Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information for

Headgroup linker modulates pK_a via acyl chain migration: Designing base-labile supramolecular assemblies

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Experimental Section and Results

Materials: Lauric acid, sodium dodecylbenzene sulfonate (SDBS), pyrene were purchased from Sigma-Aldrich. Ammonium chloride, sulfuric acid, hydrochloric acid, dioxane, NaOH, NaCl, was obtained from Merck. Ethanolamine, BOC-anhydride (di-tert-butyl dicarbonate), *N, N'*-dicyclohexylcarbodiimide (DCC), 4-dimethylaminopyridine (DMAP), tetra-butylammonium bromide, lauryl amine, lauryl bromide, tris(hydroxymethyl)aminomethane, glycine, citric acid, glucose oxidase (GOD), horseradish peroxidase (POD), *o*-dianisidine, triton-X100, solvents and other chemicals used were purchased from Sisco Research Laboratory. Milli-Q water was used in all experiments.

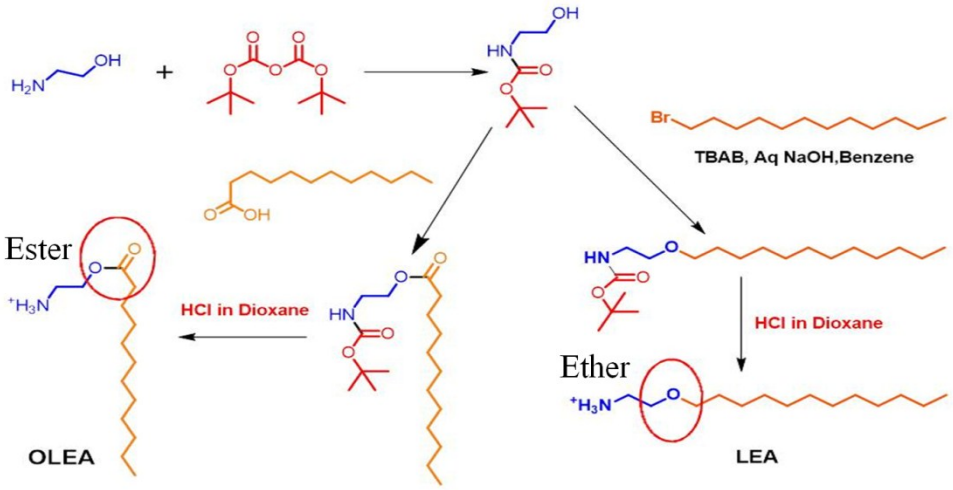
General information: Thin-layer chromatography (TLC) was performed on Merck precoated silica gel 60 F254 aluminum sheets. Chromatographic separations were carried out on silica gel (100−200 mesh). FT-Infrared (IR) spectra were obtained with a Perkin Elmer Spectrum Two spectrophotometer. Nuclear magnetic resonance (NMR) spectroscopy was performed using JEOL 400 MHz and Bruker 500 MHz spectrometers. The following buffer compositions were used in the various studies. 20 mM citrate (pH 5.0-6.0), 20 mM Tris-HCl (pH 7.0-9.0), 20 mM glycine-NaOH (pH 9.5-10.5), 20 mM phosphate-NaOH (pH 11.0).

Synthesis of *O*-lauroylethanolamine (OLEA): OLEA was synthesized according to following protocol (Scheme 1). The amino group of ethanolamine was protected using BOC-anhydride in DCM. The BOC-protected ethanolamine was esterified by condensation with lauric acid using DCC-DMAP as a coupling reagent and the product was purified by column chromatography. At last, the BOC-protected ester was deblocked with 4M HCl in dioxane (prepared by dissolving HCl gas into dioxane) to get the hydrochloride salt of OLEA. The product was characterized by IR and NMR spectroscopy. IR spectrum of OLEA shows absorption bands at 1740 cm^{-1} due to the ester linkage, at 2920 cm^{-1} and 2850 cm^{-1} due to C-H stretching and a band of medium intensity at ~3430 cm^{-1} due to N-H stretching. The ^{1}H-NMR spectrum (Fig. S10) gave the following resonances: 0.89δ (3H, t), 1.26δ (18H, s), 1.60δ (2H, p), 2.40δ (2H, t), 3.30δ (2H, m), 4.40δ (2H, t). These data are consistent with the structure of OLEA.

Synthesis of *2*-lauryloxyethanamine (LEA): The BOC-protected ethanolamine (synthesized for OLEA) was coupled with lauryl bromide in (water & benzene) biphasic medium in presence of tetra-butylammonium bromide. The reaction was carried out at 60 ^{o}C for overnight and the product was purified using column chromatography. Deprotection of the BOC-protected alkyl

ether was carried out in 4M dioxane-HCl. LEA was characterized by IR and ^{1}H-NMR spectroscopy (Fig. S11).

Synthesis of laurylamine hydrochloride (LA): It was prepared by protonation of laurylamine in presence of 4M dioxane-HCl. The solid product was separated and washed with cold ether. IR and ^{1}H-NMR were consistent with the structure (Fig. S12).



Scheme 1: Synthesis of OLEA and LEA.

UV-Turbidimetry: Turbidimetric measurements were performed at 25 ^{o}C and 37 ^{o}C using a HITACHI U-4100 UV-visible spectrometer. Aqueous solutions of cationic surfactant (OLEA, LEA and LA) and SDBS (below the CMC of either surfactant) were mixed at different ratios, kept for equilibration and the scattering at 400 nm was measured to detect supramolecular assembly. To investigate the effect of pH, the supramolecular assemblies of OLBS, LEBS and LABS was incubated in buffers of different pH and the turbidity was measured.

Fluorescence spectroscopy: Emission spectra were recorded on a Horiba Jobin Yvon Fluorescence spectrometer (Fluromax-3, Xe-150 W, 250–900 nm). OLBS, LEBS and LABS were mixed with pyrene (THF solution) by maintaining the lipid: pyrene ratio at 400: 1 and kept for 30 minutes at room temperature. The final pyrene concentration was in the μM range. Samples were excited at 335 nm and emission spectra were recorded in the range between 350 and 550 nm. The excitation and emission slit widths were set at 1.5 nm. Pyrene exhibits five bands in the spectrum and the intensity ratio of the first and third band was considered for analysis. To determine the critical micellar concentration (CMC) pyrene was mixed with various concentrations of cationic surfactant and incubated for equilibration. The intensity ratio of the first and third band was monitored to measure the CMC.

Scanning Electron Microscopy: Morphologies of OLBS, LEBS and LABS assemblies were investigated using field emission-scanning electron microscopy (FE-SEM). A small amount of liposomes was placed on a clean glass surface and dried by slow evaporation. The nanomaterial was dried under vacuum, coated with gold, and the micrographs were taken in a Zeiss SUPRA 55VP-Field Emission Scanning Electron Microscope.

Dynamic light scattering: Particle size and zeta potential of OLBS, LEBS and LABS were measured by dynamic light scattering (DLS), using a Malvern Zetasizer Nano ZS (Malvern Instruments Ltd., UK) equipped with a He-Ne laser with a wavelength of 633 nm.

Powder X-ray diffraction (PXRD): OLBS was prepared by mixing appropriate amount of OLEA and SDBS in water. The water was evaporated at high vacuum and the mixture was lyophilized before the PXRD measurements. Data was collected at ambient temperature (25 ^{o}C) on a Bruker D8 Advance diffractometer using CuKα radiation of wavelength 1.5418 Å. The PXRD data was collected within 2θ range of 5 - 40^{o} (step size 0.02^{o}).

Encapsulation of Glucose in OLBS and LEBS:

OLBS, LEBS and LABS vesicles were prepared in 300 mM Glucose solution. The excess (non-encapsulated) glucose was separated by size exclusion column equilibrated with buffer (pH 7.0). The glucose entrapped fractions were divided into two parts. In one part, pH of the solution was adjusted to 8.5 and incubated for 30 minutes at 37^{0}C. After the incubation, the pH was readjusted to 7.0 by adding HCl. The other part of the glucose entrapped fraction was treated with Triton X-100 (known as vesicle solubilizer). 400 µl of GOD-POD assay reagent (mixture of GOD, POD and *o*-dianisidine) was added to all the solutions and incubated at 37 ^{0}C for 60 minutes. Next, 400 µL of 12 N H_2SO_4 was added and the absorbance of the solutions was measured at 540 nm using control as a blank. 100% leakage was obtained from the Triton-X100 treated vesicles. Experiments were carried out at least three times and the average with standard deviation was reported.

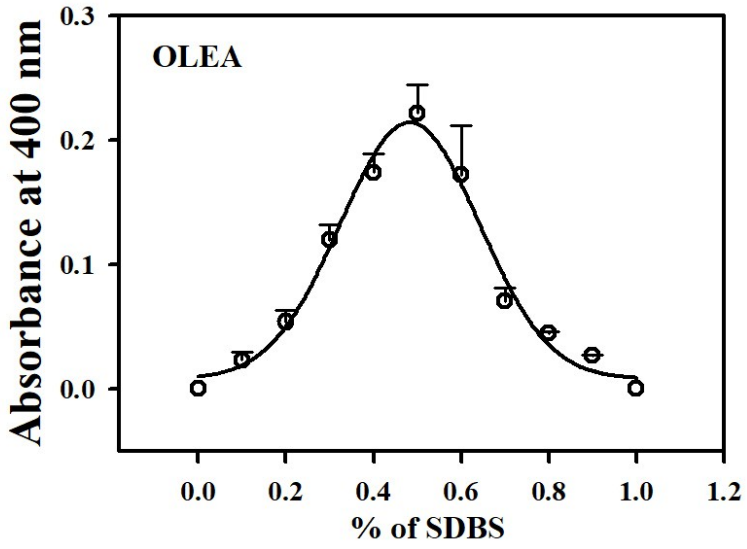


Fig. S1: Aggregate formation at various mixtures of OLEA and SDBS.

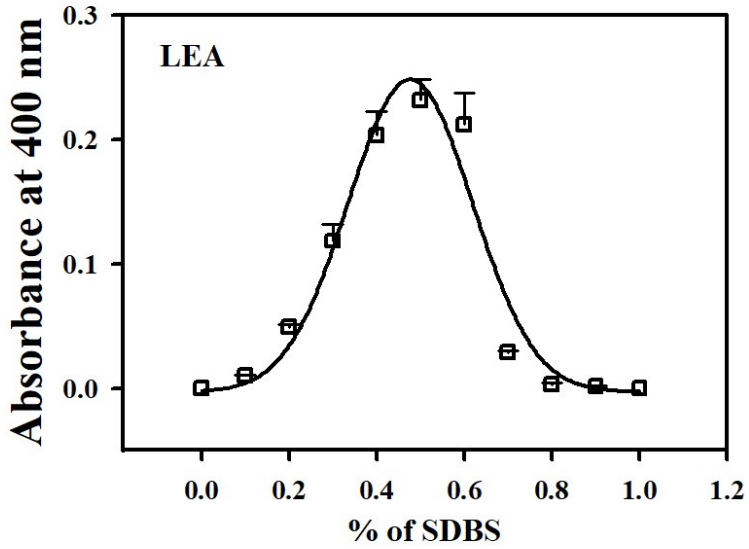


Fig. S2: Aggregate formation at various mixtures of LEA and SDBS.

Fig. S3: Aggregate formation at various mixtures of LA and SDBS.

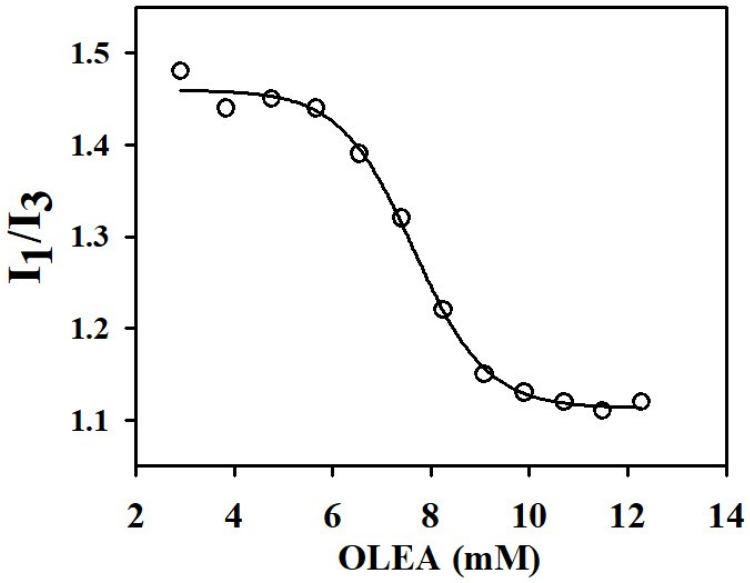


Fig. S4: Determination of the critical micellar concentration (CMC) of OLEA using pyrene fluorescence. The CMC ~ 7.7 mM was obtained by fitting the sigmoidal curve.

Fig. S5: Determination of CMC of LEA using pyrene fluorescence. The CMC ~ 6.5 mM was obtained by fitting the sigmoidal curve.

Fig. S6: Determination of CMC of LA using pyrene fluorescence. The CMC ~ 13.0 mM was obtained by fitting the sigmoidal curve.

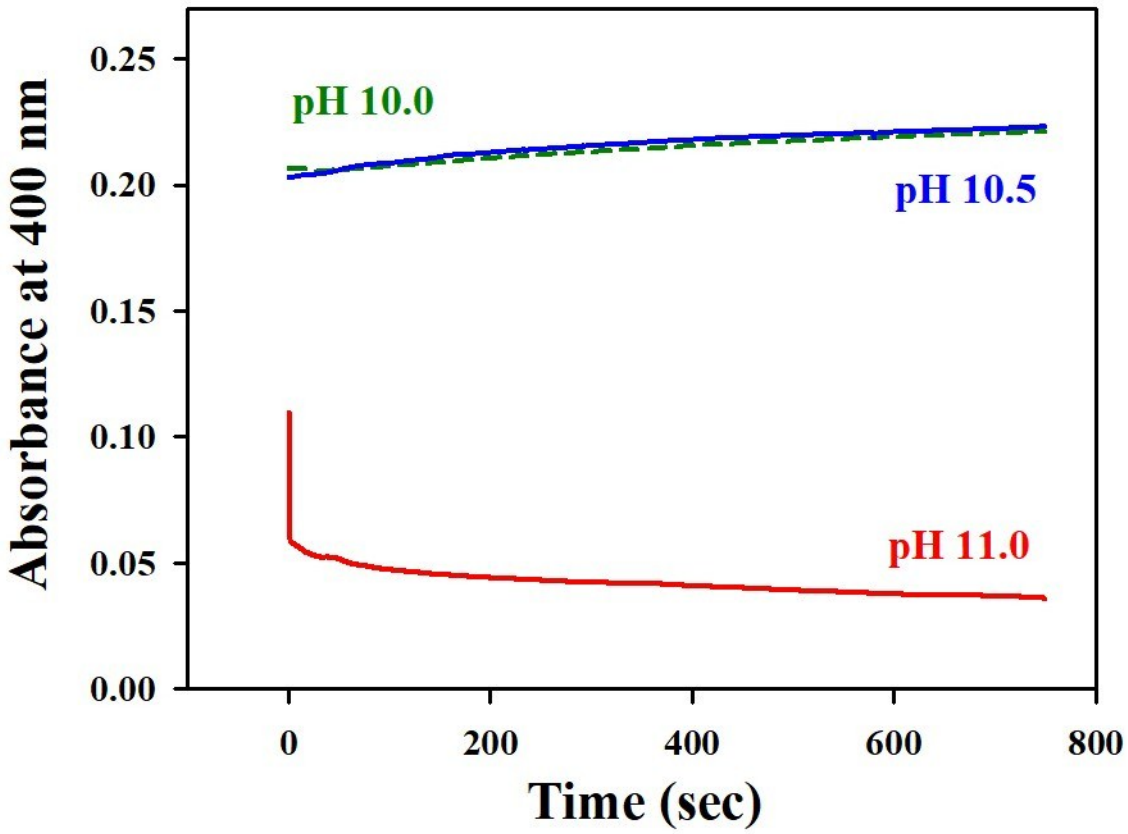


Fig S7: Time-dependent scattering of LEBS vesicles at various pH. Vesicles are stable at pH 10.5 but disrupts rapidly at pH 11.0.

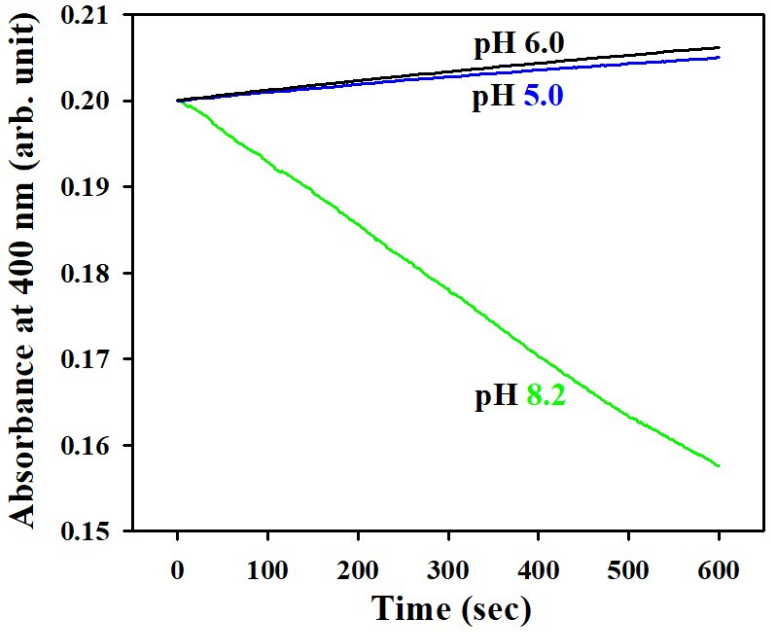


Fig S8: Kinetics of vesicle ($OL_{60}BS_{40}$) stability at acidic pH. The vesicles remain stable at acidic pH.

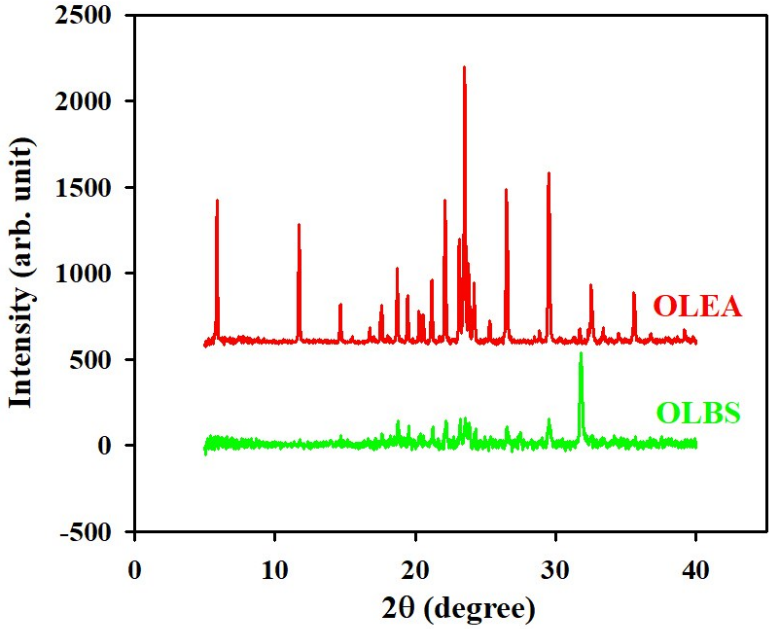


Fig S9: X-ray diffraction (XRD) data of OLEA (red line) and OLBS (green line). The catanionic mixture (OLBS) is amorphous in nature.

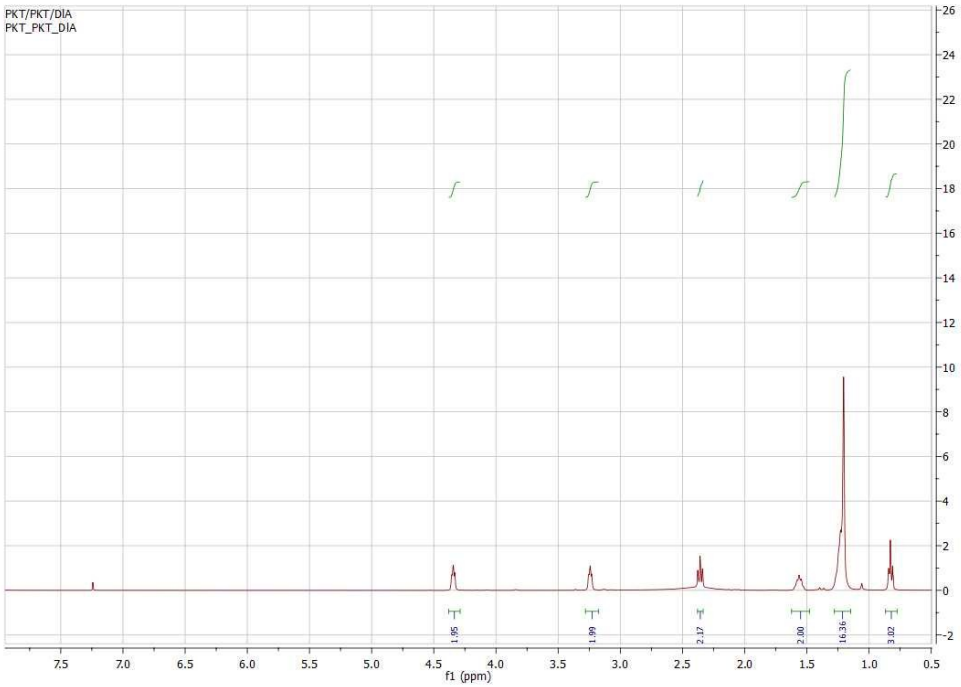


Fig S10: ^{1}H-NMR spectrum of OLEA in $CDCl_3$.

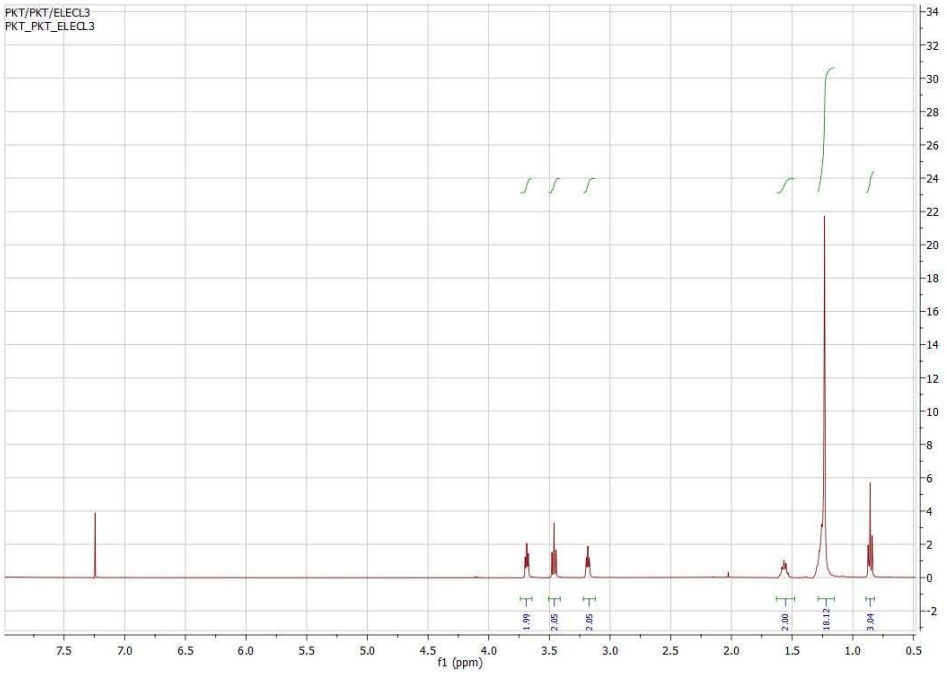


Fig S11: ^{1}H-NMR spectrum of LEA in $CDCl_3$.

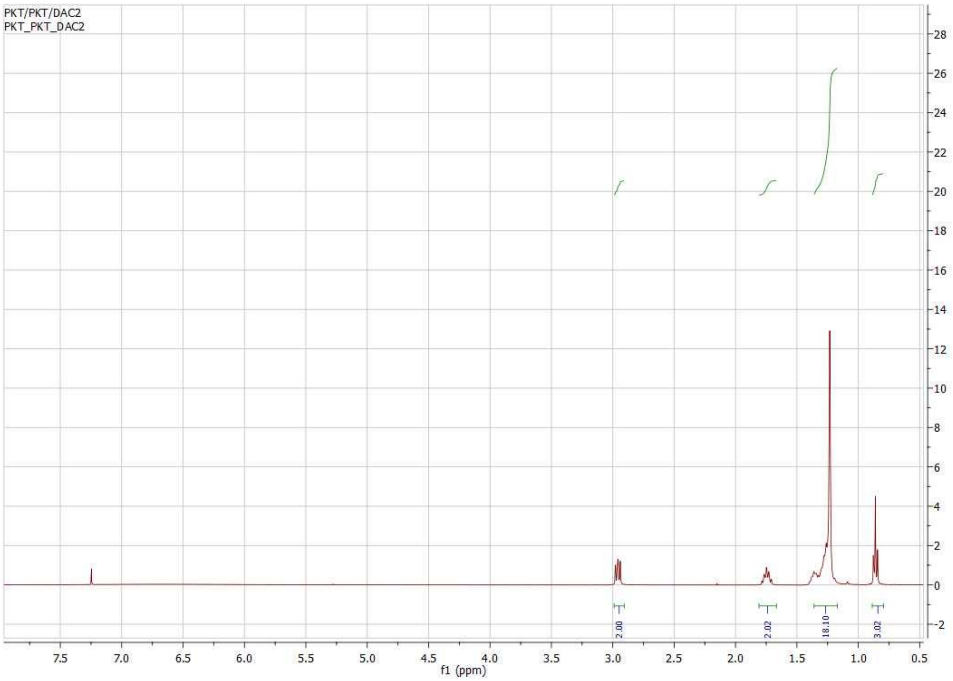


Fig S12: ^{1}H-NMR spectrum of LA in $CDCl_3$.