2-Iodoxybenzoic Acid/Tetraethylammonium Bromide/Water: An Efficient Combination for Oxidative Cleavage of Acetals

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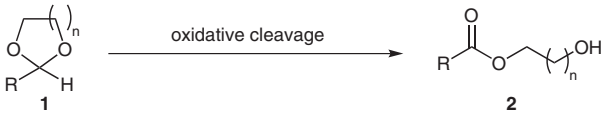
Abstract: A simple and efficient procedure has been developed for the oxidation of cyclic and acyclic acetals to the corresponding hydroxyalkyl carboxylic esters and simple esters, respectively. 2-Iodoxybenzoic acid (IBX) in the presence of tetraethylammonium bromide was employed for the reaction in aqueous media. The salient features of the protocol include short reaction time, environmentally benign reagents and solvent, and moderate to high yields.

Key words: *o*-iodoxybenzoic acid, acetals, oxidations, hydroxyalkyl esters, alcohols

Cyclic acetals are often used in organic synthesis, particularly as carbonyl protecting groups,[1] as well as for the synthesis of hydroxyalkyl carboxylic esters (Scheme 1), which are commercially important products serving as the cross-linking agents for polyesters as well as fungicides.[2] A number of oxidizing agents are used for the conversion of cyclic and acyclic acetals, and include molecular oxygen–cobalt(II),[3] di-*tert*-butyl peroxide,[4] *tert*-butyl hydroperoxide in combination with transition metals,[5] *tert*-butyl hydroperoxide–pyridinium dichromate,[6] *tert*-butyl hydroperoxide–iodine(III) compounds,[7] potassium permanganate,[8] electrochemical oxidation,[9] ozonolysis,[10] electrophilic halogen,[11] *m*-chloroperbenzoic acid in the presence of 2,2′-bipyridinium chlorochromate or boron trifluoride–diethyl ether,[12] sodium perborate in acetic anhydride,[13] and oxone.[14]



Scheme 1 Cleavage of cyclic acetals to form hydroxyalkyl carboxylic esters

Recently, the use of hypervalent iodine reagents in organic synthesis has attracted considerable interest owing to their mild, selective, and environmentally friendly properties.[15] 2-Iodoxybenzoic acid (IBX), despite its explosive properties, is a versatile oxidizing reagent due to its stability to air and moisture, mild reaction conditions, efficiency, and ease of preparation.[16] The synthetic utility of *o*-iodoxybenzoic acid as an efficient oxidizing reagent for elegant oxidative transformations has been demonstrated by several groups.[17] In continuation of our interest in the development of novel synthetic applications of *o*-iodoxybenzoic acid,[18] we disclose herein an efficient approach to hydroxyalkyl carboxylic esters by oxidative cleavage of cyclic acetals mediated by 2-iodoxybenzoic acid in the presence of tetraethylammonium bromide[19] in water.

Initially, the effect of various reaction parameters was examined, and for this 1,3-dioxolane **1a** derived from 4-nitrobenzaldehyde was utilized as the model substrate (Table 1). In the absence of tetraethylammonium bromide (entries 1–8), reactions performed at room temperature under various conditions gave unsatisfactory results, and mostly starting material was recovered (entries 1–5). Significant amounts of hydrolysis product **3a** was obtained when the reactions were carried out at elevated temperature in the absence of tetraethylammonium bromide (entries 6–8). Much to our delight, the addition of tetraethylammonium bromide (0.5 equiv) to the reaction mixture dramatically altered the situation; hydroxyalkyl ester **2a** formed in moderate to excellent conversion (entries 9–12). More importantly, water can be used as the solvent for this reaction (entry 12), providing the corresponding hydroxyalkyl ester **2a** in excellent conversion (97%). When the experiments were performed either at room temperature or with less tetraethylammonium bromide (0.25 equiv), the reactions remained incomplete and significant conversion to hydrolysis product occurred (entries 13 and 16). It should also be mentioned that no reaction took place in aqueous media in the presence of only *o*-iodoxybenzoic acid or only tetraethylammonium bromide (entries 14 and 15). Additionally, only moderate conversion occurred when the reaction of **1a** was carried out under our previously established biphasic conditions (CH_2Cl_2–H_2O, 1:1) (entries 17 and 18).[18]

The effect of the type of phase-transfer catalyst was also evaluated, as shown in Table 2. It is obvious that the type of the halide anion of the phase-transfer reagent has a considerable effect on this conversion. The presence of the bromide anion was found vital for the conversion of **1a** into **2a**. Tetraethylammonium bromide gave the best conversion (entry 1), while tetrabutylammonium bromide and cetyltrimethylammonium bromide (CTMAB) led to com-

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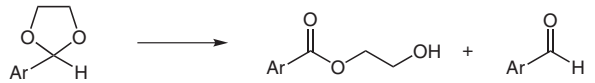
Table 1 Optimization of Reagents and Reaction Conditions for the Oxidation of Acetal **1a**



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

Ar = 4-$O_2NC_6H_4$

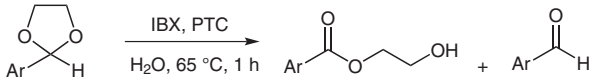
Entry	IBX/Et_4NBr (equiv)	Conditions	Conversion[a] (%)	
			2a	**3a**
1	1.1:0	CH_2Cl_2–H_2O (4:1), r.t., 24 h	0	0
2	1.1:0	acetone–H_2O (4:1), r.t., 24 h	0	0
3	1.1:0	EtOAc–H_2O (4:1), r.t., 24 h	0	2
4	1.1:0	MeCN–H_2O (4:1), r.t., 24 h	0	6
5	1.1:0	DMSO–H_2O (4:1), r.t., 24 h	0	5
6	1.1:0	MeCN–H_2O (4:1), 65 °C, 24 h	0	57
7	1.1:0	DMSO–H_2O (4:1), 65 °C, 24 h	0	53
8	1.1:0	DMSO–H_2O (4:1), 100 °C, 24 h		96
9	1.1:0.5	MeCN–H_2O (3:1), 65 °C, 1 h	67	0
10	1.1:0.5	MeCN–H_2O (1:3), 65 °C, 1 h	93	1
11	1.1:0.5	EtOAc–H_2O (1:3), 65 °C, 1 h	96	0
12	1.1:0.5	H_2O, 65 °C, 1 h	97	0
13	1.1:0.5	H_2O, r.t., 1 h	41	2
14	0:0.5	H_2O, 65 °C, 1 h	0	0
15	1.1:0	H_2O, 65 °C, 1 h	0	0
16	1.1:0.25	H_2O, 65 °C, 3 h	63	24
17	1.1:0.5	CH_2Cl_2–H_2O (1:1), r.t., 1 h	55	0
18	1.1:0.5	CH_2Cl_2–H_2O (1:1), r.t., 4 h	52	0

[a] Calculated from ^{1}H NMR (300 MHz) integration.

paratively lower conversions (entries 2 and 3). Unexpectedly, the chloride and iodide anions did not give the expected hydroxyalkyl ester **2a**, and the hydrolysis product **3a** was obtained in moderate to low yields (entries 4–6).

Having established the optimal reaction conditions [IBX (1.1 equiv), Et_4NBr (0.5 equiv), H_2O, 65 °C], we then examined the scope and the generality of the reaction, and the results are summarized in Table 3. 1,3-Dioxolane- and 1,3-dioxane-derived aldehydes representing several structural varieties were prepared according to previously reported procedures[20] and were screened for their reactivity (entries 1–21). In general, aromatic 1,3-dioxolanes underwent oxidative cleavage, yielding β-hydroxyethyl esters in good yields (55–81%, entries 1–7). Oxidation of aliphatic 1,3-dioxolanes gave the corresponding esters in

Table 2 Evaluation of Phase-Transfer Catalysts for the Transformation of **1a** into **2a**[a]



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

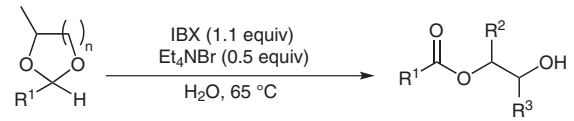
Ar = 4-$O_2NC_6H_4$

Entry	Phase-transfer reagent	Conversion[b] (%)	
		2a	**3a**
1	Et_4NBr	97	0
2	Bu_4NBr	89	0
3	CTMAB[c]	75	0
4	Et_4NCl	0	56
5	Et_4NI	0	1
6	Bu_4NI	0	2

[a] Reagents and conditions: IBX (1.1 equiv), phase-transfer reagent (0.5 equiv).
[b] Calculated from ^{1}H NMR (300 MHz) integration.
[c] CTMAB = cetyltrimethylammonium bromide.

moderate to good yields (entries 8–11). 1,3-Dioxane derivatives reacted with the reagents with almost equal facility, leading to corresponding γ-hydroxypropyl esters in comparable yields (entries 12–21). Unlike the reactions mediated by ozone,[10] electrochemical oxidation,[9] and hypervalent iodine(III),[7] the reactions of acyclic dialkyl acetals proceeded readily to give simple alkyl esters in moderate yields (entries 22 and 23). It should also be pointed out that the reaction of 1,3-dioxolane-derived 4-nitroacetophenone under standard conditions exclusively led to simple hydrolysis to the corresponding carbonyl compound.

Oxidation of unsymmetrical cyclic acetals under similar reaction conditions was also evaluated as shown in Scheme 2. Even though moderate to good yields were observed, an approximately 1:1 inseparable isomeric mixture of the hydroxyalkyl esters was obtained.



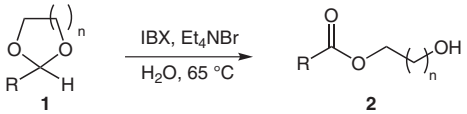
6a; R^1 = 4-$O_2NC_6H_4$
6b; R^1 = 2-$O_2NC_6H_4$

7aa; R^1 = 4-$O_2NC_6H_4$, R^2 = Me, R^3 = H, 39%
7ab; R^1 = 4-$O_2NC_6H_4$, R^2 = H, R^3 = Me, 39%
7ba; R^1 = 2-$O_2NC_6H_4$, R^2 = Me, R^3 = H, 30%
7bb; R^1 = 2-$O_2NC_6H_4$, R^2 = H, R^3 = Me, 24%

Scheme 2 Oxidation of unsymmetrical acetals

On the basis of the experimental results and literature precedents on similar acetal cleavage, a plausible reaction pathway for the formation of hydroxyalkyl esters is assumed to involve the following steps: (a) oxidation of the bromide anion by 2-iodoxybenzoic acid to give electro-

Table 3 Oxidation of Acetals with *o*-Iodoxybenzoic Acid and Tetraethylammonium Bromide in Water[a]

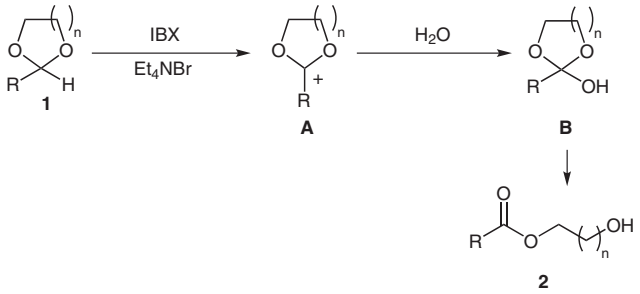


Entry	Acetal	R	n	Et_4NBr (equiv)	Time (h)	2	Yield[b] (%)
1	**1a**	4-$O_2NC_6H_4$	1	0.5	1	**2a**	81
2	**1b**	2-$O_2NC_6H_4$	1	0.5	5	**2b**	71
3	**1c**	4-BrC_6H_4	1	0.5	2	**2c**	75
4	**1d**	3-ClC_6H_4	1	0.5	1	**2d**	70
5	**1e**	4-FC_6H_4	1	0.5	1	**2e**	63
6	**1f**	Tol	1	1.0	1	**2f**	55
7	**1g**	Ph	1	0.5	1	**2g**	58
8	**1h**	Bn	1	0.5	2	**2h**	81
9	**1i**	CHMePh	1	0.5	1	**2i**	76
10	**1j**	*n*-C_8H_{17}	1	0.5	1	**2j**	62
11	**1k**	*n*-$C_{13}H_{27}$	1	0.5	1	**2k**	59
12	**1l**	4-$O_2NC_6H_4$	2	1.0	3	**2l**	50
13	**1m**	4-BrC_6H_4	2	0.5	2	**2m**	78
14	**1n**	3-ClC_6H_4	2	0.5	1	**2n**	78
15	**1o**	4-FC_6H_4	2	0.5	1	**2o**	61
16	**1p**	Tol	2	1.0	1	**2p**	42
17	**1q**	Ph	2	0.5	1	**2q**	59
18	**1r**	Bn	2	0.5	2	**2r**	83
19	**1s**	CHMePh	2	0.5	1	**2s**	79
20	**1t**	*n*-C_8H_{17}	2	0.5	1	**2t**	86
21	**1u**	*n*-$C_{13}H_{27}$	2	0.5	1	**2u**	79
22	**4a**[c]	–	–	0.5	1	**5a**[c]	60
23	**4b**[c]	–	–	0.5	2.5	**5b**[c]	56

[a] Reagents and conditions: IBX (1.1 equiv), H_2O, 65 °C, in air.
[b] Isolated yield.
[c] Phenylacetaldehyde dimethyl acetal (**4a**); 2-phenylpropanal dimethyl acetal (**4b**); methyl phenylacetate (**5a**), methyl 2-phenylpropanoate (**5b**).

philic bromine; (b) oxidation of the acetal carbon to provide stabilized acetal carbocation **A**; (c) nucleophilic attack by water to give hemiorthoester **B**; and (d) ring opening of hemiorthoester **B** to provide, finally, hydroxyalkyl ester **2** (Scheme 3).

In summary, we have developed an efficient and simple method for the oxidative cleavage of cyclic and acyclic acetals to their corresponding hydroxyalkyl carboxylic esters and simple esters, respectively, using the combination of 2-iodoxybenzoic acid and tetraethylammonium bromide in water. The method has general scope, and a clean reaction occurs, giving the products in moderate to high yields; the short reaction time in aqueous media can be of great synthetic utility in organic synthesis. The oxidative hydrolysis of acetals and ketals by 2-iodoxybenzoic acid as well as other hypervalent iodine(III) reagents is currently being investigated and will be reported in due course.



Scheme 3 Plausible reaction pathway for 2-iodoxybenzoic acid/tetraethylammonium bromide mediated oxidative cleavage of acetals

All known compounds were characterized by ^1H and ^{13}C NMR, IR, and mass spectroscopy, and their spectroscopic data were identical to those reported in the literature. All new compounds were characterized by ^1H and ^{13}C NMR, IR, and high-resolution mass spectroscopy. ^1H and ^{13}C NMR spectra were run on Bruker DPX-300 and Bruker Avance 500 spectrometers. IR spectroscopy was carried out on a Perkin Elmer GX FT-IR System spectrometer, and HRMS was carried out on a Bruker micro TOF spectrometer.

Hydroxyalkyl Carboxylic Esters 2; General Procedure

IBX (154 mg, 0.55 mmol) was added to a suspension of acetal **1** or **4** (0.5 mmol) and Et_4NBr (52.5 mg, 0.25 mmol) in H_2O (2 mL), and the reaction mixture was vigorously stirred at 65 °C for the time period shown in Table 3. Upon completion of the reaction, the reaction mixture was quenched by the addition of sat. aq $Na_2S_2O_3$ (5 mL), and basified with sat. aq $NaHCO_3$ (5 mL); further stirring was followed by extraction with EtOAc (3 × 5 mL). The combined organic extracts were washed with H_2O (10 mL) and brine (10 mL), dried (Na_2SO_4), filtered, and concentrated (aspirator). The residue was purified by column chromatography (silica gel) to furnish the analytically pure product.

2-Hydroxyethyl 4-Bromobenzoate (2c)

Compound **2c** was prepared by the general procedure from **1c** (114.5 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 7:3) gave the title compound.

Yield: 92.0 mg (75%); colorless liquid; R_f = 0.26 (hexanes–EtOAc, 7:3).

IR (neat): 3419 (O–H), 1722 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.5 Hz, 2 H), 7.58 (d, *J* = 8.5 Hz, 2 H), 4.45 (t, *J* = 4.7 Hz, 2 H), 3.96 (t, *J* = 4.7 Hz, 2 H), 2.05 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2, 131.8, 131.2, 128.8, 128.3, 66.8, 61.3.

HRMS (ESI-TOF): *m/z* [M + Na^+] calcd for $C_9H_9BrO_3Na$: 266.9633; found: 266.9659.

2-Hydroxyethyl 3-Chlorobenzoate (2d)
Compound **2d** was prepared by the general procedure from **1d** (92.3 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 3:2) gave the title compound.

Yield: 70.0 mg (70%); pale yellow liquid; R_f = 0.30 (hexanes–EtOAc, 7:3).

IR (neat): 3419 (O–H), 1723 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.04 (t, *J* = 1.8 Hz, 1 H), 7.95 (ddd, *J* = 7.9, 1.5, 1.1 Hz, 1 H), 7.55 (ddd, *J* = 7.9, 2.1, 1.1 Hz, 1 H), 7.39 (td, *J* = 7.9, 0.3 Hz, 1 H), 4.47 (t, *J* = 4.7 Hz, 2 H), 3.97 (t, *J* = 4.7 Hz, 2 H), 2.42 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7, 134.5, 133.1, 131.6, 129.68, 129.66, 127.8, 66.9, 61.1.

HRMS (ESI-TOF): *m*/*z* [M + Na^+] calcd for $C_9H_9ClO_3Na$: 223.0138; found: 223.0145.

2-Hydroxyethyl 4-Fluorobenzoate (2e)
Compound **2e** was prepared by the general procedure from **1e** (84.0 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 1:1) gave the title compound.

Yield: 58.0 mg (63%); pale yellow liquid; R_f = 0.26 (hexanes–EtOAc, 7:3).

IR (neat): 3424 (O–H), 1719 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.11–8.04 (m, 2 H), 7.15–7.09 (m, 2 H), 4.44 (t, *J* = 4.7 Hz, 2 H), 3.94 (t, *J* = 4.7 Hz, 2 H), 2.73 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 165.8 (d, *J* = 252.9 Hz), 132.2 (d, *J* = 9.4 Hz), 126.1 (d, *J* = 2.9 Hz), 115.5 (d, *J* = 21.9 Hz), 66.6, 61.2.

HRMS (ESI-TOF): *m*/*z* [M + Na^+] calcd for $C_9H_9FO_3Na$: 207.0433; found: 207.0444.

2-Hydroxyethyl 2-Phenylethanoate (2h)
Compound **2h** was prepared by the general procedure from **1h** (72.9 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 7:3) gave the title compound.

Yield: 73.0 mg (81%); pale yellow liquid; R_f = 0.22 (hexanes–EtOAc, 7:3).

IR (neat): 3418 (O–H), 1732 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.27 (m, 5 H), 4.25 (t, *J* = 4.7 Hz, 2 H), 3.81 (t, *J* = 4.7 Hz, 2 H), 3.70 (s, 2 H), 2.10 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.9, 133.8, 129.2, 128.6, 127.2, 66.4, 61.0, 41.2.

HRMS (ESI-TOF): *m*/*z* [M + Na^+] calcd for $C_{10}H_{12}O_3Na$: 203.0684; found: 203.0667.

2-Hydroxyethyl 2-Phenylpropanoate (2i)
Compound **2i** was prepared by the general procedure from **1i** (89 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 9:1 to 7:3) gave the title compound.

Yield: 73.7 mg (76%); colorless liquid; R_f = 0.24 (hexanes–EtOAc, 7:3).

IR (neat): 3426 (O–H), 1732 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.32 (m, 4 H), 7.30–7.26 (m, 1 H), 4.24–4.16 (m, 2 H), 3.79 (q, *J* = 7.2 Hz, 1 H), 3.76–3.71 (m, 2 H), 2.19 (br s, 1 H), 1.53 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.8, 140.4, 128.6, 127.3, 127.2, 66.2, 60.9, 45.4, 18.4.

HRMS (ESI-TOF): *m*/*z* [M + Na^+] calcd for $C_{11}H_{14}O_3Na$: 217.0841; found: 217.0892.

2-Hydroxyethyl Nonanoate (2j)
Compound **2j** was prepared by the general procedure from **1j** (93.0 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 7:3) gave the title compound.

Yield: 62.6 mg (62%); colorless liquid; R_f = 0.23 (hexanes–EtOAc, 7:3).

IR (neat): 3423 (O–H), 1737 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 4.19 (t, *J* = 4.7 Hz, 2 H), 3.81 (t, *J* = 4.7 Hz, 2 H), 2.75 (br s, 1 H), 2.33 (t, *J* = 7.6 Hz, 2 H), 1.70–1.55 (m, 2 H), 1.40–1.20 (m, 10 H), 0.87 (t, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.2, 65.8, 61.1, 34.1, 31.7, 29.11, 29.05, 29.01, 24.8, 22.5, 14.0.

HRMS (ESI-TOF): *m*/*z* [M + Na^+] calcd for $C_{11}H_{22}O_3Na$: 225.1467; found: 225.1466.

2-Hydroxyethyl Tetradecanoate (2k)
Compound **2k** was prepared by the general procedure from **1k** (128.0 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 7:3) gave the title compound.

Yield: 80.2 mg (59%); colorless solid; mp 44–45 °C; R_f = 0.32 (hexanes–EtOAc, 7:3).

IR (KBr): 3367 (O–H), 1737 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.23 (t, *J* = 4.7 Hz, 2 H), 3.85 (t, *J* = 4.7 Hz, 2 H), 2.37 (t, *J* = 7.6 Hz, 2 H), 1.70–1.55 (m, 2 H), 1.40–1.20 (m, 21 H), 0.90 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.2, 65.9, 61.3, 34.2, 31.9, 29.64, 29.61, 29.57, 29.43, 29.32, 29.23, 29.12, 24.9, 24.7, 22.7, 14.1.

HRMS (ESI-TOF): *m*/*z* [M + Na^+] calcd for $C_{16}H_{32}O_3Na$: 295.2249; found: 295.2299.

3-Hydroxypropyl 4-Nitrobenzoate (2l)
Compound **2l** was prepared by the general procedure from **1l** (104.5 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 3:2) gave the title compound.

Yield: 56.3 mg (50%); pale yellow liquid; R_f = 0.14 (hexanes–EtOAc, 7:3).

IR (neat): 3416 (O–H), 1724 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.29 (d, *J* = 8.7 Hz, 2 H), 8.21 (d, *J* = 8.7 Hz, 2 H), 4.54 (t, *J* = 6.1 Hz, 2 H), 3.81 (t, *J* = 6.1 Hz, 2 H), 2.05 (quin, *J* = 6.1 Hz, 2 H), 2.03 (br s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.9, 150.5, 135.5, 130.7, 123.5, 62.8, 59.0, 31.6.

HRMS (ESI-TOF): *m*/*z* [M + Na^+] calcd for $C_{10}H_{11}NO_5Na$: 248.0535; found: 248.0533.

3-Hydroxypropyl 3-Chlorobenzoate (2n)
Compound **2n** was prepared by the general procedure from **1n** (99.3 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 1:1) gave the title compound.

Yield: 83.7 mg (78%); pale yellow liquid; R_f = 0.27 (hexanes–EtOAc, 7:3).

IR (neat): 3423 (O–H), 1720 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.00 (t, *J* = 1.8 Hz, 1 H), 7.92 (dt, *J* = 7.9, 1.1 Hz, 1 H), 7.54 (ddd, *J* = 7.9, 2.1, 1.1 Hz, 1 H), 7.39 (t, *J* = 7.9 Hz, 1 H), 4.49 (t, *J* = 6.2 Hz, 2 H), 3.79 (t, *J* = 6.2 Hz, 2 H), 2.45 (br s, 1 H), 2.02 (quin, *J* = 6.2 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.7, 134.5, 133.0, 131.8, 129.7, 129.6, 127.7, 62.2, 59.0, 31.7.

HRMS (ESI-TOF): *m/z* [M + Na^+] calcd for $C_{10}H_{11}ClO_3Na$: 237.0294; found: 237.0286.

3-Hydroxypropyl 4-Fluorobenzoate (2o)

Compound **2o** was prepared by the general procedure from **1o** (91 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 1:1) gave the title compound.

Yield: 60.5 mg (61%); colorless liquid; R_f = 0.26 (hexanes–EtOAc, 7:3).

IR (neat): 3407 (O–H), 1716 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07–8.02 (m, 2 H), 7.14–7.08 (m, 2 H), 4.47 (t, *J* = 6.1 Hz, 2 H), 3.77 (t, *J* = 6.1 Hz, 2 H), 2.47 (br s, 1 H), 2.01 (quin, *J* = 6.1 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 165.8 (d, *J* = 252.6 Hz), 132.1 (d, *J* = 9.3 Hz), 126.3 (d, *J* = 3.0 Hz), 115.5 (d, *J* = 21.9 Hz), 62.0, 59.0, 31.8.

HRMS (ESI-TOF): *m/z* [M + H^+] calcd for $C_{10}H_{12}O_3F$: 199.0770; found: 199.0740.

3-Hydroxypropyl 2-Phenylethanoate (2r)

Compound **2r** was prepared by the general procedure from **1r** (89 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 1:1) gave the title compound.

Yield: 80.6 mg (83%); colorless liquid; R_f = 0.21 (hexanes–EtOAc, 7:3).

IR (neat): 3416 (O–H), 1731 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.28 (m, 5 H), 4.24 (t, *J* = 6.1 Hz, 2 H), 3.64 (s, 2 H), 3.61 (t, *J* = 6.1 Hz, 2 H), 2.49 (br s, 1 H), 1.84 (quin, *J* = 6.1 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8, 133.8, 129.0, 128.4, 126.9, 61.8, 58.8, 41.2, 31.4.

HRMS (ESI-TOF): *m/z* [M + Na^+] calcd for $C_{11}H_{14}O_3Na$: 217.0841; found: 217.0833.

3-Hydroxypropyl 2-Phenylpropanoate (2s)

Compound **2s** was prepared by the general procedure from **1s** (96 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 9:1 to 4:1) gave the title compound.

Yield: 82.2 mg (79%); colorless liquid; R_f = 0.27 (hexanes–EtOAc, 7:3).

IR (neat): 3416 (O–H), 1732 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5 H), 4.26–4.19 (m, 2 H), 3.75 (q, *J* = 7.2 Hz, 1 H), 3.59–3.51 (m, 2 H), 2.15 (br s, 1 H), 1.81 (quin, *J* = 6.1 Hz, 2 H), 1.52 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.9, 140.4, 128.5, 127.3, 127.1, 61.7, 58.9, 45.5, 31.5, 18.2.

HRMS (ESI-TOF): *m/z* [M + Na^+] calcd for $C_{12}H_{16}O_3Na$: 231.0997; found: 231.1049.

3-Hydroxypropyl Nonanoate (2t)

Compound **2t** was prepared by the general procedure from **1t** (100 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 3:2) gave the title compound.

Yield: 93.0 mg (86%); colorless liquid; R_f = 0.24 (hexanes–EtOAc, 7:3).

IR (neat): 3425 (O–H), 1737 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.22 (t, *J* = 6.1 Hz, 2 H), 3.68 (t, *J* = 6.1 Hz, 2 H), 2.36 (br s, 1 H), 2.30 (t, *J* = 7.5 Hz, 2 H), 1.86 (quin, *J* = 6.1 Hz, 2 H), 1.70–1.52 (m, 2 H), 1.40–1.15 (m, 10 H), 0.87 (t, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.3, 61.1, 59.1, 34.3, 31.7 (2 C), 29.13, 29.07, 29.03, 24.9, 22.5, 14.0.

HRMS (ESI-TOF): *m/z* [M + Na^+] calcd for $C_{12}H_{24}O_3Na$: 239.1623; found: 239.1606.

3-Hydroxypropyl Tetradecanoate (2u)

Compound **2u** was prepared by the general procedure from **1u** (135.0 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 85:15) gave the title compound.

Yield: 113.0 mg (79%); colorless liquid; R_f = 0.30 (hexanes–EtOAc, 7:3).

IR (neat): 3297 (O–H), 1736 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.24 (t, *J* = 6.1 Hz, 2 H), 3.69 (t, *J* = 6.1 Hz, 2 H), 2.32 (t, *J* = 7.6 Hz, 2 H), 1.87 (quin, *J* = 6.1 Hz, 2 H), 1.65–1.59 (m, 2 H), 1.36–1.23 (m, 21 H), 0.88 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.3, 61.1, 59.1, 34.3, 31.9, 31.7, 29.62 (2 C), 29.58, 29.54, 29.4, 29.3, 29.2, 29.1, 24.9, 22.6, 14.0.

HRMS (ESI-TOF): *m/z* [M + Na^+] calcd for $C_{17}H_{34}O_3Na$: 309.2406; found: 309.2404.

Methyl 2-Phenylpropanoate (5b)

Compound **5b** was prepared by the general procedure from **4b** (90 mg, 0.5 mmol). Column chromatography (silica gel, 13 × 2 cm; hexanes–EtOAc, 1:0 to 3:2) gave the title compound.

Yield: 46.0 mg (56%); pale yellow liquid; R_f = 0.44 (hexanes–EtOAc, 9:1).

IR (neat): 1738 (C=O) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.26 (m, 5 H), 3.75 (q, *J* = 7.2 Hz, 1 H), 3.69 (s, 3 H), 1.53 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.0, 140.6, 128.6, 127.5, 127.1, 52.0, 45.4, 18.6.

HRMS (ESI-TOF): *m/z* [M + Na^+] calcd for $C_{10}H_{12}O_2Na$: 187.0735; found: 187.0728.

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