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ULTRASOUND PROMOTED SYNTHESIS OF β -HYDROXYESTERS BY REFORMATSKY REACTION USING INDIUM METAL

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ULTRASOUND PROMOTED SYNTHESIS OF β-HYDROXYESTERS BY REFORMATSKY REACTION USING INDIUM METAL

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This paper is dedicated to Professor In-Sup Han on the occasion of his 65th birthday.

ABSTRACT

Ultrasound promoted Reformatsky reaction by the reaction of aldehydes or ketone with ethyl bromoacetate in the presence of indium metal afforded β -hydroxyesters in good to excellent yields under mild conditions.

The Reformatsky reaction, which is regarded as one of the most fundamental reactions in carbon–carbon bond formations, is the reaction between a carbonyl compound with an α -haloester in the presence of zinc

3781

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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 described.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. zinc-copper 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 Recently, we reported the indium mediated organic reaction,⁷ and in this paper we describe the beneficial effects that ultrasonic irradiation has on the indium mediated Reformatsky reaction.

To find optimum conditions for ultrasound assisted Reformatsky reaction using indium, initially benzaldehyde (entry 4) was reacted with ethyl bromoacetate in the presence of indium in various solvents. Of the several solvents tested, THF gave the best results in terms of conversion and reaction times. The reaction of benzaldehyde with ethyl bromoacetate in the presence of indium in THF afforded ethyl 3-hydroxy-3-phenylpropanoate (4) in 97% yield. Sonications 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 W. However, the yields were decreased in other solvents under the identical conditions despite longer reaction times. Ultrasound promoted reaction condition was superior to stirring condition. In the absence of sonic waves, the reaction occurs much more slowly (17 h) and the yield of the β -hydroxyester 4 is only 70%. Rate per minute (rpm) for stirring conditions is ca. 900. Ethyl iodoacetate gave the similar results to ethyl bromoacetate.

Table 1 summarizes the experimental results and illustrates the efficiency and scope of the present method.⁸ In case of aliphatic aldehydes (entries 1, 2 and 3), the reaction afforded the desired compounds 1, 2 and 3 in excellent yields. For the aromatic aldehydes, the presence of various substituents, e.g., methyl (entry 5), chloro (entry 6), bromo (entry 7), monomethoxy (entry 8), or dimethoxy (entry 9) on the aromatic ring showed little effects on the efficiency of the reactions. It should be mentioned that 2- or 3-hydroxybenzaldehyde (entries 10 and 11) that contains an acidic hydrogen was reacted with the same efficiency to provide the desired compounds 10 and 11 in 93 and 92% yields, respectively. The protocol developed here was also applied to reactions with ketone. For example, acetophenone (entry 13)



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Table 1. Preparation of β-Hydroxyesters by In-mediated Reactions of Carbonyl Compounds with Ethyl Bromoacetate

	RCHO +	Br_OEt	In / THF rt (((((R H O	`OEt	
Entry	Carbonyl Compound	ds Time / h	Products		ls	olated Yield % ^a
1	CH ₃ CH ₂ CH ₂ CHO	3	CH3CH2CH2CH(OH)	CH 2CO2Et	1	95
2	(CH ₃) ₂ CHCHO	2.5	(CH ₃) ₂ CHCH(OH)CH	l ₂CO₂Et	2	91
3	<i>с</i> -С ₆ Н ₁₁ СНО	2	<i>с</i> -С ₆ Н ₁₁ СН(ОН)СН	₂ CO ₂ Et	3	92
4	PhCHO	20	PhCH(OH)CH 2	CO₂Et	4	0 ^{b.c}
		10				0 ^{d,c}
		5				22 ^d
		17				70 ^{e,c}
		2				97'
	_	2		•		97
	о Ш		OH	0		
5	Г	2.5		OEt	5	92
					•	
	CH3 ~ 0		CH3 OH	0 II		
~	И ПО	2			6	01
0		2			v	51
	ci ^r v		сі 🗸 он	0		
	Br A		Br			
7	Т Y H	3	ĬĬĬ	OEt	7	91
	\checkmark		🗸 он	0		
	۸ Å		a L	Ļ.		
8	Г Y H	2.5	$\int \nabla $	OEt	8	90
•	MeO		MeO			
				•		
	MeO O		MeO OH	0		
	Г	2		OEt	0	90
9	\ \ \ \ \	2	- And		3	30
	~ OMe		• Ome			
	он о		ОН ОН О	2 2		
	\downarrow					
10	Γ Π	2		OEI	10	93
				0		
			HO	ĭ		
11	п∪ү∕үү	2.5		∕_`OEt	11	92
	0		ОЧ	0		
	,s. Ĭ		.s. J	ĭ		
12	(́ ∕ `н	2.5	$\langle \gamma \rangle$	`OEt	12	90
	<u> </u>		ك			
	Р		он о			
13	вь Кона	3	Ph		13	90
	013					

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^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. ^bSolvent: H₂O. ^cThe reaction mixture was stirred (rpm:~ 900). ^dsolvent: DMF. ^esolvent: THF. ^fEthyl iodoacetate was used.



3783

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was reacted under the identical conditions to give the β -hydroxyester **13** in 90% yield. However, indium promoted reaction of acetophenone with ethyl bromoacetate gave β -hydroxyester **13** in 40% yield without sonic waves. The sonicated mixture of zinc, ethyl bromoacetate, and acetophenone gave no addition product in the absence of iodine.⁶

3784

In summary, ultrasound mediated Reformatsky reaction using indium afforded β -hydroxyesters in high yields. There are several advantages of the method such as (a) the organoindium compound is prepared and used *in situ*; (b) it has a wide application for elongation of carbon chains; (c) compared to the use of zinc and tin, the reaction with indium did not require any promoter (iodine or potassium iodide); and (d) the organo-indium intermediates do not react with themselves in normal conditions. The present method complements the existing synthetic methods because of mild reaction condition and advantages of indium metal with regard to easy handling, high reactivity and selectivity, low toxicity, and operational simplicity. Further studies are now in progress.

EXPERIMENTAL SECTION

Typical procedure for indium-mediated Reformatsky reaction: Ethyl 3-hydroxy-3-phenylpropanoate (4). 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), 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 W, for 2 h, the reaction mixture was quenched with saturated aqueous NaHCO₃ solution. The aqueous layer was extracted with ether $(3 \times 25 \text{ mL})$ and the combined organic layers were washed with water (20 mL), brine (20 mL), 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-3phenylpropanoate (94.0 mg, 97%). ¹H NMR (200 MHz, CDCl₃) δ 7.4–7.25 (5H, m, Ph), 5.14 (1H, q, J = 4.0 Hz, H-3), 4.19 (2H, q, J = 7.20 Hz, H-2),3.14 (1H, br s, OH), 2.83–2.64 (2H, m, OCH₂), 1.26 (3H, J=7.00 Hz, OCH₂CH₃); ¹³C NMR (50 MHz, CDCl₃) δ 172.64 (s, C=O), 142.62 (s, Ph-1), 128.69 (s, Ph-2,6), 127.94 (s, Ph-3,5), 125.81 (s, Ph-4), 70.40 (s, C-OH), 61.02 (s, OCH₂CH₃), 43.41 (s, OCOCH₂), 14.23 (s, OCH₂CH₃); IR (film) 3460, 2980, 1720, 1490, 1450, 1395, 1370, 1295, 1260 cm⁻¹; HRMS (CI) calcd for $C_{11}H_{15}O_3 [M + H]^+$ 195.1022, found 195.1028.

Ethyl 3-hydroxyhexanoate (1). ¹H NMR (400 MHz, CDCl₃) δ 4.17 (2H, q, J = 7.15 Hz, OCH₂CH₃), 4.02 (1H, m, H-3), 3.01 (1H, d, J = 3.69 Hz,

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OH), 2.49 (1H, dd, J = 3.32, 3.16 Hz, H-2), 2.39 (1H, dd, J = 8.93, 8.93 Hz, H-2), 1.25–1.53 (4H, m, H-4,5), 1.27 (3H, t, J = 7.20 Hz, OCH₂CH₃), 0.93 (3H, t, J = 6.99 Hz, H-6); ¹³C NMR (100 MHz, CDCl₃) δ 173.13 (s, <u>C</u>=O), 67.77 (s, <u>C</u>-OH), 60.67 (s, OCH₂CH₃), 41.38 (s, OCOCH₂), 38.68 (s, <u>CH₂CH₂CH₃</u>), 18.69 (s, CH₂<u>CH₂CH₃</u>), 14.19 (s, CH₂CH₂<u>CH₃</u>), 13.97 (s, OCH₂<u>CH₃</u>); 1R (film) 3480, 3050, 2960, 1720, 1260 cm⁻¹; HRMS (CI) calcd for C₈H₁₇O₃ [M + H]⁺ 161.1179, found 161.1170.

Ethyl 3-hydroxy-4-methylpentanoate (2). ¹H NMR (400 MHz, CDCl₃) δ 4.17 (2H, q, J = 7.14 Hz, OCH₂), 3.78 (1H, m, H-3), 3.05 (1H, br s, OH), 2.50 (1H, dd, J = 2.92, 2.92 Hz, H-2), 2.40 (1H, dd, J = 9.53, 9.53 Hz, H-2), 1.72 (1H, m, H-4), 1.27 (3H, t, J = 7.15 Hz, OCH₂CH₃), 0.94 (6H, q, J = 5.99 Hz, CH(CH₃)₂); ¹³C NMR (100 MHz, CDCl₃) δ 173.86 (s, <u>C</u>=O), 73.09 (s, <u>C</u>-OH), 61.05 (s, <u>OCH₂CH₃</u>), 38.84 (s, <u>OCOCH₂</u>), 33.52 (s, <u>C</u>H(Me)₂), 18.70 (s, CH(<u>Me</u>)₂), 18.10 (s, CH(<u>Me</u>)₂), 14.52 (s, OCH₂CH₃); IR (film) 3440, 2975, 1720, 1470, 1370, 1320, 1270 cm⁻¹; HRMS (CI) calcd for C₈H₁₇O₃ [M + H]⁺ 161.1179, found 161.1185.

Ethyl 3-cyclohexyl-3-hydroxypropanoate (3). ¹H NMR (400 MHz, CDCl₃) δ 4.17 (2H, q, OCH₂CH₃), 3.79–3.75 (1H, m, H-3), 2.84 (1H, br s, OH), 2.51 (1H, dd, J= 2.80, 2.86 Hz, H-2), 2.41 (1H, dd, J= 9.50, 9.49 Hz, H-2), 1.86 (1H, d, J= 12.65 Hz, H-4), 1.76 (2H, m, H-5), 1.66 (2H, d, J= 12.30 Hz, H-9), 1.41–1.11 (9H, m, H-6,7,8); ¹³C NMR (100 MHz, CDCl₃) δ 174.60 (s, <u>C</u>=O), 73.17 (s, <u>C</u>-OH), 61.69 (s, <u>OCH₂CH₃), 44.07 (s, OCOCH₂), 39.59 (s, <u>CHCH₂CH₂CH₂CH₂CH₂CH₂), 27.44 (s, CHCH₂CH₂CH₂CH₂CH₂CH₂), 27.18 (s, CHCH₂CH₂CH₂CH₂CH₂CH₂), 27.06 (s, <u>CHCH₂CH₂CH₂CH₂CH₂CH₂), 15.20 (s, OCH₂CH₃); IR (film) 3500, 3050, 2980, 2920, 2840, 1720, 1450, 1410, 1370, 1260 cm^{-T}; HRMS (CI) calcd for C₁₁H₂₁O₃ [M + H]⁺ 201.1492, found 201.1480.</u></u></u>

Ethyl 3-hydroxy-3-(*p***-methylphenyl)propanoate (5).** ¹H NMR (400 MHz, CDCl₃) δ 7.25 (2H, d, J = 8.02 Hz, Ph-2,6), 7.14 (2H, d, J = 7.95 Hz, Ph-3,5), 5.08 (1H, q, J = 4.18 Hz, H-3), 4.16 (2H, q, J = 7.13 Hz, s, OCH₂CH₃), 3.1 (1H, br s, OH), 2.77–2.57 (2H, m, H-2), 2.33 (3H, s, 4-Me-Ph), 1.25 (3H, t, J = 7.14 Hz, s, OCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 172.80 (s, <u>C</u>=O), 140.04 (s, Ph-1), 137.84 (s, Ph-4), 129.58 (s, Ph-2,6), 126.02 (s, Ph-3,6), 70.57 (s, <u>C</u>-OH), 61.21 (s, OCH₂CH₃), 43.76 (s, OCOCH₂), 21.49 (s, 4-Me-Ph), 14.54 (s, OCH₂CH₃); IR (film) 3410, 2960, 2900, 1715, 1510, 1440, 1390, 1365, 1290, 1260 cm^{-T}; HRMS (CI) calcd for C₁₂H₁₇O₃ [M + H]⁺ 209.1179, found 209.1165.

Ethyl 3-(*p***-chlorophenyl)-3-hydroxypropanoate (6).** ¹H NMR (400 MHz, CDCl₃) δ 7.31 (4H, s, Ph), 5.09 (1H, q, *J*=4.25 Hz, H-3), 4.17 (2H, q, *J*=7.12 Hz, s, OCH₂CH₃), 3.22 (1H, br s, OH), 2.68 (2H, m, OCOCH₂), 1.25 (3H, t, *J*=7.10 Hz, s, OCH₂CH₃); ¹³C NMR (100 MHz,

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CDCl₃) & 172.24 (s, C=O), 141.03 (s, Ph-4), 133.45 (s, Ph-3,5), 128.67 (s, Ph-1), 127.09 (s, Ph-2,6), 69.62 (s, C-OH), 61.00 (s, OCH₂CH₃), 43.20 (s, OCOCH₂), 14.13 (s, OCH₂CH₃); IR (film) 3400, 2930, 2860, 1695, 1470, 1375, 1350, 1280, 1260, $12\overline{40}$ cm⁻¹; HRMS (CI) calcd for C₁₁H₁₄Cl₁O₃ $[M + H]^+$ 229.0633, found 229.0641.

3786

Ethyl 3-(*m*-bromophenyl)-3-hydroxypropanoate (7). ¹H NMR (400 MHz, CDCl₃) δ 7.55 (1H, t, J=1.62 Hz, Ph-2), 7.42–7.40 (1H, m, Ph-4), 7.30–7.19 (2H, m, Ph-5,6), 5.08 (1H, m, H-3), 4.18 (2H, q, J=7.14 Hz, OCH₂CH₃),3.41 (1H, d, J = 3.55 Hz, OH), 2.71 (2H, d, J = 6.84 Hz, OCOCH₂), 1.26 (3H, t, J = 7.17 Hz, OCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 172.23 (s, C=O), 144.78 (s, Ph-3), 130.84 (s, Ph-4), 130.12 (s, Ph-2), 128.87 (s, Ph-1), 124.28 (s, Ph-5), 122.67 (s, Ph-6), 69.59 (s, C-OH), 61.04 (s, OCH₂CH₃), 43.14 (s, OCOCH₂), 14.14 (s, OCH₂CH₃); IR (film) 3500, 3050, 2980, 1720, 1420, 1260 cm⁻¹; HRMS (CI) calcd for $C_{11}H_{14}Br_1O_3$ [M + H]⁺ 273.0128, found 273.0120.

(8). Ethyl 3-hydroxy-3-(*p*-methoxyphenyl)propanoate ¹HNMR $(400 \text{ MHz}, \text{ CDCl}_3) \delta$ 7.30 (2H, d, J = 8.09 Hz, Ph-3,5), 6.89 (2H, d, J =8.49 Hz, Ph-2,6), 5.08 (1H, t, J=4.53 Hz, H-3), 4.18 (2H, q, J=7.14 Hz, OCH₂CH₃), 3.79 (3H, s, OCH₃), 3.20 (1H, br s, OH), 2.78-2.64 (2H, m, H-2), 1.25 (3H, t, J = 7.38 Hz, OCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 172.44 (s, C=O), 159.20 (s, Ph-4), 134.73 (s, Ph-1), 126.97 (s, Ph-2,6), 113.91 (s, Ph-3,5), 69.97 (s, C-OH), 60.83 (s, OCH₂CH₃), 55.29 (s, OCH₃), 43.33 (s, OCOCH₂), 14.16 (s, OCH₂CH₃); IR (film) 3450, 2970, 2830, 1715, 1600, 1500, 1460, 1365, 1295, 1240 cm⁻¹; HRMS (CI) calcd for C₁₂H₁₇O₄ $[M + H]^+$ 255.1128, found 255.1120.

Ethyl 3-hydroxy-3-(2,5-dimethoxyphenyl)propanoate (9). ¹H NMR (400 MHz, CDCl₃) δ 7.19 (1H, t, J=8.34 Hz, Ph-4), 6.56 (2H, d, J= 8.41 Hz, Ph-3,5), 5.66 (1H, dd, J=4.21, 4.31 Hz, H-3), 4.16 (2H, q, J = 7.14 Hz, OCH₂CH₃), 3.84 (6H, s, O(Me)₂), 3.55 (1H, br s, OH), 2.99 (1H, dd, J=9.87, 9.91 Hz, H-2), 2.65 (1H, dd, J=4.25, 4.36 Hz, H-2), 1.26 (3H, t, J = 7.1 Hz, OCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 172.01 (s, C=O), 158.07 (s, Ph-2,6), 129.30 (s, Ph-1), 118.40 (s, Ph-3,5), 104.59 (s, Ph-4), 64.94 (s, C-OH), 60.79 (s, OCH₂CH₃), 56.10 (s, O(Me)₂), 42.74 (s, OCOCH₂), 14.60 (s, OCH₂CH₃); IR (film) 33525, 2960, 2920, 2820, 1720, 1580, 1460, 1365, 1260 cm^{-T}; HRMS (CI) calcd for C₁₃H₁₉O₅ [M + H]⁺ 255.1234, found 255.1225.

3-hydroxy-3-(*o*-hydroxyphenyl)propanoate (10). ¹HNMR Ethyl $(400 \text{ MHz}, \text{ CDCl}_3) \delta$ 7.18 (1H, m, Ph-3), 6.98 (1H, dd, J = 1.43, 1.43 Hz, Ph-6), 6.88–6.81 (2H, m, Ph-4,5), 5.27 (1H, dd, J = 3.06, 3.06 Hz, H-3), 4.21 (2H, q, J = 7.14 Hz, OCH₂CH₃), 2.95 (1H, dd, J = 10.27, 10.25 Hz, H-2), 2.72 (1H, dd, J=3.16, 3.11 Hz, H-2), 1.28 (3H, t, J=7.15 Hz, OCH₂CH₃); ¹³CNMR (100 MHz, CDCl₃) δ 173.08 (s, C=O), 155.66 (s, Copyright © Marcel Dekker, Inc. All rights reserved

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Ph-2), 129.32 (s, Ph-1), 126.66 (s, Ph-3), 125.31 (s, Ph-6), 119.97 (s, Ph-4), 117.48 (s, Ph-5), 71.48 (s, C-OH), 61.28 (s, OCH₂CH₃), 40.95 (s, OCOCH₂), 14.11 (s, OCH₂CH₃); IR (film) 3370, 2980, 1700, 1610, 1490, 1450, 1370, 1350, 1220 cm⁻¹; HRMS (CI) calcd for $C_{11}H_{15}O_4$ [M + H]⁺ 211.0972, found 211.0985.

Ethyl 3-hydroxy-3-(m-hydroxyphenyl)propanoate (11). ¹H NMR (400 MHz, CDCl₃) δ 7.15 (1H, t, J=7.8 Hz, Ph-2), 6.83 (1H, d, J= 7.08 Hz, Ph-4,6), 6.73 (2H, m, Ph-5), 5.05 (3H, q, J=4.32 Hz, H-3, OH), 4.14 (2H, q, J=7.13 Hz, OCH₂CH₃), 2.72 (1H, dd, J=9.02, 9.02 Hz, H-2), 2.65 (1H, dd, J=3.95, 3.94 Hz, H-2), 1.23 (3H, t, J=7.13 Hz, OCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 172.64 (s, C=O), 156.18 (s, Ph-3), 143.96 (s, Ph-2), 129.81 (s, Ph-1), 117.74 (s, Ph-4), 115.10 (s, Ph-6), 112.77 (s, Ph-5), 70.38 (s, C-OH), 61.15 (s, OCH₂CH₃), 43.18 (s, OCOCH₂), 14.07 (s, OCH₂CH₃); IR (film) 3380, 3050, 2980, 1720, 1600, 1450, 1420, 1250 cm⁻¹; HRMS (CI) calcd for C₁₁H₁₅O₄ [M+H]⁺ 211.0972, found 211.0970.

Ethyl 3-hydroxy-3-(2-thienyl)propanoate (12). ¹H NMR (400 MHz, CDCl₃) δ 7.26–7.23 (1H, m, S-CH), 6.96–6.94 (2H, m, SCH=CH-CH), 5.36 (1H, m, H-3), 4.58 (2H, q, J=7.14 Hz, OCH₂CH₃), 3.55 (1H, d, J=4.27 Hz, OH), 2.90–2.79 (1H, m, H-2), 1.26 (3H, t, J=7.2 Hz, OCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 172.32 (s, <u>C</u>=O), 146.78 (s, thienyl-2), 127.1 (s, thienyl-5), 125.24 (s, thienyl-3), 124.03 (s, thienyl-4), 66.95 (s, <u>C</u>-OH), 61.39 (s, O<u>C</u>H₂CH₃), 43.61 (s, OCO<u>C</u>H₂), 14.53 (s, OCH₂<u>C</u>H₃); HRMS (CI) calcd for C₉H₁₃O₃S₁ [M + H]⁺ 201.0587, found 201.0581.

Ethyl 3-hydroxy-3-phenylbutanoate (13). ¹H NMR (400 MHz, CDCl₃) δ 7.43 (2H, m, Ph-2,6), 7.33 (2H, m, Ph-3,5), 7.25–7.21 (1H, m, Ph-4), 4.39 (1H, s, OH), 4.05 (2H, q, J=7.13 Hz, OCH₂CH₃), 2.88 (2H, dd, J=15.8, 15.9 Hz, H-2), 1.54 (3H, s, CCH₃), 1.12 (3H, t, J=7.2 Hz, OCH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 172.72 (s, <u>C</u>=O), 146.83 (s, Ph-1), 128.23 (s, Ph-2,6), 126.84 (s, Ph-3,5), 124.45 (s, Ph-4), 72.74 (s, <u>C</u>-OH), 60.73 (s, OCH₂CH₃), 46.41 (s, OCO<u>C</u>H₂), 30.66 (s, CCH₃), 13.98 (s, OCH₂<u>C</u>H₃); IR (film) 3460, 3020, 2960, 2900, 1690, 1480, 1430, 1360, 1320, 1240 cm⁻¹; HRMS (CI) calcd for C₁₂H₁₇O₃ [M + H]⁺ 209.1179, found 209.1173.

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3789

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