

Highly tunable polyurethanes: organocatalyzed polyaddition and subsequent post-polymerization modification of pentafluorophenyl ester sidechains†

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A facile method for the synthesis of high molecular weight functionalized polyurethanes from a novel pentafluorophenyl ester-containing diol precursor is described. Specifically, polyurethanes containing the activated ester sidechains were synthesized *via* triflic acid-catalyzed polyaddition of the above diol with diisocyanates. This was followed by quantitative postpolymerization modification of the sidechains with various primary amines. This method represents an efficient and modular synthetic strategy for the preparation of functionalized polyurethanes.

Introduction

Polyurethanes (PUs) are among the most versatile polymeric materials due to their ability to exhibit thermoplastic, elastomeric, and thermosetting behavior depending on their chemical and morphological makeup.^{1–3} Because of their utility and relatively low cost, these materials account for nearly 5 wt% of the total worldwide polymer production.⁴ Nowadays, PUs are almost entirely synthesized by reacting diisocyanates with diols, although alternative, “greener” isocyanate-free approaches have been developed in the last decade.^{3,5–8}

In general, the properties of PUs are easily tailored by the appropriate selection of the individual monomeric units, many of which are commercially available.^{9,10} Conversely, developing new methods for synthesizing polyurethanes with modifiable reactive groups along their backbone remains an open challenge.^{5,11} A post-polymerization functionalization strategy based on chemically modifying these reactive groups would provide a complementary method to the more traditional routes for functional PU synthesis. Such a platform is especially useful in

cases where the desired functional groups are incompatible with the polymerization conditions.

Within the context of PU chemistry, an ideal post-polymerization functionalization approach is one that directly incorporates reactive and/or readily functionalizable side-chains into linear PUs during the polymerization reaction, but does not interfere with the polymerization process. Previously, the frequent incompatibility of diisocyanates with various reactive functional groups has necessitated the use of protection/deprotection strategies prior to polymerization.^{5,12,13} For example, Du Prez and co-workers incorporated different “clickable” synthetic handles such as alkynes for Huisgen cycloaddition,^{13,14} or alkene and maleimide groups for conjugation with thiols,^{12,15,16} in order to incorporate diverse functionalities. However, in some of these cases, the use of metal catalysts and/or cumbersome protection/deprotection protocols inherently limits their usefulness.

Apart from the incorporation of functionality using isocyanate chemistry, a straightforward method for the synthesis of functionalized polyurethanes, based on amine–thiol–ene conjugation was recently described.⁵ In spite of the success of this new isocyanate-free approach for introducing functionality, the multi-step monomer synthesis and the inability to incorporate different soft segments such as polyethers, polyesters, or polycarbonates, considerably diminish the scope of possible functional materials.

With the discovery of various organocatalysts as effective alternatives to tin-based catalysts,^{17–19} new opportunities for the preparation of functionalized polyurethanes have emerged. The development of organocatalyzed PU syntheses provides greater accessibility, faster kinetics, convenience, and most importantly, functional group tolerance.^{17,20} Cramail *et al.* showed the ability of bicyclic alkylated guanidines to efficiently catalyze alcohol/isocyanate polymerization.^{21,22} Similarly, we have shown that certain organic acids are able to promote polyurethane formation under mild polymerization conditions and low catalyst loadings.²³ The use of acid catalysis can expand the

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range of polymerizable monomers that contain amides or other functionalities that are sensitive to base catalysis.^{24,25}

Herein we describe the synthesis and post-polymerization modification of PUs containing pendant activated pentafluorophenyl esters. First, we describe a method to synthesize a novel diol monomer containing a pentafluorophenyl ester moiety, followed by the triflic acid-catalyzed polymerization of this diol with diisocyanates to yield chemically modifiable polyurethanes. Finally, we show that the resulting polymers can be functionalized quantitatively on the sidechains using various amines to give more complex functional polyurethanes.

Result and discussion

In recent years, the post-polymerization modification of pentafluorophenyl esters has been used in order to incorporate functionalities into various polymer backbones.^{26–31} Therefore, we explored the use of 2,2-bis(hydroxymethyl)propanoic acid (bis-MPA) as a precursor to a versatile pentafluorophenyl ester-containing diol monomer (bis-MPA-C₆F₅) (Scheme 1) for PU synthesis and post-functionalization. Our design was based on the relative tolerance and compatibility of pentafluorophenyl esters toward the PU polymerization conditions.^{31,32} Thus, the esters remain intact after polymerization, and can be easily displaced by suitable nucleophiles under mild conditions in the post-polymerization modification step.

Synthesis of pentafluorophenyl ester-containing diol (bis-MPA-C₆F₅) monomer

Reaction of bis-MPA with 1.1 equiv. of commercially available bis(pentafluorophenyl) carbonate (PFC) resulted in the one-pot transformation of the carboxylic acid into a pentafluorophenyl

ester. The use of a base such as triethylamine (TEA) activated the carboxylic acid and solubilized the bis-MPA starting material in solvents such as THF, DMF, and acetonitrile, while stoichiometric control of PFC effectively prevented significant amounts of ring closure to the corresponding cyclic carbonate. Presumably, the esterification proceeds through an anhydride intermediate as shown in Scheme 1, based on the observation of a significant amount of gas evolution (*i.e.*, CO₂) during the early stages of the reaction. Following completion of the reaction, purification by column chromatography and recrystallization afforded bis-MPA-OC₆F₅ as a white crystalline powder in 65% yield. The structure was confirmed by ¹H and ¹⁹F NMR spectroscopy. The synthesized bis-MPA-C₆F₅ can be easily stored and handled on the benchtop.

Synthesis of a HDI-based pentafluorophenyl ester-containing polyurethane, *i.e.* poly(MPA-C₆F₅-HDI) urethane

Polymerization studies were performed using hexamethylene diisocyanate (HDI) and bis-MPA-C₆F₅ (Scheme 2). The polymerization was accomplished by dissolving equimolar amounts of HDI and bis-MPA-C₆F₅ in dichloromethane (0.1 M) followed by addition of triflic acid (5 mol%).²³

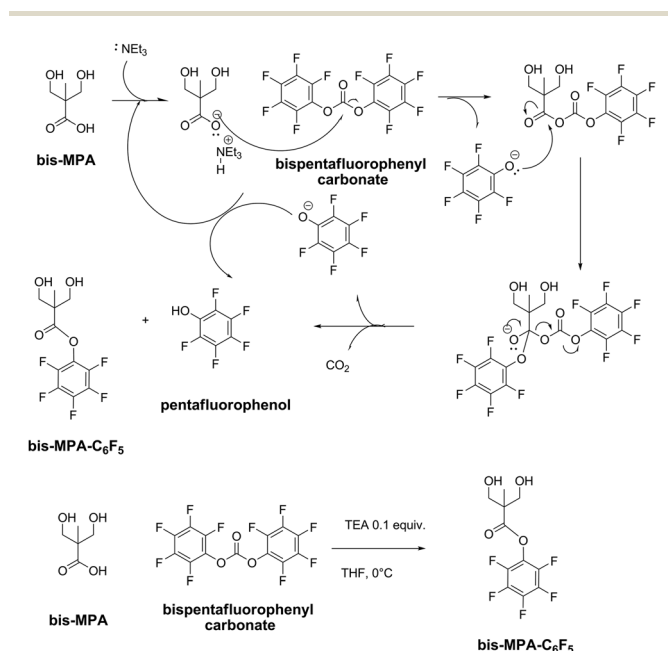
The polymerization was confirmed by ¹H NMR spectroscopy (CDCl₃) by monitoring the disappearance of HDI methylene protons (δ 3.32 ppm, adjacent to the isocyanate peak) and the concomitant appearance of protons adjacent to the urethane peak at δ 3.15 ppm (Fig. 1). ¹⁹F NMR spectroscopy was also utilized to confirm that the pentafluorophenyl esters remain untouched after the polymerization (see ESI†). To further verify the formation of high molecular weight polymers, gel permeation chromatography (GPC) analysis was performed (see ESI†), which confirmed that the polyurethanes exhibited the following characteristics after 24 h: M_n = 25–37 kDa; polydispersity index (D) = 1.4. These values are in good agreement with the values that we had recently obtained from triflic acid-catalyzed isocyanate-alcohol polymerization.²³

Synthesis of pentafluorophenyl ester-containing segmented polyurethanes

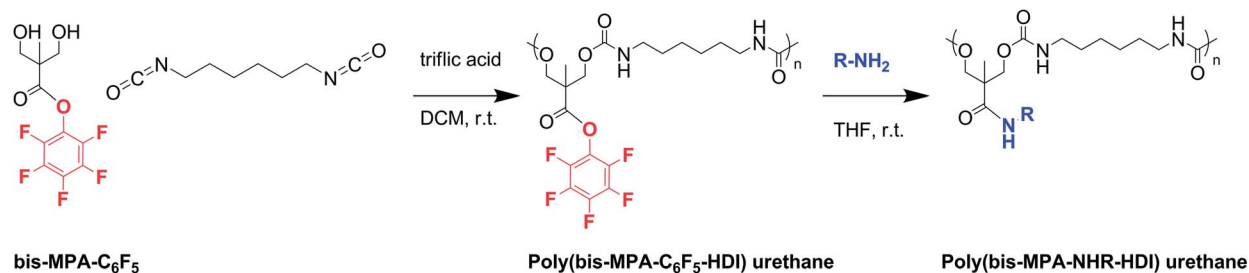
Apart from the bis-MPA-C₆F₅-based polyurethane, segmented polyurethanes were synthesized utilizing PEG₁₅₀₀ diol (ESI†). Segmented polyurethanes are attractive synthetic targets because of their ability to phase separate, imparting unusual morphological and physical properties to the polymer.³³ In this case the reaction was performed in two steps: first, the polyol (the less reactive alcohol) was reacted with a twofold excess of diisocyanate. The reaction was monitored by ¹H NMR spectroscopy to ensure successful chain propagation (ESI†), after which bis-MPA-C₆F₅ was added. The polymerization produced polymers ranging between M_n = 25.0 and 30.0 kDa; D = 1.5 as determined by GPC (ESI†). In this case, due to the different reactivity of the diols, a multimodal molar mass distribution was obtained.

Post-polymerization modification using primary amines

A convenient single-step post-polymerization modification of poly(MPA-C₆F₅-HDI) urethane provides access to polyurethanes



Scheme 1 General synthesis route toward the pentafluorophenyl ester-containing diol (bis-MPA-C₆F₅) from bis-MPA.



R = H, Hexyl, Benzyl, Pyrenemethyl

Scheme 2 General synthesis of functionalized polyurethanes from a precursor polymer bearing pendant pentafluorophenyl esters.

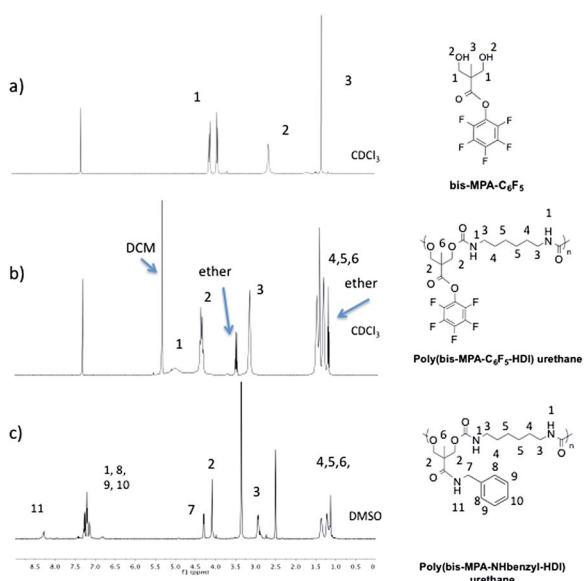


Fig. 1 ^1H NMR of (a) bis-MPA- C_6F_5 in CDCl_3 , (b) poly(bis-MPA- C_6F_5 -HDI) urethane with pentafluorophenyl ester sidechains in CDCl_3 , and (c) poly(bis-MPA-NHbenzyl-HDI) with *N*-benzylamide sidechains in DMSO-d_6 .

exhibiting a wide variety of functionalities. Furthermore, this avoids the need for protection/deprotection sequences, and functionalities can be easily incorporated using mild post-polymerization modification conditions. Several nucleophilic small molecules were selected for post-polymerization

modification studies (Table 1). For instance, when a primary amide was desired, the precursor polymer was treated with excess ammonium acetate (*i.e.* ammonia equivalent). Within 20 min, complete conversion of the activated ester to the corresponding amide was observed (ESI^+), as determined by ^1H NMR spectroscopy. Similarly, to obtain secondary amides, the precursor polymer was treated with 1.05 equiv. of a primary amine such as 1-hexylamine or benzylamine. In these cases, addition of an equivalent amount of triethylamine (TEA) was necessary for complete conversion to the desired amides within 45 min (Table 1 & Fig. 1).

Our modular synthetic strategy also lends itself well to the preparation of random and/or segmented polymers. Two different strategies were used; in the first, the statistical incorporation of two distinct primary amines was carried out. Specifically, a mixture of 1-aminomethylpyrene and 1-hexylamine (1 : 4 ratio) was reacted with the polymer. As shown in the ^1H NMR spectrum (ESI^+), the functionalization was successfully performed, resulting in a statistically functionalized copolymer whose composition closely matched the feed ratio of the two primary amines used. The polymer was also subsequently analyzed by GPC using both ultraviolet (UV) and refractive index (RI) signals. As shown in the ESI^+ , the UV and RI GPC traces matched up well, indicating that the pyrene chromophore had been introduced equally in all polymer chains. In the second approach, the aforementioned segmented polyurethane, poly(MPA-OC $_6\text{F}_5$ -HDI-PEG) urethane, was treated with 1-hexylamine (ESI^+), resulting in quantitative amide formation as indicated by ^1H NMR spectroscopy (ESI^+). The

Table 1 Summary of the substituted polyurethanes

Precursor polymer	Sidechain	Time (min)	Conversion % (^1H NMR)	M_n (g mol^{-1}) (GPC)	D (GPC)
Poly(bis-MPA- C_6F_5 -HDI) urethane	Amide	30	≥ 98	N/A ^a	N/A ^a
Poly(bis-MPA- C_6F_5 -HDI) urethane	1-Hexylamide	40	≥ 98	28	1.3
Poly(bis-MPA- C_6F_5 -HDI) urethane	1-Benzylamide	45	≥ 98	32	1.4
Poly(bis-MPA- C_6F_5 -HDI) urethane	1-Hexylamide- 1-pyrenemethanamide (4 : 1)	40	≥ 98	29	1.4
Poly(bis-MPA- C_6F_5 -HDI-PEG)	1-Benzylamide	120	≥ 98	39	1.6

^a Amide-functionalized polymer was not soluble in THF.

above reactions demonstrate a high degree of control over the post-polymerization chemical modification of both homopolymers and block copolymers.

Notably, GPC analysis before and after the chemoselective amine functionalization confirmed that the PU backbone remained intact under the reaction conditions. In general, we found that the molecular weights increased slightly upon post-polymerization functionalization, while minimal broadening of the *D* was observed (Table 1).

Conclusions

In conclusion, we have reported a novel synthetic method that enables a broad range of functionality to be incorporated into linear polyurethanes *via* a versatile pentafluorophenyl ester intermediate. We have also successfully demonstrated the organocatalyzed polymerization of the pentafluorophenyl ester-containing diol with diisocyanate, and the subsequent functionalization of the resulting polymer to generate primary and secondary amide sidechains. This post-polymerization functionalization provides rapid access to a wide range of functional polyurethanes with minimal synthetic steps. In view of the ever-increasing need for biodegradable and biocompatible polyurethanes, we envisage that this metal-free route will provide a versatile and convenient platform for the synthesis of many new and innovative materials.

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