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Synthesis of Carboxylated Derivatives of Poly(isobutylene-*co*-isoprene) by Azide-alkyne "Click" Chemistry

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ABSTRACT

The synthesis of carboxylated derivatives of poly(isobutylene-*co*-isoprene) (isobutylene-isoprene rubber, IIR) with substitution levels ranging from 1-4 mol% and different spacer lengths was accomplished by azide-alkyne Huisgen cycloaddition. Azido-functionalized IIR was first prepared by reacting brominated IIR to full conversion with sodium azide in a tetrahydrofuran/N,N-dimethylacetamide 90:10 mixture. The click reaction of the azido-functionalized IIR with acetylenic acids, using the copper(I) bromide/N,N,N′,N″,N″-pentamethyldiethylenetriamine catalyst system in tetrahydrofuran, gave the carboxylated IIRs. The products were characterized by ^{1}H NMR and FT-IR spectroscopy, and their molecular weight was determined by size exclusion chromatography analysis. The conversion to carboxylated groups reached up to 100%, as determined by NMR spectroscopy, but was highly dependent on the type of solvent and the amounts of catalyst and reactants used in the procedures.

Keywords: poly(isobutylene-*co*-isoprene), IIR, bromobutyl rubber, ionomer, azide-alkyne click

Introduction

Copolymers of isobutylene and isoprene, also known as isobutylene-isoprene rubber (IIR),

have found multiple applications in different areas due to their unusual physical properties. Some of the characteristics of IIR include excellent impermeability to air, good electrical resistivity, excellent resistance to moisture, oxidation and heat, and good flex properties resulting from its low unsaturation level.[1–4] The range of properties displayed by IIR were further extended by introducing a low concentration of ionic moieties such as sulfonic acid groups bound along the polymer chains, to produce ionomers.[5] The synthesis of phosphonium and ammonium salts based on IIR has also been reported. Such derivatives were typically prepared from brominated IIR (BIIR) containing ca. 1 mol% of allylic bromide moieties.[6] The allylic bromide in BIIR can be displaced by a wide variety of nucleophiles, since it is a good leaving group.[7-10] The post-polymerization chemical modification of BIIR by nucleophilic substitution is therefore useful to synthesize derivatives (such as ionomers) that cannot be obtained by copolymerization.

Click chemistry is a powerful tool for polymer modification. Introduced by Sharpless in 2001,[11] the copper-catalyzed azide–alkyne Huisgen 1,3-dipolar cycloaddition reaction has attracted a lot of interest because it is facile, selective, proceeds in high yield under mild conditions, and has excellent tolerance to functional groups.[12–15] In contrast to traditional 1,3-dipolar Huisgen cycloaddition, the copper-catalyzed azide–alkyne click reaction can be carried out at room temperature in a wide range of solvents including water, THF and ethanol.[16–18] Additionally, the Cu(I)-catalyzed azide-alkyne cycloaddition reaction is usually much ($\geq 10^7$ times) faster than the uncatalyzed reaction,[19] and is rather insensitive to the steric and electronic properties of the groups attached to the azide and alkyne centers.[17] In fact primary, secondary or even tertiary, electron-rich or electron-deficient azides usually react well with substituted terminal alkynes. Moreover, the triazole unit formed in the reaction has several interesting properties including a high chemical stability (being inert to hydrolytic, oxidizing and reducing conditions), good hydrogen bonding

ability, and aromatic character.[20] The triazole group can also interact effectively with biological molecules, similarly to amide bonds.[21,22] Considering these factors, the azide-alkyne click reaction seems to be a good candidate to generate functional IIR derivatives.

Over the past few decades, different synthetic methods have been applied to modify IIR and improve its properties.[6,23–26] Among these, the synthesis of carboxylated IIR is of particular interest because polar groups like carboxylate moieties enhance adhesion as compared to IIR, which is very hydrophobic in nature.[27–29] The introduction of carboxylate groups also increases the modulus and tensile strength of rubbery materials,[30–33] and allows further functionalization/modification of IIR. Gillies and coworkers recently reported the synthesis of carboxylated IIR via ring opening of cyclic anhydrides or the introduction of poly(carboxylic acid)s,[34] but to the best of our knowledge there have been no reports on the synthesis of carboxylated IIR by click chemistry. It is now shown that azide-alkyne click chemistry, under appropriate conditions, can serve to generate carboxylated IIR derivatives in high yield.

Experimental Section

^{1}H NMR spectra were recorded on a Bruker 300 MHz spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as internal standard. FT-IR spectra were acquired on a Bruker Vector 22 FT-IR Spectrophotometer from 400 to 4000 cm^{-1}. The molecular weight of the IIR samples was determined on a Viscotek GPCmax size exclusion chromatography (SEC) instrument with a VE 2001 GPC Solvent/sample Module. The unit was equipped with a TDA 305 triple detector array with refractive index (RI), light scattering and viscometer detectors, as well as a UV detector (Viscotek 2600) and three PolyAnalytik organic mixed bed columns for an overall polystyrene molecular weight range of 10^3 to 10^7 g/mol. The samples were analyzed in THF at a flow rate of 1

mL/min.

Copper bromide (99.99%), sodium azide (99%)**,** bromine (≥99.5%), sodium hydroxide (≥97%), N,N,N′,N″,N″-pentamethyldiethylenetriamine (PMDETA, 99%), cyclohexanone (≥99%), 10-undecenoic acid (95%), and PEG-200 were all purchased from Aldrich and used without further purification. Hydrogen peroxide (30%) was purchased from Fisher Scientific. Brominated poly(isobutylene-*co*-isoprene) (BIIR) samples containing either 1, 1.9 or 4 mol% of brominated isoprene units (all experimental grades with M_w = 280-380 kg/mol) were supplied by Lanxess Canada Inc. Solvents such as THF, N,N-dimethylacetamide (DMA), N,N-dimethylformamide (DMF), methanol and chloroform were purchased from Caledon and used as received.

Azidation of BIIR (4.0 mol% brominated isoprene units). In a 250-mL round-bottomed flask (RBF), BIIR (1 g, 6.74×10^{-4} mol brominated isoprene units) was dissolved in 90 mL of THF before adding 10 mL of DMA. Sodium azide (0.88 g, 0.0135 mol, 20 eq with respect to brominated isoprene units) was added and the mixture was stirred on a magnetic stirrer at room temperature for 4 d. The solution was then filtered to remove excess sodium azide, concentrated, and precipitated into methanol. The product was further purified twice by dissolution in 25 mL of THF followed by precipitation into methanol. Recovery yield = 0.87 g (90%), substitution level 4.0 mol% (100% conversion). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 5.45 (1H, b, C=C**H**), 5.16 and 5.03 (2H of isoprene, s), 3.82-3.61 (3H, bm, C**H**-N_3 and C**H**$_2$- N_3), 2.4-0.75 (aliphatic protons from isobutylene and isoprene units). **Note:** Caution must be applied in designing reactions with sodium azide since that compound is dangerous, particularly in large quantities. Inorganic azides are highly toxic and potentially explosive compounds. Metal spatulas should not be used to handle sodium azide, to avoid the formation of shock-sensitive heavy metal azides. Solutions of sodium azide

may be absorbed through the skin, and can generate highly toxic hydrazoic acid when exposed to water. Therefore, the reactions should only be carried out in a well-ventilated fume hood and with appropriate personal protective equipment.

Click reaction of azidated IIR (4.0 mol% azidated isoprene units) with 4-phenyl-1-butyne. To a solution of azidated IIR (0.5 g in 50 mL of THF, 3.46×10^{-4} mol azide moieties) in a 100-mL RBF, PMDETA (0.3 g, 1.73×10^{-3} mol, 5 eq with respect to azide), and 4-phenyl-1-butyne (0.23 g, 1.73×10^{-3} mol, 5 eq with respect to azide) were added and the flask was purged with nitrogen for 30 min. To this mixture CuBr (0.1 g, 7.01×10^{-4} mol, 2 eq with respect to azide) was added against nitrogen flow. The reaction was allowed to proceed at room temperature for 3 d, the THF was evaporated, and the residue was redissolved in $CHCl_3$ (100 mL) for extraction with water (5 × 50 mL) to remove the copper salts. The $CHCl_3$ solution was then concentrated, precipitated into methanol or acetone, and further purified twice by dissolution in 15 mL of THF and precipitation into methanol or acetone. Recovery yield = 0.89 g (82%), substitution level 4.0 mol% (100% conversion). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.37-7.70 (5H, Ar), 6.98 (1H, s, N-C**H**=C), 5.43 (1H, b, C=C**H**), 5.18-5.03 (3H, b, C**H**-N_3 and C**H**$_2$-N_3), 5.12 and 5.01 (2H of isoprene, s), 3.01 (4H, b, -C**H**$_2$-C**H**$_2$-Ar), 2.35-0.65 (aliphatic protons of isobutylene and isoprene units).

Synthesis of 5-hexenoic acid. Hydrogen peroxide (30% aqueous solution, 115 mL, 1 mol) was added to a stirred solution of cyclohexanone (49 g, 0.5 mol) in methanol (50 mL) over 30 min at 20-25 °C. This mixture was then added to a stirred solution of ferrous sulfate heptahydrate (138 g, 0.9 mol) and cupric sulfate pentahydrate (125 g, 0.8 mol) in water (900 mL) over 2 h while maintaining the mixture at 18-20 °C. The reaction was then stirred at the same temperature for 1 h longer before extraction with diethyl ether (6 × 100 mL), concentration to 150 mL, and washing with 20% aq NaOH (4 × 50 mL). The alkaline extract was acidified to pH 2 with

sulfuric acid and extracted with diethyl ether (3 × 100 mL). Removal of the solvent at reduced pressure gave the crude 5-hexenoic acid as a clear oil which was purified by distillation. Yield: 40 g (70%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 11.1 (br s, 1H, CH_2=CH-CH_2-CH_2-CH_2-COO**H**), 5.74 (m, 1H, CH_2=C**H**-CH_2-CH_2-CH_2-COOH), 5.01 (dd, 2H, C**H$_2$**=CH-CH_2-CH_2-CH_2-COOH), 2.35 (t, 2H, CH_2=CH-CH_2-CH_2-C**H$_2$**-COOH), 2.08 (q, 2H, CH_2=CH-C**H$_2$**-CH_2-CH_2-COOH), 1.72 (quint, 2H, CH_2=CH-CH_2-C**H$_2$**-CH_2-COOH).

Synthesis of 5,6-dibromohexanoic acid. A solution of bromine (55 g, 0.34 mol) in dichloromethane (70 mL) was added at -40 °C with vigorous stirring over 1 h to a solution of 5-hexenoic acid (39.3 g, 0.34 mol) in CH_2Cl_2 (130 mL). The mixture was stirred at the same temperature for 1 h longer. Removal of the solvent gave 5,6-dibromohexanoic acid as an orange-yellow oil. Yield: 93.5 g (99%). The product was used in the next step without additional purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 10.61 (br s, 1H, $BrCH_2$-CHBr-CH_2-CH_2-CH_2-COO**H**), 4.10 (m, 1H, BrC**H**$_2$-CHBr-CH_2-CH_2-CH_2-COOH), 3.83 (dd, 1H, BrC**H**$_2$-CHBr-CH_2-CH_2-CH_2-COOH), 3.61 (t, 1H, $BrCH_2$-C**H**Br-CH_2-CH_2-CH_2-COOH), 2.42 (t, 2H, $BrCH_2$-CHBr-CH_2-CH_2-C**H$_2$**-COOH), 2.28-2.10, 2.01-1.65 (both m, 1H and 3H, $BrCH_2$-CHBr-C**H$_2$**-C**H$_2$**-CH_2-COOH).

Synthesis of 5-hexynoic acid. A mixture of PEG-200 (180 mL) and NaOH pellets (36 g, 0.91 mol) was stirred in an oil bath at 80 °C until all the NaOH dissolved and 5,6-dibromohexanoic acid (50 g, 0.18 mol) was added drop-wise to this solution over 30 min. The mixture was heated further at 80-85 °C for 3-4 h before adding water (150 mL) and acidifying with HCl to pH 2 and cooling. The mixture was then extracted with diethyl ether and concentrated. The combined organic layers were washed with water, then with a brine solution, and dried. The crude product was distilled in a Kugelrohr apparatus under reduced pressure (80 °C, 5 torr) to yield a colorless

oil. Yield = 14 g (70%).^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 11.56 (br s, 1H, CH≡C-CH_2-CH_2-CH_2-COO**H**), 2.49 (t, 2H, CH≡C-CH_2-CH_2-C**H$_2$**-COOH), 2.26 (m, 2H, CH≡C-C**H$_2$**-CH_2-CH_2-COOH), 1.96 (t, 1H, C**H**≡C-CH_2-CH_2-CH_2-COOH), 1.82 (quint, 2H, CH≡C-CH_2-C**H$_2$**-CH_2-COOH). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 179.40 (C), 83.0 (C), 69.5 (CH), 32.6 (CH_2), 23.1 (CH_2), 17.7 (CH_2). HRMS (ESI−) calcd for $C_6H_7O_2$ [M − H]− 111.0446, found 111.0439.

Synthesis of 10,11-dibromoundecanoic acid. This acid was synthesized from 10-undecenoic acid (25 g) by the procedure described above for 5,6-dibromohexanoic acid. Removal of the solvent gave 10,11-dibromoundecanoic acid as an orange-yellow crystalline compound. The product was used in the next step without additional purification. Yield = 46.2 g (99%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 10.66 (br s, 1H, $BrCH_2$-CHBr-CH_2-$(CH_2)_5$-CH_2-CH_2-COO**H**), 4.15 (m, 1H, $BrCH_2$-CHBr-CH_2-$(CH_2)_5$-CH_2-CH_2-COOH), 3.82 (dd, 1H, $BrCH_2$-CHBr-CH_2-$(CH_2)_5$-CH_2-CH_2-COOH), 3.61 (t, 1H, $BrCH_2$-C**H**Br-CH_2-$(CH_2)_5$-CH_2-CH_2-COOH), 2.33 (t, 2H, $BrCH_2$-CHBr-CH_2-$(CH_2)_5$-CH2-C**H$_2$**-COOH), 2.10, 1.76 (both m, 1H and 1H, $BrCH_2$-CHBr-C**H$_2$**-$(CH_2)_5$-CH_2-CH_2-COOH), 1.61 (m, 2H, $BrCH_2$-CHBr-$(CH_2)_5$-C**H$_2$**-CH_2-CH_2-COOH), 1.30 (m, 10H, $BrCH_2$-CHBr-**-$(CH_2)_5$-**CH_2-CH_2-CH_2-COOH).

Synthesis of 10-undecynoic acid. The procedure used was as described for 5-hexynoic acid. The crude product was distilled in a Kugelrohr apparatus under reduced pressure (110 °C, 1 torr) to yield a colorless oil which solidified to a white powder at room temperature. Yield = 18.4 g (75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 11.37 (br s, 1H, CH≡C-CH_2-$(CH_2)_5$-CH_2-CH_2-COO**H**), 2.32 (t, 2H, CH≡C-CH_2-$(CH_2)_5$-CH_2-C**H$_2$**-COOH), 2.14 (m, 2H, CH≡C-C**H$_2$**-$(CH_2)_5$-CH_2-CH_2-COOH), 1.91 (s, 1H, C**H**≡C-CH_2-$(CH_2)_5$-CH_2-CH_2-COOH), 1.60, 1.49 (both m, 1H and 1H, CH≡C-CH_2-$(CH_2)_5$-C**H$_2$**-CH_2-COOH), 1.28 (m, 10H, CH≡C-CH_2-**$(CH_2)_5$-**CH_2-CH_2-COOH). ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 180.4 (C), 84.7 (C), 68.1 (CH), 34.1 (CH_2), 29.1 (CH_2), 28.9

(CH_2), 28.8 (CH_2), 28.6 (CH_2), 28.4 (CH_2), 24.6 (CH_2), 18.4 (CH_2). HRMS (ESI−) calcd for $C_{11}H_{17}O_2$ [M − H]− 181.1229, found 181.1226.

Synthesis of carboxylated IIR. The carboxylated IIR samples were prepared using BIIR containing 1.0 to 4.0 mol% of azidated isoprene units and the different acetylenic acids synthesized, following the procedure given above for 4-phenyl-1-butyne. Recovery yield for the reaction of IIR (1 mol% azidated isoprene units) with 10-undecynoic acid = 88%, substitution level 1 mol % (100% conversion). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.15 (1H, s, N-C**H**=C), 5.49 (1H, b, C=C**H**), 5.06 (3H, b, C**H**-N_3, C**H**$_2$-N_3 and IIR), 4.93 and 4.84 (2H of isoprene, s), 2.78-2.36 (4H, C-C**H**$_2$- and -C**H**$_2$-C=O), 2.05-0.73 (aliphatic protons of isobutylene and isoprene units). Recovery yield for the reaction of IIR (1.9 mol% azidated isoprene units) with 10-undecynoic acid = 85%, substitution level 1.9 mol % (100% conversion). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.15 (1H, s, N-C**H**=C), 5.48 (1H, b, C=C**H**), 5.10 (3H, b, C**H**-N_3 and C**H**$_2$-N_3), 4.93 and 4.85 (2H of isoprene, s), 2.68-2.40 (4H, C-C**H**$_2$- and -C**H**$_2$-C=O), 2.03-0.75 (aliphatic protons of isobutylene and isoprene units). Recovery yield for the reaction of IIR (4 mol% azidated isoprene units) with 10-undecynoic acid = 85%, substitution level 4 mol % (100% conversion). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm: 7.17 (1H, s, N-C**H**=C), 5.46 (1H, b, C=C**H**), 5.05 (3H, b, C**H**-N_3 and C**H**$_2$-N_3), 4.91 and 4.81 (2H of isoprene, s), 2.65-2.34 (4H, C-C**H**$_2$- and -C**H**$_2$-C=O), 1.97-0.70 (aliphatic protons of isobutylene and isoprene units). The reactions of azidated IIR with 5-hexynoic acid gave yields similar to 10-undecynoic acid and 100% conversion.

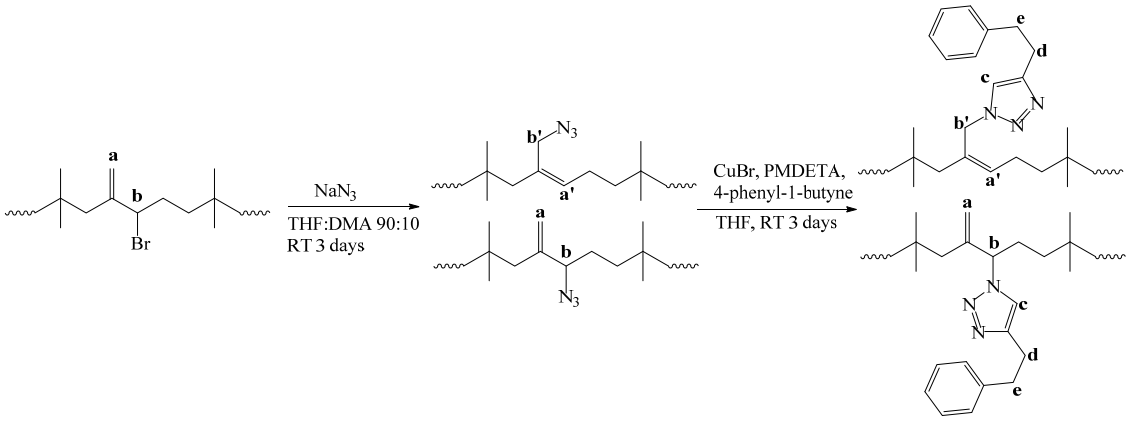
Results and Discussion

The copper-catalyzed azide–alkyne reaction based on Huisgen 1,3-dipolar cycloaddition was employed to synthesize carboxylated derivatives of IIR. The synthetic process included two main

steps, namely the conversion of brominated IIR (BIIR) to the corresponding azide-functionalized polymer (IIR-N_3), followed by clicking with the acetylenic acids. To optimize the reaction conditions, BIIR was selected containing ~4 mol% of brominated isoprene units with an exomethylene structure. Azidated IIR was obtained by treating BIIR with a large excess of sodium azide (20 equiv with respect to the brominated isoprene units) in THF/DMA 90:10 v/v under vigorous stirring for 3-4 days. The procedure used for the synthesis of click-modified IIR and the corresponding ^{1}H NMR spectra are provided in Scheme 1 and Figure 1, respectively. The ^{1}H NMR spectrum for BIIR (Figure 1A) had two singlets at 5.39 and 5.02 ppm corresponding to the exomethylene structural unit, and a peak at 4.32 ppm for the allylic bromide proton. Upon azidation the peak at 4.32 ppm vanished and a new broad peak appeared at 3.82-3.61 ppm, indicating complete conversion of the bromide to azide. An azidation level of 4.0 mol% was calculated from the ^{1}H NMR spectrum, corresponding to 100% conversion. The azidation reaction also led to the isomerization of IIR, as seen by the appearance of a peak at 5.45 ppm, corresponding mainly to an exomethylene microstructure (~55%) and approximately 45% of the endo isomer based on the peaks at 5.45 ppm and 5.16 ppm.[35]

The azidation reaction was also attempted in THF/DMF mixtures, but this approach was found to produce gel particles and the azidated polymer obtained was unstable. It should be considered that the BIIR samples used had very high molecular weights ($M > 10^5$ g/mol, corresponding to degrees of polymerization $X > 1700$), and the formation of a gel is expected when a mole fraction of only $1/1700 \approx 0.06\%$ of the structural units are involved in cross-linking reactions. This is well below the detection limit of any of the analytical techniques currently available for polymers, and hence any discussion of the nature of the reactions leading to gel formation can only be speculative. Two hypotheses are suggested for the formation of gel particles

in the THF/DMF mixtures. The photochemical degradation of DMF produces minute amounts of CN^-/HCN as an impurity.[36] When DMF is used as a solvent for azidation, this can lead to the transformation of some alkyl halide groups to alkyl nitriles, which may react with the azide functionalities on other chains to form tetrazole cross-links (Scheme S1a). This possibility appears somewhat unlikely however, since the formation of tetrazoles from azides and nitriles typically requires a temperature around 100-150°C,[37] while the azidation reaction was done at room temperature in the present case. Another (more likely) explanation for gel formation is the presence of trace amounts of dimethylamine in DMF, arising from hydrolysis.[38] This compound, by reacting with two allylic bromide functionalities on different chains, would yield quaternary amine cross-links (Scheme S1b). Reactions carried out with 5 or 10 equiv of sodium azide in THF/DMF mixtures did not lead to full azidation, as evidenced by NMR analysis (Supporting Information, Figure S1). The slower rate of azidation achieved under these conditions would make competing side reactions involving nitrile or amine groups more likely to induce gel formation. The choice of solvent and the amount of sodium azide used are therefore important parameters to be considered for azidation.



Scheme 1. Optimization of the azidation and azide-alkyne click reactions.

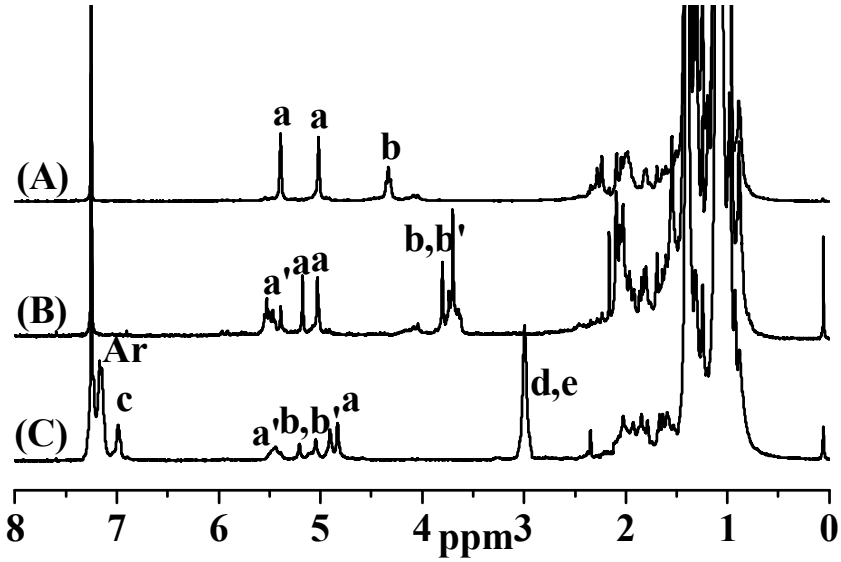


Figure 1. ^{1}H NMR spectra for the optimization of the azidation and azide-alkyne click reactions: (A) BIIR; (B) IIR-N_3; (C) IIR-Ph. The peak assignments are provided in Scheme 1.

The click reaction of IIR-N_3 with 4-phenyl-1-butyne served as model reaction using the copper(I) bromide/N,N,N′,N″,N″-pentamethyldiethylenetriamine (PMDETA) catalyst system at room temperature. To assess the efficiency of the click reaction, a series of reactions were carried out by varying parameters such as amount of catalyst and ligand, and the solvent system used (Table 1). A THF/DMA 90:10 solvent mixture was investigated initially, since DMA is useful to increase the solubility of CuBr. Unfortunately, at high DMA concentrations the IIR derivatives were insoluble. As shown for Entry 1 in Table 1, a reaction using only one equiv of CuBr, PMDETA and alkyne (1:1:1 with respect to the azide) in THF/DMA did not yield any product. A 1:2:2 ratio gave the same result, while increasing the amounts of reagents to 2:2:2 led to gelation of the reaction in less than 10 minutes. It was therefore concluded that there was a strong dependence between the type of solvent used and the amount of catalyst required in the

reaction.[39,40] To confirm this, THF and toluene were also explored as solvents while varying the ratio of CuBr, PMDETA and alkyne. The experimental details provided in Table 1 show that in THF, for a 2:2:2 ratio of CuBr:PMDETA:alkyne, the reaction proceeded without gelation but only reached 20% conversion in two days. Interestingly, the amount of 4-phenyl-1-butyne incorporated increased significantly in THF upon increasing the ratio to 2:5:5 (90% in two days). The progress of the reaction also could be monitored through a color change from pale green to orange, probably due to the formation of a complex of triazole with CuBr and PMDETA. Whenever no color change was observed, the reaction failed. Further increase in substitution level was achieved when the reaction was allowed to proceed for 3 days. No gelation was observed under these conditions, and the product obtained had excellent solubility even in comparison to its precursor. While toluene is a good solvent for IIR, the click reactions in toluene yielded mixed and irreproducible results. This again demonstrates the strong influence of the solvent used on the success of azide-alkyne click reactions.[41] Excess PMDETA also ensured the complete dissolution of CuBr, which led to homogeneous reactions, in contrast to lower ratios. A higher ligand concentration would be expected to enhance the reaction rate, by increasing the solubility of CuBr and protecting Cu(I) from oxidation, and thereby maintain a high concentration of catalytically active complex throughout the reaction.[42,43]

Table 1. Optimization of the conditions for the azide-alkyne click reactions.

CuBr (eq)	PMDETA (eq)	Alkyne (eq)	Solvent (50 mL for 0.5 g of IIR)	Time	Conversion %
1	1	1	THF/DMA (90:10)	2 days	0
1	2	2	THF/DMA (90:10)	2 days	0
2	2	2	THF/DMA (90:10)	10 min	gelled
2	2	2	THF	2 days	20
2	3	3	THF	2 days	44
2	5	5	THF	3 days	100
2	5	5	Toluene	1-3 days	gel/no reaction*

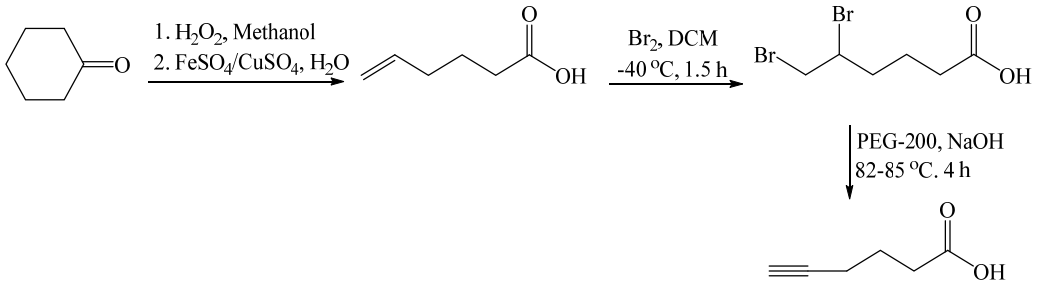
*Irreproducible

The ^{1}H NMR spectrum for the product of the reaction between azidated butyl rubber and 4-phenyl-1-butyne (IIR-Ph) is provided in Figure 1B. The click reaction resulted in the disappearance of the resonance at 3.82-3.61 ppm, corresponding to the protons close to the azide group, and the appearance of aromatic proton signals at 7.24-7.11 ppm, and at 6.97 ppm[44] for the proton on the triazole ring. The broad singlet at 3.01 ppm is attributed to the aliphatic protons from 4-phenyl-1-butyne. On the basis of these results, it was concluded that a CuBr:PMDETA:alkyne ratio of 2:5:5 in THF worked best for the click reaction with azidated IIR. FT-IR spectra obtained for the products (Figure S2) also show the appearance of a strong azide stretching vibration at 2092 cm^{-1} upon azidation, which disappeared after the click reaction.

Synthesis of acetylenic acids

The acetylenic acids were synthesized by modifying the procedure of Starostin et al.[45] The synthesis of 5-hexynoic acid (6-COOH) is described in Scheme 2. Cyclohexanone was first treated with 30% H_2O_2 to form cyclohexanone peroxide, which upon reaction with $FeSO_4$/$CuSO_4$

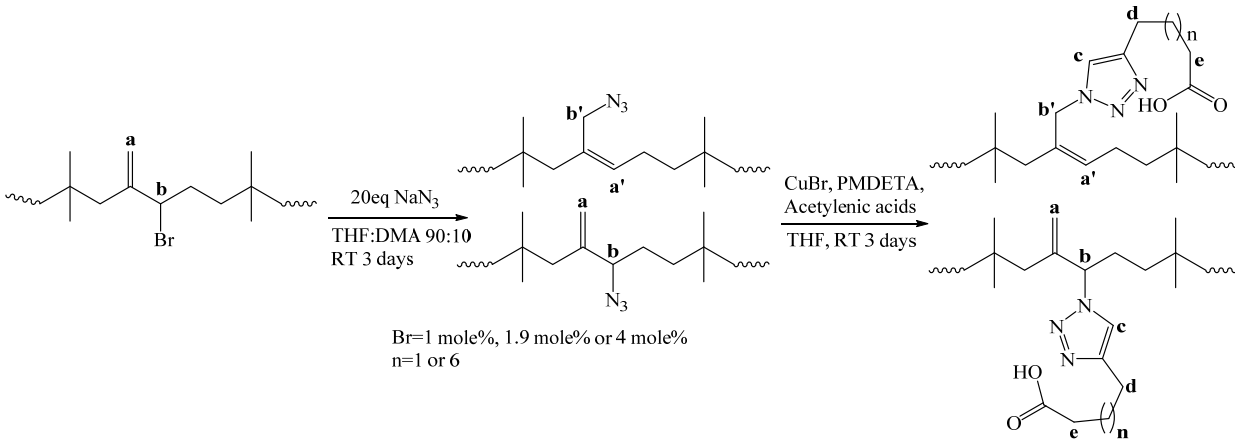
decomposed to give 5-hexenoic acid in 70% yield. The addition of bromine to 5-hexenoic acid at -40 °C yielded 5,6-dibromohexanoic acid, which could be dehydrobrominated with $NaNH_2$, KOH or NaOH. While these bases are most commonly used for that purpose, $NaNH_2$ and KOH have disadvantages: Impurities in $NaNH_2$ can decrease its reactivity and cause explosions, and KOH promotes migration of the acetylenic bond to the center of the chain.[45,46] Consequently we preferred using NaOH, with PEG-200 acting as a phase transfer catalyst. This method was found to favor the formation of 5-hexynoic acid as compared with an aqueous NaOH solution (Figure S3). The dehydrobromination of 5,6-dibromohexanoic acid with NaOH yielded a mixture of 6-bromohex-5-enoic acid and 5-hexynoic acid that were separated by distillation in a Kugelrohr apparatus under reduced pressure, to yield 5-hexynoic acid as a colorless liquid in 70% yield. It should be noted that the reaction temperature must be maintained between 80-85 °C, because higher temperatures lead to the formation of other isomeric products and 4-hexynoic acid. The ^{1}H NMR spectra corresponding to the different steps of the 5-hexynoic acid synthesis are provided as Supporting Information (Figure S4), and the ^{13}C NMR spectrum for the final product is shown in Figure S5. The synthesis of 10-undecynoic acid (11-COOH) started from 10-undecenoic acid by the same procedure described above. The ^{1}H NMR and ^{13}C NMR spectra for the products are given in Figures S6 and S5, respectively. The spectral characteristics for these molecules were similar to previously reported data.[47]



Scheme 2. Synthesis of 5-hexynoic acid.

Synthesis of carboxylated IIR

Samples of carboxylated IIR were prepared as depicted in Scheme 3, using the optimized reaction conditions described above. BIIR substrates with three different brominated isoprene unit contents, namely 1, 1.9 and ~4 mol%, were used for this part of the investigation. The reaction of BIIR having 1.9 mol% brominated units with 5-hexynoic acid and 10-undecynoic acid is discussed below. The progress of these reactions was monitored by ^{1}H NMR and FT-IR spectroscopy. ^{1}H NMR spectra for the reaction are provided in Figure 2, starting with BIIR for comparison. The peak marked with an asterisk corresponds to non-brominated isoprene units.[48] Similarly to the 4.0 mol% substrate, the azidation of BIIR in THF/DMA proceeded to full conversion. The success of the azidation reaction was further confirmed by FT-IR analysis, through the appearance of a peak at 2092 cm^{-1} (Figure 3).[49] Upon reaction with the acetylenic acids a new signal appeared at 7.15 ppm for the proton on the 1,2,3-triazole ring,[44] as well as a broad signal at 2.81-2.29 ppm for the aliphatic protons on the substituent closer to the triazole ring and the carboxylic acid group (Figures 2C-D). The signal at 3.81-3.64 ppm in the azidated product disappeared, again confirming the purity of the product obtained. Disappearance of the strong azide stretching vibration at 2092 cm^{-1} in the FT-IR spectrum, as well as the appearance of a peak at 1720 cm^{-1} for the carboxylic acid C=O further confirmed the success of the coupling reaction (Figures 3C-D). Quantification of the substitution level by ^{1}H NMR analysis of the reaction products with both 5-hexynoic acid and 10-undecynoic acid confirmed full conversion. Click reactions starting from BIIR with 1 and 4 mol% brominated isoprene units yielded results similar to the other reactions, except for their relative signal intensities. The ^{1}H NMR and FT-IR spectra for these products are provided as Supporting Information (Figures S7-S9).



Scheme 3. Synthesis of carboxylated IIR by azide-alkyne click reaction.

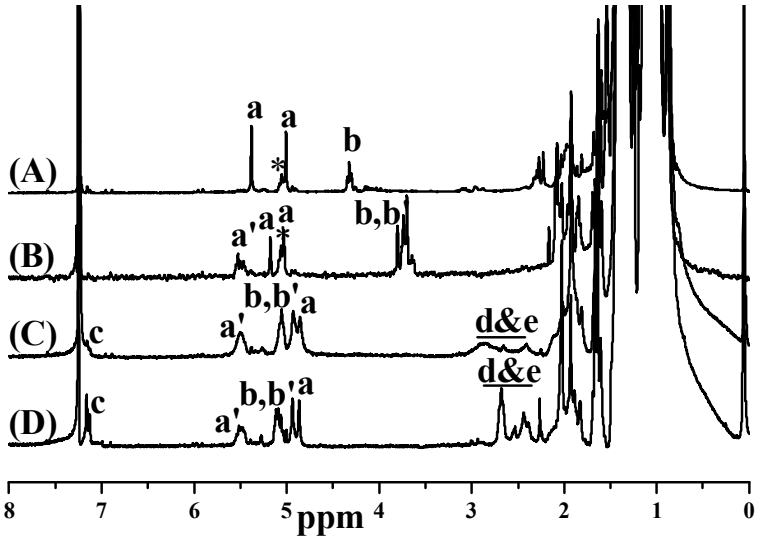


Figure 2. ^{1}H NMR spectra for the synthesis of carboxylated IIR (1.9 mol% brominated isoprene units) by the azide-alkyne click reaction. (A) BIIR (B) IIR-N_3 (C) IIR-6COOH and (D) IIR-11COOH. The peak assignments are provided in Scheme 3.

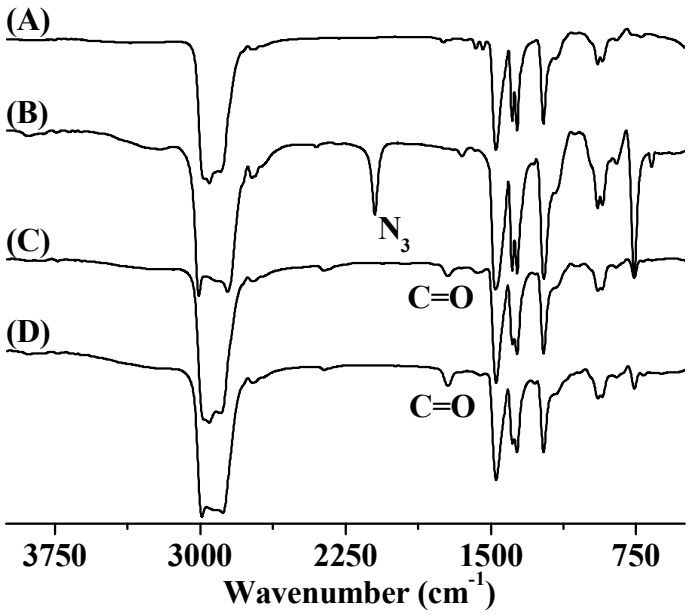


Figure 3. FT-IR spectra for the synthesis of carboxylated IIR (1.9 mol% brominated isoprene units) by the azide-alkyne click reaction. (A) BIIR (B) IIR-N_3 (C) IIR-6COOH and (D) IIR-11COOH.

Size exclusion chromatography (SEC) analysis was carried out to monitor potential changes in the molecular weight distribution of the products resulting from either cross-linking or chain cleavage. A series of SEC traces starting with BIIR containing 1.9 mol% brominated units and the different derivatives synthesized are provided in Figure 4. The SEC analysis of IIR is known to be problematic,[50,51] and it was indeed difficult to prepare solutions of BIIR and the carboxylated IIR derivatives concentrated enough for the SEC measurements (0.5 mg/mL) while also avoiding clogging of the columns. It was indeed reported that THF is a poor solvent as mobile phase for both halogenated IIR and its derivatives.[52] Due to these considerations, the results are only provided to demonstrate trends among the samples. The weight-average molar mass measured for BIIR (1.9 mol%) was $M_w = 3.8\times10^5$ g/mol, as compared to 2.3×10^5 and 2.7×10^5 g/mol for IIR-

6COOH and IIR-11COOH, respectively. It is therefore clear from SEC analysis that there were no significant changes in the molecular weight distribution of the carboxylated derivatives as compared with BIIR, both being on the order of 10^5 g/mol, which suggests that no significant degradation nor cross-linking of the IIR derivatives took place in the azidation and click reaction steps. Analysis of the products derived from BIIR with 1 mol% and ~4 mol% brominated isoprene units by SEC displayed similar trends (Supporting information, Figures S10 and S11).

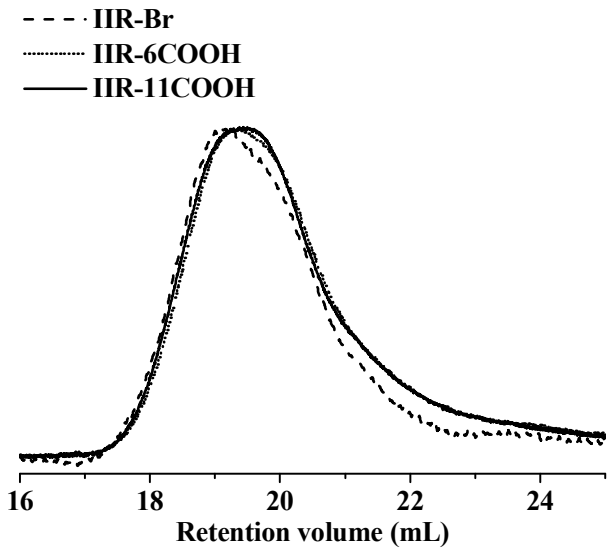


Figure 4. SEC traces for IIR derivatives (1.9 mol% brominated isoprene units).

Conclusions

Carboxylated BIIR derivatives with different substitution levels and alkyl spacer lengths were successfully synthesized by the azide-alkyne click coupling methodology. The success of the azidation and click reactions of IIR strongly depended on the type of solvent and the stoichiometry of the catalyst system used. This approach provides a new dimension to the modification of IIR. The high fidelity coupling of alkynes with azide-functionalized polymers offers a useful tool for

the modification of IIR, potentially enabling the generation of a wide range of derivatives.

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Polym Chem. 1993;31:2437–44.

Synthesis of Carboxylated Derivative of Poly(isobutylene-*co*-isoprene) (IIR) by Azide-alkyne "Click" Chemistry

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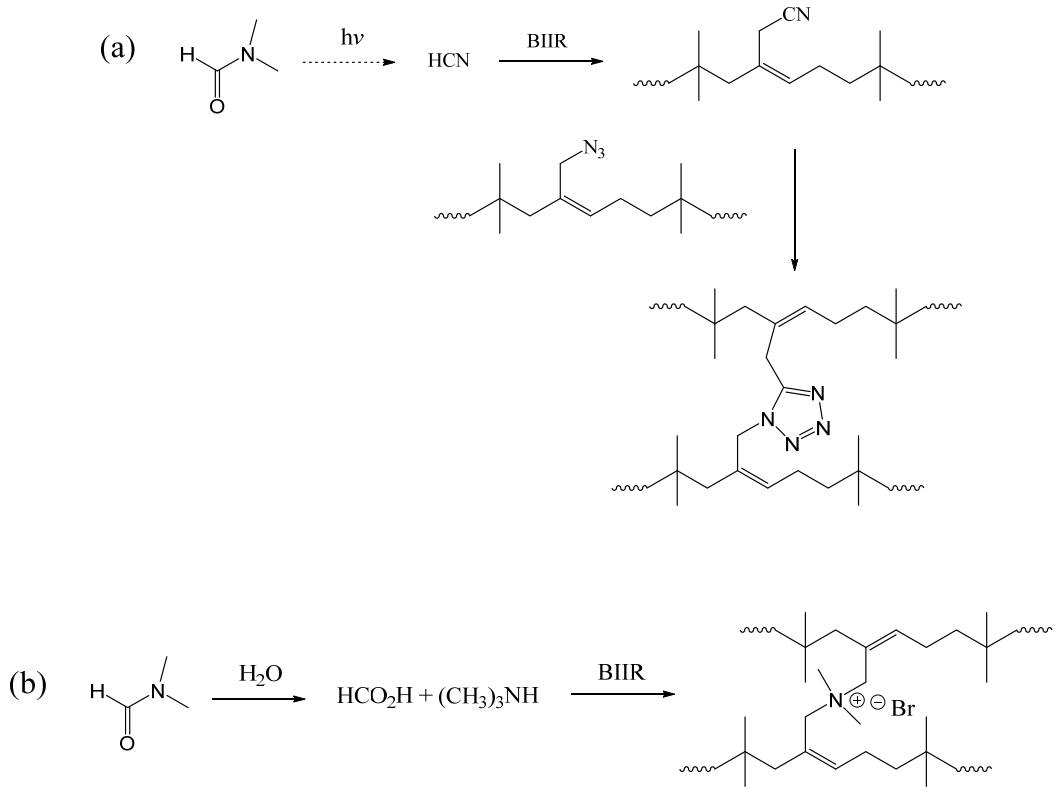


Scheme S1. Possible side reactions leading to gel formation in THF/DMF mixtures: (a) intermolecular tetrazole rings by reaction of nitrile and azide groups, (b) intermolecular quaternary amine cross-links induced by dimethylamine. For simplicity, only the allylic forms are shown.

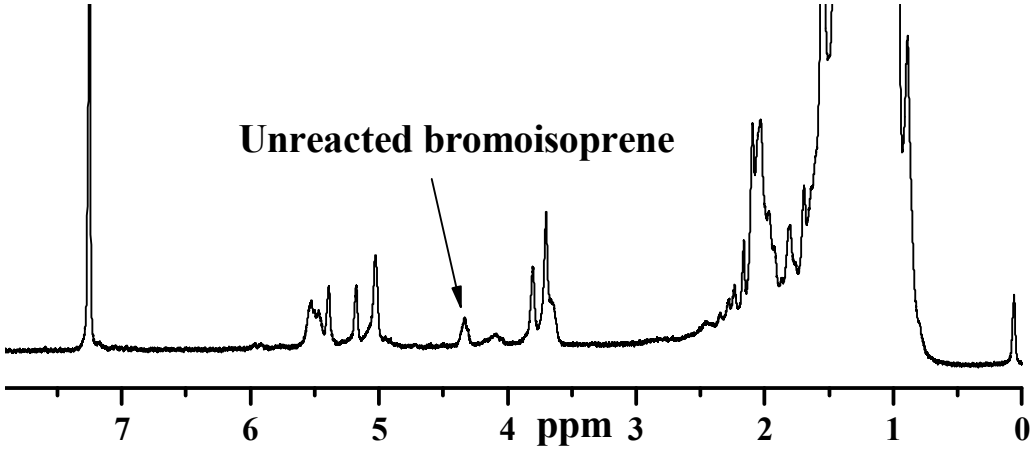


Figure S1. ^{1}H NMR spectra for azidated butyl rubber (IIR-N_3) showing the presence of unreacted brominated isoprene units after reaction of BIIR with 10 eq NaN_3.

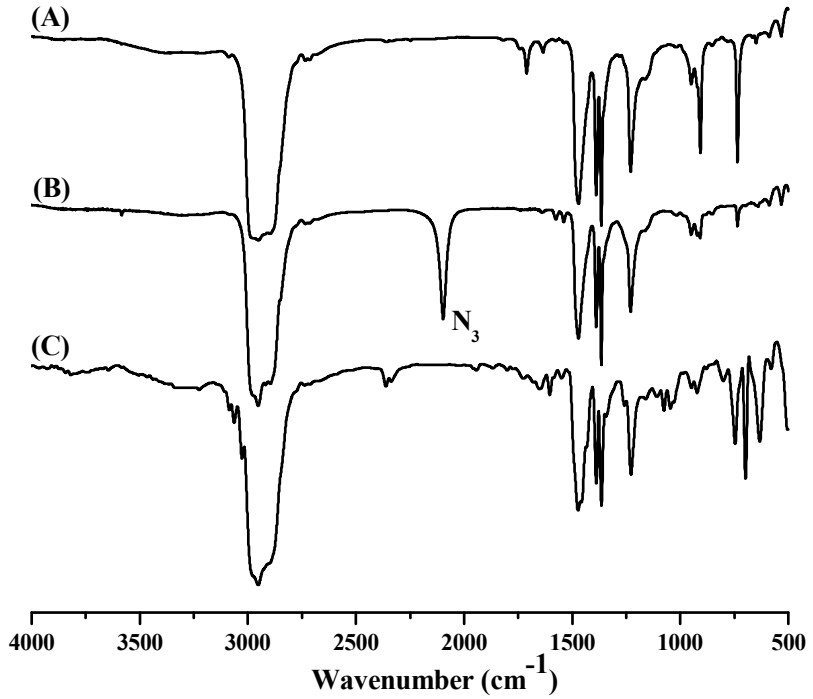


Figure S2. FT-IR spectrum for the optimization of azidation and azide-alkyne click reactions: (A) BIIR, (B) IIR-N_3, and (C) IIR-Ph.

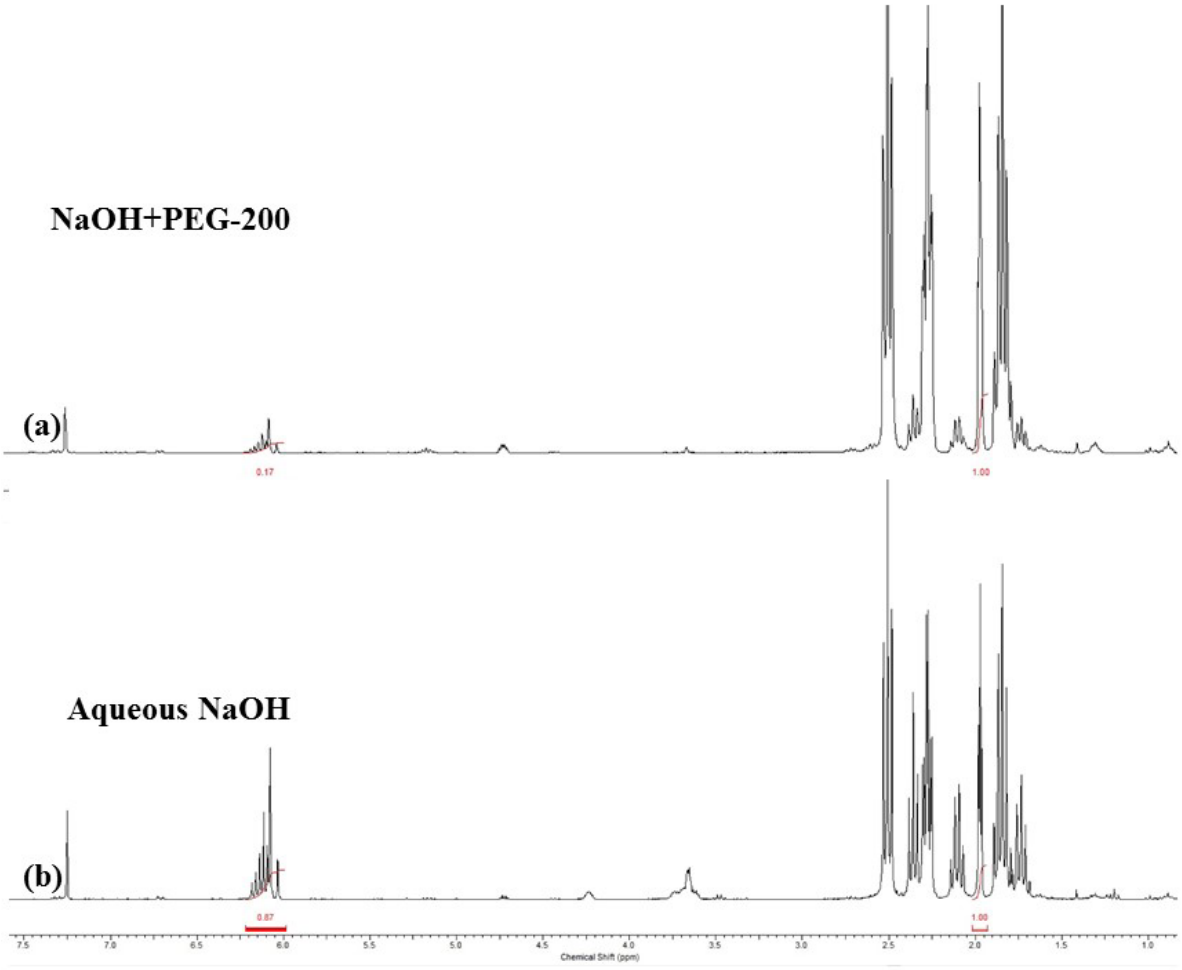


Figure S3. ^{1}H NMR spectra for 5-hexynoic acid isolated before purification in synthesis using (a) NaOH+PEG-200, and (b) aqueous NaOH. Using NaOH with PEG-200 was found to favor the formation of 5-hexynoic acid as compared with aqueous NaOH alone.

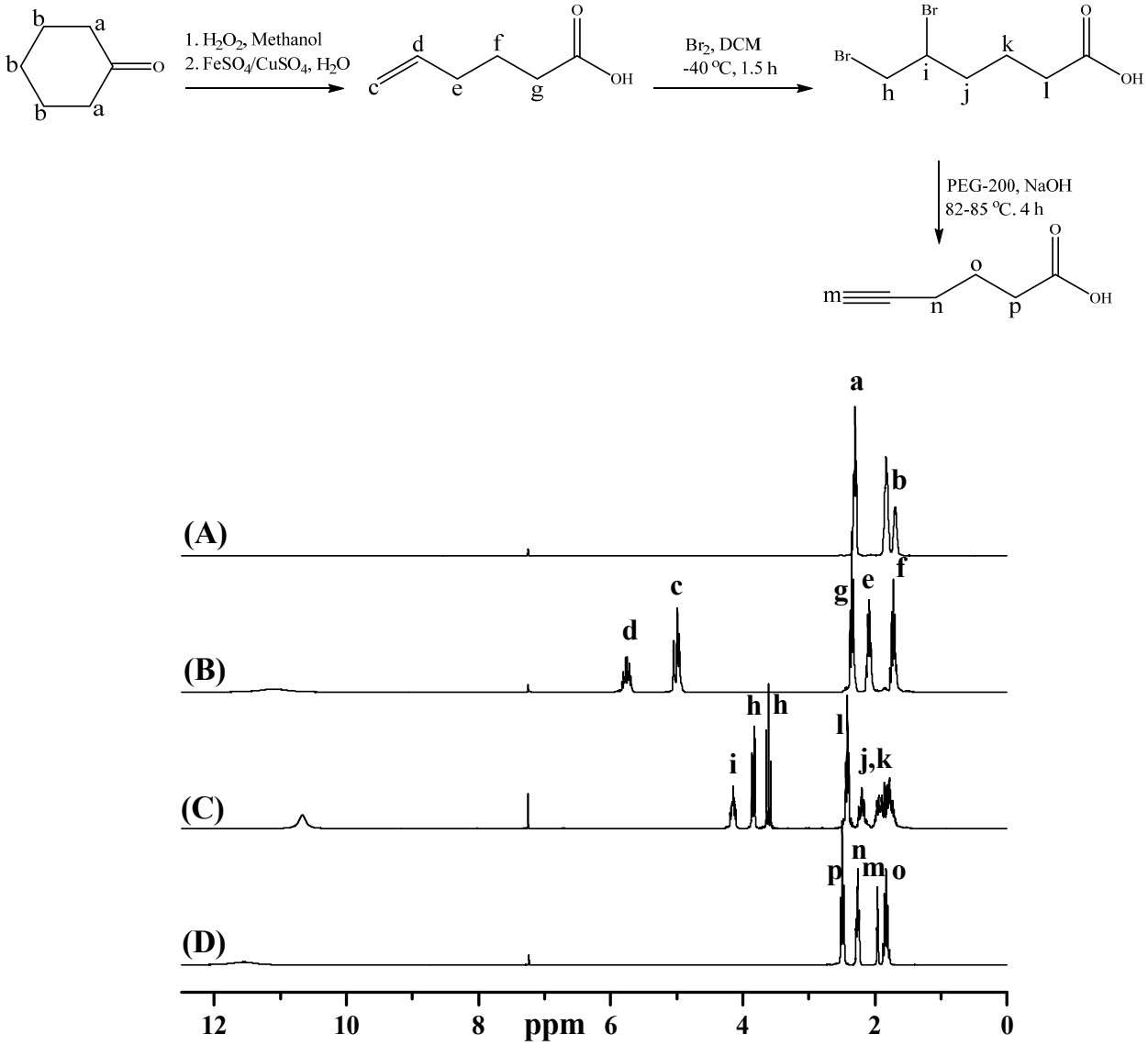


Figure S4. ^{1}H NMR spectra for the synthesis of 5-hexynoic acid: (A) Cyclohexanone, (B) 5-hexenoic acid, (C) 5,6-dibromohexanoic acid, and (D) 5-hexynoic acid.

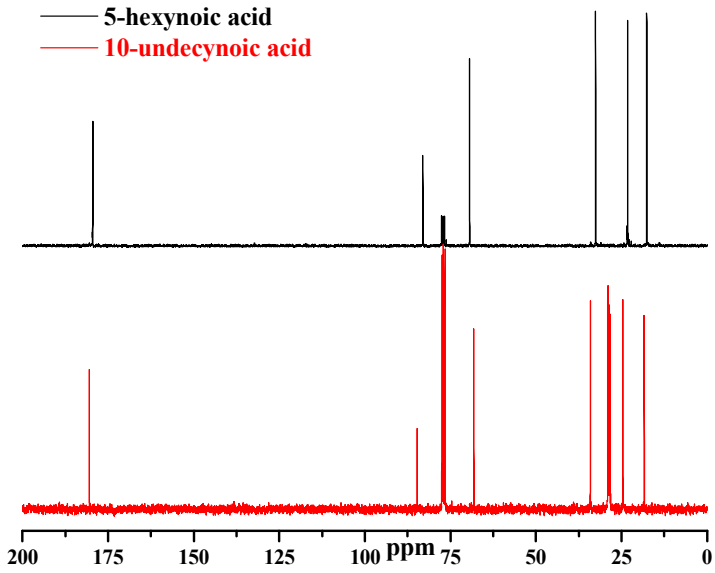


Figure S5. ^{13}C NMR spectra for 5-hexynoic acid and 10-undecynoic acid.

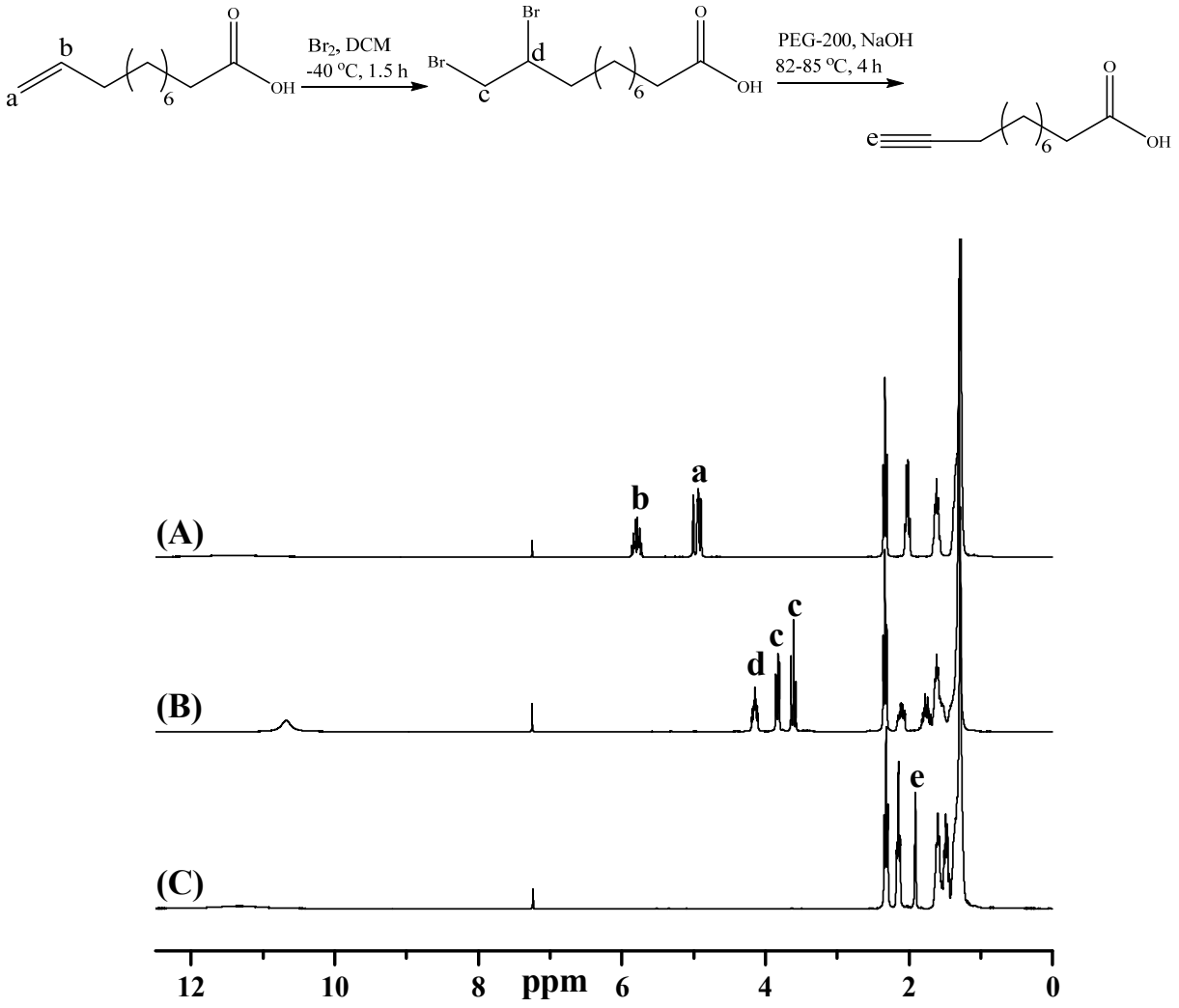


Figure S6. ^{1}H NMR spectra for the synthesis of 10-undecynoic acid: (A) 10-undecenoic acid, (B) 10,11-dibromoundecanoic acid, and (C) 10-undecynoic acid.

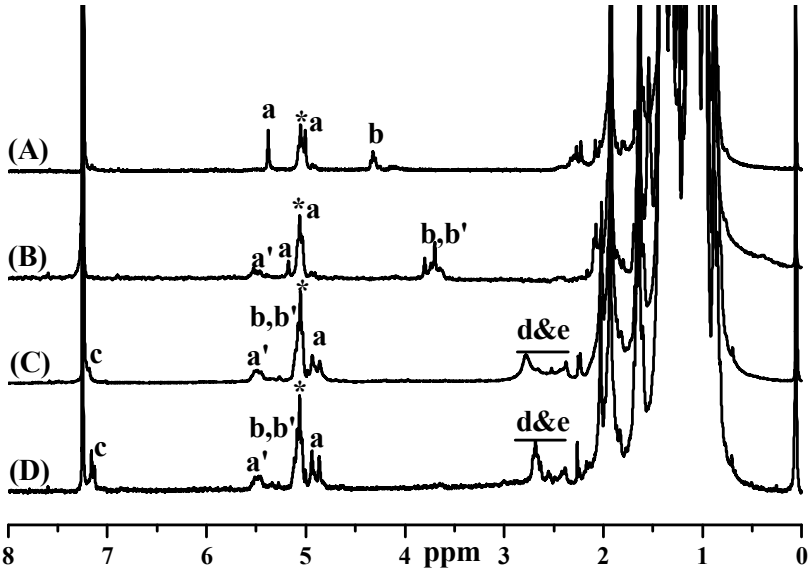


Figure S7. NMR spectra for the synthesis of carboxylated IIR (1 mol% brominated isoprene units) by azide-alkyne click reaction: (A) BIIR, (B) IIR-N_3, (C) IIR-6COOH, and (D) IIR-11COOH.

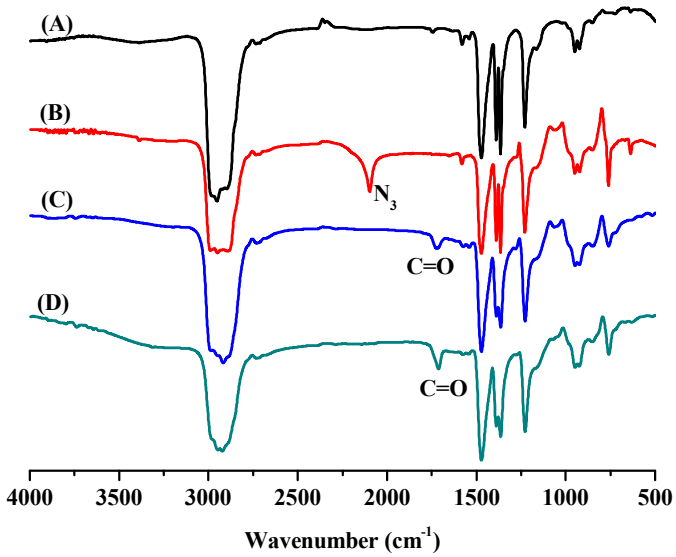


Figure S8. FT-IR spectra for the synthesis of carboxylated IIR (1 mol% brominated isoprene units) by azide-alkyne click reaction: (A) BIIR, (B) IIR-N_3, (C) IIR-6COOH, and (D) IIR-11COOH.

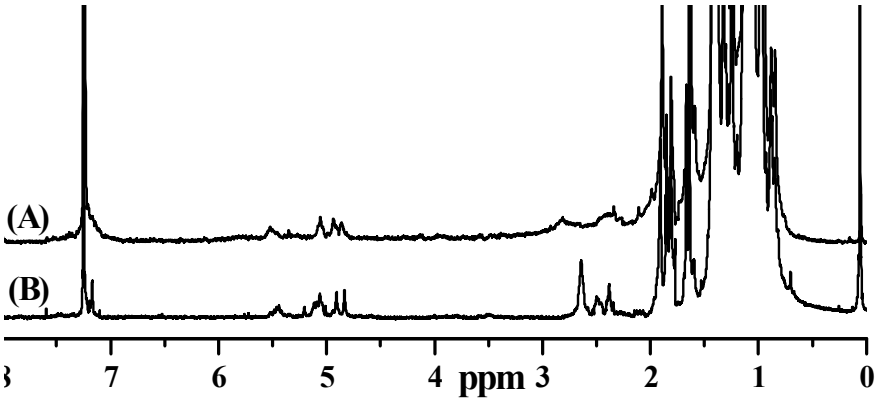
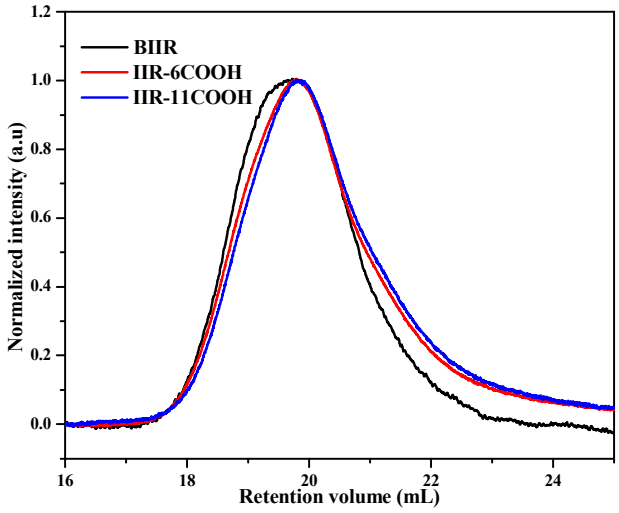


Figure S9. NMR spectra for the synthesis of carboxylated IIR (~4 mol% brominated isoprene units) by azide-alkyne click reaction: (A) IIR-6COOH, and (B) IIR-11COOH.



M_w(IIR-Br) = 2.8×10^5, M_w(IIR-6COOH) = 1.9×10^5, M_w(IIR-11COOH) = 1.8×10^5

Figure S10. SEC traces for IIR derivatives (1 mol% brominated isoprene units).

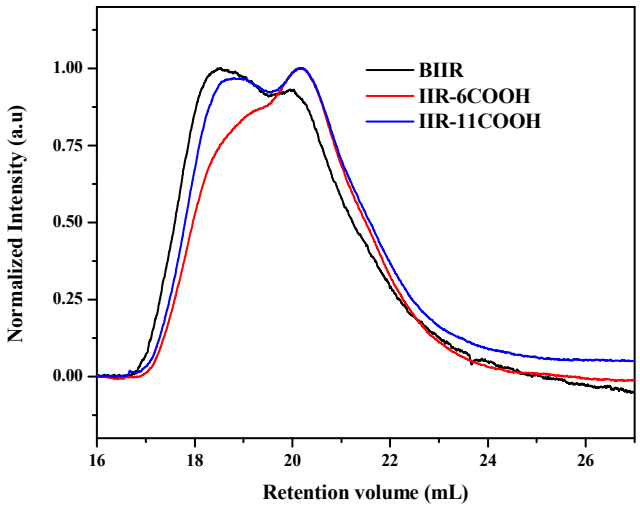


Figure S11. SEC traces for IIR derivatives (~4 mol% brominated isoprene units).