

## Supporting Information

### **Membrane Transport Inspired Hydrolysis of Non-activated Esters at Near Physiological pH**

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†Both authors contributed equally

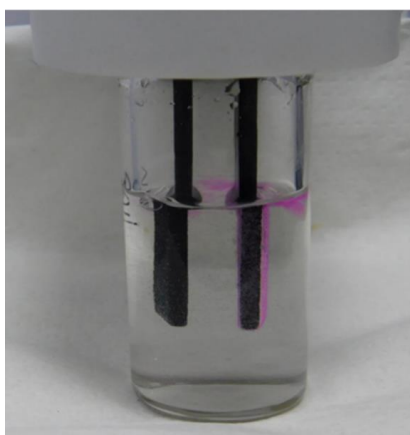
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**General Information:** Reactions were performed under air using pre-dried glassware and standard reaction tube. De-ionized water was taken from ELIX to prepare bis-tris 20 mM buffer (pH 7.0). Electrochemical reactions were performed on IKA Electrasyn 2.0 and electrodes were purchased from IKA. Substrates obtained from commercial sources (Sigma Aldrich, Alfa Aesar, Sisco Research Laboratories) were used without further purification. Yields refer to isolated compounds, estimated to be >95% pure as determined by  $^1\text{H}$  NMR. Thin-layer chromatography (TLC) was performed on Merck precoated silicagel 60F254 aluminum sheets with detection under UV light at 254nm. Chromatographic separations were carried out on Chempure silica gel (60-120 mesh or 100–200 mesh). High-resolution mass spectra (HRMS, m/z) were recorded on a Bruker Micro-TOF spectrometry. Zeta potential measurement was carried on Malvern, Zetasizer ZS, UK. UV measurements were performed on BiOTeK, EPOCH Microplate Reader and Fluorescence spectra were measured on F-7000, HITACHI spectrofluorometer. Nuclear magnetic resonance (NMR) spectroscopy was performed using JEOL 400 MHz and Bruker 500 MHz spectrometers. Chemical shifts ( $\delta$ ) are provided in ppm. IUPAC names were obtained from Chem Draw software.

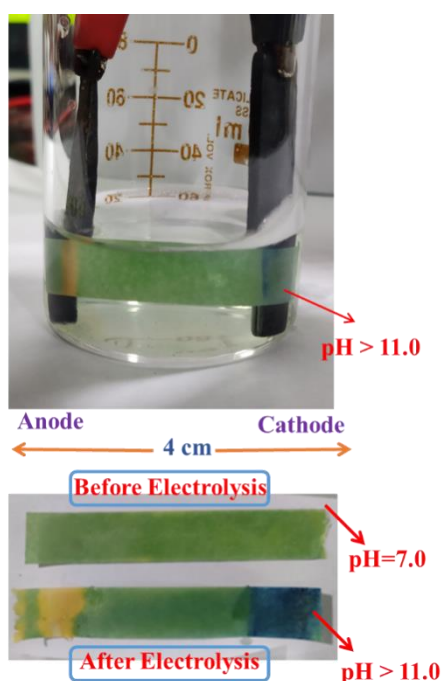
**Proof of the localization of hydroxide near the cathode surface:**

**A) Proof of hydroxide accumulation by phenolphthalein indicator (Fig. S1):** 2,4,6-tribromophenyl hexanoate (0.04 mmol), CTAB (3.6 wt%), 1 drop of phenolphthalein indicator in pH 7.0 bis-tris buffer (8 ml) were charged in a reaction tube equipped with graphite (5.2 cm $\times$ 0.8 cm $\times$ 0.2 cm) both as anode and cathode. Without employing current between two electrodes, no color was observed near the cathode surface. After that, electrolysis was turned on and the solution of the cathode surface becomes pink because of the high local concentration of the hydroxyl anion at the surface of the electrode (Fig. S1). After 10 minutes, the potentiostat was turned off and gradually, the pink color vanished from the electrode surface.



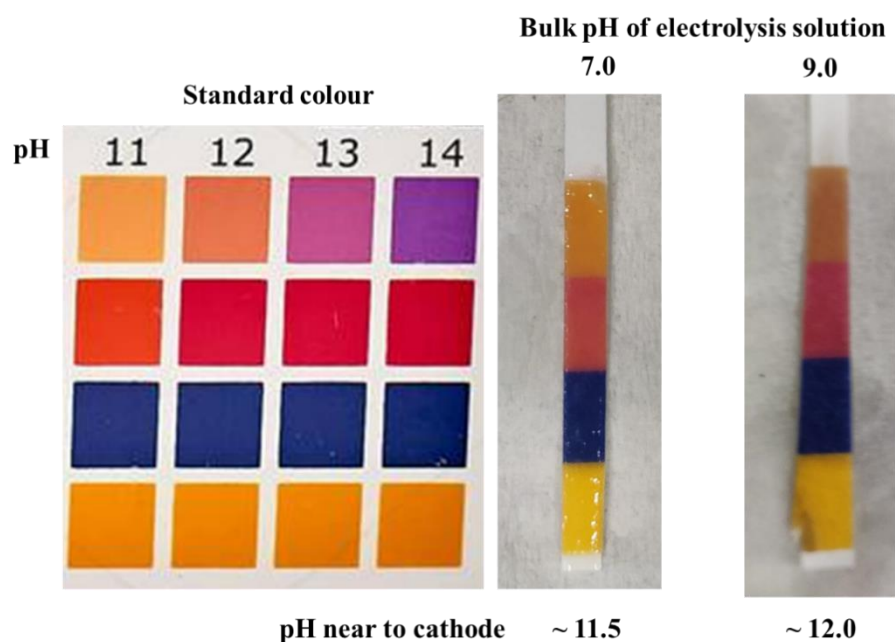
**Figure S1:** Localization of hydroxide near the cathode. Phenolphthalein was added as acid-base indicator. The pink color suggests that the pH near to cathode is > 8.2.

**B) pH paper experiment (Fig. S2):** 2,4,6-tribromophenyl hexanoate (0.04 mmol), CTAB (3.6 wt%), in pH 7.0 bis-tris buffer (8 ml) were charged in a standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. Both the electrodes were tied with a thin pH paper, as shown in Fig. S2. Without employing current between two electrodes, the whole pH paper shown lime green colour, which corresponds to pH 7.0. After that electrolysis was turned on and the pH paper near the cathode surface turned to blue because of the high local concentration of the hydroxyl anion at the surface of the electrode. This experiment was performed multiple times and a representative picture is shown in Fig. S2A. This experiment and phenolphthalein experiment suggest that the local pH near to cathode is basic and probably greater than 11.0.



**Figure S2A:** Localization of hydroxide near to cathode from pH paper experiment.

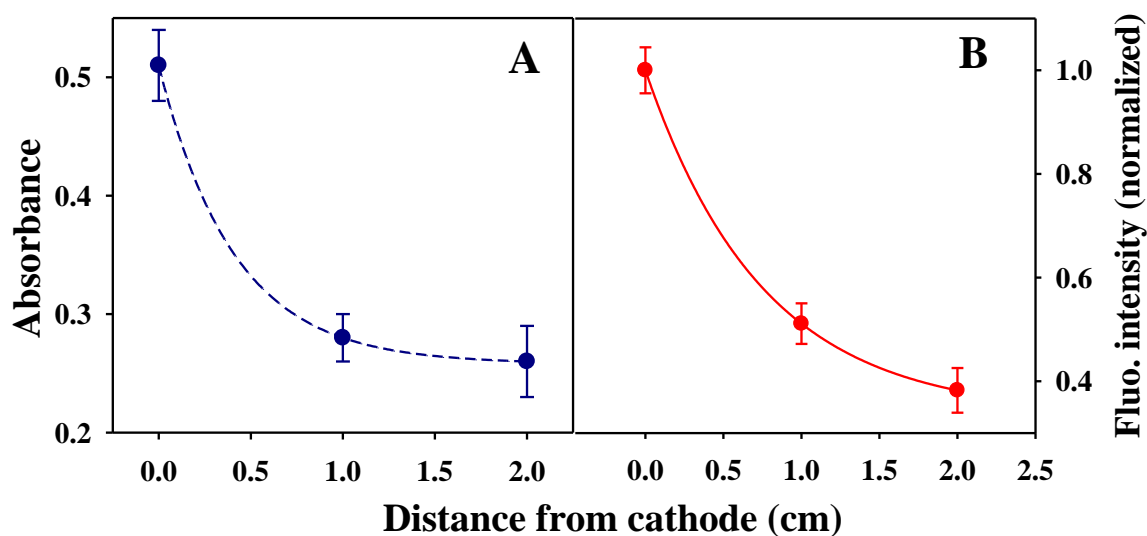
To obtain a more accurate estimation of pH near to cathode the aliquot near to the cathode was dropped in a universal pH paper strip and the value matches in between 11.0 and 12.0. We estimated the pH near to cathode as  $11.5 \pm 0.5$  and the pH of the electrolysis solution was 7.0. This experiment was performed multiple times and a representative picture is shown in Fig. S2B). Similar pH measurements were performed under electrolytic conditions at pH 9.0 buffer and the value of pH near to cathode was estimated to  $12.0 \pm 0.5$ .



**Figure S2B:** pH near to the cathode at different electrolytic buffer. Middle: bulk pH 7.0, right: bulk pH 9.0.

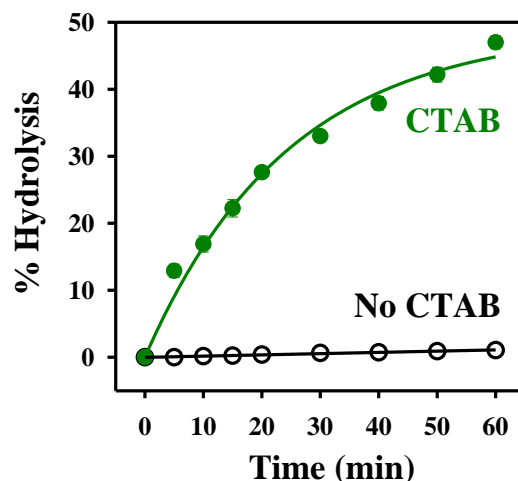
**CTAB trafficking towards Cathode (Fig. S3A):** 0.1 mol% Rhodamine labeled phosphatidylethanolamine, Rh-PE (Avanti Polar Lipids, USA), CTAB (3.6 wt%) in pH 7.0 bis-tris buffer (20 ml) were placed in a standard glass beaker equipped with graphite (5.2 cm×0.8 cm×0.2 cm) as anode and cathode. The electrodes were separated by 4 cm. The reaction was performed under electrochemical conditions with 10 mA constant current at ambient temperature. After 5 minutes of electrolysis, 50  $\mu$ l aliquots were collected at various distances from the cathode and diluted with 950  $\mu$ l of pH 7.0 Bis-tris buffer. The absorbance of Rh-PE was measured at 560 nm.

**Fluorescence measurement CTAB Guided Rh-PE towards Cathode (Fig. S3B):** 0.1 mol% Rh-PE, CTAB (3.6 wt%) in pH 7.0 bis-tris buffer (20 ml) were placed in a standard glass beaker equipped with graphite (5.2 cm×0.8 cm×0.2 cm) as anode and cathode. The electrodes were separated by 4 cm. The reaction was performed under electrochemical conditions with 10 mA constant current at ambient temperature. After 5 minutes of electrolysis, 50  $\mu$ l aliquots were collected at various distances from the cathode and diluted with 950  $\mu$ l of pH 7.0 Bis-tris buffer. The fluorescence spectra were measured by exciting at 540 nm and emission at 550 to 650 nm in a HITACHI 7000 spectrofluorometer.



**Figure S3:** Rhodamine PE doped (0.1 mol%) CTAB micelles trafficked selectively near the cathode. The absorbance (A) and fluorescence intensity (B) of Rh-PE doped CTAB micellar solutions at various distance from the cathode. The fluorescence intensity was normalized. The lines were the fitted in exponential equation.

**Kinetics of hydrolysis (Fig. 2A):** 2,4,6-tribromophenyl hexanoate (0.04 mmol), CTAB (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were placed in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) as anode and cathode. The reaction was performed under electrochemical condition with 10 mA constant current at ambient temperature for 1 h without stirring the solution. At various time intervals, 50  $\mu$ l aliquot was taken from the reaction mixture and the absorbance was measured at 320 nm in 950  $\mu$ l of pH 7.0 bis-tris buffer. Before taking the aliquots, the solution was stirred to equilibrate the electrode-bound micelles into the bulk solution. The % hydrolysis was calculated from the extinction coefficient and plotted vs. time. The UV measurements were repeated with anionic micelle, SDS (3.6 wt%) and neutral micelle Triton X-100 (3.6 wt%) surface and the % hydrolysis were plotted with time.

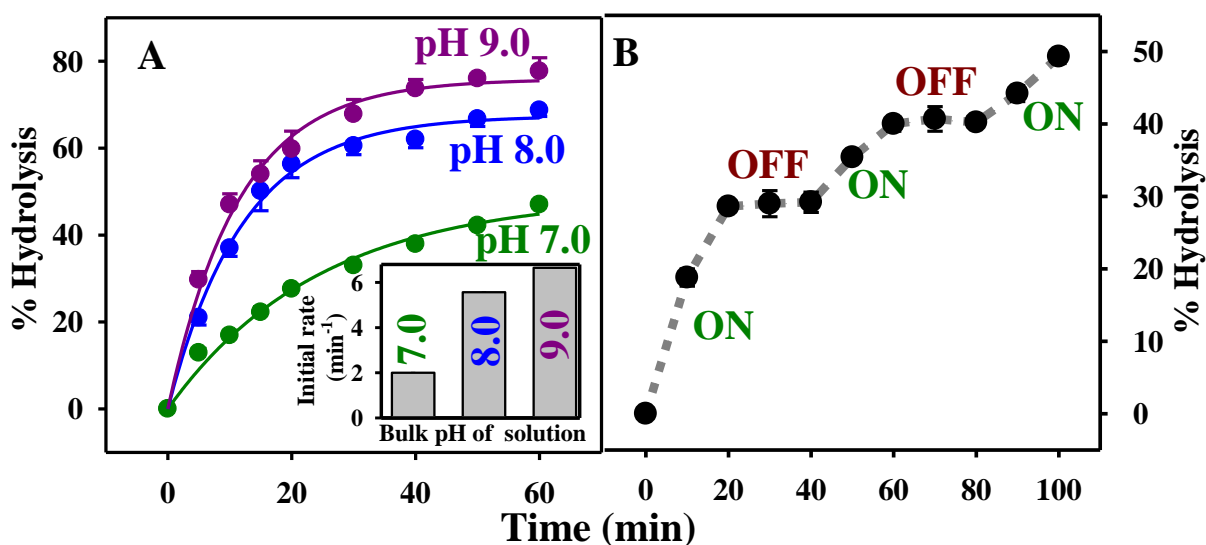


**Figure S4.** Kinetics of the hydrolysis of hexyl tribromophenolic ester in CTAB micelles under electrochemical condition. In absence of CTAB no hydrolysis was observed.

**Kinetics of ester hydrolysis at different pH (Fig. S5A):** 2,4,6-tribromophenyl hexanoate (0.04 mmol), CTAB (3.6 wt%) in pH 8.0 tris buffer (8 ml) were placed in a standard glass reaction tube at ambient temperature for 1 h. The % hydrolysis was measured by following the above protocol and the experiment was repeated with pH 9.0 tris-HCl buffer. The control experiments were performed without applying the current. The ester remains stable at pH 7.0-9.0 under the control condition (no electrolysis). Experiments were performed three times and the average data were plotted in Figure 2A-B. The kinetic data were fitted to a mono exponential equation ( $y = ae^{-bx}$ ) and the initial rate was calculated as  $IR = a \cdot b$ .

**Kinetics experiment by tuning the surface composition and zeta potential (Fig. 2B):** 2,4,6-tribromophenyl hexanoate (0.04 mmol), Triton X-100 (1.8 wt%) in pH 7.0 bis-tris buffer (8 ml) were mixed and placed in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) electrode as anode and cathode. The reaction was initiated under the electrochemical condition with 10 mA constant current at ambient temperature for 20 min. During the reaction, at various intervals, 50 µl aliquot was taken from the reaction mixture and the absorbance was measured at 320 nm in 950 µl of pH 7.0 bis-tris buffer. Then CTAB (1.8 wt%) was added to the reaction mixture and the reaction was continued for another 20 min. At different time intervals, 50 µl aliquot was taken from the reaction mixture and absorbance was measured. Finally, SDS (3.6 wt%) was added to the reaction mixture and the reaction was continued for another 20 min. Similarly, at various time intervals, 50 µl aliquot was taken from the reaction mixture and absorbance was measured in a microplate reader. The procedure was repeated for three times and the average was plotted. The zeta potential of the sample was measured in Triton X-100, after addition of CTAB and SDS.

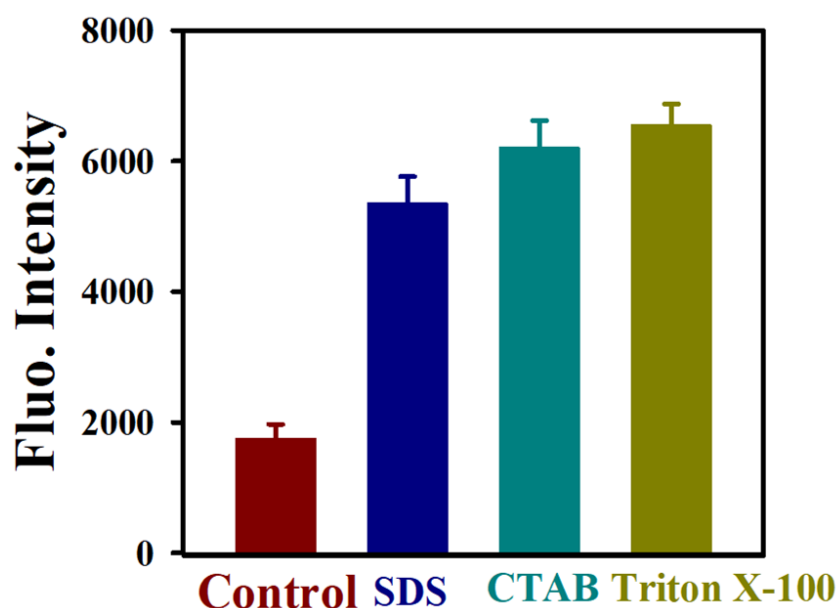
**On-Off experiment of the ester hydrolysis (Fig. S5B):** 2,4,6-tribromophenyl hexanoate (0.04 mmol), CTAB (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were mixed and placed in a standard glass reaction tube equipped with graphite electrode (5.2 cm×0.8 cm×0.2 cm) as anode and cathode. The reaction was initiated with 10 mA constant current at ambient temperature for 20 min. During the reaction, 50  $\mu$ l aliquot was taken at various time intervals from the reaction mixture and the absorbance was measured. After 20 minutes, the power supply was shut down and the aliquots were collected. The entire process was repeated for another two times and absorbance was measured.



**Figure S5.** Kinetics of the hydrolysis of hexyl tribromophenolic ester in CTAB micelles. A) The initial rate and extent of the hydrolysis under electrochemical condition increases with the bulk pH of the reaction mixture. B) Role of constant current on the extent of hydrolysis.

#### Ester solubility in the different micelle core:

Fluorescence measurement was performed with 1  $\mu$ M methyl ester of pyrene butyric acid in pH=7.0 buffer by exciting at 334 nm and emission at 350 to 550 nm. There after we have measured fluorescence intensity in different micelle (SDS, CTAB, Triton X-100) with 20 mM concentration. The increment of the measured intensity compared to the blank suggests the solubility or incorporation of the ester in the different micelle core is similar. We compared the solubility of esters (methyl ester of pyrene butyric acid) into SDS, triton X-100 and CTAB core using fluorescence to rule out the incorporation ability and effective hydrolysis (Figure S6).



**Figure S6:** Ester solubility in the different micelle core by fluorescence measurement.

**General procedure of the synthesis of ester (GP1):** Ester molecules were synthesized by following below-mentioned procedures.

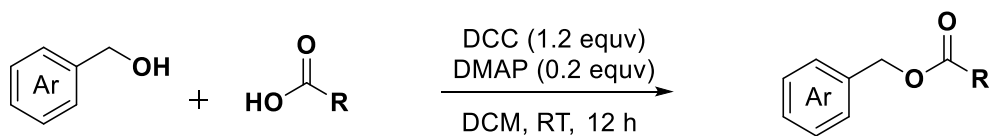
A)



Following reported procedure<sup>[1]</sup> a mixture of aryl alcohol (6 mmol), acyl chloride (6 mmol), was placed in a pre-dried single neck round bottom flask filled with argon. A dry solvent (DCM, 10 ml) was added via a syringe. After that Et<sub>3</sub>N (6.6 mmol) was added slowly to the reaction mixture at 0 °C and stirred for 4 h at RT. After completion of the reaction, the solvent was evaporated under vacuum affording white solid. The crude product was extracted with EtOAc and washed with the same amount of water. Thereafter organic layer was collected and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the concentrated crude product was purified by column chromatography on silica gel to obtain the corresponding esters. This procedure was followed for the synthesis of the compounds (**1aa-1ca**, **1ac-1cc**, **1ad-1cd**). The purity of the product(s) was determined by <sup>1</sup>H-NMR and Mass spectrometry.

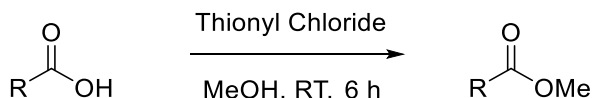


**B)**



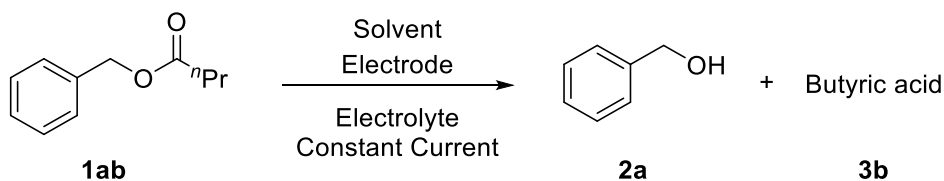
Following a reported procedure<sup>[2]</sup>, the corresponding aryl alcohol (6 mmol), aliphatic acid (6 mmol), DCC (7.2 mmol) and DMAP (1.2 mmol) were dissolved in dry DCM solvent (15 ml) in a round bottom flask and stirred overnight at room temperature. After the full consumption of alcohol, the reaction mixture was concentrated by evaporation on a rotary evaporator and solid product was dissolved and filtered using EtOAc on a sintered funnel. The residue was evaporated on a rotary evaporator and concentrated crude mixture was purified by column chromatography on silica gel to obtain the corresponding ester. This procedure was followed for the synthesis of the compounds (**1ab-1cb**). The purity of the product(s) was determined by <sup>1</sup>H-NMR and Mass spectrometry.

**C)**



Following a reported procedure<sup>[3]</sup> aliphatic acid (1.5 mmol) was taken in a dried round bottom flask and dissolved in methanol (10 ml) under nitrogen atmosphere at room temperature. Then the reaction was stirred for 5 min and thereafter thionyl chloride (6 mmol) was added in ice-cooled condition and the reaction was continued for another 6 h. Upon completion of the reaction, methanol was evaporated using a solvent distillation setup and yielded a white solid. Hexane was added and a white precipitate was obtained. The white solid was filtered and further purified by column chromatography (**1e**, **1f**). The purity of the product(s) was determined by <sup>1</sup>H-NMR and Mass spectrometry.

### Optimization studies for the hydrolysis of benzyl butyrate(**1ab**) (Table S1):



Benzyl Butyrate (**1ab**, 0.2 mmol), electrolyte (3.6 wt% or 0.1 M) in solvent (8 ml) were mixed in a pre-dried standard glass reaction tube equipped with the cathode (5.2 cm×0.8 cm×0.2 cm) and anode

(5.2 cm×0.8 cm×0.2 cm). The reaction was performed under electrochemical condition with 10-25 mA constant current at ambient temperature under air for 4 h. The distance between cathode and anode was kept at 1 cm. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under vacuum. <sup>1</sup>H NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.

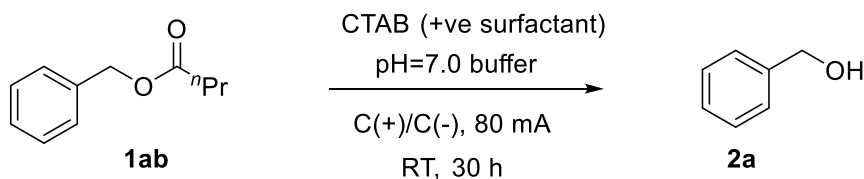
**Table S1.** Optimization of the guided ester hydrolysis conditions.<sup>[a]</sup>

CCCC(=O)OCc1ccccc1 (1ab)  $\xrightarrow[\text{Electrolyte, Constant Current}]{\text{Solvent, Electrode}}$  OCc1ccccc1 (2a) + CCCC(=O)O (3b)

Entry	Solvent	Electrode	Electrolyte	Current	Yield <sup>[b]</sup>
1	pH 7 buffer	C(+)/C(-)	CTAB	20 mA	58%
2	pH 7 buffer	C(+)/C(-)	CTAB	10 mA	52%
3	pH 7 buffer	C(+)/C(-)	CTAB	25 mA	51%
4	H <sub>2</sub> O	C(+)/C(-)	CTAB	10 mA	40%
5	H <sub>2</sub> O	C(+)/C(-)	LiClO <sub>4</sub>	10 mA	ND
6	H <sub>2</sub> O	C(+)/C(-)	Bu <sub>4</sub> NBr	10 mA	ND
7	MeCN	C(+)/C(-)	LiClO <sub>4</sub>	10 mA	ND
8	pH 7 buffer	C(+)/Ni(-)	CTAB	20 mA	35%
9	pH 7 buffer	C(+)/RVC(-)	CTAB	20 mA	52%
10	pH 7 buffer	C(+)/Pt(-)	CTAB	20 mA	20%
11 <sup>[c]</sup>	pH 7 buffer	C(+)/C(-)	CTAB	20 mA	79% (77%) <sup>[d]</sup>
12	pH 7 buffer	C(+)/C(-)	CTAB	0 mA	ND

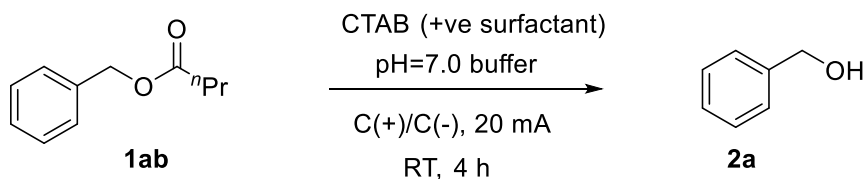
<sup>[a]</sup>Reaction conditions: **1ab** (0.2 mmol), electrolyte (3.6 wt% or 0.1 M) in solvent (8 mL), in an undivided cell with constant current = 10-25 mA, at r.t. under air for 4 h. <sup>[b]</sup><sup>1</sup>H NMR yield of **2a**. <sup>[c]</sup>Reaction was conducted without stirring. <sup>[d]</sup>Yield of pure **2a**.

### Procedure for gram scale hydrolysis of benzyl butyrate (**1ab**):



Benzyl Butyrate (**1ab**, 1.07 gm, 6 mmol), CTAB (3.6 wt%) in pH 7.0 bis-tris buffer (50 ml) were charged in a glass reaction vial equipped with graphite (5.2 cm×3.2 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 80 mA constant current at ambient temperature for 30 h. After completion of the reaction, the mixture was extracted with EtOAc (50 ml), washed with brine (20 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under vacuum. The product benzyl alcohol (**2a**) was purified by column chromatography and colorless liquid (420 mg, 65%) was obtained. <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>) δ 7.28-7.36 (m, 5H), 4.67 (s, 2H), <sup>13</sup>C NMR (101MHz, CDCl<sub>3</sub>) δ 141.0, 128.6, 127.6, 127.1, 77.6 (CDCl<sub>3</sub>), 77.3 (CDCl<sub>3</sub>), 77.0 (CDCl<sub>3</sub>), 65.0.

### Recyclability of the designed hydrolysis (Fig. S7):



Benzyl butyrate (**1ab**, 0.2 mmol), CTAB (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were charged in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction MTBE (5 ml) was added and the organic layer was collected and dried over Na<sub>2</sub>SO<sub>4</sub>, concentrated under vacuum, and <sup>1</sup>H NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard. The aqueous solution was collected in the same glass reaction tube and benzyl butyrate (**1ab**, 0.2 mmol) and sodium bromide (1.2 wt%) were added to the aqueous medium. The resulted solution was electrolyzed further with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction MTBE (5 ml) was added and organic layer was collected and dried over Na<sub>2</sub>SO<sub>4</sub>, concentrated under vacuum, and <sup>1</sup>H NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard. The same procedure was repeated for the third cycle and yield of **2a** was calculated by <sup>1</sup>H NMR using 1,1,2,2-tetrachloroethane as the internal standard.

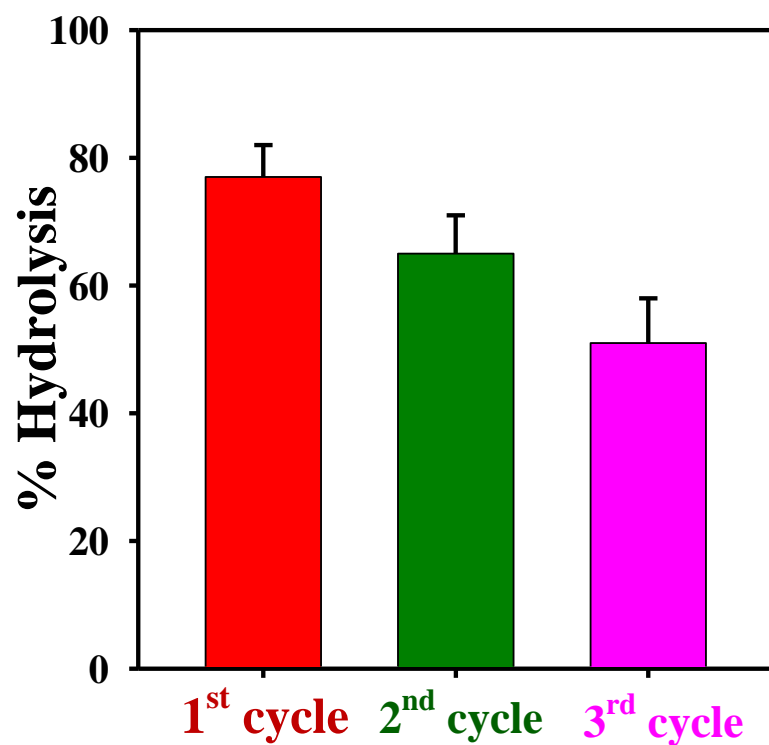
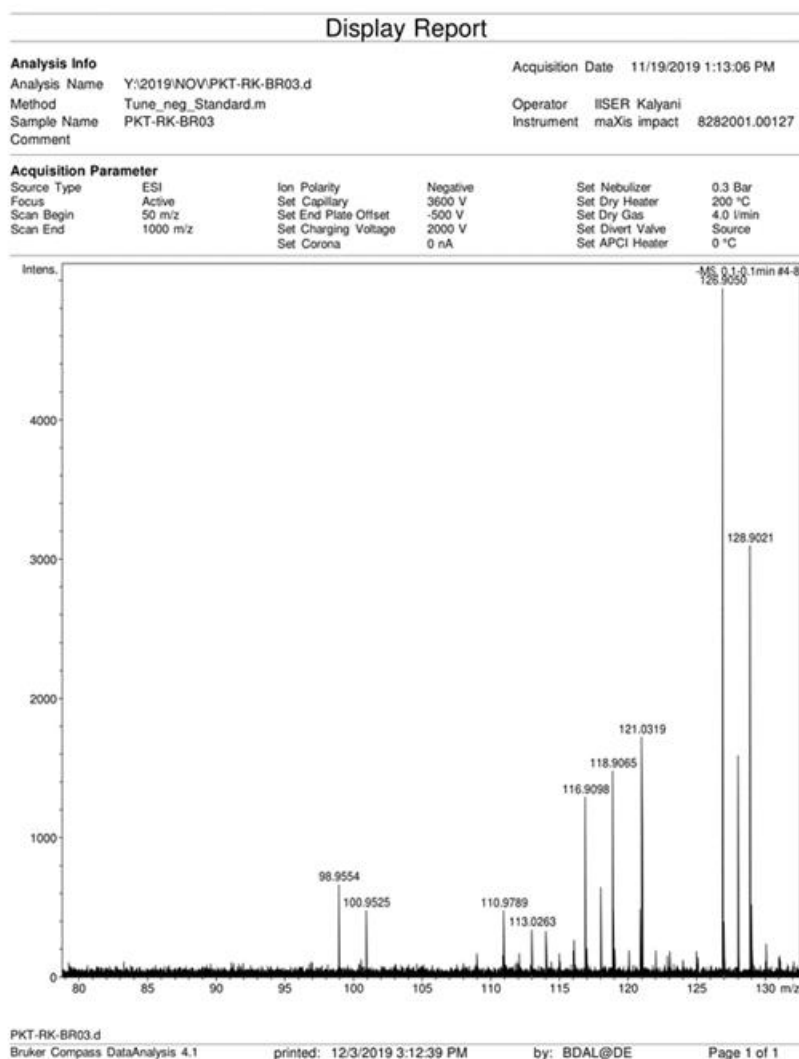


Figure S7: The % of hydrolysis at different cycles.

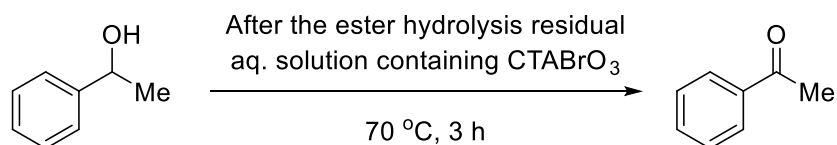
**Negative Mode Mass Spectrometric Data for Bromate Anion:**

HRMS-ESI (m/z): calcd for  $\text{BrO}_3^-$  [M]<sup>-</sup> 128.9010, 126.9031; found 128.9021, 126.9050



**Figure S8:** Mass spectroscopic characterization of  $\text{BrO}_3^-$ .

### Application of bromate ion for the oxidation of alcohol:

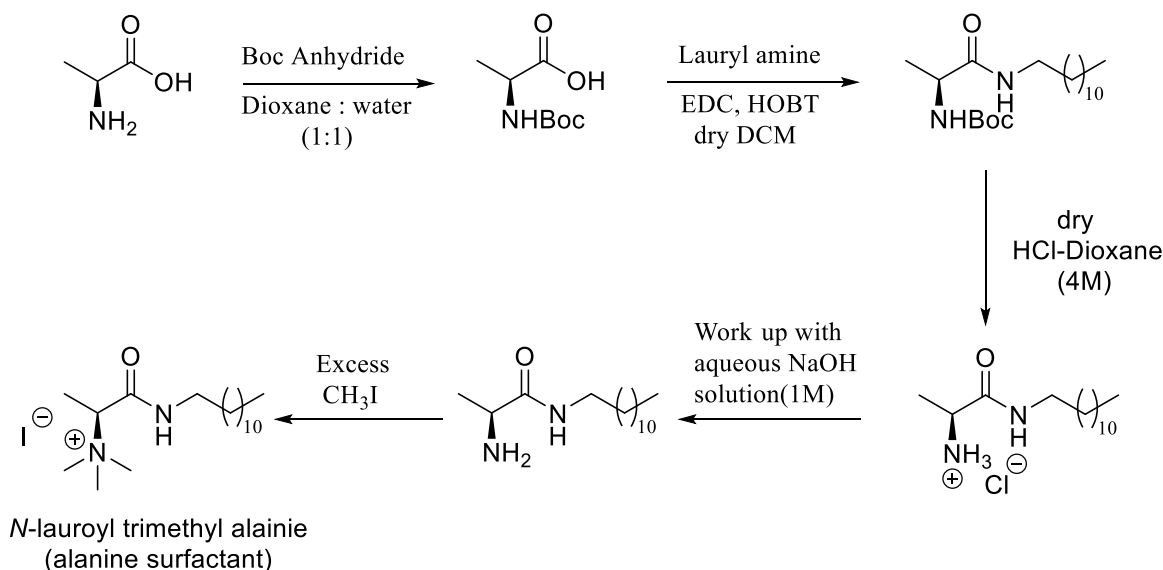


**Figure S9:** The byproduct ( $\text{CTABrO}_3$ ) was used to oxidize a secondary alcohol.

Ester (0.2 mmol), CTAB (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were mixed thoroughly and kept in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the organic compound of the reaction mixture was removed by EtOAc (8 ml). The aqueous solution was then collected in the same glass reaction tube and 1-phenylethanol (0.2 mmol) was added to the aqueous

medium. The resulted solution was stirred with a magnetic bar at 70°C under air for 3 h. After completion of the reaction, EtOAc (8 ml) was added and the organic layer was collected and dried over Na<sub>2</sub>SO<sub>4</sub>, concentrated under vacuum and purified by column chromatography to yield acetophenone as a colourless liquid (16 mg, 67%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.14 – 7.81 (m, 2H), 7.67 – 7.53 (m, 1H), 7.45 (ddd, *J* = 6.8, 4.3, 1.1 Hz, 2H), 2.60 (s, 3H), <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 198.3, 137.2, 133.2, 128.6, 128.4, 26.7.

### Synthesis of *N*-Lauroyl trimethyl alanine (alanine surfactant):



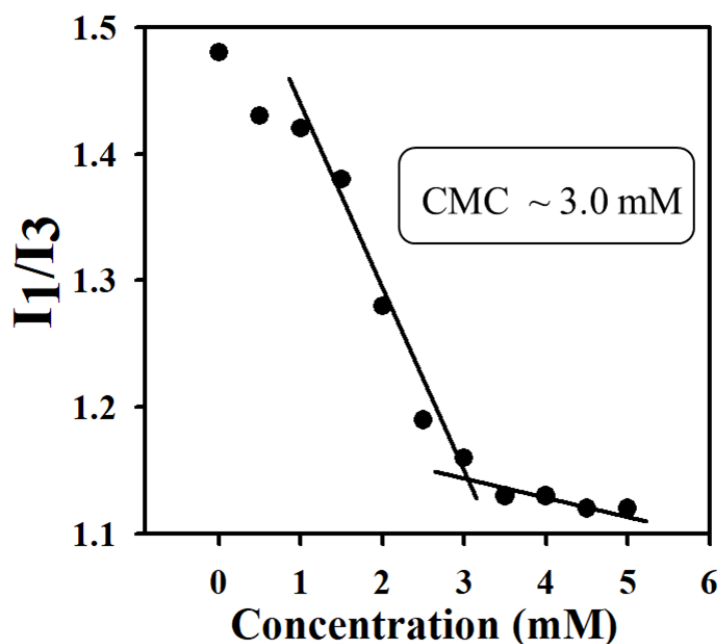
A solution of *L*-Alanine in a mixture of dioxane (10 ml), water (5 ml) and 1M NaOH (5 ml) was stirred and cooled in an ice bath. Boc anhydride (1.2 equivalent) was added and stirring was continued at room temperature for overnight. The dioxane was removed from the solution in vacuum. The solution was acidified with a dilute solution of KHSO<sub>4</sub> to pH 2-3 in ice-bath. The aqueous phase was extracted with ethyl acetate thrice and solvent was evaporated to get *N*-Boc Alanine. The yield was 98%.

The *N*-Boc was coupled with lauryl amine by using EDC and HOBT in dry DCM solvent. The reaction was continued for 24 hrs. After reaction was complete, DCM was evaporated under reduced pressure and the solution was washed with water 2 times and with sodium bicarbonate solution 2 times to remove extra EDC, EDU and HOBT. The product was extracted with ethyl acetate and purified by column chromatography. The yield was 65%. Deprotection of the Boc group to get *N*-lauryl alanine was carried out using dioxane-HCl. The yield was 75%. Then *N*-lauryl alanine was neutralized with 1M NaOH solution and extracted with ethyl acetate. The solution was concentrated, and excess methyl iodide was added to get the *N*-lauroyl trimethyl alanine (alanine surfactant, bio-degradable). The reaction mixture was stirred for 3 hrs and after that diethyl ether was added. The precipitate was washed and filtered by filter paper to get the final pure product. The purity of the compound was checked by

$^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$  and HRMS.  $^1\text{H NMR}$  (400 MHz, DMSO- $\text{D}_6$ )  $\delta$  8.47 (t,  $J = 5.3$  Hz, 1H), 3.98 (q,  $J = 6.8$  Hz, 1H), 3.21 – 3.00 (m, 11H), 1.48 (d,  $J = 6.8$  Hz, 3H), 1.45 – 1.39 (m, 2H), 1.24 (m, 18H), 0.85 (t,  $J = 6.9$  Hz, 3H).

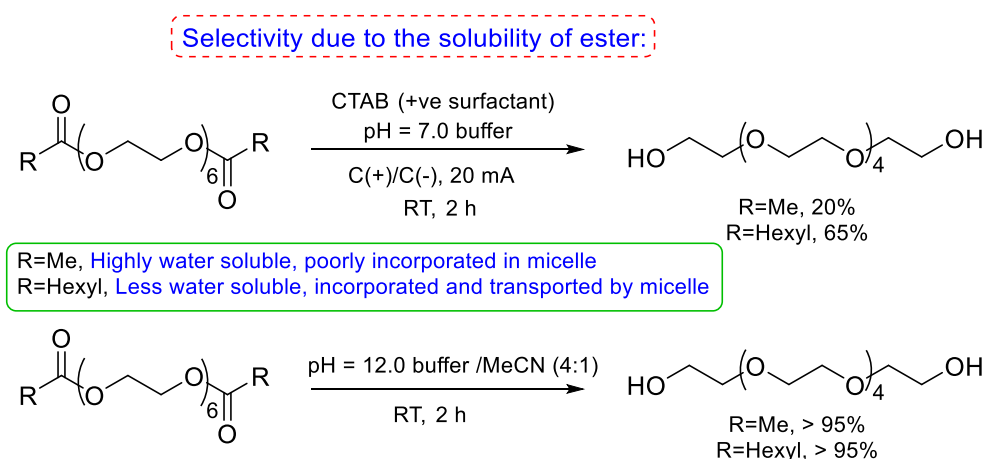
$^{13}\text{C NMR}$  (126 MHz, DMSO)  $\delta$  166.90, 69.84, 51.74, 39.18, 31.76, 29.50, 29.47, 29.44, 29.41, 29.17, 29.08, 28.91, 26.78, 22.56, 14.42, 13.21. HRMS mass expected  $[\text{C}_{18}\text{H}_{39}\text{N}_2\text{O}]^+$ : 299.3057 found  $[\text{C}_{18}\text{H}_{39}\text{N}_2\text{O}]^+$ : 299.3107.

**Critical micellar concentration (CMC) of alanine surfactant:** CMC of the alanine surfactant was measured by standard procedure using pyrene as fluorophore.<sup>[4]</sup> Initially 2  $\mu\text{M}$  pyrene was taken in buffer pH 7.0 (hydrophilic environment) and excited at 334 nm. The excitation and emission slit widths were set at 2.5 nm. The  $I_1/I_3$  (intensity ratio of first and third emission peak) value remain high (around 1.5) suggesting it resides in hydrophilic region. Then the alanine surfactant was added to the buffer and the pyrene  $I_1/I_3$  was monitored after equilibration. With increase in the surfactant concentration, the  $I_1/I_3$  decreases. By plotting  $I_1/I_3$  the CMC of the surfactant was estimated (Figure S10,  $\sim 3$  mM).



**Figure S10:** Critical micellar concentration of alanine surfactant.

## Selective hydrolysis of esters via guided delivery of micelles to cathode:

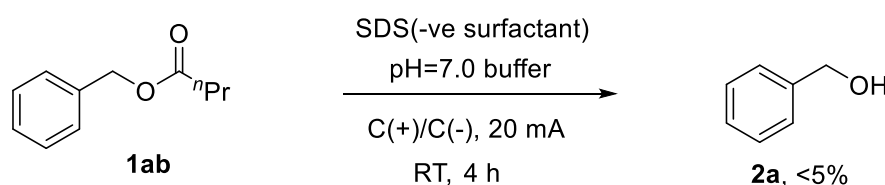


**Figure S11:** Selective hydrolysis of esters. A more hydrophobic (hexyl) ester was hydrolyzed more selectively in our method. Conventional bulk high pH hydrolysis does not show any selectivity.

To showcase the advantage of transient high local pH over a bulk high pH system, the ester hydrolysis was carried out using the developed condition (pH = 7.0 buffer) with a comparison to pH = 12.0 buffer solution (without surfactant). It was observed that a water-soluble ester with PEG moiety (R = Me) got hydrolyzed quantitatively in the solution of pH = 12.0, but only 20% of the hydrolyzed product was obtained in the guided vehicular delivery inspired electrochemical condition (bulk solution of pH = 7.0). In contrast, a more hydrophobic ester containing a longer alkyl chain length of the acid got hydrolyzed with higher efficiency (65%) under the micellar condition and quantitatively at pH 12.0 buffer (Figure S11). This clearly demonstrates that selective hydrolysis of the ester can be achieved by adopting our guided vehicular delivery inspired approach based on the solubility of the esters.

## Control Experiments and Mechanistic Studies:

### Hydrolysis of Ester in negatively charged micelle (SDS):

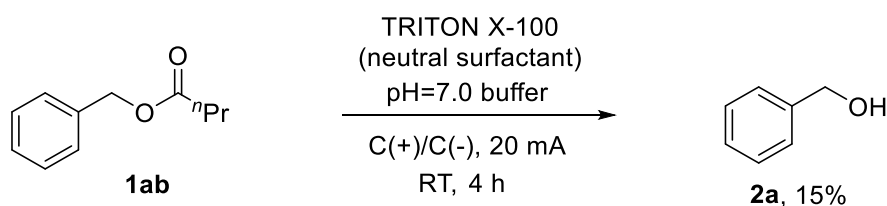


Benzyl butyrate (**1ab**, 0.2 mmol), SDS (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were charged in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under



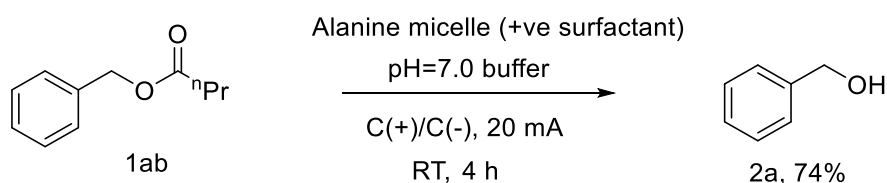
vacuum.  $^1\text{H}$  NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.

#### Hydrolysis of Ester in neutral micelle Triton X-100:

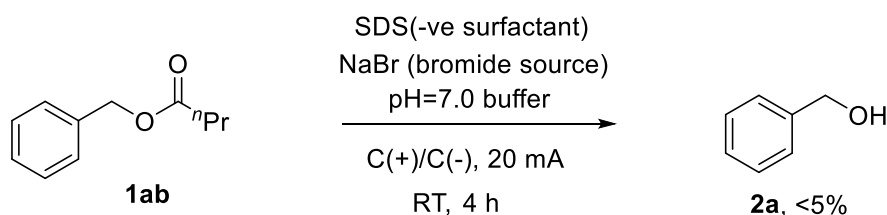


Benzyl butyrate (**1ab**, 0.2 mmol), TRITON X-100 (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were charged in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated under vacuum.  $^1\text{H}$  NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.

**Hydrolysis of benzyl butyrate (1ab) in alanine surfactant:** Benzyl butyrate (**1ab**, 0.2 mmol), alanine surfactant (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were charged in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated under vacuum.  $^1\text{H}$  NMR yield (74%) of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.



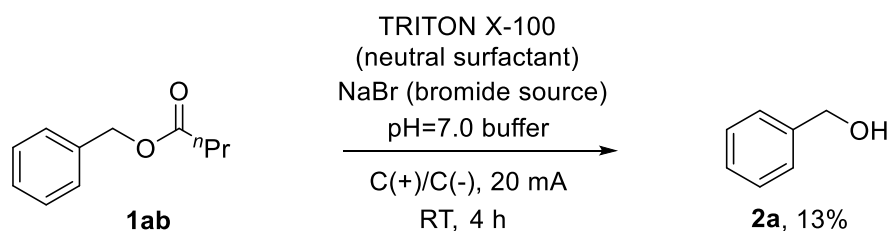
#### Hydrolysis of Ester in negatively charged micelle (SDS) with oxidizable counterion:



Benzyl butyrate (**1ab**, 0.2 mmol), SDS (3.6 wt%), NaBr (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were charged in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2

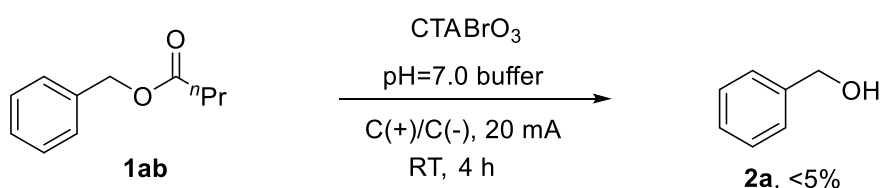
cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under vacuum. <sup>1</sup>H NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.

### Hydrolysis of Ester in neutral micelle (Triton X-100) with oxidisable counterion:



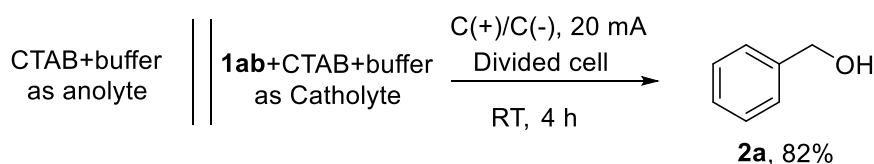
Benzyl butyrate (**1ab**, 0.2 mmol), Triton X-100 (3.6 wt%), NaBr (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were charged in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under vacuum. <sup>1</sup>H NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.

### Hydrolysis of ester in a positively charged surface with non-oxidizable counter anion CTABrO<sub>3</sub>:



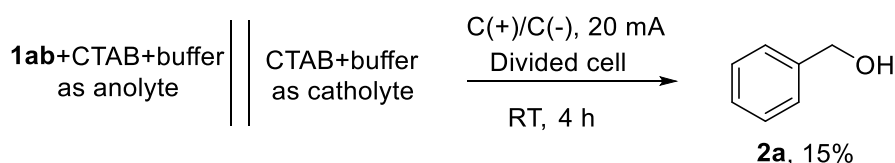
Benzyl butyrate (**1ab**, 0.2 mmol), CTABrO<sub>3</sub> (3.6 wt%) in pH 7.0 bis-tris buffer (8 ml) were charged in a pre-dried standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under vacuum. <sup>1</sup>H NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.

### Hydrolysis of ester in divided cell and ester as catholyte:



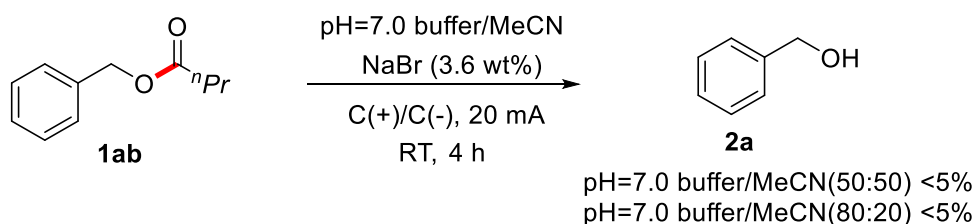
Benzyl butyrate (**1ab**, 0.2 mmol), CTAB (1.8 wt%) were charged in cathodic chamber whereas CTAB (1.8 wt%) was charged in the anodic chamber in pH 7.0 bis-tris buffer in a pre-dried standard divided cell separated by G3 sintered equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under vacuum. <sup>1</sup>H NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.

### Hydrolysis of ester in divided cell with ester as anolyte:



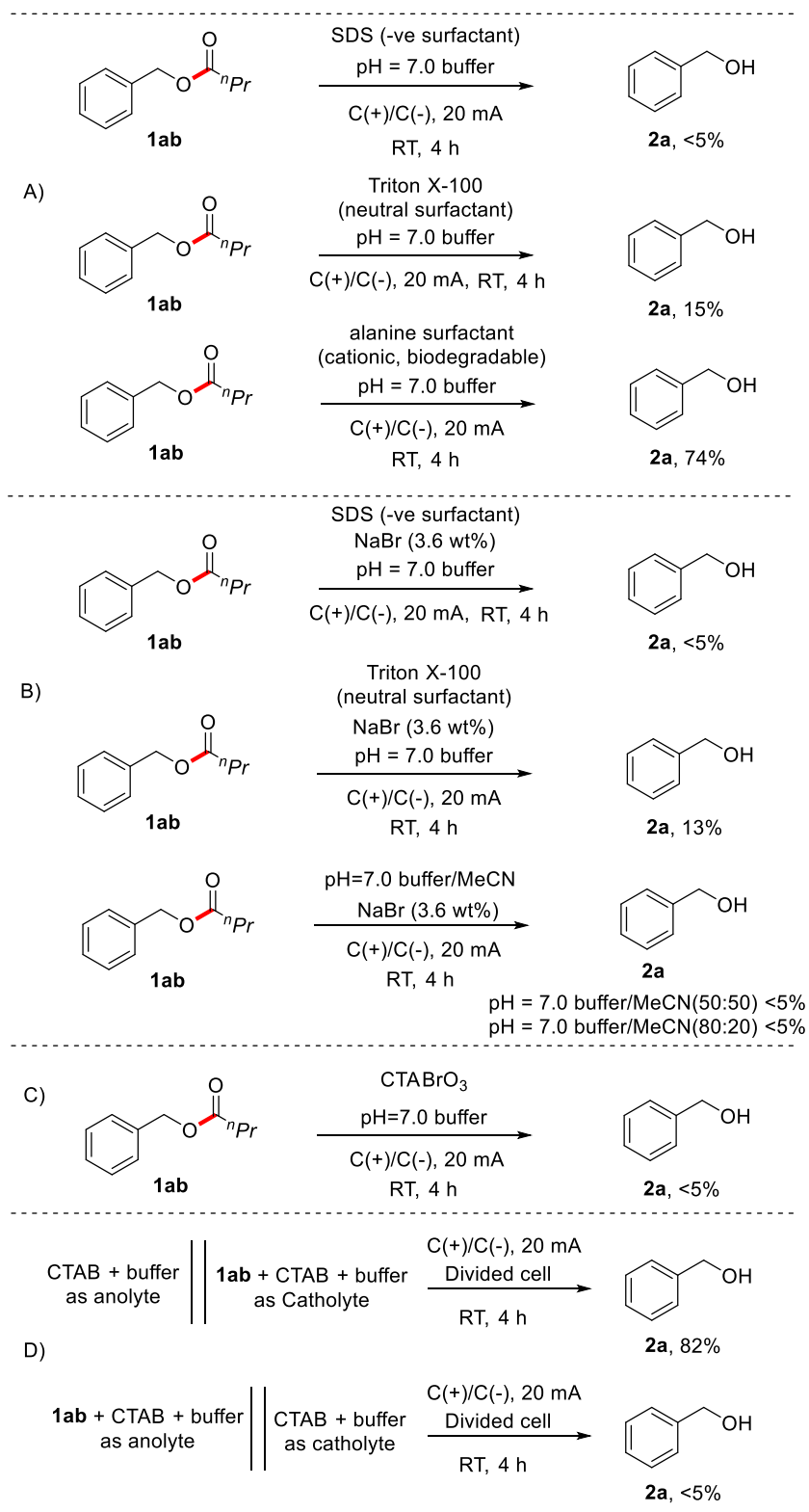
Benzyl butyrate (**1ab**, 0.2 mmol), CTAB (1.8 wt%) were charged in anodic chamber whereas CTAB (1.8 wt%) was charged in the cathodic chamber in pH 7.0 bis-tris buffer in a pre-dried standard divided cell separated by G3 sintered equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under vacuum. <sup>1</sup>H-NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.

### Hydrolysis of Ester in H<sub>2</sub>O/MeCN mixture with oxidisable counterion:



Benzyl butyrate (**1ab**, 0.2 mmol) and NaBr (3.6 wt%) in pH 7.0 bis-tris buffer (4 ml) / MeCN (4 ml) mixture and pH 7.0 bis-tris buffer (6.4 ml) / MeCN (1.6 ml) were charged in two different pre-dried

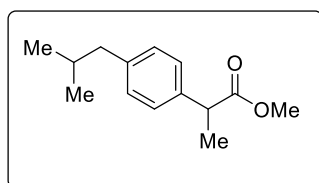
standard glass reaction tube equipped with graphite (5.2 cm×0.8 cm×0.2 cm) both as anode and cathode. The reaction was performed under the electrochemical condition with 20 mA constant current at ambient temperature under air for 4 h. After completion of the reaction, the mixture was extracted with EtOAc (10 ml), washed with brine (8 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated under vacuum. <sup>1</sup>H NMR yield of **2a** was determined by using 1,1,2,2-tetrachloroethane as the internal standard.



**Figure S12:** Mechanistic investigations of guided transport inspired hydrolysis. The role of various A) surfactants (SDS: anionic; Triton X-100: neutral; alanine surfactant: cationic, biodegradable), B) surfactants or organic solvent with sacrificial bromide, and C) counterion on the extent of hydrolysis of **1ab**, D) Control experiments in a divided cell suggest that the localization of CTAB near the cathode is necessary for successful hydrolysis.

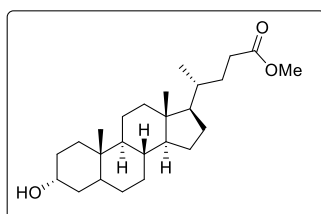
## Characterization Data for Isolated Compounds:

### Methyl 2-(4-isobutylphenyl) propanoate:



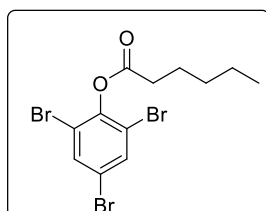
**GP1C** was followed using 2-(4-isobutylphenyl) propanoic acid (309 mg, 1.5 mmol), Thionyl Chloride (714 mg, 6 mmol). After 6 h, solvent was evaporated and followed by hexane wash gave white solid (313 mg, 95%).  $^1\text{H NMR}$  (400 MHz, DMSO- $\text{D}_6$ )  $\delta$  7.12 (d,  $J = 7.8$  Hz, 2H), 7.05 (d,  $J = 7.8$  Hz, 2H), 3.70 (q,  $J = 7.0$  Hz, 1H), 3.52 (s, 3H), 2.36 (d,  $J = 7.1$  Hz, 2H), 1.75 (m, 1H), 1.31 (d,  $J = 7.1$  Hz, 3H), 0.80 (d,  $J = 6.5$  Hz, 6H).

### Methyl lithocholate:



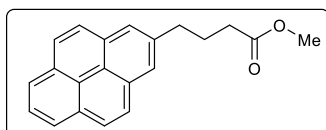
**GP1C** was followed using lithocholic acid (564 mg, 1.5 mmol), Thionyl Chloride (714 mg, 6 mmol). After 6 h, solvent was evaporated and hexane wash to achieve white solid (550 mg, 94%).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  3.87 – 3.49 (m, 4H), 2.35 (m, 1H), 2.28 – 2.16 (m, 1H), 1.95 (d,  $J = 9.9$  Hz, 1H), 1.90 – 0.97 (m, 26H), 1.02 – 0.81 (m, 6H), 0.64 (s, 3H).

### 2,4,6-tribromophenyl hexanoate:



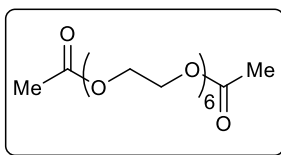
**GP 1B** was followed using 2,4,6-tribromophenol (1.98 gm, 6 mmol), Hexanoic acid (700mg, 6 mmol), DCC (7.2 mmol) and DMAP (1.2 mmol). After 6 h, The residue was evaporated on rotavapour and concentrated crude mixture was purified by flash column chromatography on silica gel to afford 2,4,6-tribromophenyl hexanoate (2.3gm, 90%).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 (s, 2H), 2.65 (t,  $J = 7.5$  Hz, 2H), 1.82 (dt,  $J = 15.1, 7.5$  Hz, 2H), 1.52 – 1.30 (m, 4H), 0.93 (t,  $J = 7.1$  Hz, 3H).

### Methyl 4-(pyren-2-yl) butanoate:



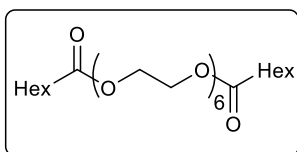
**GP1C** was followed using pyrene butyric acid (1.5 mmol), Thionyl Chloride (6 mmol) in MeOH (10 ml) solvent. After 6 h, solvent was evaporated and did hexane wash to achieve white solid (92%).  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.31 (d,  $J = 9.2$  Hz, 1H), 8.17 (dd,  $J = 7.4, 3.7$  Hz, 2H), 8.13 (d,  $J = 3.0$  Hz, 1H), 8.11 (s, 1H), 8.03 (s, 2H), 7.99 (t,  $J = 7.6$  Hz, 1H), 7.86 (d,  $J = 7.7$  Hz, 1H), 3.69 (s, 3H), 3.42 – 3.38 (m, 2H), 2.47 (t,  $J = 7.3$  Hz, 2H), 2.28 – 2.13 (m, 2H).

### 3,6,9,12,15-pentaoxaheptadecane-1,17-diyl diacetate:



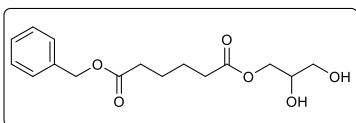
**GP 1A** was followed using hexaethylene glycol (6 mmol), Acetyl chloride (12 mmol), Et<sub>3</sub>N (13.2 mmol). After 4 h, The residue was evaporated on rotavapour and concentrated crude mixture was purified by flash column chromatography on silica gel to afford 3,6,9,12,15-pentaoxaheptadecane-1,17-diyl diacetate (90%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.26 – 4.16 (m, 4H), 3.73 – 3.66 (m, 4H), 3.64 (s, 16H), 2.06 (s, 6H).

### 3,6,9,12,15-pentaoxaheptadecane-1,17-diyl diheptanoate:



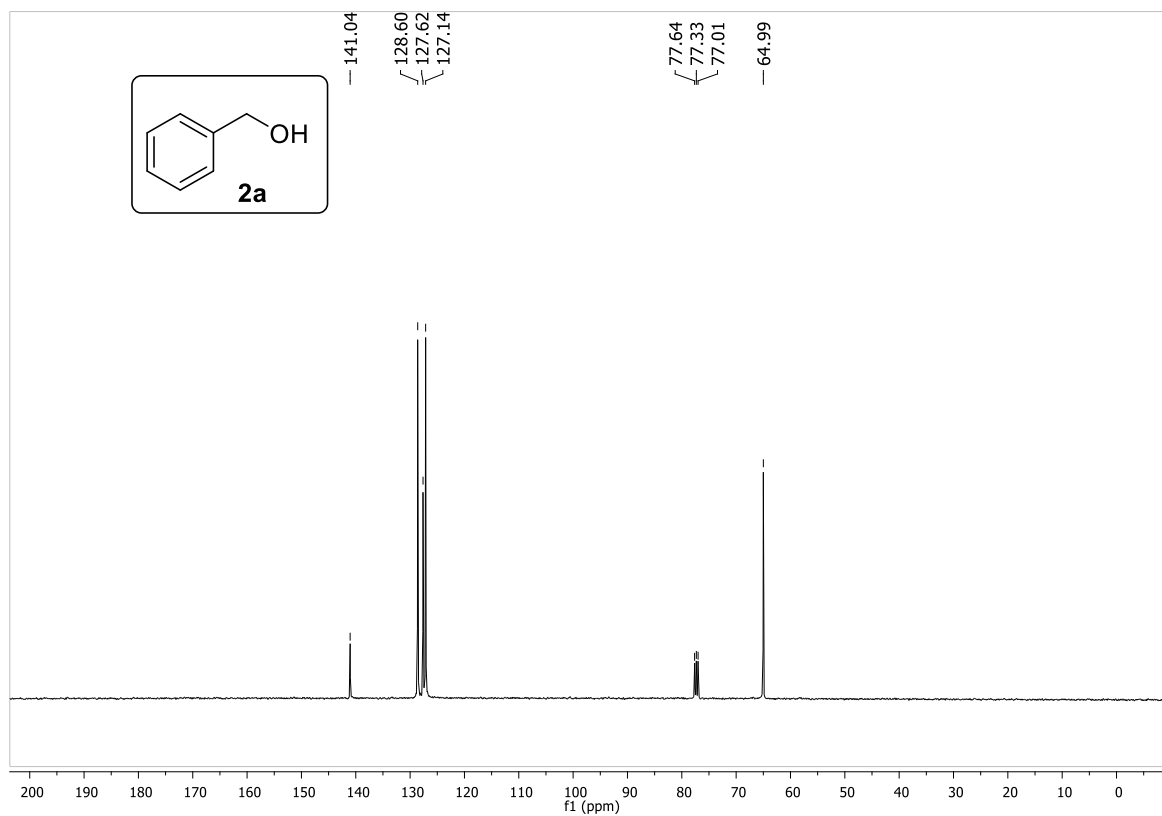
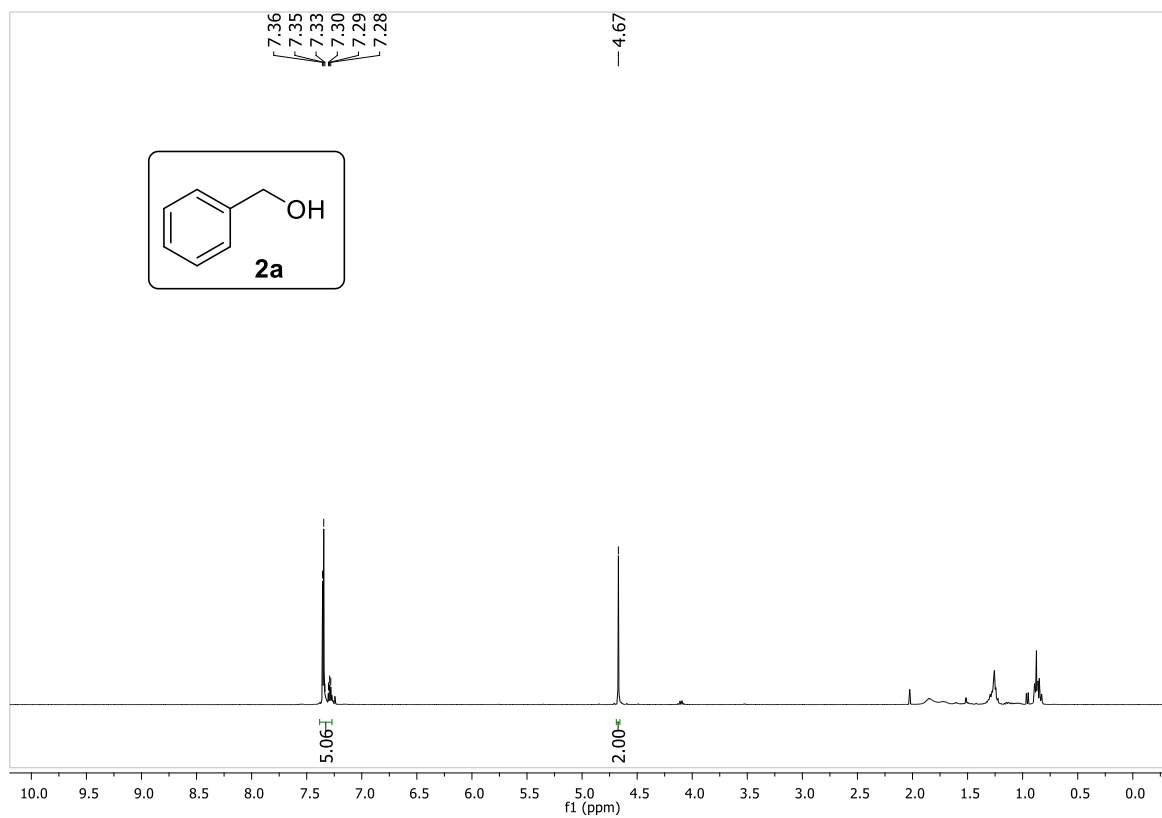
**GP 1A** was followed using hexaethylene glycol (6 mmol), Hexanoyl chloride (12 mmol), Et<sub>3</sub>N (13.2 mmol). After 4 h, The residue was evaporated on rotavapour and concentrated crude mixture was purified by flash column chromatography on silica gel to afford 3,6,9,12,15-pentaoxaheptadecane-1,17-diyl diacetate (87%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.27 – 4.18 (m, 4H), 3.71 – 3.66 (m, 4H), 3.64 (s, 16H), 2.32 (t, *J* = 7.6 Hz, 4H), 1.70 – 1.55 (m, 4H), 1.30 (m, 8H), 0.88 (t, *J* = 6.9 Hz, 6H).

### Benzyl (2,3-dihydroxypropyl) adipate:

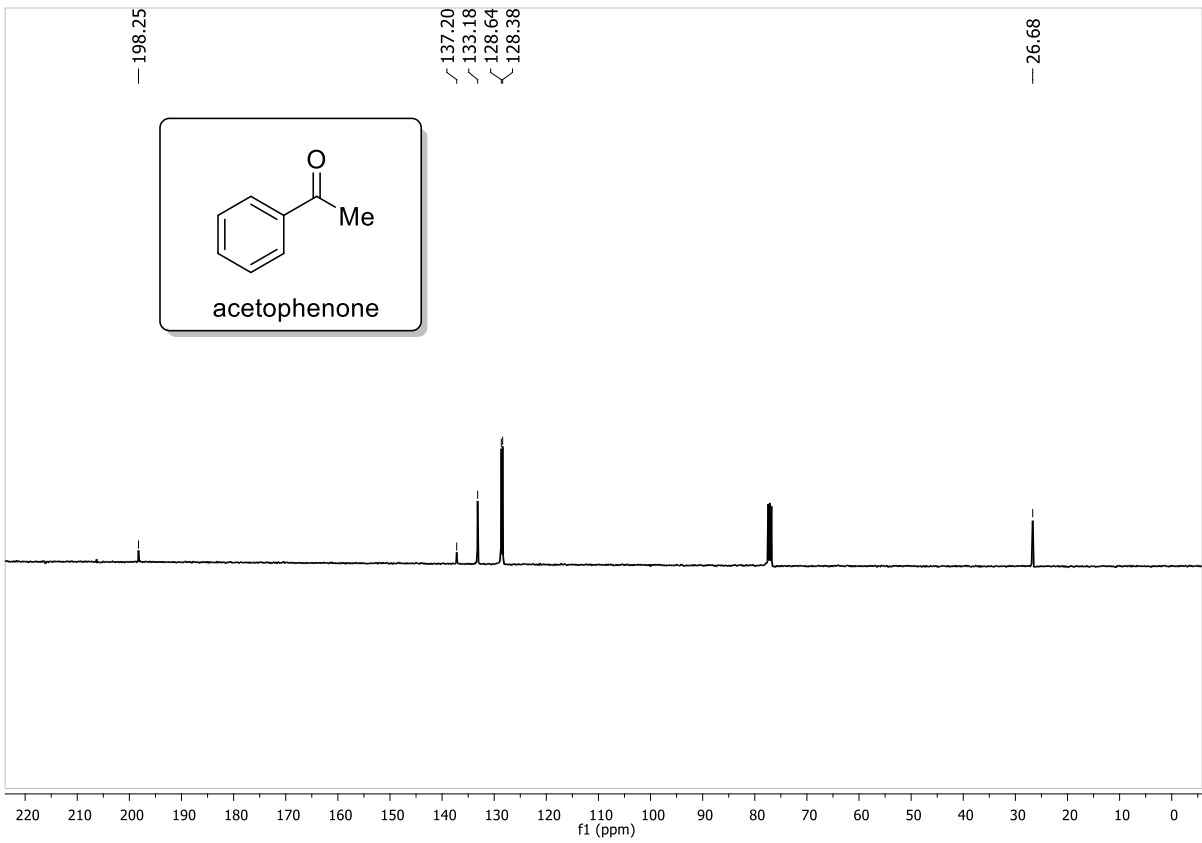
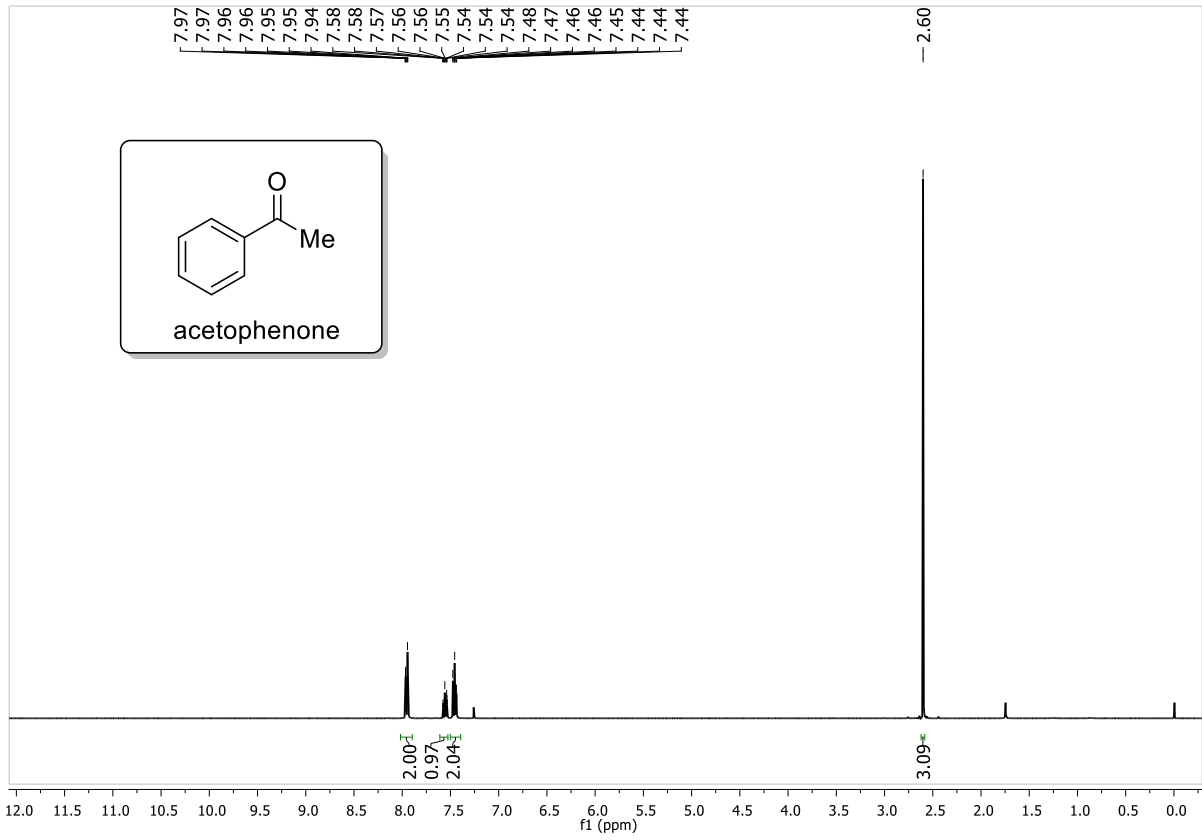


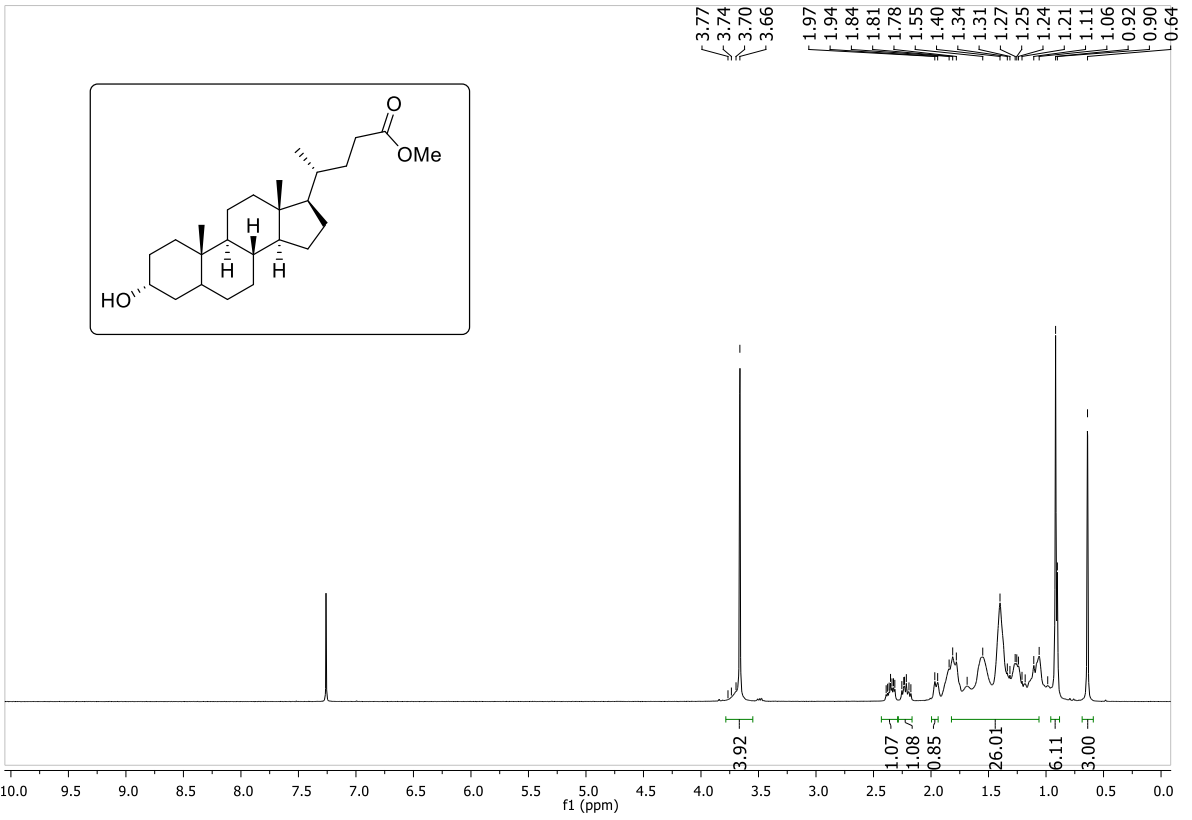
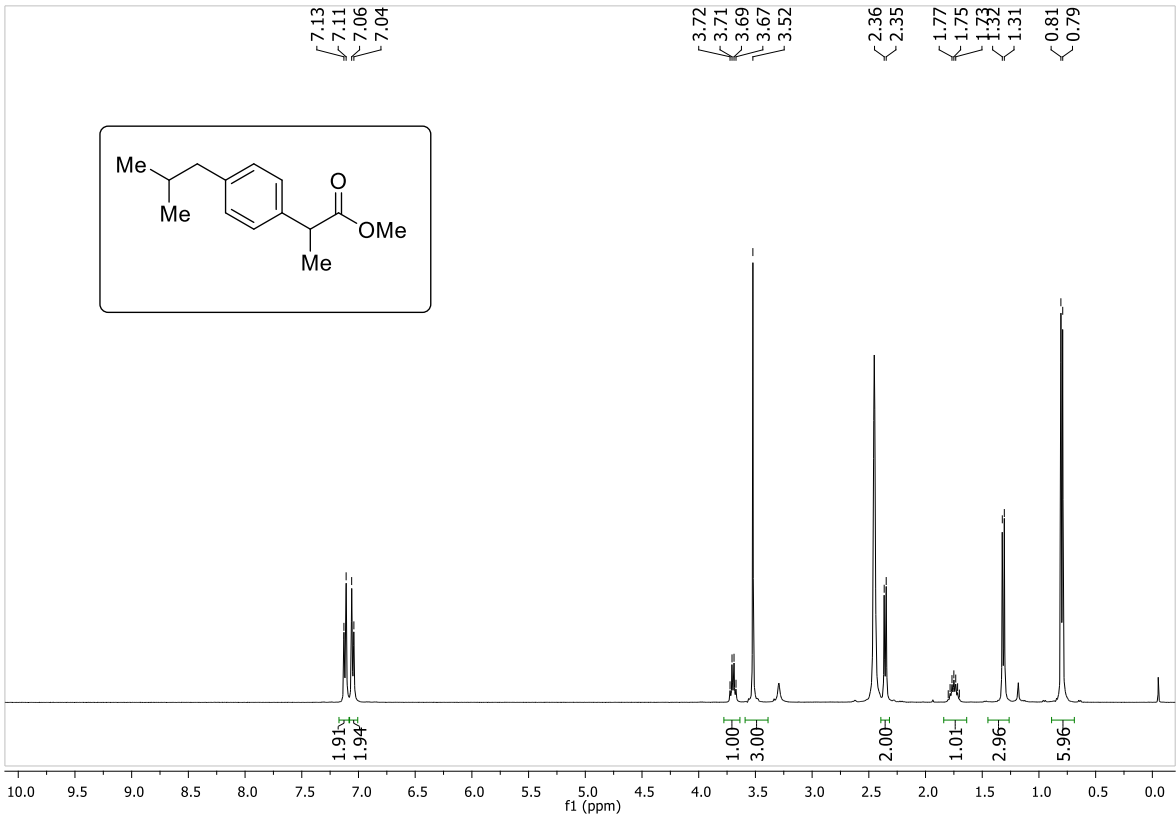
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.35 (s, 5H), 5.11 (s, 2H), 4.20 (dd, *J* = 11.6, 4.6 Hz, 1H), 4.14 (dd, *J* = 11.6, 6.3 Hz, 1H), 3.93 (ddd, *J* = 10.4, 6.0, 4.3 Hz, 1H), 3.69 (dd, *J* = 11.5, 4.1 Hz, 1H), 3.59 (dd, *J* = 11.5, 5.9 Hz, 1H), 2.38 (m, 4H), 1.75 – 1.61 (m, 4H).

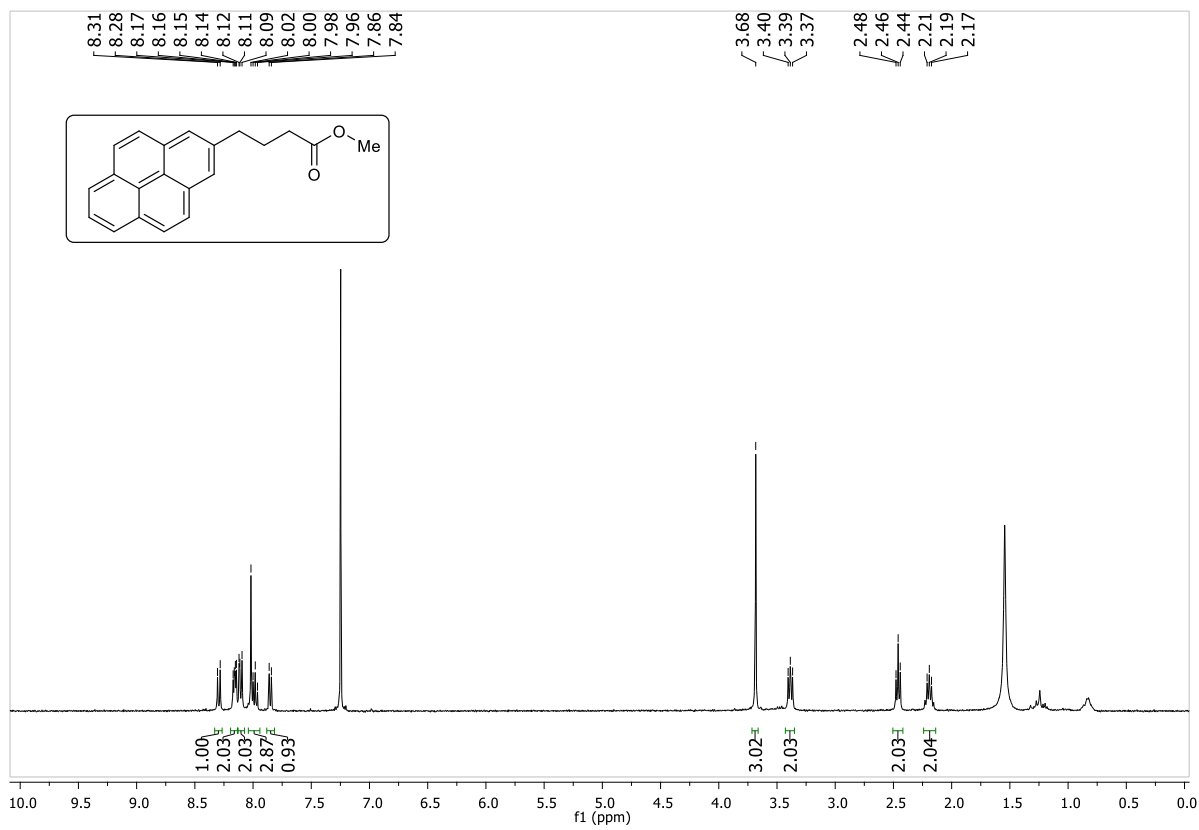
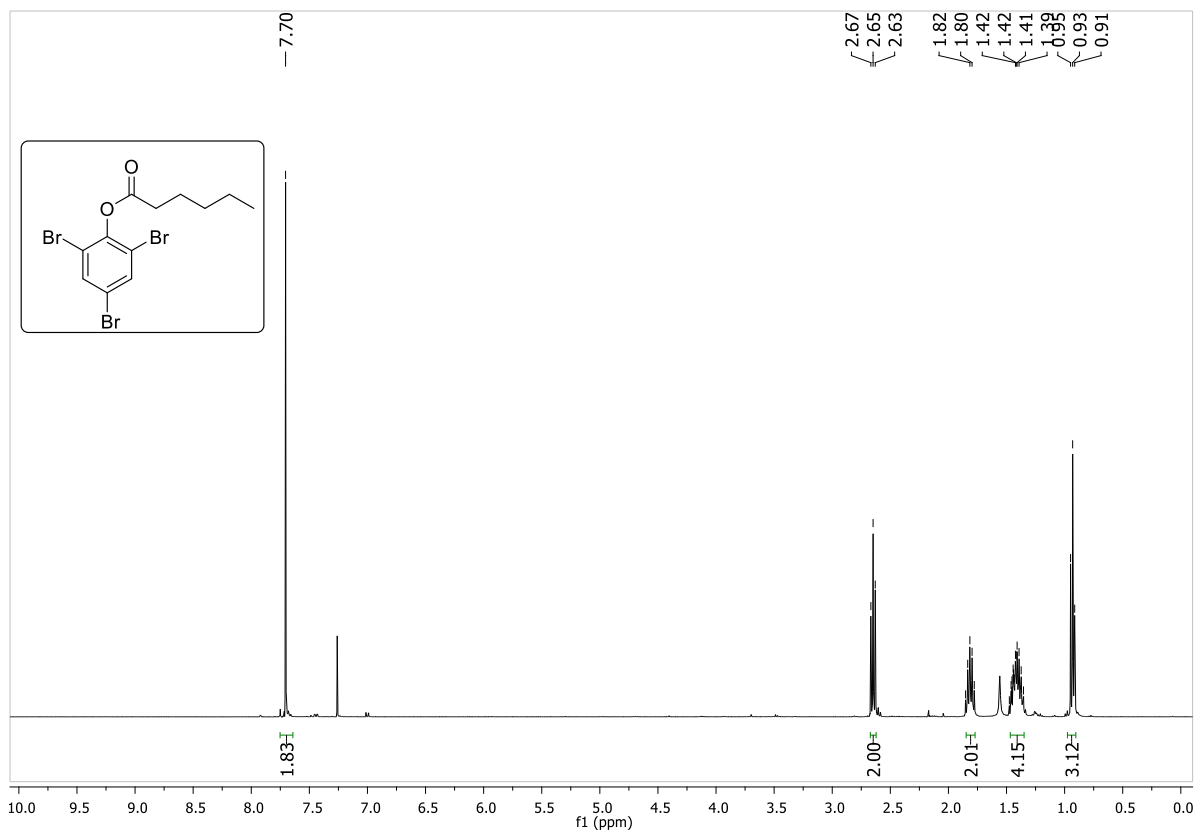
## NMR Spectra of Synthesized Compounds:

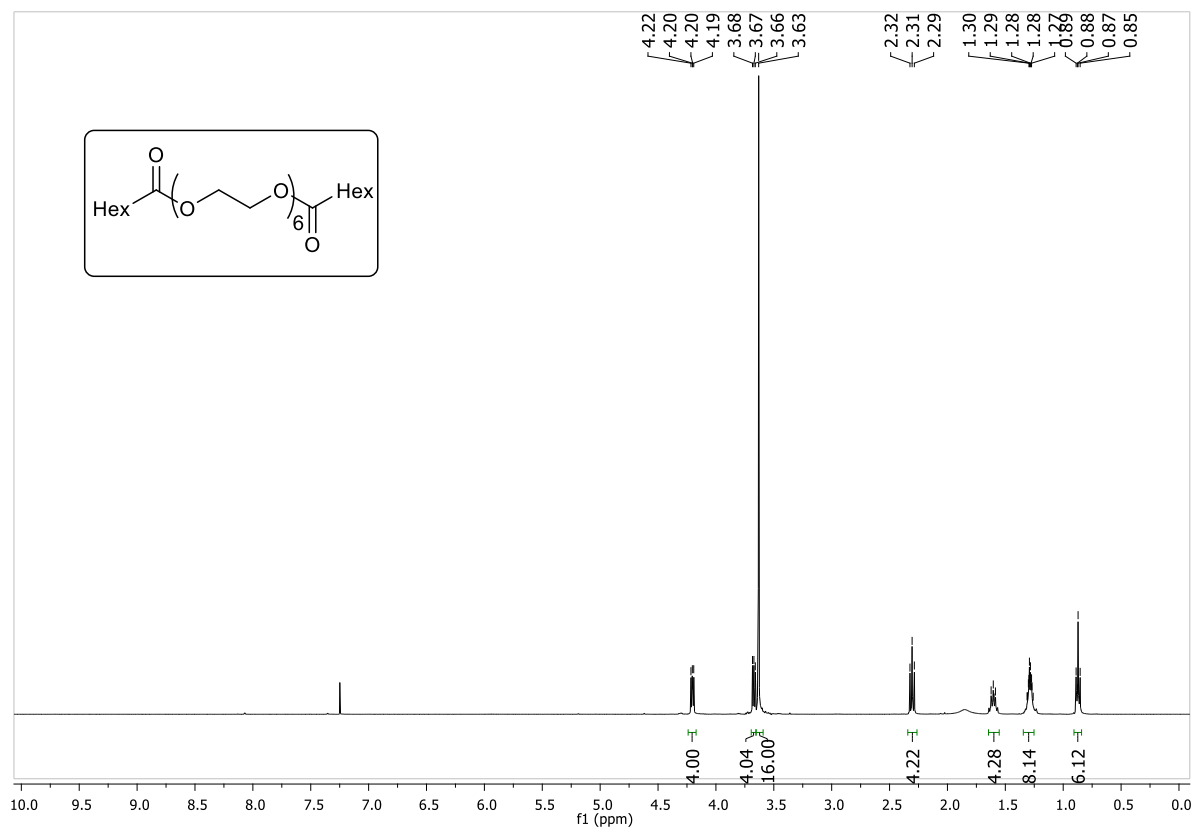
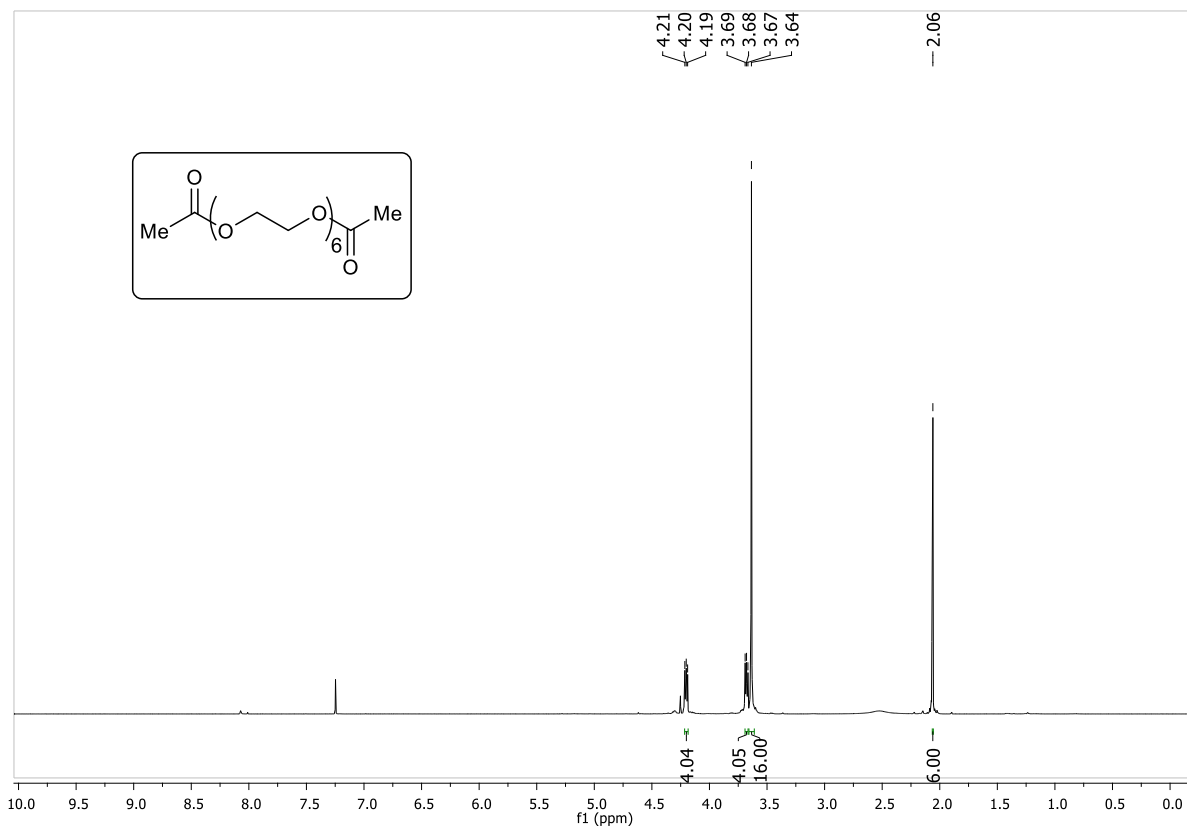


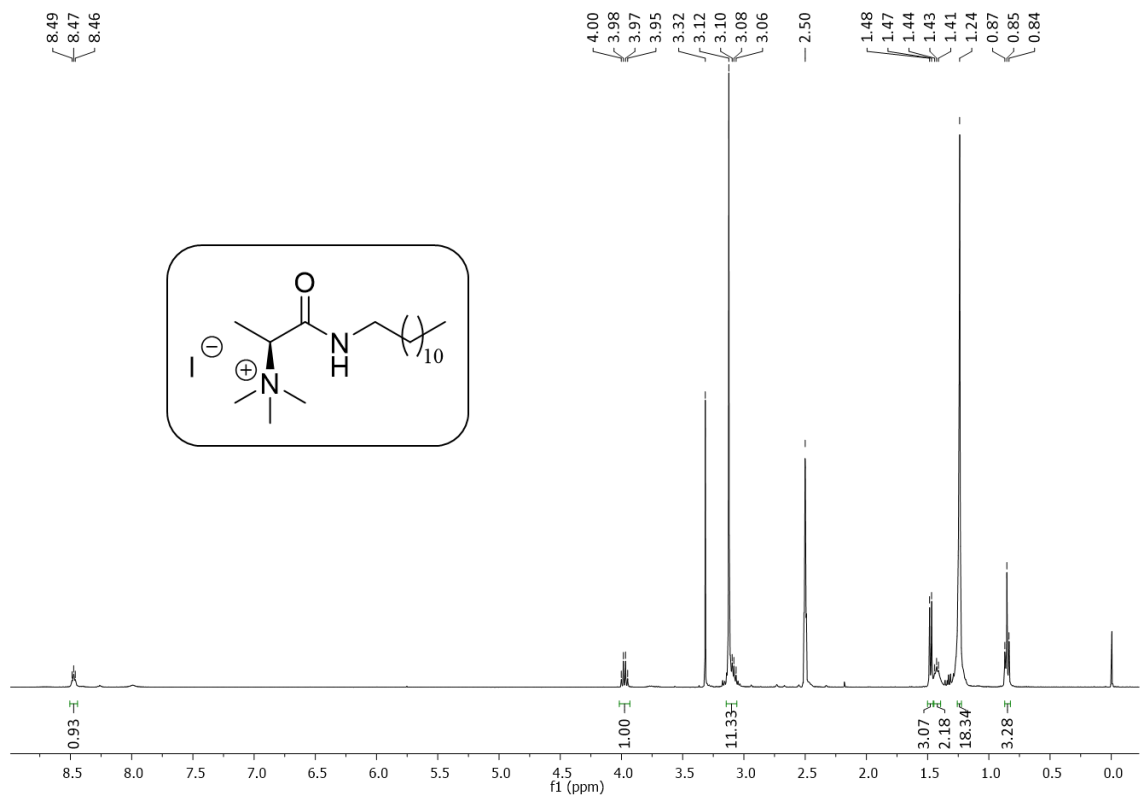
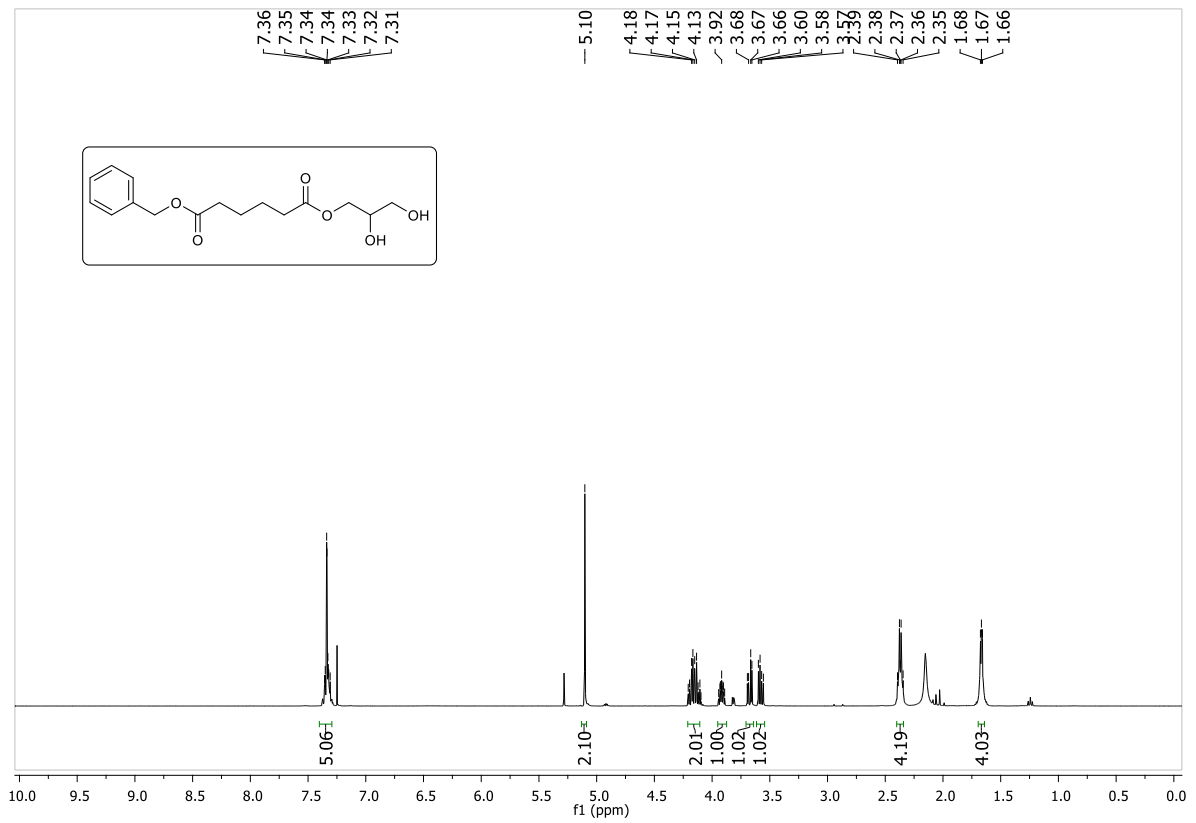


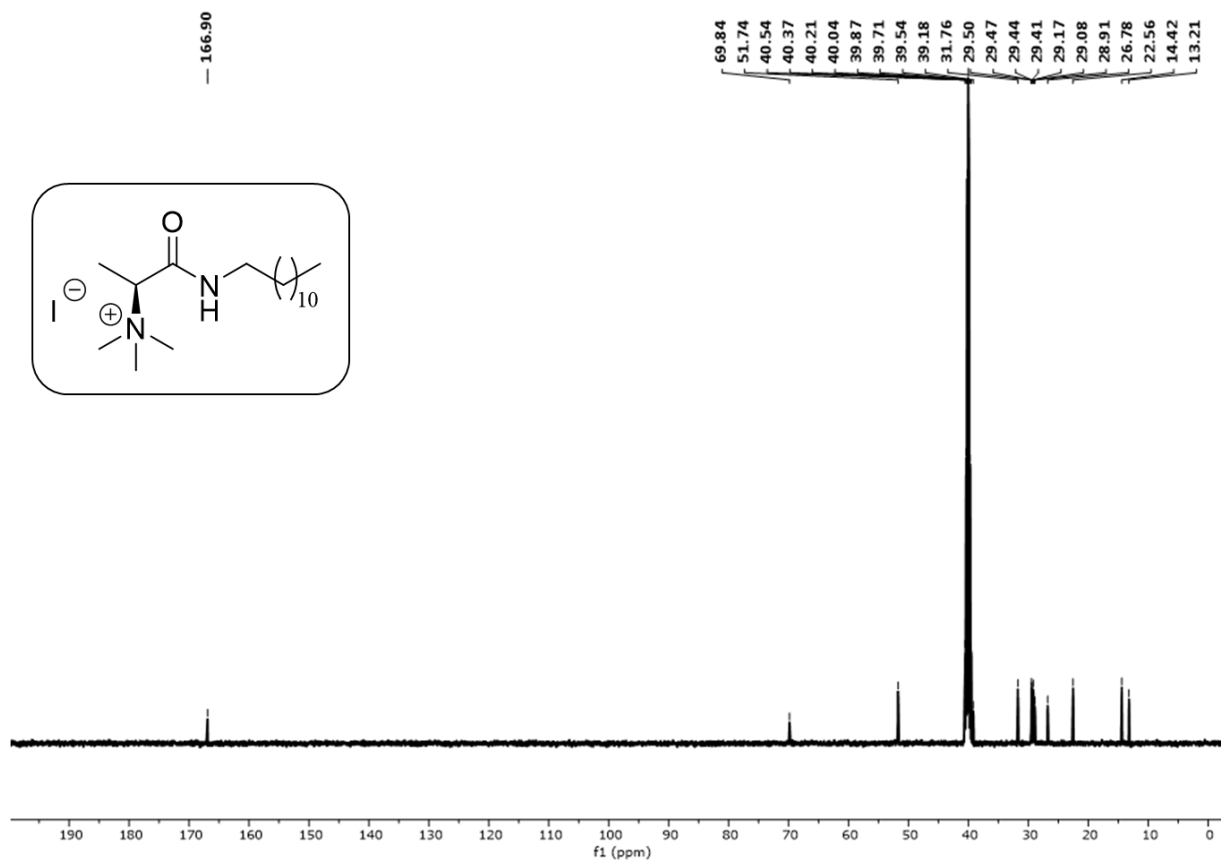












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- 4) K. Kalyanasundaram, J.K. Thomas, *J. Am. Chem. Soc.* **1977**, *99*, 2039-2044.