that 2- or

**Scheme 2**

3-hydroxybenzaldehyde that contains an acidic hydrogen reacted with ethyl bromoacetate to provide the desired compounds **13** and **14** in 93% and 92% yields, respectively. (entries 13 and 14). In the case of 2-furaldehyde and 2-thiophenecarboxaldehyde, β -hydroxyesters were obtained in good yields (entries 15 and 16). Cinnamaldehyde was treated with ethyl bromoacetate to produce the desired compound in 93% yield (entry 17). The protocol developed here was also applied to reactions with ketone. For example, acetone and cyclohexanone reacted with ethyl bromoacetate to produce the desired compounds in 73% and 82% yields, respectively (entries 18 and 19). For the aromatic ketones, the treatment of acetophenone (entry 20) and *p*-methoxyacetophenone (entry 21) with ethyl bromoacetate gave the β -hydroxyesters **20** and **21** in 90% and 88% yields, respectively. However, indium-promoted reaction of acetophenone with ethyl bromoacetate gave β -hydroxyester **20** in 40% yield without sonic wave. The sonicated mixture of zinc, ethyl bromoacetate, and acetophenone gave no addition product in the absence of iodine.⁶

In the case of alkyl substituted ethyl bromoacetate, the desired products were obtained in good to excellent yields (Scheme 2). Benzaldehyde reacted with ethyl 2-bromopropanoate and ethyl 2-bromo-2-methylpropanoate in the presence of indium to give β -hydroxyesters **22** and **23** in 76% (dr = 2.5 : 1) and 82% yields, respectively.

To investigate chemoselectivity of aldehyde and ketone group, the mixture of benzaldehyde and acetophenone was treated with ethyl bromoacetate and indium to produce selectively ethyl 3-hydroxy-3-phenylpropanoate (**6**) as major compound. The results are summarized in Table 3.

In summary, sonochemical Reformatsky reaction using indium afforded β -hydroxyesters in high yields. There are several advantages of the method such as (a) the organo-indium compound was prepared and used in situ; (b) it has a wide application for elongation of carbon chains; (c) in comparison to the use of zinc and tin, the reaction with indium was not required any promoter (iodine or potassium iodide); (d) the organoindium intermediates did not react with themselves in normal conditions; (e) It should be men-

tioned that 2- or 3-hydroxybenzaldehyde that contains an acidic hydrogen reacted with ethyl bromoacetate to provide the desired compounds with the same efficiency; and (f) reaction of aldehyde with indium reagent in the presence of ketone group proceeded chemoselectively. The present method complements the existing synthetic methods of β -hydroxyester because of mild reaction condition and advantages of indium metal with regard to easy handling, high reactivity and selectivity, low toxicity, and operational simplicity.

Experimental Section

The ¹H NMR and ¹³C NMR spectra were recorded on Bruker IFS 48 (400 MHz) spectrometer. Proton chemical shifts (δ) were reported in ppm downfield from tetramethylsilane (TMS), and ¹³C resonances were recorded using the 77.0 ppm CDCl₃ resonance peak of the solvent as internal reference. Fourier transform infrared (FTIR) spectra were recorded on a JASCO IR 100 spectrophotometer. Mass spectra were obtained on a Autospec, M363 series. Column chromatography was performed on silica gel (Merck, 230-400 mesh). The gas chromatograms were obtained on HP 5890.

Typical procedure for indium-mediated sonochemical Reformatsky reaction: Ethyl 3-hydroxy-3-phenylpropanoate (6). To a solution of indium [indium powder (99.99%) purchased from Aldrich Chem Co.: 58.0 mg, 0.5 mmol] in THF (1.0 mL) was added ethyl bromoacetate (125.0 mg, 0.75 mmol) and then benzaldehyde (53.0 mg, 0.5 mmol) under nitrogen at room temperature. After sonicating in a Fisher Scientific ultrasonic cleaner bath, which delivered a 43 kHz wave with a fixed electrical power of 435 Watts for 2 hr, the reaction mixture was quenched with saturated aqueous NaHCO₃ solution. The aqueous layer was extracted with ether (3 × 25 mL) and the combined organic layers were washed with water (20 mL) and brine (20 mL) and dried with MgSO₄, filtered and concentrated *in vacuo*. The residue was purified by silica gel chromatography (hexane : EtOAc = 5 : 1) leading to ethyl 3-hydroxy-3-phenylpropanoate (94.0 mg, 97%). ¹H NMR (200 MHz, CDCl₃) δ 7.4-7.25 (5H, m), 5.14 (1H, q, *J* = 4.0 Hz), 4.19 (2H, q, *J* = 7.20 Hz), 3.14 (1H, br s), 2.83-2.64 (2H, m), 1.26 (3H, t, *J* = 7.00 Hz); ¹³C NMR (50 MHz, CDCl₃) δ 172.64, 142.62, 128.69, 127.94, 125.81, 70.40, 61.02, 43.41, 14.23; IR (film) 3460, 2980, 1720, 1490, 1450, 1395, 1370, 1295, 1260 cm⁻¹; MS (CI) calcd for C₁₁H₁₃O₃ [M+H]⁺ 195, found 195.

Ethyl 3-hydroxyhexanoate (1) ¹H NMR (400 MHz, CDCl₃) δ 4.17 (2H, q, *J* = 7.15 Hz), 4.02 (1H, m), 3.01 (1H, d, *J* = 3.69 Hz), 2.49 (1H, dd, *J* = 3.32, 3.16 Hz), 2.39 (1H, dd, *J* = 8.93, 8.93 Hz), 1.25-1.53 (4H, m), 1.27 (3H, t, *J* = 7.20 Hz), 0.93 (3H, t, *J* = 6.99 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 173.13, 67.77, 60.67, 41.38, 38.68, 18.69, 14.19, 13.97; IR (film) 3480, 3050, 2960, 1720, 1260 cm⁻¹; MS (CI) calcd for C₈H₁₇O₃ [M+H]⁺ 161, found 161.

Ethyl 3-hydroxy-5-phenylpentanoate (2) ¹H NMR (400 MHz, CDCl₃) δ 7.30-7.25 (m, 2H), 7.21-7.16 (m, 3H), 4.17 (q, *J* = 7.15 Hz, 2H), 4.02 (m, 1H), 3.07 (d, *J* = 3.96 Hz, 1H), 2.82-2.78 (m, 1H), 2.73-2.68 (m, 2H), 1.89-1.82 (m, 1H).

Table 3. Competition reaction of benzaldehyde and acetophenone

Entry	Equiv of reactants				G.C ratio	
	a	b	c	d	6	20
1	1.0	1.0	1.5	1.0	4.2	1
2	1.0	1.0	1.0	1.0	237	1
3	5.0	5.0	1.5	1.0	10.1	1
4	5.0	5.0	1.0	1.0	10.1	1

1.75-1.72 (m, 1H), 1.26 (t, $J = 7.08$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 174.19, 142.91, 129.63, 129.59, 127.06, 68.38, 61.90, 42.46, 39.28, 32.93, 15.34; IR (film) 3420, 2920, 1710, 1600, 1490, 1445, 1360, 1295, 1245 cm^{-1} ; MS (CI) calcd for $\text{C}_{13}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{H}]^+$ 223, found 223.

Ethyl 3-hydroxy-4-phenylbutanoate (3) ^1H NMR (400 MHz, CDCl_3) δ 7.30 (m, 2H), 7.22 (m, 3H), 4.26 (m, 1H), 4.13 (q, $J = 4.73$ Hz, 2H), 2.98 (d, $J = 3.86$ Hz, 1H), 2.85 (q, $J = 6.89$ Hz, 1H), 2.76 (q, $J = 6.56$ Hz, 1H), 2.39-2.25 (m, 2H), 1.25 (t, $J = 7.16$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.71, 137.71, 129.45, 128.53, 126.60, 69.05, 60.71, 42.95, 40.54, 14.16; IR (film) 3420, 2970, 2920, 1720, 1490, 1450, 1370, 1300, 1260 cm^{-1} ; MS (CI) calcd for $\text{C}_{12}\text{H}_{16}\text{O}_3$ $[\text{M}+\text{H}]^+$ 209, found 209.

Ethyl 3-hydroxy-4-methylpentanoate (4) ^1H NMR (400 MHz, CDCl_3) δ 4.17 (2H, q, $J = 7.14$ Hz), 3.78 (1H, m), 3.05 (1H, br s), 2.50 (1H, dd, $J = 2.92, 2.92$ Hz), 2.40 (1H, dd, $J = 9.53, 9.53$ Hz), 1.72 (1H, m), 1.27 (3H, t, $J = 7.15$ Hz), 0.94 (6H, q, $J = 5.99$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 173.86, 73.09, 61.05, 38.84, 33.52, 18.70, 18.10, 14.52; IR (film) 3440, 2975, 1720, 1470, 1370, 1320, 1270 cm^{-1} ; MS (CI) calcd for $\text{C}_8\text{H}_{14}\text{O}_3$ $[\text{M}+\text{H}]^+$ 161, found 161.

Ethyl 3-cyclohexyl-3-hydroxypropanoate (5) ^1H NMR (400 MHz, CDCl_3) δ 4.17 (2H, q), 3.79-3.75 (1H, m), 2.84 (1H, br s), 2.51 (1H, dd, $J = 2.80, 2.86$ Hz), 2.41 (1H, dd, $J = 9.50, 9.49$ Hz), 1.86 (1H, d, $J = 12.65$ Hz), 1.76 (2H, m), 1.66 (2H, d, $J = 12.30$ Hz), 1.41-1.11 (9H, m); ^{13}C NMR (100 MHz, CDCl_3) δ 174.60, 73.17, 61.69, 44.07, 39.59, 29.80, 29.27, 27.44, 27.18, 27.06, 15.20; IR (film) 3500, 3050, 2980, 2920, 2840, 1720, 1450, 1410, 1370, 1260 cm^{-1} ; MS (CI) calcd for $\text{C}_{11}\text{H}_{20}\text{O}_3$ $[\text{M}+\text{H}]^+$ 201, found 201.

Ethyl 3-hydroxy-3-(*p*-methylphenyl)propanoate (7) ^1H NMR (400 MHz, CDCl_3) δ 7.25 (2H, d, $J = 8.02$ Hz), 7.14 (2H, d, $J = 7.95$ Hz), 5.08 (1H, q, $J = 4.18$ Hz), 4.16 (2H, q, $J = 7.13$ Hz), 3.1 (1H, br s), 2.77-2.57 (2H, m), 2.33 (3H, s), 1.25 (3H, t, $J = 7.14$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 172.80, 140.04, 137.84, 129.58, 126.02, 70.57, 61.21, 43.76, 21.49, 14.54; IR (film) 3410, 2960, 2900, 1715, 1510, 1440, 1390, 1365, 1290, 1260 cm^{-1} ; MS (CI) calcd for $\text{C}_{12}\text{H}_{17}\text{O}_3$ $[\text{M}+\text{H}]^+$ 209, found 209.

Ethyl 3-(*p*-chlorophenyl)-3-hydroxypropanoate (8) ^1H NMR (400 MHz, CDCl_3) δ 7.31 (4H, s), 5.09 (1H, q, $J = 4.25$ Hz), 4.17 (2H, q, $J = 7.12$ Hz), 3.22 (1H, br s), 2.68 (2H, m), 1.25 (3H, t, $J = 7.10$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 172.24, 141.03, 133.45, 128.67, 127.09, 69.62, 61.00, 43.20, 14.13; IR (film) 3400, 2930, 2860, 1695, 1470, 1375, 1350, 1280, 1260, 1240 cm^{-1} ; MS (CI) calcd for $\text{C}_{11}\text{H}_{14}\text{ClO}_3$ $[\text{M}+\text{H}]^+$ 229, found 229.

Ethyl 3-(*m*-bromophenyl)-3-hydroxypropanoate (9) ^1H NMR (400 MHz, CDCl_3) δ 7.55 (1H, t, $J = 1.62$ Hz), 7.42-7.40 (1H, m), 7.30-7.19 (2H, m), 5.08 (1H, m), 4.18 (2H, q, $J = 7.14$ Hz), 3.41 (1H, d, $J = 3.55$ Hz), 2.71 (2H, d, $J = 6.84$ Hz), 1.26 (3H, t, $J = 7.17$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 172.23, 144.78, 130.84, 130.12, 128.87, 124.28, 122.67, 69.59, 61.04, 43.14, 14.14; IR (film) 3500, 3050, 2980, 1720, 1420, 1260 cm^{-1} ; MS (CI) calcd for $\text{C}_{11}\text{H}_{14}\text{BrO}_3$ $[\text{M}+\text{H}]^+$ 273, found 273.

Ethyl 3-hydroxy-3-(*p*-methoxyphenyl)propanoate (10) ^1H NMR (400 MHz, CDCl_3) δ 7.30 (2H, d, $J = 8.09$ Hz), 6.89 (2H, d, $J = 8.49$ Hz), 5.08 (1H, t, $J = 4.53$ Hz), 4.18 (2H, q, $J = 7.14$ Hz), 3.79 (3H, s), 3.20 (1H, br s), 2.78-2.64 (2H, m), 1.25 (3H, t, $J = 7.38$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 172.44, 159.20, 134.73, 126.97, 113.91, 69.97, 60.83, 55.29, 43.33, 14.16; IR (film) 3450, 2970, 2830, 1715, 1600, 1500, 1460, 1365, 1295, 1240 cm^{-1} ; MS (CI) calcd for $\text{C}_{12}\text{H}_{17}\text{O}_4$ $[\text{M}+\text{H}]^+$ 255, found 255.

Ethyl 3-hydroxy-3-(2,6-dimethoxyphenyl)propanoate (11) ^1H NMR (400 MHz, CDCl_3) δ 7.19 (1H, t, $J = 8.34$ Hz), 6.56 (2H, d, $J = 8.41$ Hz), 5.66 (1H, dd, $J = 4.21, 4.31$ Hz), 4.16 (2H, q, $J = 7.14$ Hz), 3.84 (6H, s), 3.55 (1H, br s), 2.99 (1H, dd, $J = 9.87, 9.91$ Hz), 2.65 (1H, dd, $J = 4.25, 4.36$ Hz), 1.26 (3H, t, $J = 7.1$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 172.01, 158.07, 129.30, 118.40, 104.59, 64.94, 60.79, 56.10, 42.74, 14.60; IR (film) 3352.5, 2960, 2920, 2820, 1720, 1580, 1460, 1365, 1260 cm^{-1} ; MS (CI) calcd for $\text{C}_{13}\text{H}_{19}\text{O}_5$ $[\text{M}+\text{H}]^+$ 255, found 255.

Ethyl 3-hydroxy-3-(*o*-nitrophenyl)propanoate (12) ^1H NMR (400 MHz, CDCl_3) δ 7.95 (dd, $J = 0.95, 1.15$ Hz, 1H), 7.89 (dd, $J = 0.76, 0.66$ Hz, 1H), 7.67 (m, 1H), 7.44 (m, 1H), 5.66 (d, $J = 9.37$ Hz, 1H), 4.2 (q, $J = 7.14$ Hz, 2H), 3.86 (d, $J = 2.59$ Hz, 1H), 2.96 (dd, $J = 2.76, 2.76$ Hz, 1H), 2.66 (dd, $J = 9.4, 9.36$ Hz, 1H), 1.27 (t, $J = 7.12$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.66, 147.73, 138.5, 134.16, 128.83, 128.54, 124.83, 66.33, 61.5, 42.78, 14.49; IR (film) 3420, 2960, 1700, 1500, 1320, 1280, 1250 cm^{-1} ; MS (CI) calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_5$ $[\text{M}+\text{H}]^+$ 240, found 240.

Ethyl 3-hydroxy-3-(*o*-hydroxyphenyl)propanoate (13) ^1H NMR (400 MHz, CDCl_3) δ 7.18 (1H, m), 6.98 (1H, dd, $J = 1.43, 1.43$ Hz), 6.88-6.81 (2H, m), 5.27 (1H, dd, $J = 3.06, 3.06$ Hz), 4.21 (2H, q, $J = 7.14$ Hz), 2.95 (1H, dd, $J = 10.27, 10.25$ Hz), 2.72 (1H, dd, $J = 3.16, 3.11$ Hz), 1.28 (3H, t, $J = 7.15$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 173.08, 155.66, 129.32, 126.66, 125.31, 119.97, 117.48, 71.48, 61.28, 40.95, 14.11; IR (film) 3370, 2980, 1700, 1610, 1490, 1450, 1370, 1350, 1220 cm^{-1} ; MS (CI) calcd for $\text{C}_{11}\text{H}_{15}\text{O}_4$ $[\text{M}+\text{H}]^+$ 211, found 211.

Ethyl 3-hydroxy-3-(*m*-hydroxyphenyl)propanoate (14) ^1H NMR (400 MHz, CDCl_3) δ 7.15 (1H, t, $J = 7.8$ Hz), 6.83 (1H, d, $J = 7.08$ Hz), 6.73 (2H, m), 5.05 (3H, q, $J = 4.32$ Hz, H-3), 4.14 (2H, q, $J = 7.13$ Hz), 2.72 (1H, dd, $J = 9.02, 9.02$ Hz), 2.65 (1H, dd, $J = 3.95, 3.94$ Hz), 1.23 (3H, t, $J = 7.13$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 172.64, 156.18, 143.96, 129.81, 117.74, 115.10, 112.77, 70.38, 61.15, 43.18, 14.07; IR (film) 3380, 3050, 2980, 1720, 1600, 1450, 1420, 1250 cm^{-1} ; MS (CI) calcd for $\text{C}_{11}\text{H}_{15}\text{O}_4$ $[\text{M}+\text{H}]^+$ 211, found 211.

Ethyl 3-hydroxy-3-(2-furyl)propanoate (15) ^1H NMR (400 MHz, CDCl_3) δ 7.36 (t, $J = 0.89$ Hz, 1H), 6.33-6.26 (m, 2H), 5.13 (q, $J = 4.23$ Hz, 1H), 4.18 (q, $J = 7.11$ Hz, 2H), 3.25 (s, 1H), 2.92-2.79 (m, 2H), 1.26 (t, $J = 7.16$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 170.29, 153.2, 14.59, 108.62, 104.65, 62.55, 59.33, 38.24, 12.5; IR (film) 3450, 2960, 2920, 1715, 1640, 1500, 1360, 1280, 1240 cm^{-1} ; MS (CI) calcd for $\text{C}_9\text{H}_{12}\text{O}_4$ $[\text{M}+\text{H}]^+$ 185, found 185.

Ethyl 3-hydroxy-3-(2-thienyl)propanoate (16) ^1H NMR

(400 MHz, CDCl_3) δ 7.26-7.23 (1H, m), 6.96-6.94 (2H, m), 5.36 (1H, m), 4.58 (2H, q, $J = 7.14$ Hz), 3.55 (1H, d, $J = 4.27$ Hz), 2.90-2.79 (1H, m), 1.26 (3H, t, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 172.32, 146.78, 127.1, 125.24, 124.03, 66.95, 61.39, 43.61, 14.53; MS (CI) calcd for $\text{C}_9\text{H}_{13}\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+$ 201, found 201.

Ethyl 3-hydroxy-5-phenyl-4-pentenoate (17) ^1H NMR (400 MHz, CDCl_3) δ 7.38-7.21 (m, 5H), 6.65 (d, $J = 16.04$ Hz, 1H), 6.22 (dd, $J = 6.12$ Hz, 1H), 4.72 (m, 1H), 4.18 (q, $J = 7.15$ Hz, 2H), 2.95 (s, 1H), 2.68-2.57 (m, 2H), 1.27 (t, $J = 7.17$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.65, 136.85, 131.16, 130.37, 128.98, 128.21, 126.95, 69.29, 61.27, 41.93, 14.59; IR (film) 3400, 2960, 1710, 1490, 1440, 1380, 1360, 1270, 1230 cm^{-1} ; MS (CI) calcd for $\text{C}_{13}\text{H}_{16}\text{O}_3$ $[\text{M}+\text{H}]^+$ 221, found 221.

Ethyl 3-hydroxy-3-methylbutanoate (18) ^1H NMR (400 MHz, CDCl_3) δ 4.18 (q, $J = 7.16$ Hz, 2H), 3.6 (s, 1H), 2.48 (s, 2H), 1.3-1.25 (m, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 173.04, 69.00, 60.64, 46.31, 29.14, 14.19; IR (film) 3440, 2960, 2910, 1710, 1370, 1200 cm^{-1} ; MS (CI) calcd for $\text{C}_7\text{H}_{14}\text{O}_3$ $[\text{M}+\text{H}]^+$ 147, found 147.

1-Ethoxycarbonylmethylcyclohexanol (19) ^1H NMR (400 MHz, CDCl_3) δ 4.17 (q, $J = 7.14$ Hz, 2H), 3.44 (s, 1H), 2.46 (s, 2H), 1.72-1.62 (m, 4H), 1.56-1.47 (m, 1H), 1.46-1.32 (m, 4H), 1.27 (m, 4H); ^{13}C NMR (100 MHz, CDCl_3) δ 173.32, 70.31, 60.92, 45.65, 37.80, 25.98, 22.36, 14.56; IR (film) 3500, 2910, 2850, 1705, 1450, 1370, 1310, 1230 cm^{-1} ; MS (CI) calcd for $\text{C}_{10}\text{H}_{18}\text{O}_3$ $[\text{M}+\text{H}]^+$ 187, found 187.

Ethyl 3-hydroxy-3-phenylbutanoate (20) ^1H NMR (400 MHz, CDCl_3) δ 7.43 (2H, m), 7.33 (2H, m), 7.25-7.21 (1H, m), 4.39 (1H, s), 4.05 (2H, q, $J = 7.13$ Hz), 2.88 (2H, dd, $J = 15.8, 15.9$ Hz), 1.54 (3H, s), 1.12 (3H, t, $J = 7.2$ Hz); ^{13}C NMR (100 MHz, CDCl_3) δ 172.72, 146.83, 128.23, 126.84, 124.45, 72.74, 60.73, 46.41, 30.66, 13.98; IR (film) 3460, 3020, 2960, 2900, 1690, 1480, 1430, 1360, 1320, 1240 cm^{-1} ; MS (CI) calcd for $\text{C}_{12}\text{H}_{17}\text{O}_3$ $[\text{M}+\text{H}]^+$ 209, found 209.

Ethyl 3-hydroxy-3-(*p*-methylphenyl)propanoate (21) ^1H NMR (400 MHz, CDCl_3) δ 7.43 (m, 2H), 7.33 (m, 2H), 7.25-7.21 (m, 1H), 4.39 (s, 1H), 4.05 (q, $J = 7.13$ Hz, 2H), 2.88 (dd, $J = 15.8, 15.9$ Hz, 2H), 1.54 (s, 3H), 1.12 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.72, 146.83, 128.23, 126.84, 124.45, 72.74, 60.73, 46.41, 30.66, 13.98; IR (film) 3460, 3020, 2960, 2900, 1690, 1480, 1430, 1360, 1320, 1240 cm^{-1} ; MS (CI) calcd for $\text{C}_{12}\text{H}_{16}\text{O}_3$ $[\text{M}+\text{H}]^+$ 222, found 222.

Ethyl 3-hydroxy-2-methyl-3-phenylpropanoate (22) ^1H NMR (200 MHz, CDCl_3) δ 7.35 (m, 5H), 5.01 (t, $J = 4.63$ Hz, 1H), 3.70 (d, $J = 11.90$ Hz, 3H), 3.01 (m, 1H), 2.82 (m, 1H), 1.11 (d, $J = 7.33$ Hz, 3H).

3-Hydroxy-2,2-dimethyl-3-phenylpropanoate (23) ^1H NMR (200 MHz, CDCl_3) δ 7.31 (m, 5H), 4.91 (d, $J = 4.27$ Hz, 1H), 4.17 (q, $J = 7.01$ Hz, 2H), 3.18 (d, $J = 4.17$ Hz, 1H), 1.27 (t, $J = 7.01$ Hz, 3H), 1.13 (d, $J = 5.19$ Hz, 6H).

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References

- (a) Shriner, R. L. *Org. React.* **1946**, *1*, 1. (b) Rathke, M. W. *Org. React.* **1975**, *22*, 423. (c) Gensler, W. J. *Chem. Rev.* **1957**, *57*, 265. (d) Diaper, D. G. M.; Kuskis, A. *Chem. Rev.* **1959**, *59*, 89.
- (a) Becker, D.; Brodsky, N.; Kalo, I. *J. Org. Chem.* **1978**, *43*, 2557. (b) Barco, A.; Bennett, S.; Pollini, G. P. *J. Org. Chem.* **1980**, *45*, 4776. (c) Klipa, D. K.; Hart, H. J. *J. Org. Chem.* **1981**, *46*, 2815. (d) West, F. G.; Gunawardena, G. V. J. *J. Org. Chem.* **1993**, *58*, 5043. (e) Witzemann, J. S.; Nottingham, W. D. *J. Org. Chem.* **1989**, *54*, 3258 and references cited therein.
- (a) March, J. *Advanced Organic Chemistry*; Wiley: New York, 1992; p 929. (b) Marioka, K.; Hashimoto, S.; Kitagawa, Y.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 7705. (c) Harada, T.; Mukaiyama, T. *Chem. Lett.* **1982**, 161. (d) Imamoto, T.; Kusumoto, T.; Tawarayama, Y.; Sugiura, Y.; Yokoyama, M. *J. Org. Chem.* **1984**, *49*, 3904. (e) Nokami, J.; Tamaoka, T.; Ogawa, H.; Wakabayashi, S. *Chem. Lett.* **1986**, 541. (f) Shen, Z.; Zhang, J.; Zou, H.; Yang, M. *Tetrahedron Lett.* **1997**, *38*, 2733. (g) Gabriel, T.; Wessjohann, L. *Tetrahedron Lett.* **1997**, *38*, 1363. (h) Gabriel, T.; Wessjohann, L. *Tetrahedron Lett.* **1997**, *38*, 4387. (i) Chao, L.-C.; Rieke, R. D. *J. Org. Chem.* **1975**, *40*, 2253. (j) Araki, S.; Ito, H.; Butsugan, Y. *Synth. Commun.* **1988**, *18*, 453. (k) Araki, S.; Ito, H.; Katsumura, N.; Butsugan, Y. *J. Organomet. Chem.* **1989**, *369*, 291. (l) Araki, S.; Katsumura, N.; Kawasaki, K.; Butsugan, Y. *J. Chem. Soc. Perkin Trans. 1* **1991**, 499. (m) Johar, P. S.; Araki, S.; Butsugan, Y. *J. Chem. Soc. Perkin Trans. 1* **1992**, 711. (n) Schick, H.; Ludwig, R.; Schwarz, K.-H.; Kleiner, K.; Kunath, A. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1191. (o) Cahiez, G.; Chavant, P.-Y. *Tetrahedron Lett.* **1989**, *30*, 7373. (p) Kagan, H. B.; Namy, J.-L.; Girard, P. *Tetrahedron* **1981**, *37*, 175. (q) Tabuchi, T.; Kawamura, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 3889. (r) Molander, G. A.; Etter, J. B. *J. Am. Chem. Soc.* **1987**, *109*, 6556. (s) Huang, X.; Xie, L.; Wu, H. *Tetrahedron Lett.* **1987**, *28*, 801.
- (a) Fustner, A. *Synthesis* **1989**, 571. (b) Fustner, A. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 164.
- Rieke, R. D.; Uhm, S. J. *Synthesis* **1975**, 452.
- (a) Mason, T. J.; Lorimer, J. P. *Sonochemistry: Theory, Applications and Uses of Ultrasound in Chemistry*; Ellis Horwood Limited: Chichester, 1988. (b) Han, B. H.; Boudjouk, P. J. *J. Org. Chem.* **1982**, *47*, 5030. (c) Nishiyama, T.; Woodhall, J. F.; Lawson, E. N.; Kitching, W. J. *J. Org. Chem.* **1989**, *54*, 2184.
- (a) Lee, P. H.; Bang, K.; Lee, K.; Lee, C.-H.; Chang, S. *Tetrahedron Lett.* **2000**, *41*, 7521. (b) Lee, P. H.; Bang, K.; Ahn, H.; Lee, K. *Bull. Korean Chem. Soc.* **2001**, *22*, 1385. (c) Lee, P. H.; Seomoon, S.; Lee, K. *Bull. Korean Chem. Soc.* **2001**, *22*, 1380. (d) Lee, P. H.; Lee, K.; Sung, S.-Y.; Chang, S. *J. Org. Chem.* **2001**, *66*, 8646. (e) Lee, P. H.; Lee, K.; Kim, S. *Org. Lett.* **2001**, *3*, 3205. (f) Lee, P. H.; Sung, S.-Y.; Lee, K. *Org. Lett.* **2001**, *3*, 3201. (g) Lee, P. H.; Lee, K.; Chang, S. *Synth. Commun.* **2001**, *31*, 3189. (h) Lee, P. H.; Ahn, H.; Lee, K.; Sung, S.-Y.; Kim, S. *Tetrahedron Lett.* **2001**, *42*, 37. (i) Lee, P. H.; Sung, S.-Y.; Lee, K.; Chang, S. *Synlett* **2002**, 146.
- Lee, P. H.; Bang, K.; Lee, K.; Sung, S.-Y.; Chang, S. *Synth. Commun.* **2001**, *31*, 3781.