

# A Modified Synthesis of Oxetan-3-ol

X. Y. Xia<sup>a</sup>, W. Sun<sup>a</sup>, W. He<sup>a</sup>, Y. Feng<sup>a</sup>, L. Zhan<sup>a</sup>, and Y. Luo<sup>a,\*</sup>

<sup>a</sup> Shanghai Engineering Research Center of Molecular Therapeutics and New Drug Development,  
School of Chemistry and Molecular Engineering, East China Normal University, Shanghai, 200241 China  
\*e-mail: yluo@chem.ecnu.edu.cn

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**Abstract**—A highly regioselective ring opening reaction of terminal epoxides with 2-bromobenzoic acid catalyzed by tetrabutylammonium bromide was accomplished. The procedure is operationally simple and practical for the synthesis of a series of  $\beta$ -hydroxy esters. Using this protocol, oxetan-3-ol could be prepared efficiently in a good yield.

**Keywords:**  $\beta$ -hydroxy esters, 2-bromobenzoic acid, epoxide, epichlorohydrin, oxetan-3-ol

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Terminal epoxides are versatile substrates in organic synthesis because of the easy synthesis and ability to undergo ring opening reactions under the action of various nucleophiles [1]. Among such reactions, the reaction of carboxylic acids with terminal epoxides has attracted special attention [2], since it provides a convenient synthetic approach to 1,2-diol monoesters [3–4].

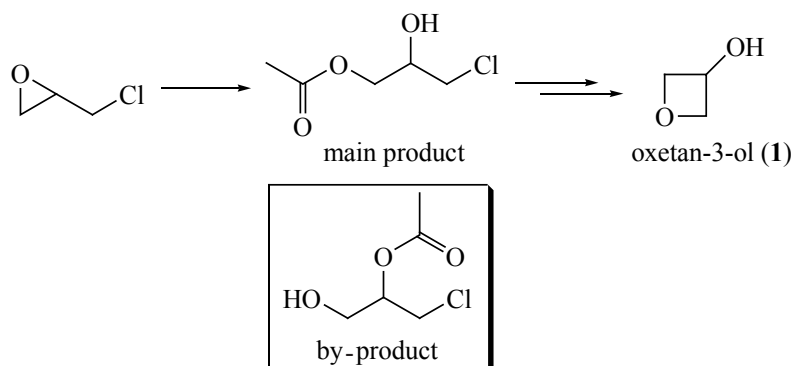
Many  $\beta$ -hydroxy esters are crucial precursors for the synthesis of natural products, pharmaceuticals, and fragrances [5–9]. For instance, oxetan-3-ol (**1**), a popular moiety in pharmaceutical industry, could be prepared from a  $\beta$ -hydroxy ester intermediate via ring opening in epichlorohydrin (Scheme 1) [10, 1]. Although several works have published on ring opening reaction in terminal epoxides with carboxylic acids, this reaction

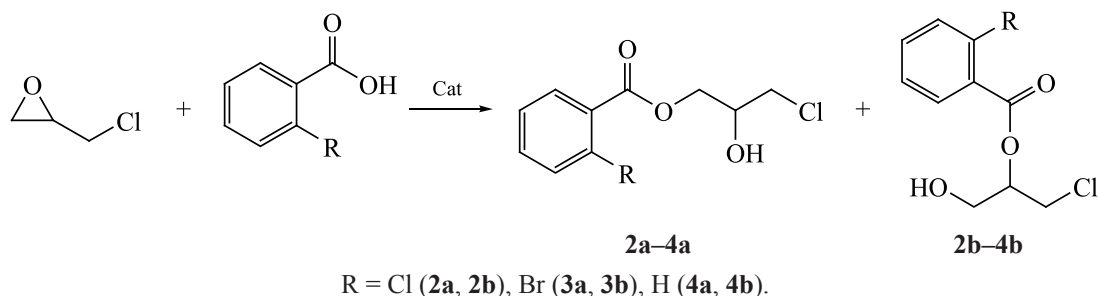
still calls for further investigations [12–14], because in some works the regioselectivity was not good enough, while in other works, insufficient regioselectivity data were reported [15, 16].

Recently, in an effort to develop a practical synthetic protocol for oxetan-3-ol (**1**), we obtained better results in the ring opening reactions of epichlorohydrin with benzoic acids, because the benzyloxy groups were less prone to isomerization and migration to the vicinal hydroxy group [17, 18]. Herein, we report the results of detailed investigations into the synthesis of this building block.

First we selected the reaction of 2-chlorobenzoic acid with epichlorohydrin as a model reaction (Table 1). We examined the effect of different phase-

**Scheme 1.**



**Table 1.** Screening of catalysts and solvents for ring opening in epichlorohydrin

Entry no.	Product no.	Catalyst	Solvent	Total yield, %	Regioisomeric ratio (a/b)
1	<b>2a/2b</b>	—	EtOAc	No reaction	—
2	<b>2a/2b</b>	TBAB	CH <sub>3</sub> CN	74	>99/1
3	<b>2a/2b</b>	TBAB	DMF	84	>99/1
4	<b>2a/2b</b>	TBAB	EtOAc	86	>99/1
5	<b>2a/2b</b>	TBAC	EtOAc	80	>99/1
6	<b>2a/2b</b>	TEBAC	EtOAc	77	>99/1
7	<b>3a/3b</b>	TBAB	EtOAc	93	>99/1
8	<b>4a/4b</b>	TBAB	EtOAc	87	5.8/1

transfer catalysts, including tetrabutylammonium bromide (TBAB), tetrabutylammonium chloride (TBAC), and benzyltriethylammonium chloride (TEBAC). As seen from Table 1, the reaction did not occur in the absence of a catalyst (Table 1, entry 1). As a remarkable advantage of our approach one can notice a dramatically reduced degree of isomerization, which can be associated with enhanced steric hindrance (Table 1, entries 2–7). However, the regioselectivity of the reaction with benzoic acid proved to be not so high (Table 1, entry 8). The best results were obtained with 1.1 equiv of 2-bromobenzoic acid, 5 mol % TBAB as the catalyst, and ethyl acetate as the solvent (Table 1, entry 7).

To explore the scope of the proposed protocol, a variety of epoxides were reacted with 2-bromobenzoic acid in the optimal conditions (Table 2). As seen, satisfactory yields were obtained with all the tested terminal epoxides.

Thus, a modified synthesis of oxetan-3-ol (**1**) could be developed. As the next step, 3-chloro-2-hydroxypropyl 2-bromobenzoate (**3a**) was treated with ethyl vinyl ether to obtain compound **11** (yield 85%) (Scheme 2). The subsequent hydrolysis of the latter gave alcohol **12** in a yield of 90%. However, we further found that cyclization

was another key step in the synthesis of oxetan-3-ol (**1**), which had to be optimized. To develop an efficient cyclization protocol, different bases and solvents were screened (Table 3). As seen from the Table 3, oxetane **13** was obtained in low yields in aprotic solvents, such as THF and DMF (entries 1, 2, and 10). Among the five protic solvents tested, *t*-BuOH usually gave better yields. Furthermore, among the five bases tested, *t*-BuONa and *t*-BuOK were more efficient than the other bases (Table 3, entries 8 and 11). We gave preference to *t*-BuONa, because it was cheaper than *t*-BuOK.

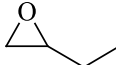
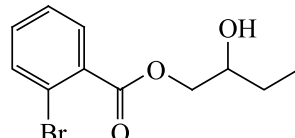
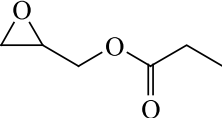
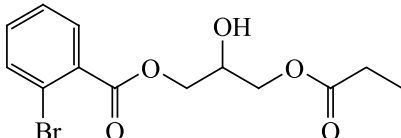
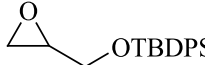
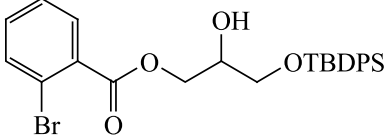
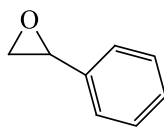
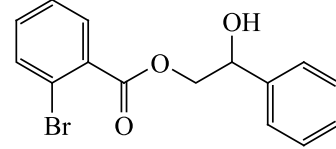
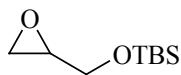
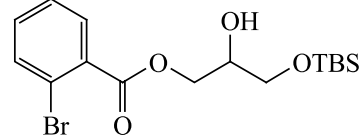
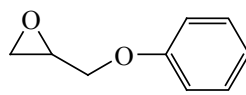
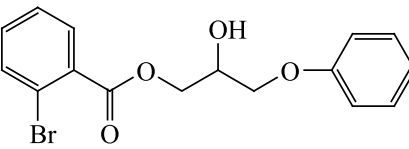
Finally, 3-(1-ethoxyethoxy)oxetane (**13**) was hydrolyzed with water in the presence of a catalytic amount of toluenesulfonic acid to obtain oxetan-3-ol (**1**) in 77% yield.

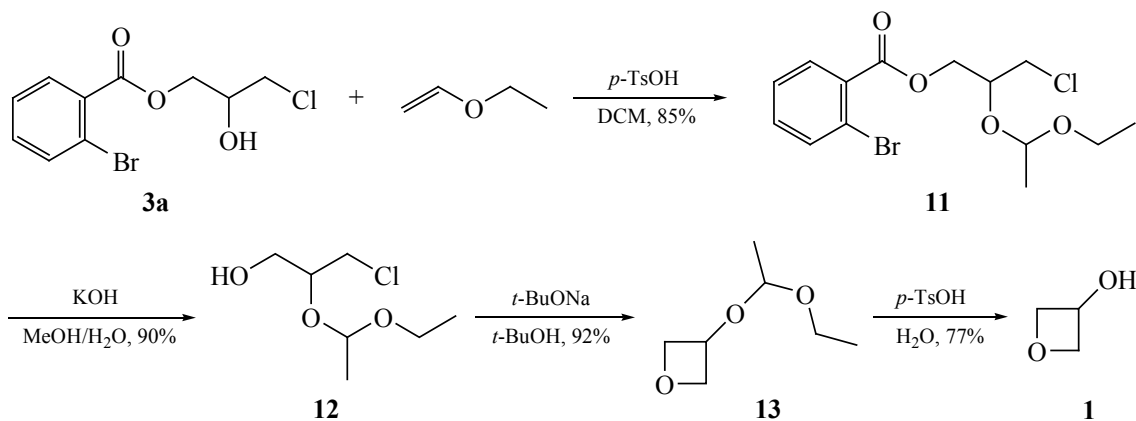
In conclusion, we developed an improved and facile five-step synthesis of oxetan-3-ol (**1**) with a total yield of 50%.

## EXPERIMENTAL

Commercial reagents were used without further purification. The IR spectra were run on a Bruker Tensor 27 FTIR spectrometer. The <sup>1</sup>H NMR spectra were recorded on Bruker DRX-400 (400 MHz) or Bruker

**Table 2.** Epoxide ring opening with 2-bromobenzoic acid

Entry no.	Epoxide	Product	Comp. no.	Yield, %
1			<b>5</b>	87
2			<b>6</b>	83
3			<b>7</b>	85
4			<b>8</b>	89
8			<b>9</b>	83
9			<b>10</b>	88

**Scheme 2.**

**Table 3.** Effect of bases and solvents on the cyclization of alcohol **12** into oxetane **13**

Entry no.	Base	Solvent	<i>T</i> , °C	Yield, %
1	NaH	THF	65	24
2	NaH	DMF	80	28
3	EtONa	EtOH	70	62
4	EtONa	<i>t</i> -BuOH	70	65
5	NaOH	MeOH	70	51
6	NaOH	EtOH	70	48
7	NaOH	<i>t</i> -BuOH	70	45
8	<i>t</i> -BuOK	<i>t</i> -BuOH	70	90
9	<i>t</i> -BuOK	EtOH	70	74
10	<i>t</i> -BuONa	THF	65	38
11	<i>t</i> -BuONa	<i>t</i> -BuOH	70	92
12	<i>t</i> -BuONa	EtOH	70	77

DRX-500 (500 MHz) spectrometers. The  $^{13}\text{C}$  NMR spectra were obtained on a JNM-EX400 (100 MHz) spectrometer. The chemical shifts were measured in ppm relative to TMS. The high-resolution mass spectra (ESI) were obtained on a Bruker MicroTof II mass spectrometer.

**Ring opening in epichlorohydrin (general procedure).** Epichlorohydrin (21.2 mmol) and TBAB (5 mol %) were added to a solution of carboxylic acid (19.2 mmol) in EtOAc. The reaction mixture was refluxed at 65°C for 4 h and then cooled down to room temperature and washed with a saturated  $\text{Na}_2\text{CO}_3$  solution. The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated to dryness, and the product was purified by column chromatography on silica gel, eluent petroleum ether–ethyl acetate, 5 : 10.

**3-Chloro-2-hydroxypropyl 2-chlorobenzoate (2a)** was prepared following the general procedure using 2-chlorobenzoic acid. Yield 4.10 g (86%), oil.  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 2.71 br.s (1H, OH), 3.69–3.76 m (2H,  $\text{CH}_2\text{Cl}$ ), 4.22–4.23 m (1H, CH), 4.47–4.48 m (2H,  $\text{OCH}_2$ ), 7.32–7.35 m ( $1\text{H}_{\text{arom}}$ ), 7.42–7.47 m ( $2\text{H}_{\text{arom}}$ ), 7.84–7.86 m ( $1\text{H}_{\text{arom}}$ ).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 45.9, 66.1, 69.4, 126.7, 129.4, 131.1, 131.7, 133.1, 133.6, 165.6. Mass-spectrum, found,  $m/z$ : 270.9912 [ $M$  ( $^{35}\text{Cl}$ ,  $^{35}\text{Cl}$ ) +  $\text{Na}$ ] $^+$ .  $\text{C}_{10}\text{H}_{10}\text{O}_3\text{Cl}_2\text{Na}$ . Calculated,  $m/z$ : 270.9905. Found,

$m/z$ : 272.9880 [ $M$  ( $^{35}\text{Cl}$ ,  $^{37}\text{Cl}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 272.9875.

**3-Chloro-2-hydroxypropyl 2-bromobenzoate (3a)** was prepared following the general procedure using 2-bromobenzoic acid. Yield 5.25 g (93%), oil.  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 2.80 br.s (1H, OH), 3.70–3.77 m (2H,  $\text{CH}_2\text{Cl}$ ), 4.22–4.25 m (1H, CH), 4.45–4.50 m (2H,  $\text{OCH}_2$ ), 7.35–7.41 m ( $2\text{H}_{\text{arom}}$ ), 7.67–7.68 m ( $1\text{H}_{\text{arom}}$ ), 7.81–7.83 m ( $1\text{H}_{\text{arom}}$ ).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 44.1, 64.4, 65.0, 121.7, 127.2, 131.4, 132.8, 134.4, 134.4, 165.8. Mass-spectrum, found,  $m/z$ : 314.9394 [ $M$  ( $^{35}\text{Cl}$ ,  $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ .  $\text{C}_{10}\text{H}_{10}\text{O}_3\text{BrClNa}$ . Calculated,  $m/z$ : 314.9394. Found,  $m/z$ : 316.9369 [ $M$  ( $^{37}\text{Cl}$ ,  $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 316.9374. Found,  $m/z$ : 318.9345 [ $M$  ( $^{37}\text{Cl}$ ,  $^{81}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 318.9344.

**3-Chloro-2-hydroxypropyl benzoate (4a)** was prepared following the general procedure using benzoic acid. Yield 3.58 g (87%), oil.  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 2.91 br.s (1H, OH), 3.63–3.73 m (2H,  $\text{CH}_2\text{Cl}$ ), 4.19–4.22 m (1H, CH), 4.44–4.48 m (2H,  $\text{OCH}_2$ ), 7.41–7.45 m ( $2\text{H}_{\text{arom}}$ ), 7.54–7.58 m ( $1\text{H}_{\text{arom}}$ ), 8.01–8.04 m ( $2\text{H}_{\text{arom}}$ ).

**2-Hydroxybutyl 2-bromobenzoate (5)** was prepared following the general procedure from 2-bromobenzoic acid (5.97 mmol), 1,2-epoxybutane (4.85 mmol), and TBAB (0.34 mmol). Yield 1.18 g (87%), oil. IR

spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2966, 2873, 1722, 1249.  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 0.94–1.02 m (3H,  $\text{CH}_2\text{CH}_3$ ), 1.56–1.59 m (2H,  $\text{CH}_2\text{CH}_3$ ), 2.27 br.s (1H, OH), 3.88–3.92 m (1H, CH), 4.17–4.41 m (2H,  $\text{OCH}_2$ ), 7.26–7.37 m (2H<sub>arom</sub>), 7.62–7.64 m (1H<sub>arom</sub>), 7.77–7.79 m (1H<sub>arom</sub>).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 8.8, 25.3, 68.5, 70.1, 120.4, 126.3, 130.5, 131.1, 131.7, 133.3, 165.3. Mass-spectrum, found,  $m/z$ : 294.9935 [ $M$  ( $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ .  $\text{C}_{11}\text{H}_{13}\text{O}_3\text{BrNa}$ . Calculated,  $m/z$ : 294.9940. Found,  $m/z$ : 296.9901 [ $M$  ( $^{81}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 296.9919.

**2-Hydroxy-3-(propanoyloxy)propyl 2-bromobenzoate (6)** was prepared following the general procedure from 2-bromobenzoic acid (4.97 mmol), 2,3-epoxypropyl propanoate (4.15 mmol), and TBAB (0.29 mmol). Yield 1.14 g (83%), oil. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2983, 1728, 1293, 1243.  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 1.11–1.15 m (3H,  $\text{CH}_2\text{CH}_3$ ), 2.35–2.40 m (2H,  $\text{CH}_2\text{CH}_3$ ), 3.02 br.s (1H, OH), 4.23–4.45 m (5H,  $\text{CH}_2\text{CHCH}_2$ ), 7.33–7.38 m (2H<sub>arom</sub>), 7.64–7.66 m (1H<sub>arom</sub>), 7.80–7.82 m (1H<sub>arom</sub>).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 9.0, 27.4, 65.1, 66.2, 68.0, 121.6, 127.3, 131.5, 131.6, 132.9, 134.4, 166.1, 174.6. Mass-spectrum, found,  $m/z$ : 352.9977 [ $M$  ( $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ .  $\text{C}_{15}\text{H}_{15}\text{O}_5\text{BrNa}$ . Calculated,  $m/z$ : 352.9995. Found,  $m/z$ : 354.9952 [ $M$  ( $^{81}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 354.9975.

**3-[[*tert*-Butyl(diphenyl)silyl]oxy]-2-hydroxypropyl 2-bromobenzoate (7)** was prepared following the general procedure from 2-bromobenzoic acid (5.72 mmol), *tert*-butyl(oxiran-2-ylmethoxy)diphenylsilane (4.80 mmol), and TBAB (0.34 mmol). Yield 2.10 g (85%), oil. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3071, 2928, 1728, 1243.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 1.08 s [9H,  $\text{C}(\text{CH}_3)_3$ ], 2.59 br.s (1H, OH), 3.76–3.83 m (2H,  $\text{OCH}_2$ ), 4.08–4.11 m (1H, CH), 4.41–4.47 m (2H,  $\text{OCH}_2$ ), 7.32–7.46 m (8H<sub>arom</sub>), 7.66–7.67 m (5H<sub>arom</sub>), 7.73–7.76 m (1H<sub>arom</sub>).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 18.5, 26.1, 63.8, 65.4, 69.2, 121.0, 126.4, 127.1, 129.2, 131.0, 131.1, 132.0, 132.1, 133.6, 134.8, 165.3. Mass-spectrum, found,  $m/z$ : 535.0920 [ $M$  ( $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ .  $\text{C}_{26}\text{H}_{29}\text{O}_4\text{BrNaSi}$ . Calculated,  $m/z$ : 535.0911. Found,  $m/z$ : 537.0913 [ $M$  ( $^{81}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 537.0890.

**2-Hydroxy-2-phenylethyl 2-bromobenzoate (8)** was prepared following the general procedure from 2-bromobenzoic acid (4.97 mmol), styrene oxide

(4.16 mmol), and TBAB (0.29 mmol). Yield 1.2 g (89%), oil. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 3060, 2939, 1717, 1249.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 2.20 br.s (1H, OH), 3.84–3.94 m (2H,  $\text{CH}_2$ ), 6.01–6.02 m (1H, CH), 7.22–7.39 m (7H<sub>arom</sub>), 7.58 d (1H<sub>arom</sub>,  $J$  7.4 Hz), 7.76 d (1H<sub>arom</sub>,  $J$  7.2 Hz).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 65.2, 77.7, 120.9, 126.1, 126.6, 127.8, 128.0, 131.0, 131.3, 132.1, 133.7, 135.9, 164.9. Mass-spectrum, found,  $m/z$ : 342.9920 [ $M$  ( $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ .  $\text{C}_{15}\text{H}_{13}\text{O}_3\text{BrNa}$ . Calculated,  $m/z$ : 342.9940. Found,  $m/z$ : 344.9910 [ $M$  ( $^{81}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 344.9920.

**3-[[*tert*-Butyl(dimethyl)silyl]oxy]-2-hydroxypropyl 2-bromobenzoate (9)** was prepared following the general procedure from 2-bromobenzoic acid (7.46 mmol), *tert*-butyldimethylsilyl glycidyl ether (6.37 mmol), and TBAB (0.45 mmol). Yield 2.04 g (83%), oil. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2958, 2851, 1718, 1243.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 0.08–0.10 m [6H,  $\text{Si}(\text{CH}_3)_2$ ], 0.91–0.92 m [9H,  $\text{C}(\text{CH}_3)_3$ ], 2.65 br.s (1H, OH), 3.73–3.77 m (2H,  $\text{OCH}_2$ ), 3.97–4.11 m (1H, CH), 4.38–4.42 m (2H,  $\text{OCH}_2$ ), 7.31–7.42 m (2H<sub>arom</sub>), 7.66 d (1H<sub>arom</sub>,  $J$  7.4 Hz), 7.79–7.85 m (1H<sub>arom</sub>).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: –4.85, 18.8, 26.4, 64.4, 66.8, 70.4, 122.2, 127.8, 132.1, 132.6, 133.3, 134.9, 166.8. Mass-spectrum, found,  $m/z$ : 411.0580 [ $M$  ( $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ .  $\text{C}_{16}\text{H}_{25}\text{O}_4\text{BrNaSi}$ . Calculated,  $m/z$ : 411.0598. Found,  $m/z$ : 413.0544 [ $M$  ( $^{81}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 413.0577.

**2-Hydroxy-3-phenoxypropyl 2-bromobenzoate (10)** was prepared following the general procedure from 2-bromobenzoic acid (7.03 mmol), 2-(phenoxyethyl)oxirane (5.85 mmol), and TBAB (0.41 mmol). Yield 1.80 g (88%), oil. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 2935, 2884, 1722, 1230.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 2.80 br.s (1H, OH), 4.13–4.16 m (2H,  $\text{OCH}_2$ ), 4.40–4.42 m (1H, CH), 4.53–4.61 m (2H,  $\text{OCH}_2$ ), 6.94–6.96 m (2H<sub>arom</sub>), 6.99–7.02 m (1H<sub>arom</sub>), 7.28–7.33 m (2H<sub>arom</sub>), 7.38–7.40 m (2H<sub>arom</sub>), 7.67–7.69 m (1H<sub>arom</sub>), 7.83–7.85 m (1H<sub>arom</sub>).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 66.4, 68.5, 68.7, 114.6, 121.4, 121.6, 127.3, 129.6, 131.6, 131.8, 132.9, 134.4, 158.3, 166.3. Mass-spectrum, found,  $m/z$ : 373.0021 [ $M$  ( $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ .  $\text{C}_{16}\text{H}_{15}\text{O}_4\text{BrNa}$ . Calculated,  $m/z$ : 373.0046. Found,  $m/z$ : 375.0000 [ $M$  ( $^{81}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 375.0025.

**3-Chloro-2-(1-ethoxyethoxy)propyl 2-bromobenzoate (11).** Ethyl vinyl ether (8.1 g, 110 mmol) and

toluenesulfonic acid (0.94 g, 3.75 mmol) were added to a solution of 3-chloro-2-hydroxypropyl 2-bromobenzoate (22 g, 75 mmol) in dichloromethane (90 mL). The reaction mixture was stirred at room temperature for 3 h and then washed with water (80 mL). The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated to give 23.3 g (85%) of compound **11** as a light yellow oil.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 1.14–1.21 m (3H,  $\text{CH}_2\text{CH}_3$ ), 1.33–1.37 m (3H,  $\text{CHCH}_3$ ), 3.64–3.73 m (4H,  $\text{CH}_2\text{Cl}$ ,  $\text{CH}_2\text{CH}_3$ ), 4.16–4.18 m (1H, CH), 4.44–4.53 m (2H,  $\text{OCH}_2$ ), 4.88–4.90 m (1H,  $\text{OCHO}$ ), 7.26–7.37 m (2H<sub>arom</sub>), 7.65–7.66 m (1H<sub>arom</sub>), 7.77–7.80 m (1H<sub>arom</sub>).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 15.2, 20.2, 44.1, 60.6, 65.0, 72.8, 99.9, 121.7, 127.2, 131.5, 131.8, 132.8, 134.4, 165.8. Mass spectrum, found,  $m/z$ : 386.9977 [ $M$  ( $^{35}\text{Cl}$ ,  $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ .  $\text{C}_{10}\text{H}_9\text{O}_3\text{Cl}_3\text{Na}$ . Calculated,  $m/z$ : 386.9975. Found,  $m/z$ : 388.9961 [ $M$  ( $^{37}\text{Cl}$ ,  $^{79}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 388.9954. Found,  $m/z$ : 388.9946 [ $M$  ( $^{35}\text{Cl}$ ,  $^{81}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 388.9945. Found,  $m/z$ : 390.9930 [ $M$  ( $^{37}\text{Cl}$ ,  $^{81}\text{Br}$ ) +  $\text{Na}$ ] $^+$ . Calculated,  $m/z$ : 390.9925.

**3-Chloro-2-(1-ethoxyethoxy)propanol (12).** Compound **11** (35 g, 95.7 mmol) and KOH (6.4 g, 0.11 mol) were added to a mixture of methanol (80 mL) and water (80 mL), and the reaction mixture was allowed to stand at room temperature for 5 h. Methanol was then removed under reduced pressure, and the residue was extracted with dichloromethane (100 mL) and washed with water (100 mL). The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated to obtain 15.7 g (90%) of compound **12** as a light yellow oil.  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 1.23–1.26 m (3H,  $\text{CH}_2\text{CH}_3$ ), 1.38 d (3H,  $\text{CHCH}_3$ ,  $J$  5.3 Hz), 1.76 br.s (1H, OH), 3.53–3.73 m (6H,  $\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{Cl}$ ,  $\text{CH}_2\text{CH}_3$ ), 3.85–3.88 m (1H, OCH), 4.79–4.82 m (1H,  $\text{OCHO}$ ).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 15.2, 20.2, 43.5, 61.2, 63.2, 78.9, 101.1.

**3-(1-Ethoxyethoxy)oxetane (13).** Sodium *tert*-butylethoxide (7.6 g, 78.9 mmol) was added to a solution of compound **12** (12 g, 65.7 mmol) in *t*-BuOH (60 mL). The reaction mixture was heated at 70°C for 4 h, cooled to room temperature, and filtered. The filtrate was concentrated to dryness under reduced pressure. The residue was extracted with dichloromethane (100 mL) and washed with water (300 mL). The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated to give a crude product, which was purified by vacuum distillation to obtain 8.8 g (92%) of compound **13** as a

light yellow oil.  $^1\text{H}$  NMR spectrum (500 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 1.15–1.18 m (3H,  $\text{CH}_2\text{CH}_3$ ), 1.27 d (3H,  $\text{CHCH}_3$ ,  $J$  5.4 Hz), 3.42–3.62 m (2H,  $\text{CH}_2\text{CH}_3$ ), 4.63–4.82 m (6H,  $2\text{CH}_2\text{O}$ ,  $\text{OCH}$ ,  $\text{OCHO}$ ).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 15.2, 20.1, 61.2, 67.2, 79.0, 79.9, 99.2.

**Oxetan-3-ol (1).** *p*-Toluenesulfonic acid (0.2 g, 1.05 mmol) was added to a solution of compound **13** (25 g, 171 mmol) in water (10 mL). The reaction mixture was allowed to stand at 25°C for 2 h and, after the addition of aqueous  $\text{NaHCO}_3$  to pH 8, it was filtered. The filtrate was evaporated to dryness, the residue was dissolved in ethyl acetate (30 mL), and the solution was filtered. The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and evaporated to leave a crude product, which was distilled to obtain 9.7 g (77%) of compound **1** as a colorless oil.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 4.53–4.52 m (CH, OH), 4.80–4.77 m (4H,  $\text{CH}_2\text{OCH}_2$ ).  $^{13}\text{C}$  NMR spectrum (126 MHz,  $\text{CDCl}_3$ ),  $\delta$ , ppm: 65.0, 80.6.

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#### CONFLICT OF INTEREST

The authors declare no conflict of interest.

#### SUPPLEMENTARY MATERIALS

Supplementary materials are available for this article at <https://doi.org/10.1134/S107042802005022X> and are accessible for authorized users.

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