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# 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 proper 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 high reactivity of diisocyanates together with the reactive nature of the incorporated functional group 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 the Huisgen cycloaddition,[13, 14] or alkene and maleimide groups for conjugation with thiols,[12, 15, 16] in order to incorporate diverse functionality. However, in some of these cases, the use of metal catalysts and/or cumbersome protection/deprotection protocols inherently limits their usefulness.

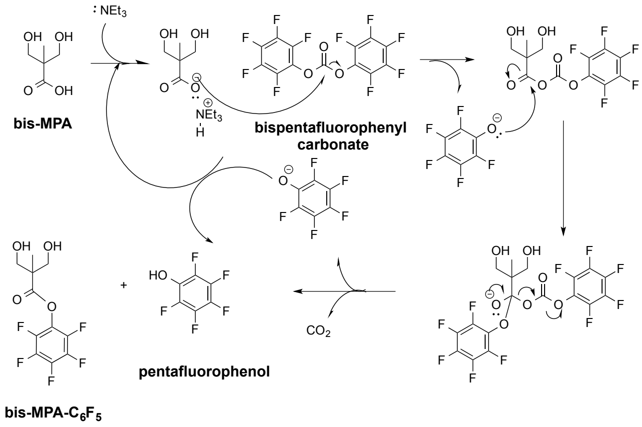
Apart from the incorporation of functionality using isocyanate chemistry, a straightforward method for the synthesis of functionalized polyurethanes, based on amine–thiol-ene conjugation was recently described. [5] In spite of the success of this new isocyanate-free approach for introducing functionality, 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 polymerizations.[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 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 pentafluorophenyl activated 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 functionality 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-$C_6F_5$) (Scheme 1) for PU synthesis and post-functionalization. Our design was based on the relative tolerance and compatibility of the 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.



Scheme 1. General synthetic route toward the pentafluorophenyl ester-containing diol (bis-MPA-$C_6F_5$) from bis-MPA.

## Synthesis of pentafluorophenyl ester-containing diol (bis-MPA-$C_6F_5$) 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., $CO_2$) during the early stages of the reaction. Following completion of the reaction, purification by column chromatography and recrystallization afforded bis-MPA-$OC_6F_5$ as a white crystalline powder in 65% yield. The structure was confirmed by $^1$H, and $^{19}$F NMR spectroscopy. The synthesized bis-MPA-$C_6F_5$ is easily stored and handled on the benchtop.

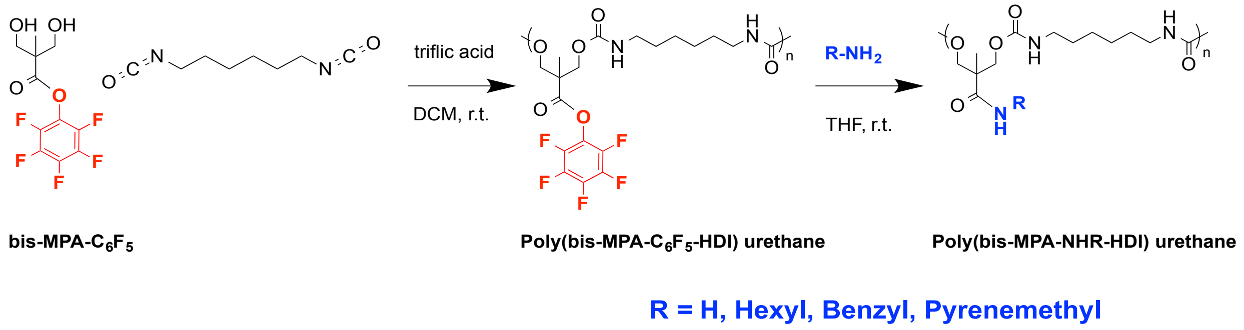
## Synthesis of a HDI-based pentafluorophenyl ester containing polyurethane, i.e. poly(MPA-$C_6F_5$-HDI) urethane

Polymerization studies were performed using hexamethylene diisocyanate (HDI) and bis-MPA-$C_6F_5$ (Scheme 2). The polymerization was accomplished by dissolving equimolar amounts of HDI and bis-MPA-$C_6F_5$ in dichloromethane (0.1 M) followed by addition of triflic acid (5 mol %).[23]

Polymerization was confirmed by $^1$H NMR spectroscopy ($CDCl_3$) by evaluating the disappearance of HDI methylene protons (δ 3.32 ppm, adjacent to the isocyanate) and the concomitant appearance of protons adjacent to the urethane at δ 3.15 ppm (Figure 1). $^{19}$F NMR spectroscopy was also utilized to confirm that the pentafluorophenyl esters remain untouched after the polymerization (see Supporting Information). To further verify the formation of high molecular weight polymer, gel permeation chromatography (GPC) analysis was performed (see Supporting Information), which confirmed that the polyurethanes exhibited the following characteristics after 24 h: $M_n$ = 25-37 kDa; Polydispersity index (Đ) = 1.4. These values are in good agreement with the values that we recently obtained for triflic acid-catalyzed isocyanate-alcohol polymerizations.[23]

## Synthesis of pentafluorophenyl ester-containing segmented polyurethanes

Apart from the bis-MPA-$C_6F_5$-based polyurethane, segmented polyurethanes were synthesized utilizing $PEG_{1500}$ diol, Supporting Information). 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 $^1$H NMR spectroscopy to ensure successful chain propagation (Supporting Information), after which bis-MPA-$C_6F_5$ was added. The polymerization



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

produced polymers ranging between $M_n$ = 25.0-30.0 kDa; Đ = 1.5 as determined by GPC (Supporting Information). In this case, due to the different reactivity of the diols, a multimodal molar mass distribution was obtained.

**Post-polymerization modification using primary amines.**

Convenient single-step post-polymerization modification of poly(MPA-C$_6$F$_5$-HDI)urethane provides access to polyurethanes exhibiting a wide variety of functionalities. Furthermore, this avoids the need for protecting/deprotecting sequences, and functionalities can be easily incorporated using mild post-polymerization 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 (Supporting Information), as determined by $^1$H 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 & Figure 1).

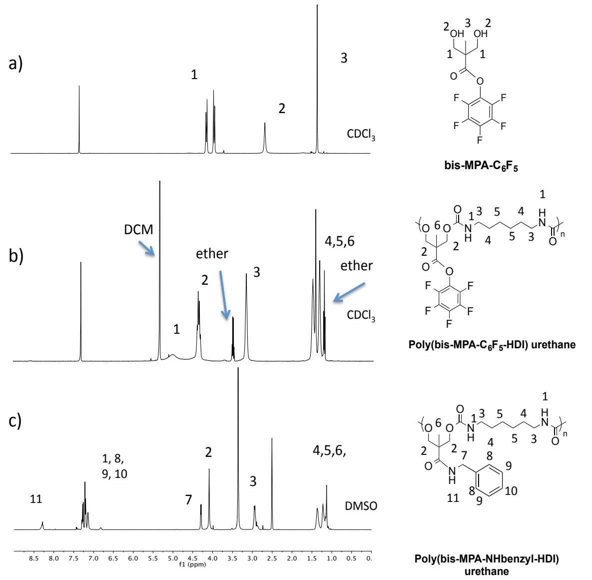


Figure 1. $^1$H NMR of (a) bis-MPA-C$_6$F$_5$ in CDCl$_3$, (b) poly(bis-MPA-C$_6$F$_5$-HDI) urethane with pentafluorophenyl ester sidechains in CDCl$_3$, and (c) poly(bis-MPA-NHbenzyl-HDI) with *N*-benzylamide sidechains in DMSO-d$_6$.

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-pyrenemethylamine and 1-hexylamine (1:4 ratio) was reacted with the polymer. As shown in the $^1$H NMR spectrum (Supporting Information), the functionalization was successfully performed, resulting in a statistically functionalized copolymer whose composition closely matched of 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 Supporting Information, the UV and RI GPC traces match 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$_6$F$_5$-HDI-PEG)urethane, was treated with 1-hexylamine (Supporting Information), resulting in quantitative amide formation as indicated by $^1$H NMR spectroscopy (Supporting Information). The above reactions demonstrate a high degree of control for 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 Đ was observed (Table 1).

## Conclusions

Table 1. Summary of the substituted polyurethanes.

| Precursor Polymer | Sidechain | Time (min) | Conversion % ($^1$H NMR) | Mn (g.mol$^{-1}$) (GPC) | Đ (GPC) |
|---|---|---|---|---|---|
| Poly(bis-MPA-$C_6F_5$-HDI) urethane | amide | 30 | ≥ 98 | N/A* | N/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 |

* amide-functionalized polymer was not soluble in THF.

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, it is envisioned 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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## Notes and references

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