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Cite this: DOI: 10.1039/c0xx00000x

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PAPER

Controlled RAFT Synthesis of Side-Chain Oleic Acid Containing Polymers and Their Post-Polymerization Functionalization†

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

This study provides new insights into the design and controlled synthesis of side-chain unsaturated fatty acid containing polymers, with specific attention from facile post-polymerization modification reactions. Methacrylate derivative of oleic acid, 2-(methacryloyloxy)ethyl oleate (MAEO), has been synthesized and polymerized by reversible addition-fragmentation chain transfer (RAFT) process to obtain poly(2-(methacryloyloxy)ethyl oleate) (PMAEO) with controlled molecular weight, narrow molecular weight distribution (*Đ*) and known chain ends. The PMAEO is capable of subsequent chain extension to form well-defined block copolymers *via* RAFT technique. Double bonds in oleate side-chains in PMAEO are further reacted with various organic thiol compounds *via* thiol–ene based thia-Michael addition reactions in the presence of 2,2´-azobisisobutyronitrile (AIBN) as radical source at 60 $^{\circ}$C in tetrahydrofuran (THF) solvent. The ^{1}H NMR spectroscopy indicated quantitative conversion of double bonds with ethanethiol, butanethiol, dodecanethiol and 3-mercaptopropanoic acid, whereas 2-mercaptoethanol gave ~90% thioether product. The side-chain double bonds of PMAEO were quantitatively epoxidized using *meta*-chloroperbenzoic acid (mCPBA) at room temperature in dichoromethane, which was further cross-linked by 1, 3-diaminopropane. Therefore, side-chain oleate pendants are ideal for various post-polymerization modifications to prepare renewable resource derived controlled macromolecular architectures with potential practical applications in the field such as paints, adhesives, electrical insulators, thermoplastics, etc.

Introduction

The synthesis of polymers from renewable resources is receiving increasing attention to the researchers of the academic and industrial world due to their low cost, sustainability and biocompatibility.[1,2] Fatty acid based renewable resources have been reported in construction of materials such as thermoplastics elastomers,[3] biocomposites and thermosetting resins by using fatty acid based monomers *via* different types of polymerization techniques.[4] Polycondensation polymerization mechanism has been extensively utilized to prepare polyesters, polyethers, polyamides, epoxy and polyurethane resins, etc.[5,6] For example, a series of ω-hydroxyfatty acid monomers and their methyl ester derivatives from fatty acid and its alcohols were used to prepare thermoplastic poly(ω-hydroxyfatty acid)s *via* melt polycondensation method.[7] Also, Quinzler and Mecking reported novel semicrystalline polyesters with long-chain hydrocarbon segments based on complete linear incorporation of oleic acid and erucic acid through polycondensation reactions.[8] Controlled radical polymerization (CRP) techniques have also been used to prepare fatty acid containing polymers mainly with saturated fatty acid derived monomers. Merier et al. prepared fatty acid functionalized norbornenes and polymerized by the ring-opening metathesis polymerization (ROMP) in a controlled fashion, where they were able to tune the thermal property of polymers by varying the chain length of fatty acid.[9] Atom transfer radical polymerization (ATRP) of fatty acid containing methacrylates produced side-chain fatty acid containing polymers with controlled molecular weights and molecular weight distributions.[10] Lauryl methacrylate (LMA) has been polymerized by reversible addition-fragmentation chain transfer (RAFT) method.[11,12] In our previous report, we have demonstrated controlled RAFT polymerization of series of methacrylate monomers with side-chain fatty acids, such as caprylic, capric, lauric, mysritic, palmitic and stearic acid. By changing the alkyl chain length in the fatty acid, homopolymers displayed different physical properties such as crystallinity and solubility.[13] Other methods[14] such as cationic and anionic polymerizations have also been applied to prepare fatty acid containing materials.

Unsaturated fatty acids such as linoleic acid, oleic acid and erucic acid, etc. have a wide range of applications in the industry.[15] Among the various unsaturated fatty acids, oleic acid is important due to its low cost, large availability and high oxidative stability compared to other unsaturated fatty acids.[16] Since derivatization of alkenes through the thia-Michael type conjugate addition with thiol-containing molecules is highly selective and is tolerant to a variety of functional groups such as hydroxyl, carboxyl, and amine,[17] plant oils have been modified by several thiol-ene reactions.[18] The efficient thiol addition onto oleic acid, leading to bio-based polyol, was demonstrated elsewhere.[19] Sulfur-containing plasticizers have been developed based on the thiol–ene addition of alkyl thiols to the double bond of technical oleic acid, followed by oxidation of the sulfide group.[20] The bulk cationic ring-opening polymerization of 2-(dec-9-enyl)-2-oxazoline, a fatty acid based monomer with pendant alkene groups, and subsequent thiol–ene reactions with dodecanethiol and 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glycopyranose in 'green' solvents is demonstrated.[21] Although there are several reports on the Michael-type conjugate addition onto oleic acid, side-chain fatty acid derived polymers by free radical polymerization methods have never been modified by versatile thiol-ene reactions. Barandiaranet and co-workers have synthesized oleic acid methacrylate monomer and polymerized it by conventional free radical miniemulsion polymerization.[22] The radical polymerization of 2-(acryloyloxy) ethyl oleate resulted corresponding polymer with molecular weight in the range from 20,000 to 30,000 g/mol.[23] In both the above reports, the side-chain double bond in oleate moiety was unreactive towards radical polymerization upto reasonably high molecular weights, which inspired us to check the feasibility of controlled radical polymerization techniques such as RAFT to polymerize side-chain oleic acid containing methacrylate monomer, 2-(methacryloyloxy) ethyl oleate (MAEO). Therefore, the purpose of this work is to make polymer from MAEO monomer in a controlled fashion and incorporate new functional groups to the side-chain double bonds *via* simple organic chemistry approach such as thiol-ene and epoxidation reactions.[24] The epoxidized polymer was cured by using a diamine, which may be potentially useful for many industrial applications.[25] These polymeric architectures are very likely to have good biocompatibility due to the presence of fatty acid pendants. In this context, it is worth to mention that due to the facile chain transfer reactions, polymerization of sulphur containing monomers (such as, with free –SH, disulphide, tetrasulphide, etc.) to obtain corresponding polymers usually requires multi-step process involving protection and deprotection of the functional groups before and after the polymerization,[26] which may result in low overall yields as well as degradation of polymers.

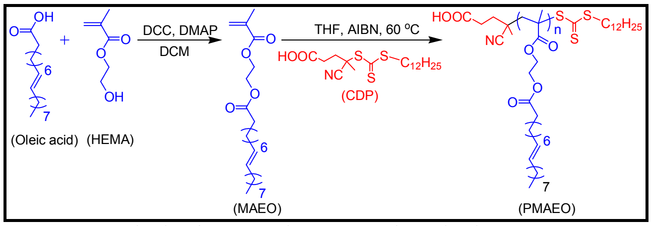
Experimental Section

Materials

Oleic acid (OA, ≥ 99%), dicyclohexylcarbodiimide (DCC, 99%), 4-dimethylaminopyridine (DMAP, 99%), 2-hydroxyethyl methacrylate (HEMA, 97%), *meta*-choloroperbenzoic acid (mCPBA), 1, 3-diaminopropane (≥ 99%), ethanethiol (≥98%), butanethiol (≥98%), dodecanethiol (≥98%) and 3-mercaptopropanoic acid (98%) were purchased from Sigma-Aldrich and used without any further purification. The 2-mercaptoethanol (99%) was purchased from Sisco Research Laboratories Pvt. Ltd., India. Poly(ethylene glycol) methyl ether methacrylate (PEGMA, M_n = 300 g/mol, 99%) and methyl methacrylate (MMA, 99%) were obtained from Sigma-Aldrich and passed through a basic alumina column prior to polymerization. The RAFT chain transfer agent (CTA), 4-cyano-(dodecylsulfanylthiocarbonyl)sulfanylpentanoic acid (CDP), was synthesized following the standard literature procedure,[27] and 2,2´-azobisisobutyronitrile (AIBN, Sigma, 98%) was recrystallized from methanol. $CDCl_3$ (99.8% D) was obtained from Cambridge Isotope Laboratories, Inc., USA for NMR spectroscopy. Regular solvents such as dichloromethane (DCM), tetrahydrofuran (THF), methanol (MeOH), ethyl acetate (EtOAc), hexanes (mixture of isomers), acetone, etc. were purified by simple distillation.

Instrumentation

Molecular weights and molecular weight distributions (dispersity, *Đ*) of polymers were determined by gel permeation chromatography (GPC) instrument, which contains one Waters 515 HPLC pump, one Waters 2414 refractive index (RI) detector and two columns (Styragel HT4 and Styragel HT3) in THF at 30 °C at 1.0 mL/min flow rate. Poly(methyl methacrylate) (PMMA) standards were used to construct conventional calibration curve, which was used to determine molecular weights of polymers. ^1H NMR spectra were acquired in a Bruker Avance^{III} 500 spectrometer operating at 500 MHz at 25 °C. FT-IR spectroscopic measurements were carried out on KBr pellets using a Perkin-Elmer Spectrum 100 FT-IR spectrometer. Positive mode electrospray ionization mass spectrometry (ESI-MS) was performed on a maXis impact (ESI-Q TOF) high resolution mass spectrometer (Bruker Daltonics). Matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry was carried out on a Bruker ultrafleXtreme^{TM} instrument equipped with a smart beam-II laser in the reflector mode and 22 kV acceleration voltages. 2,5-Dihydroxybenzoic acid (DHB, Bruker) was used as matrix during MALDI-TOF measurements.



Scheme 1 Synthesis of PMAEO by RAFT polymerization.

Synthesis of MAEO Monomer

The OA (0.024 mol, 8.0 g) and DMAP (1.40 mmol, 0.353 g) were dissolved in 30 mL dry DCM in a 250 mL double necked round bottom (RB) flask equipped with a magnetic stir bar. Then, the RB flask was put on ice-water bath and dry N_2 gas was purged through it. In a separate beaker DCC (0.027 mol, 6.426 g) was dissolved in minimum volume of DCM and was added to the reaction mixture through a dropping funnel. Then, HEMA (0.027 mol, 3.22 g) was added drop wise for 30 min. The ice-water bath was removed after 20 min and the resulting reaction mixture was stirred for overnight at room temperature. After competition of reaction, it was filtered to remove the white precipitate and 60 mL distilled water was added to the filtrate. The organic layer was washed with saturated $NaHCO_3$ (80 mL × 4) and brine solution (80 mL × 2), and dried over anhydrous Na_2SO_4 for 18 h. The solvent was removed by rotary evaporator and purified by column chromatography using silica gel as stationary phase and hexanes/EtOAc (95:5, v/v) as an eluent to obtain a colorless liquid (yield: 75 %). ^1H NMR (Fig. 1, 500 MHz, in $CDCl_3$): δ (ppm) = 6.12 and 5.58 (C=C$\boldsymbol{H}_2$, 2H, d), 5.37 (-CH$_2$-CH$_2$-C$\boldsymbol{H}$=C$\boldsymbol{H}$-CH$_2$-CH$_2$-, 4.32 (-OC$\boldsymbol{H}_2$C$\boldsymbol{H}_2$O-, 4H, t), 2.32 (O=CC$\boldsymbol{H}_2$, 2H, t), 1.61 (O=CCH$_2$C$\boldsymbol{H}_2$CH$_2$CH$_2$-, 2H, m), 1.28 (-(C$\boldsymbol{H}_2$)$_6$-CH$_2$-CH=CH-CH$_2$-(C$\boldsymbol{H}_2$)$_4$-, 20H, m), 1.94 (CH$_2$=CC$\boldsymbol{H}_3$, 3H, s), 0.87 (-CH$_2$C$\boldsymbol{H}_3$, 3H, t). FT-IR (cm^{-1}, Fig. S1): 3000, 2934 (C–H), 1735 (C=O), 1634 (C=C), 1455, 1367, 1296, 1220, 1162 (C–O), 1062, 938, 862, 816, 768. ESI-MS (Fig. S2): *m*/*z* for [M + Na$^+$]; calculated: 417.308, observed: 417.309.

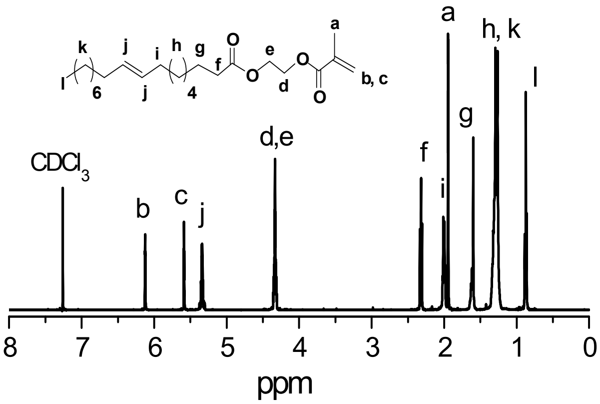


Fig. 1 ^{1}H NMR spectrum of MAEO in CDCl$_3$.

RAFT Polymerization of MAEO

A representative RAFT polymerization procedure is as follows: MAEO (5.06 mmol, 2.00 g), CDP (0.20 mmol, 81 mg), AIBN (40 µmol, 6.63 mg; from stock solution) and 8 mL THF were added to a 20 mL septa sealed glass vial equipped with a magnetic bar. The reaction vial was purged with dry N$_2$ gas for 15 min keeping the vial on ice-water bath. Then, the vial was put in a preheated reaction block at 60 ^{o}C for 13 h. Polymerization reaction was quenched by cooling the vial in ice-water bath, and the polymer (PMAEO) was purified by reprecipitation in MeOH at least five times (from acetone solution) and dried under high vacuum at room temperature to obtain a yellowish sticky material.

Chain Extension Reactions

Typically, MAEO (74.0 mg, 0.188 mmol), PMAEO macroCTA (number average molecular weight obtained from GPC ($M_{\mathrm{n,GPC}}$) = 9000 g mol^{-1}, $Đ$ = 1.10, 100.0 mg, 7.5 µmol), AIBN (1.5 µmol, 0.24 mg ; 48.0 mg solution of 10.0 mg AIBN in 2.0 g THF) and 0.822 g THF were added to the 20 mL polymerization vial equipped with a magnetic stir bar and purged with dry N$_2$ for 15 min on a ice-water bath. The reaction vial was placed in a preheated reaction bath at 60 ^{o}C for 7 h, quenched by cooling in ice-water bath, and purified as mentioned above for the homopolymer.

Synthesis of Block Copolymers

Generally, PEGMA (0.33 mmol, 100.0 mg), PMAEO macroCTA ($M_{\mathrm{n,GPC}}$ = 9000 g mol^{-1}, $Đ$ = 1.10, 60.0 mg, 6.7 µmol), AIBN (1.33 µmol, 0.21 mg; 42.0 mg solution of 10.0 mg AIBN in 2.0 g THF), and THF (0.758 g) were added in a 20 mL polymerization vial equipped with a magnetic bar and deoxygenated with dry N$_2$ gas for 15 min on an ice-water bath. The polymerization reaction was carried out at 60 ^{o}C for 7 h, quenched by cooling the vial in ice-water bath and the resulting reaction mixture was then purified by precipitation in MeOH as mentioned above.

Thiol-Ene Reaction

PMAEO (0.07 g, 1.0 equivalent) was dissolved in 1.5 mL dry THF in a 20 mL vial, and then AIBN (0.2 equivalent, 6.0 mg) and ethanethiol (0.165 g, 15.0 equivalents) was added into the vial. The vial was purged with dry N$_2$ on an ice-water bath for 10 min, and was stirred at 60 ^{o}C for 12 h. The resulting polymer was purified by precipitation in MeOH (at least 4 times to ensure complete removal of unreacted ethanethiol), and finally the product was dried under high vacuum at room temperature.

Epoxidation of Homopolymer

PMAEO ($M_{\mathrm{n,GPC}}$ = 9000 g mol^{-1}, $Đ$ = 1.10, 1.26 mmol, 500 mg) and mCPBA (3.78 mmol, 656 mg) was dissolved in 2.0 mL DCM in a 20 mL glass vial. The reaction mixture was stirred for 12 h at room temperature. It was then purified by precipitation in MeOH (from acetone solution, at least 4 times) and dried under high vacuum at room temperature to get a waxy type compound. The yield was quantitative.

Cross-linking

Epoxidized polymer (1.70 mmol, 700 mg) and 1, 3-diaminopropane (2.56 mmol, 300 mg) were mixed in 2.0 mL dry DCM in a 20 mL vial. The reaction mixture was placed at 50 ^{o}C for 24 h. It was then purified by reprecipitation from MeOH and dried under high vacuum at room temperature.

Results and Discussion

Monomer and Polymer Synthesis

The MAEO was synthesized by simple coupling reaction of oleic acid and HEMA in the presence of DCC and DMAP (Scheme 1).[13] Structure of MAEO was confirmed by using ^{1}H NMR, ESI-MS, and FT-IR spectroscopy. In the ^{1}H NMR spectrum of MAEO (Fig. 1), the signal at 5.37 ppm is assigned to the double bond present in the side-chain oleate moiety and two peaks at 6.12 and 5.58 ppm correspond to the vinyl protons from methacrylate part. The assignment of all resonance signals has been depicted in Fig. 1. The structure of MAEO was further verified by ESI-MS study and we noticed excellent agreement between the observed molecular mass of [MAEO + Na]$^+$ = 417.309 *m*/*z* with the theoretical [MAEO + Na]$^+$ = 417.308 *m*/*z* value (Fig. S2). The FT-IR spectrum of MAEO showed characteristic absorptions corresponding to stretching vibrations of the ester carbonyl C=O (1739 cm^{-1}) and the CH$_2$ = C(CH$_3$)- double bond (1638 cm^{-1}) (Fig. S1). These results confirmed the success of the synthetic procedure and no side reactions from the side-chain double bonds in oleate moiety.

To ensure control of the polymerization and to obtain PMAEO with a desirable molecular weight, RAFT polymerization of MAEO was conducted in THF at 60 ^{o}C in the presence of AIBN as radical initiator and CDP as a CTA. This trithiocarbonate CTA was chosen because of its efficiency in polymerizing side-chain fatty acid containing methacrylate derivatives.[13] The polymerization reactions were carried out at different ratios of monomer (M) to CDP between 25 and 200, while the molar ratios of [CDP]/[AIBN] = 5:1 kept constant. For all the [M]/[CDP] ratios, unimodal GPC RI traces without shoulder and tailing confirmed no bimolecular termination reactions during the RAFT polymerization (Fig. 2A). Figure 2B shows that the $M_{n,GPC}$ increases linearly with the increase of [M]/[CDP] ratio upto 100 with narrow $Đ$ (1.12-1.44), and $M_{n,GPC}$ values match reasonably well with the theoretical number average molecular weights ($M_{n,theo}$) based on monomer conversion (Table 1). Although molecular weight depends on [M]/[CDP] ratio and monomer conversion, note that the polymerization time is different for different [M]/[CDP] ratios. Substantial deviation is observed for the $M_{n,GPC}$ values from the $M_{n,theo}$ line at higher [M]/[CDP] ratios of 150/1 and 200/1, indicating side reactions at higher monomer concentrations. This is presumably due to the presence of impurities in the monomer, concentration of which increases with increasing monomer concentration ([M]/[CDP] ratios) to provide chain-breaking events to the propagating macro-radicals. Kinetic studies were also carried out using [MAEO]/[CDP]/[AIBN] = 25:1:0.2 in THF at 60 °C. Linear first-order plot was observed up to high conversion, 75 % (Fig. S3A). The M_n of the PMAEO increased linearly with conversion and was in reasonably good agreement with the $M_{n,theo}$ calculated from polymerization stoichiometry and monomer conversion (Fig. S3B). Note that the measured $M_{n,GPC}$'s (based on conventional calibration) are apparent values relative to PMMA standard. Although the $M_{n,GPC}$ and $M_{n,theo}$ values matches well upto the [M]/[CDP] = 100:1 ratios, hydrodynamic volume of PMMA standards are likely to be different compared to the compact PMAEO polymers. Reasonable agreements between $M_{n,GPC}$ and $M_{n,theo}$ values are already reported for the RAFT polymerization of LMA,[28] and various fatty acid based polymers with different side-chain lengths,[13] where $M_{n,GPC}$ values were calculated based on conventional calibration curve. The unimodal, symmetrical nature of the GPC chromatograms coupled with the clear shift to lower elution volumes is qualitatively indicative of the controlled nature of the RAFT polymerization of MAEO.

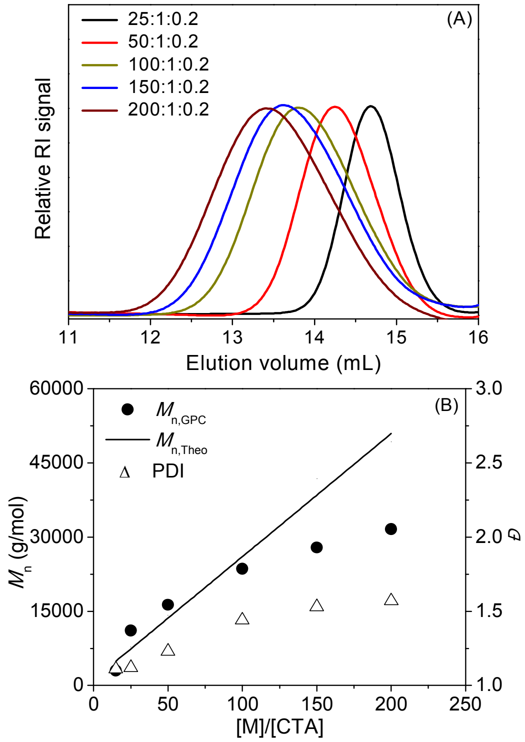


Fig. 2 GPC RI traces of PMAEO obtained at different [MAEO]/[CDP] ratios (A), and dependence of M_n and $Đ$ on [MAEO]/[CDP] ratios (B) for the RAFT polymerization of MAEO in THF at 60 °C.

The PMAEO was soluble in most of the common solvents except in water, alcohols, DMF, DMSO and acetonitrile (Table S1). The ^{1}H NMR spectrum of purified PMAEO shows no peaks at 6.12 and 5.58 ppm, indicating complete removal of unreacted monomers *via* repeated precipitation (Fig. 3A). All the resonance signals have been assigned in Fig. 3A, corresponding to the PMAEO structure. The HOOC-C$\boldsymbol{H}_2$-C$\boldsymbol{H}_2$-C(CN)(CH$_3$)- moiety at the polymer chain end was observed at 2.4-2.6 ppm.[29] The integration areas of these terminal protons (4 protons) and the repeating unit protons at 4.03-4.39 ppm (for four -OC$\boldsymbol{H}_2$C$\boldsymbol{H}_2$O- proton) are compared to calculate the number-average molecular weight ($M_{n,NMR}$) from the NMR spectroscopy. Table 1 shows reasonable agreement between $M_{n,NMR}$ and $M_{n,theo}$ values, indicating presence of CTA moiety at the polymer chain ends which is expected if RAFT mechanism works during the polymerization. Furthermore, the MALDI-TOF mass spectrum of PMAEO ($M_{n,GPC}$ = 3000 g/mol) is well-resolved and the peaks are separated by 395.168 mass units (Fig. S4), which corresponds to the molecular weight of MAEO monomer (394.308 g/mol).

Table 1 Results from the RAFT polymerization of MAEO in THF at 60 °C

Polymer^a	[MAEO]/[CDP]^b	Time (h)	Conv.^{c} (%)	$M_{n,GPC}$^{d} (g/mol)	$Đ^d$	$M_{n,theo}$^{e} (g/mol)	$M_{n,NMR}$^{f} (g/mol)
P15	15	7	65	3000	1.10	4200	3900
P25	25	11	75	11100	1.12	7800	11800
P50	50	14	70	16300	1.23	14200	21300
P100	100	15	60	23600	1.44	24100	22500
P 150	150	16	70	27900	1.53	41800	24200
P 200	200	17	62	31600	1.57	49300	26300

^{a}P15 means homopolymer of MAEO at [MAEO]/[CDP] = 15. ^{b}[CDP]/[AIBN] = 1/0.2. ^{c}Determined by gravimetric analysis. ^{d}Measured by GPC in THF. ^{e}$M_{n,theo}$= [([MAEO]/[CDP] × molecular weight (MW) of MAEO × conversion) + (MW of CDP)]. ^{f}Calculated by ^{1}H NMR spectroscopy from the integration areas of the terminal -C$\boldsymbol{H}_2$-C$\boldsymbol{H}_2$- protons (from HOOC-CH$_2$-CH$_2$-C(CN)(CH$_3$)- chain end) at 2.4-2.6 ppm and the repeating unit protons at 4.03-4.39 ppm due to the -O-C$\boldsymbol{H}_2$-C$\boldsymbol{H}_2$-O- protons.

Chain Extension and Block Copolymerization

To further demonstrate the retention of the trithiocarbonate end-groups and the controlled nature of MAEO polymerization, the synthesized PMAEO was used as a macroCTA ($M_{n,GPC}$ = 9000 g/mol, $Đ$ = 1.10) for the chain extension polymerization with MAEO and block copolymerization with MMA and PEGMA. Detailed polymerization conditions and characterization results are summarized in Table 2. Figure 4 shows shift of signals from lower molecular weight for PMAEO macroCTA to higher molecular weights for chain extended homopolymer (PMAEO-*b*-PMAEO) and block copolymers (PMAEO-*b*-PPEGMA and PMAEO-*b*-PMMA). Also, we did not observe any bimolecular termination products or unreacted macroCTA in Fig. 4, indicating the high efficiency of the PMAEO macroCTA in controlling the polymerization of methacrylate monomers. The $M_{n,GPC}$ values for these block copolymers are somewhat lower than the $M_{n,theo}$ values determined from conversion data (Table 2). This could due to the block copolymer's morphology in solution or conventional calibration curve, which we have used to determine $M_{\mathrm{n,GPC}}$ values. The ^{1}H NMR spectra of block copolymers (Fig. S5A and Fig. S6) in $CDCl_3$ confirmed successful incorporation of MMA and PEGMA units in the block copolymer chains, where characteristic signals for both the blocks are clearly observed. Comparison of the integration areas of terminal protons at 2.4-2.6 ppm (from HOOC-C$\boldsymbol{H}_2$-C$\boldsymbol{H}_2$-C(CN)(CH_3)- chain ends) with the repeating unit protons allowed the calculation of number average degrees of polymerization for PMAEO ($DP_{\mathrm{n,PMAEO}}$) and PPEGMA/PMMA ($DP_{\mathrm{n,PEGMA/MMA}}$) blocks. The $M_{\mathrm{n,NMR}}$ values were calculated by using the formula (Table 2); $M_{\mathrm{n,NMR}}$ = [($DP_{\mathrm{n,PMAEO}}$ × molecular weight of MAEO) + ($DP_{\mathrm{n,PEGMA/MMA}}$ × molecular weight of PEGMA/MMA) + molecular weight of CDP]. Table 2 shows reasonable agreement between the $M_{\mathrm{n,theo}}$ and $M_{\mathrm{n,NMR}}$ values, thus demonstrating successful synthesis of block copolymers using PMAEO macroCTA.

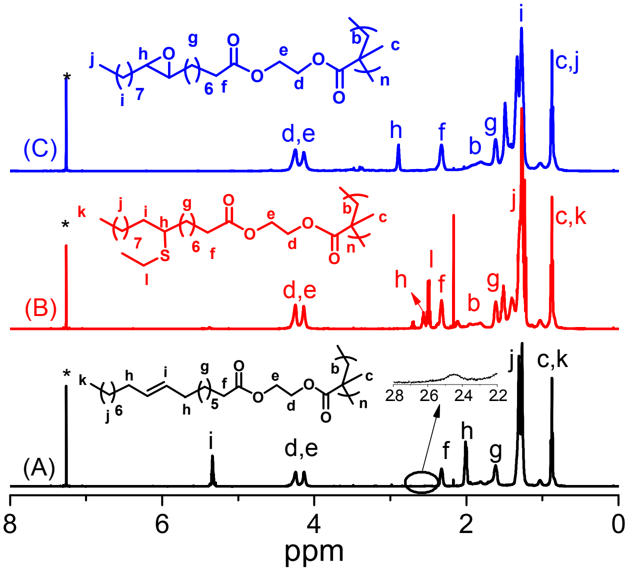


Fig. 3 ^{1}H NMR spectra of (A) PMAEO, (B) product from thiol-ene reaction of PMAEO with ethanethiol, and (C) epoxide of PMAEO. The * indicates $CDCl_3$.

Thiol-Ene Reaction

Post polymerization modification is a very useful synthetic tool to incorporate new functional groups into the polymer which cannot be always introduced before polymerization.[30] The PMAEO polymers with alkene side chains could be modified using thiol-functionalized compounds.[31] The thiol-ene reaction is known to follow a radical pathway *via* an anti-Markovnikov fashion, where the addition of a thiyl radical to a double bond is followed by chain transfer to thiol.[32,33] The thiol-ene modification was performed with various thiols (R-SH) such as ethanethiol, butanethiol, dodecanethiol, 3-mercaptopropanoic acid and 2-mercaptoethanol in the presence of AIBN as a radical source in THF at 60 °C. Initially, [MAEO repeating unit]/[butanethiol] ratios were varied from 1:3 to 1:15 at a constant ratio of [MAEO repeating unit]/[AIBN] = 1:1. 23, 35, 52, 70 and 100 % alkene bond conversions were noticed after 12 h (Fig. S7). Therefore, high excess of thiol compounds (15 equivalents compared to the alkene) were used for further experiments because the double bond is in the middle of a long chain, for which reactivity is expected to be low compared to the terminal double bonds.[18,34] For example, the thiol-ene reaction for the 1:1 molar mixtures showed that 1-hexene is 8 times more reactive than *trans*-2-hexene and 18 times more reactive than *trans*-3-hexene, since both *trans*-2-hexene and *trans*-3-hexene have internal double bonds.[35] Interestingly, quantitative conversion of side chain alkene groups was achieved using a [MAEO repeatingunit]/[R-SH]/[AIBN] ratio of 1:15:1 after 12 h (Scheme 2) for ethanethiol, butanethiol, dodecanethiol and 3-mercaptopropanoicacid as confirmed by the analysis of reaction product by ^{1}H NMR.

Table 2 Results from the RAFT polymerization of MAEO, MMA and PEGMA in the presence of PMAEO macroCTA in THF at 60 °C.[a]

Polymer	[M]/ [macroCTA]	Conv.[b] (%)	$M_{\mathrm{n,GPC}}$[c] (g/mol)	Đ[c]	$M_{\mathrm{n,theo}}$[d] (g/mol)	$M_{\mathrm{n,NMR}}$[e] (g/mol)
PMAEO-*b*-PMAEO	25	72	11000	1.19	16000	16900
PMAEO-*b*-PPEGMA	50	71	15600	1.37	19600	17000
PMAEO-*b*-PMMA	50	61	9800	1.44	12000	14000

[a] [PMAEO macroCTA]/[AIBN] = 1/0.2, polymerization time = 7 h. [b] Determined gravimetrically. [c] Obtained from GPC in THF. [d] $M_{\mathrm{n,theo}}$= ([Monomer (M)]/[PMAEO macroCTA] × average molecular weight (MW) of monomer × conversion) + (MW of PMAEO macroCTA). [e] Calculated by ^{1}H NMR spectroscopy.

All corresponding peaks of the starting material (PMAEO, Fig. 3A) and the products (Fig. 3B for ethanethiol) are assigned in the ^{1}H NMR spectra, which shows complete disappearance of resonance signal at 5.37 ppm corresponding to the side-chain double bonds in PMAEO and appearance of new peak at 2.3 ppm due to the H_3C-C$\boldsymbol{H}_2$-S- protons. Similar observations were noticed for thiol-ene reactions of PMAEO with 3-mercaptopropanoic acid, butanethioland and dodecanethiol (Fig. S8), where the peak at 5.37 ppm due to the side-chain double bonds in PMAEO disappeared after thiol-ene reactions. GPC RI traces of the polymers after the thiol-ene reactions of PMAEO with ethanethiol, butanethiol and dodecanethiol revealed that the reaction system did not involve any detectable degradation, high molecular weight shoulders or cross-linking of the polymer chains (Fig. 5). Interestingly, incorporation of 3-merceptopropanoic acid in pendent oleate chains through thiol-ene reaction converts the hydrophobic PMAEO homopolymer to hydrophilic material.

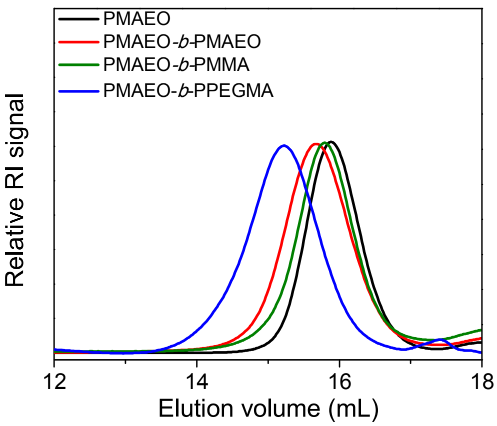
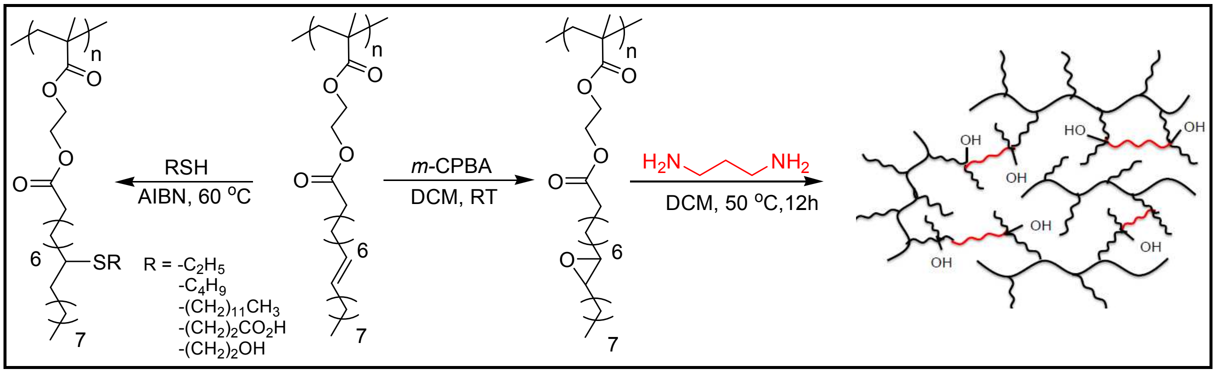


Fig. 4 GPC RI traces of PMAEO, PMAEO-*b*-PMAEO, PMAEO-*b*-PMMA and PMAEO-*b*-PPEGMA.



Scheme 2 Post-polymerization modifications of the double bonds in PMAEO *via* thiol-ene and epoxidation reactions, and synthesis of cross-linked network from the reaction of epoxydized PMAEO with 1, 3-diaminopropane.

On the other hand, in the case of 2-mercaptoethanol, even at extended reaction periods, i.e. 72 h, it was not possible to reach quantitative conversion values at [MAEO repeating unit]/[2-mercaptoethanol]/[AIBN] ratio of 1:15:1. To accelerate this reaction, the [MAEO repeating unit]/[2-mercaptoethanol]/[AIBN] ratio was varied from 1/15/1 to 1/15/25 and the kinetics was followed by ^{1}H NMR spectroscopy. Here, all the reactions were carried out for 24 h. The purified polymer was analyzed by ^{1}H NMR to determine conversion of alkene group by comparing the intensity of $–CH_2C\boldsymbol{H}{=}C\boldsymbol{H}CH_2–$ peak at 5.37 ppm with respect to-$OC\boldsymbol{H}_2$-$C\boldsymbol{H}_2$-O- protons at 4.03-4.39 ppm (Fig. 6). The alkene bond conversion versus [MAEO repeating unit]/[AIBN] plot at a constant [MAEO repeating unit]/[2-mercaptoethanol] = 1:15 is shown in Fig. 7, which shows maximum of ~90% thioether product formation. One explanation of the low reactivity of 2-mercaptoethanol is the presence of –OH functionality resulting in radical quenching and the subsequent non-generation of thioether.

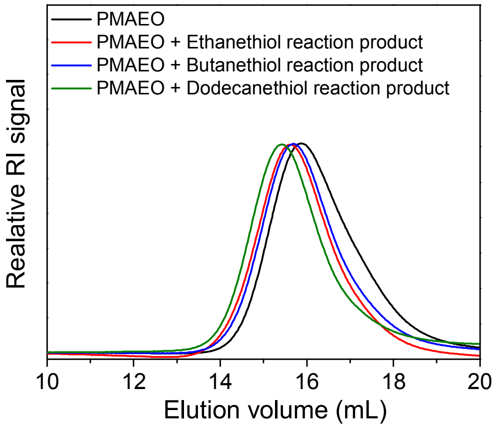


Fig. 5 GPC RI traces of products from the thiol-ene reaction of PMAEO with ethanethiol, butanethiol and dodecanethiol.

Epoxidation of Homopolymer and Subsequent Cross-linking

Epoxy resins find extensive applications in different kinds of fields such as paints, adhesives, engineering building block, etc.,[36] which after curing can have good mechanical strength, chemical resistance and electrical insulation properties. The epoxide groups can be used directly to construct thermoset networks by cationic polymerization of the epoxide groups or by ring opening reactions with cross-linking agents with nucleophilic groups.[37] A saturated acrylate was reported by epoxidizing the double bond in methyl oleate and subsequently ring-opening the epoxide groups with acrylic acid.[38] Therefore, in the next stage, oxidation of double bonds in PMAEO to produce the epoxide functionality has been studied. The epoxidation was carried out in DCM using mCPBA as oxidant at room temperature for 12 h. Figure 3C confirmed that all the double bonds present in PMAEO (at 5.37 ppm) were converted to epoxide when the reaction was performed with three equivalents (excess) of mCPBA compared to the MAEO repeating units in PMAEO. A new signal at 2.88 ppm is appeared due to the CH protons adjacent to epoxide group.

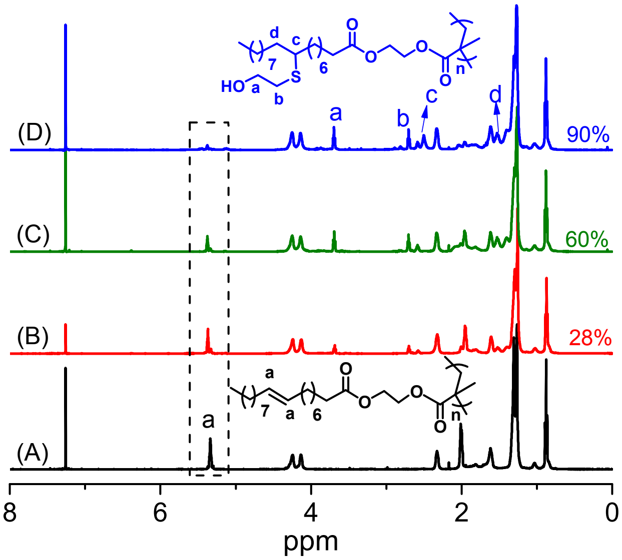


Fig. 6 ^{1}H NMR spectra of PMAEO (A), products from thiol-ene reaction of PMAEO with 2-mercaptoethanol at [MAEO repeating unit]/[2-mercaptoethanol]/[AIBN] 1:15:1 (B), 1:15:5 (C) and 1:15:25 (D). For comparison PMAEO spectrum is provided, which is same as in Fig. 3A.

When the epoxidation was carried out at [MAEO repeating unit]/[mCPBA] = 2:1 ratio (Scheme S1), approximately 50 % of the double bonds in PMAEO are transformed to epoxide with some remaining double bonds in the polymer side-chain (Fig. S9). The completely epoxidized polymer is partially soluble in

DCM. However, the partially (50 %) epoxidized product from [MAEO repeating unit]/[mCPBA] = 1.0:0.5 was fully soluble in DCM. FT-IR analysis shows that the intensity of stretching band centered at 3010 cm^{-1} associated to sp^2 C-H stretching frequency in PMAEO reduced after 50% epoxide formation (Fig. 8B). In addition, we observed a weak broad peak at around 3500 cm^{-1} due to the –OH stretching, which arose from the ring opening reaction during the epoxidation.[39] The ring stretching absorption band for epoxy functional group appeared near about 1220 cm^{-1}. Furthermore, epoxidation of PMAEO-*b*-PMMA block copolymer at [MAEO repeating unit]/[mCPBA] = 1:3 ratio was studied for 12 h in DCM at room temperature. The ^{1}H NMR of the epoxidized product of block copolymer revealed quantitative epoxidation, where the peak at 5.37 ppm due to the side-chain double bond in PMAEO block completely disappeared and a new peak emerged at 2.88 ppm corresponding to the protons adjacent to epoxide (Fig. S5).

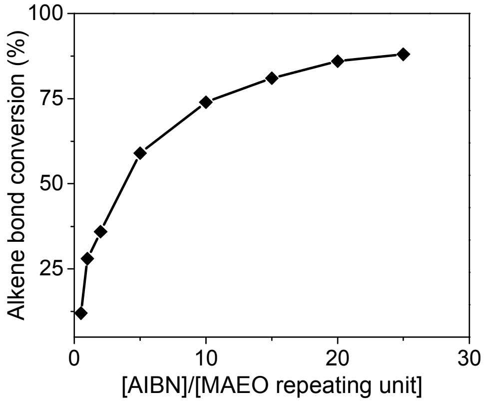


Fig. 7 Alkene bond conversion versus ratios of [AIBN]/[MAEO repeating unit] plot for PMAEO reacting with 2-mercaptoethanol at a constant [MAEO repeating unit]/[2-mercaptoethanol] = 1:15 in THF at 60 ºC. Note: conversion values were calculated by ^{1}H NMR spectroscopy based on the consumption of the alkene bonds.

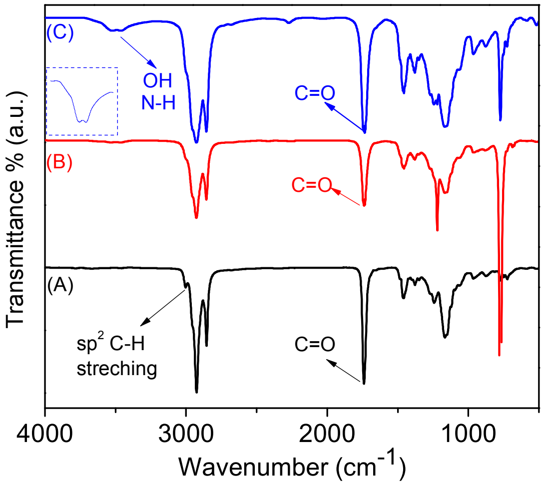


Fig. 8 FT-IR spectra of (A) PMAEO, (B) 50 % epoxydized PMAEO, and (C) cross-linked product from the reaction of 50 % epoxydized PMAEO and 1, 3-diaminopropane.

Finally, 1, 3-diaminopropane was used to cross-link the epoxydized PMAEO (Scheme 2), where hydroxyl groups were generated from epoxy rings by the reaction with primary amine and epoxy curing with diamine is well documented in the literature.[40,41] The cross-linked polymer was insoluble in almost all organic solvents, indicating that a high level of cross-linking had been obtained. Characterization of the cross-linked product by FT-IR spectroscopy (Fig. 8C) showed appearance of a new band at 3210 cm^{-1} due to the N-H stretching vibration along with the –OH stretching at 3500 cm^{-1}. Thermal stabilities of epoxdized PMAEO and corresponding cross-linked product were studied by TGA in N_2 atmosphere. Figure 9 displays the plots of percentage of weight loss against temperature. As expected cross-linked products shows relatively higher stability than epoxdized PMAEO due to its highly cross-linked network structure.

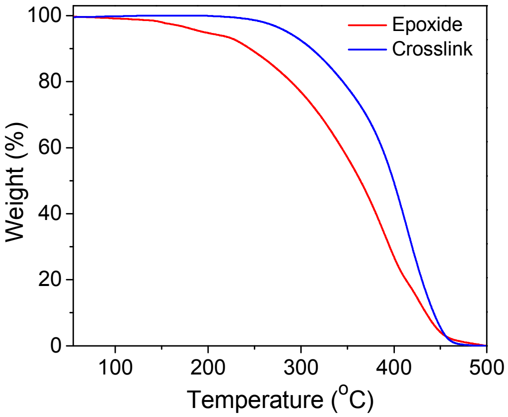


Fig. 9 TGA thermograms of epoxdized PMAEO and cross-linked product from the reaction of epoxydized PMAEO and 1, 3-diaminopropane.

Conclusion

In summary, the carbon-carbon double bond in side-chain oleic acid containing methacrylate monomer is unreactive during the RAFT polymerization and we have successfully prepared PMAEO with controlled molecular weight upto 24,000 g/mol, narrow *Đ* between 1.10 to 1.44 and precise trithiocarbonate chain end functionality. The PMAEO can be used as macroCTA to prepare diblock copolymers with other methacrylate monomers such as MMA and PEGMA. We have shown that the internal double bonds in oleate pendants can be modified by versatile thiol-ene reactions in order to introduce new functionalities, water solubility (3-merceptopropanoic acid modified polymer was soluble in aqueous media) and epoxide groups, which was further cross-linked by using a diamine. Quantitative and ~90% conversions of double bonds with ethane/butane/dodecane-thiols and 2-mercaptoethanol were observed, respectively. The incomplete level of internal double bond functionalization remain as a major challenge that need to be addressed to further enhance the general utility of a synthetic polymer that could be modified using thiol-functionalized proteins, cholesterols, sugars, or other biological structures. Nevertheless, this study suggests that controlled macromolecular architectures perhaps possible *via* RAFT technique with other unsaturated fatty acids such as linoleic, linolenic, petroselinic, erucic, calendic, etc., and we are currently investigating controlled RAFT polymerization of their (meth)acrylate monomers.

Acknowledgements

BM acknowledges Council of Scientific and Industrial Research (CSIR), Government of India, for the junior research fellowship.

Notes and references

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† Electronic Supplementary Information (ESI) available: FT-IR and ESI-MS spectra of MAEO, solubility of MAEO and PMAEO in different solvents, First-order kinetic plot and M_n versus monomer conversion plot for the RAFT polymerization of MAEO, MALDI-TOF spectrum of PMAEO, Scheme for epoxidation reactions at [MAEO repeating unit]/[mCPBA] = 2:1 ratio, alkene bond conversion versus ratios of [MAEO repeating unit]/[butanethiol] plot, ^{1}H NMR spectra of block copolymers, epoxides and thiol-ene reaction products. See DOI: 10.1039/b000000x/

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