

## Synthesis of aryl-substituted polyisobutylenes as precursors for ligands for greener, phase-selectively soluble catalysts\*

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**Abstract:** General synthetic approaches to functional derivatives of polyisobutylene (PIB) that contain arene groups that can be used as catalysts or as precursors to catalyst ligands are discussed. The emphasis is on reactions that use commercially available terminally functionalized PIB derivatives as starting materials. Both successful and unsuccessful electrophilic aromatic substitution processes are described, and potential problems of this process and ways to circumvent the problem of depolymerization of the intermediate polyisobutyl cation in substitutions of less reactive arenes are detailed. Examples that lead to polyisobutyl-containing arenes that are known and potentially useful as ligands or ligand precursors for greener homogeneous catalysts that are phase-selectively soluble and recoverable in heptane are emphasized.

**Keywords:** catalysis; green chemistry; ligands; polyisobutylene; polymer supports.

### INTRODUCTION

Polyisobutylene (PIB) and related polymers like **1** and **2** containing di- and trisubstituted alkenes at their termini are commercially available inexpensive materials [1]. PIB in particular is noncrystalline and soluble in a wide range of organic solvents including simple alkanes, aromatics, ethers like tetrahydrofuran (THF), and in various halogenated organic solvents [2]. Though PIB polymers and their derivatives are soluble in mixtures of alkanes and polar protic or polar aprotic solvents, they are not very soluble in pure polar protic solvents like ethanol, in pure dimethylformamide (DMF), or in acetonitrile. PIB and its derivatives with a variety of terminal functional groups are insoluble in water. In many respects, terminally functionalized derivatives of these hydrocarbon polymers can be considered to be nonpolar analogs of the poly(ethylene glycol) (PEG) polymers that are soluble in polar solvents that PIB derivatives do not dissolve in. Moreover, just as PEG is often used to support catalysts or reagents in polymer-supported chemistry [3], PIB can be similarly used [4]. PEG derivatives are typically recovered and separated from products by solvent precipitation. This is not the case for PIB derivatives. While non-



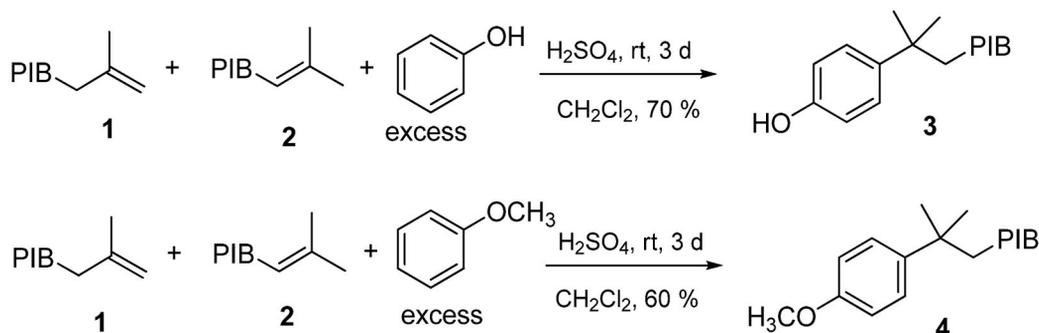
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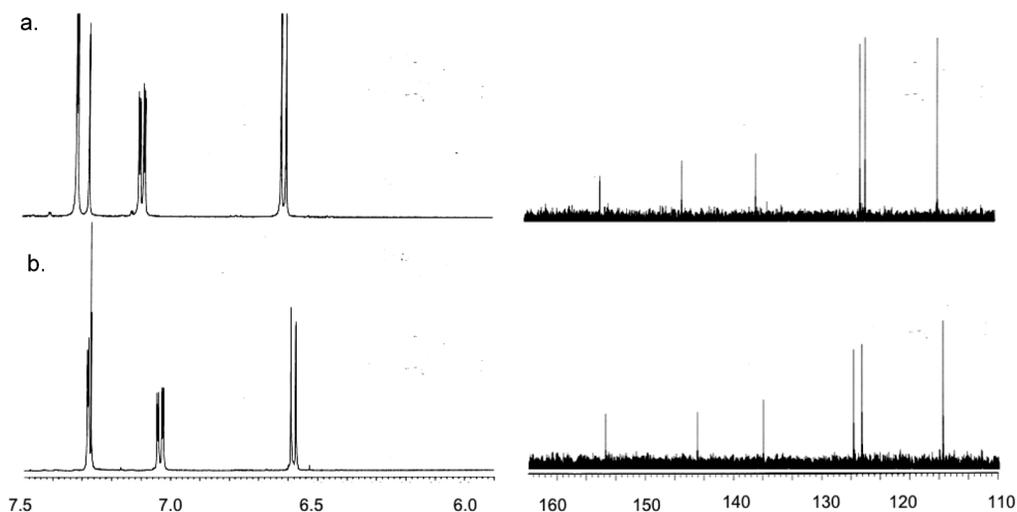
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crystalline PIB polymers or their derivatives cannot readily be recovered by precipitation as is the case for more crystalline hydrocarbon polymers or as is the case for many derivatives of PEG, PIB and its derivatives can be separated from polar organic materials by solvent extraction or by a gravity separation of a biphasic hydrocarbon/polar solvent mixture [5,6]. Our group has already shown that functional derivatives of PIB can be used in a variety of green catalytic chemistry as phase anchors to recover homogeneous catalysts [7–11]. These studies have shown that PIB, like PEG, can be used to support many different sorts of transition-metal catalysts if suitable ligands can be introduced onto the terminus of the PIB. Organocatalysts too can be supported on these sorts of polymers. This paper describes both the utility and limitations of electrophilic aromatic substitution as a route for the synthesis of terminally functionalized PIBs that serve as precursors of catalysts or catalyst ligands. It describes successful and unsuccessful routes to several classes of functionalized arenes, which are useful hydrocarbon PIB phase anchored ligand precursors that are phase-selectively soluble in saturated hydrocarbon solvents.

### POLYISOBUTYLATION OF PHENOL

In our initial work, we examined the electrophilic substitution of phenols and phenol derivatives [8,10]. This chemistry shown below for reaction of a mixture of **1** and **2** to form either **3** or **4** was quite successful. Good yields of 4-substituted products were isolated using phenol, anisole, and substituted phenols like 2-*tert*-butylphenol starting with commercially supplied PIB samples that contain a mixture of **1** and **2**. The percentage of **2** in these mixtures varies from 10 to 25 % but does not affect the overall process as the electrophilic aromatic substitution chemistry proceeds via the same carbocation. The substitution regiochemistry was also high. The only product isolated from the nonpolar phase after evaporation of the solvent, dissolution of the crude product into a biphasic mixture of hexanes and a polar solvent (e.g., aqueous ethanol, acetonitrile, *N,N*-DMF), and extraction of the product mixture with hexanes and evaporation of the hexanes was a PIB aryl derivative where the polyisobutyl group was introduced at the *para* position of these activated oxygenated arenes. Reactions of phenol with excess PIB did not yield any 2,4-bis(polyisobutyl)phenol, a somewhat surprising result since it is possible to introduce *tert*-butyl groups *ortho* and *para* to the phenolic hydroxyl group in phenol. In these cases, it was convenient to use an excess of phenol or anisole in electrophilic substitution using mixtures of **1** and **2**. In these reactions, separation of the product from the excess polar reactant was readily effected because PIB derivatives are soluble in saturated hydrocarbon solvents like heptane or hexanes, while the phenol or anisole are soluble in more polar hexane immiscible solvents and can be extracted from hexane solutions of the product PIB derivatives. As noted, good yields of product are generally obtained. The products of these reactions are also easily characterized. A PIB-substituted derivative of 2-*tert*-butylphenol, for example, has <sup>1</sup>H and <sup>13</sup>C NMR spectra that are nearly indistinguishable from <sup>1</sup>H and <sup>13</sup>C NMR spectra of 2,4-di-*tert*-butylphenol where a *tert*-butyl group is present in place of the polyisobutyl group as shown in Figs. 1a and 1b.



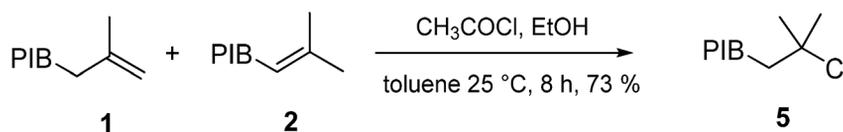


**Fig. 1** Aryl region of the  $^1\text{H}$  NMR spectra of (a) 4-polyisobutyl-2-*tert*-butylphenol, and (b) 2,4-di-*tert*-butylphenol and the  $^{13}\text{C}$  NMR spectra of these two compounds showing similar chemical shifts and spectral quality for the PIB and low-molecular-weight analogs of similarly substituted arenes.

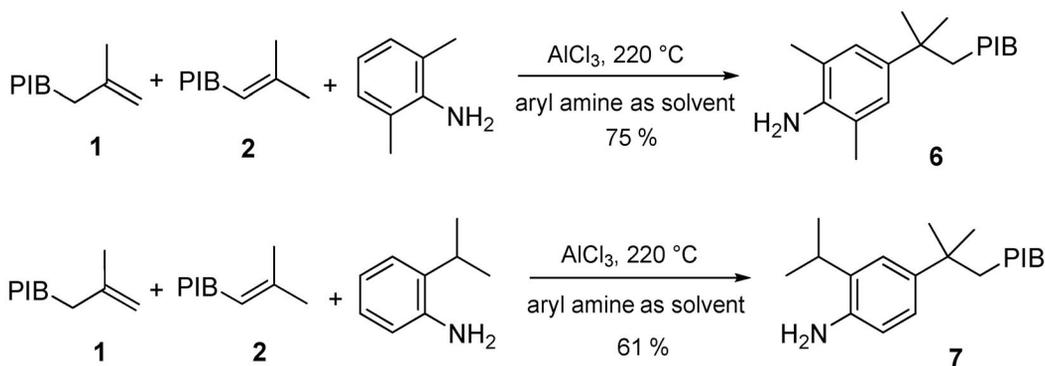
We have previously shown that phenol-substituted PIB derivatives can serve as precursors to a variety of catalyst ligands. For example, we have shown that the product of addition of a vinyl-terminated PIB to phenol or a substituted phenol can be used to prepare salen ligands for recoverable Cr polymerization catalysts [8] and can be used to prepare benzylidene ligands for Grubbs–Hoveyda metathesis precatalysts [10]. Phenols can also be converted into sulfonated esters, and compounds like a PIB aryl triflate could in principle serve as a precursor to an arylamine or an arylphosphine in a Pd-catalyzed aryl amination or phosphination reaction [12,13]. Thus, the phenolic derivatives of PIB are generally useful precursors to a variety ligands commonly used for transition-metal catalysts. Since the PIB can also serve as a hydrocarbon phase anchor in a biphasic separation of heptane and a more polar immiscible solvent, these ligands are expected to be useful in development of new greener versions of homogeneous catalysts that have demonstrated utility in the synthesis of fine chemicals in the chemical industry.

## POLYISOBUTYL DERIVATIVES OF ALKYL-SUBSTITUTED ANILINES

Given the importance of aminoarenes as catalyst ligand precursors in the formation of *N*-heterocyclic carbenes, we examined extension of the electrophilic substitution chemistry of phenols to the synthesis of PIB-substituted anilines. We expected this could be more difficult than the phenol chemistry because of the basicity of aniline derivatives. Indeed, our initial attempt to prepare a 4-PIB-substituted 2,6-dimethylaniline by reaction of the alkenes **1** and **2** with 2,6-dimethylaniline was unsuccessful. Likewise, a reaction of the alkenes **1** and **2** with the acetamide of 2,6-dimethylaniline in the presence of  $\text{H}_2\text{SO}_4$  or the reaction of the tertiary chloride **5** (formed as shown below from HCl generated in situ in toluene from acetyl chloride and ethanol) with the acetamide of 2,6-dimethylaniline in the presence of  $\text{AlCl}_3$  (or  $\text{AlBr}_3$ ) failed too. Nonetheless, we continued to pursue this synthesis because direct formation of

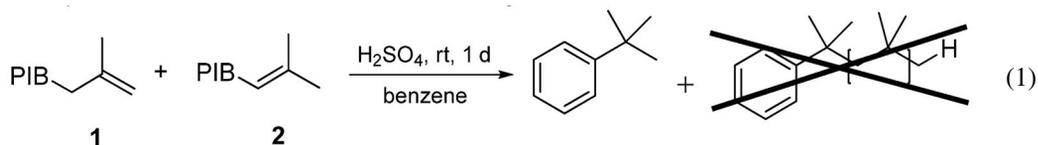


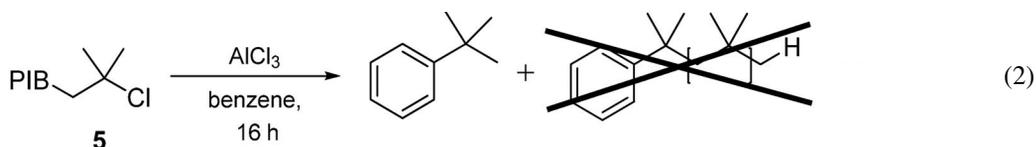
PIB aryl amines by electrophilic aromatic substitution would likely be less expensive and more direct than the aforementioned Pd-catalyzed aryl amination chemistry. Fortunately, a procedure in the patent literature provided guidance [14], and we were successful in using electrophilic aromatic substitution chemistry shown below to prepare PIB-substituted dialkyl and monoalkylanilines like **6** and **7**. The example of most initial interest was **6**, 4-polyisobutyl-2,6-dimethylaniline as 4-polyisobutyl-2,6-dimethylaniline is a direct analog of mesitylamine—a widely used precursor of an important class of *N*-heterocyclic carbene ligands [15]. We were able to prepare this PIB derivative **6** in 75 % isolated yield on a 10 g scale. The chemistry shown uses a mixture of the alkene-terminated PIB polymers **1** and **2** as substrates with 2,6-dimethylaniline as the solvent. While the vinyl-terminated PIB polymers are used as the starting materials, we speculate that either HCl and/or tertiary chlorides are actually produced in situ. In this scenario, HCl either reacts with this polymeric alkene to directly form a tertiary carbocation or forms an intermediate tertiary chloride that in turn leads to a tertiary carbocation on reaction with AlCl<sub>3</sub>. This chemistry was successfully extended to include monoalkylanilines like 2-isopropylaniline to form **7**. However, this chemistry was not successful in initial work with aniline itself because aniline and the vinyl-terminated PIB starting material are immiscible even at elevated temperature. The PIB derivative of the monoalkyl aniline 2-isopropylaniline was prepared on a >2 g scale and in a 61 % isolated yield. As was true for the PIB phenol derivatives, purification of the PIB-substituted anilines was facilitated by the alkane solubility of the PIB group.



### POLYISOBUTYL DERIVATIVES OF UNACTIVATED ARENES

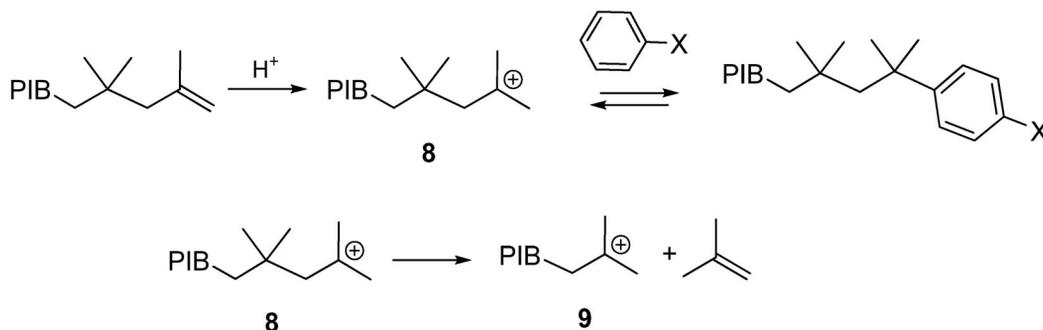
We next turned our attention to electrophilic aromatic substitution of less activated arenes like toluene or benzene itself. However, these efforts were unexpectedly unsuccessful even with large excesses of arenes as solvents at elevated temperature. Both conventional heating and microwave heating were attempted but all attempts to effect electrophilic aromatic substitution on simple alkylbenzenes or on benzene itself by using PIB oligomers with tertiary halides on their termini or by using PIB oligomers terminated with vinyl groups proved unsuccessful. However, while alkylation of benzene with a vinyl-terminated PIB or a PIB terminated with a tertiary chloride group (**5**) under Friedel–Crafts conditions did not give the desired product, we did observe some arene substitution. What was seen was that *tert*-butyl benzene was generated (eqs. 1 or 2). We attribute the formation of this product to depolymerization of the intermediate tertiary carbocations formed from the PIB starting materials under the reaction conditions.





While we did not usually isolate *tert*-butyl substituted phenol or anilines in reactions that led to PIB-bound arenes **3**, **4**, and **6**, we did not extensively analyze the polar phase in these reactions as our initial focus was the synthesis and isolation of hydrocarbon-soluble phenols and arylamines. We subsequently went back and looked at the polar phase of the reactions shown above that formed PIB-bound phenol **3** and 2,6-dimethylaniline **6**. These analyses confirmed the presence of some *tert*-butyl substituted phenol and 2,6-dimethylaniline in both the formation of PIB-substituted phenol and 2,6-dimethylaniline. The observation that 4-*tert*-butylphenol and 2,6-dimethyl-4-*tert*-butylaniline is present in these cases suggests that simple *tert*-butylation seen as the exclusive product in reactions 1 and 2 is a side reaction in this other chemistry too.

We speculate that the formation of *tert*-butylbenzene in the reactions shown in eqs. 1 and 2 is a result of depolymerization of the polyisobutyl cation intermediate. Loss of isobutylene from the tertiary carbocation **8** as shown in Scheme 1 can produce isobutylene and a new tertiary carbocation **9** with one less repeat unit in the polyisobutyl chain under the reaction conditions. It is also possible that any PIB-substituted arenes that did form could undergo proteolysis to reform the same intermediate polyisobutyl cation **8** since the reversibility of arene alkylation in the presence of acid has been long known to be a viable process that can remove *tert*-alkyl groups bound to arenes by what is in effect a proteolysis [16].



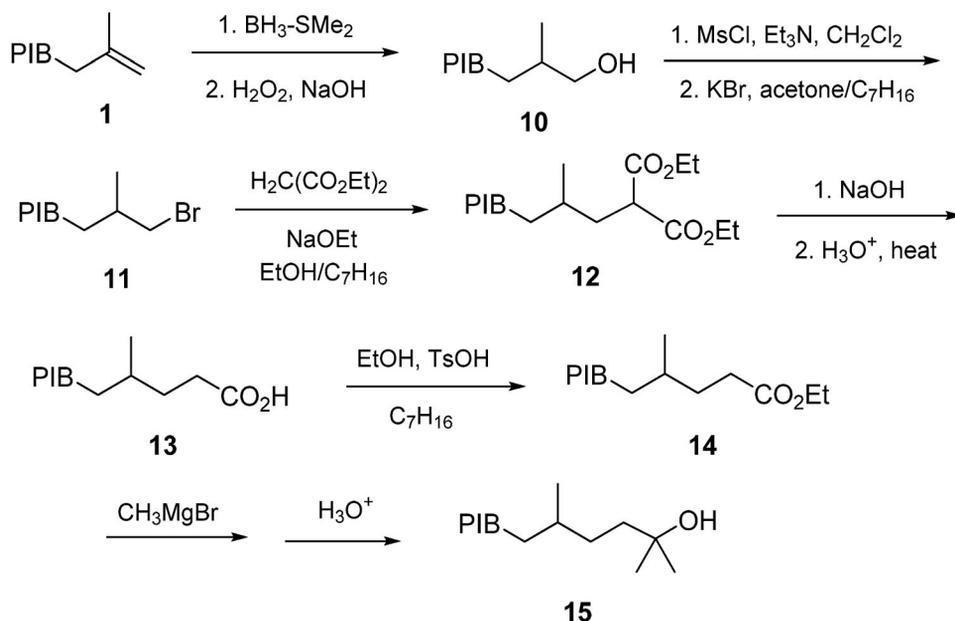
**Scheme 1** Postulated depolymerization polyisobutyl cation intermediates in electrophilic aromatic substitutions of less activated arene substrates.

The premise that a terminal polyisobutyl cation could form isobutylene and in turn produce *tert*-butyl cations is also supported in earlier results described by both the Ipatieff and Sanford groups. These groups noted that *tert*-butylbenzene was a product in electrophilic aromatic substitutions using either diisobutylene or triisobutylene as the alkylating agent [17,18].

In this explanation of formation of *tert*-butylbenzene in place of PIB, the PIB-alkene or PIB-*tert*-butyl chloride is converted to a tertiary carbocation terminated polymer **8** under Friedel–Crafts conditions. This carbocation once formed can either react with the substrate arene to form a  $\sigma$ -complex that can lead to the desired polyisobutyl arene, lose a proton to reform the starting alkene-terminated PIB (**1** or **2**), or this polyisobutyl cation **8** can lose isobutylene in an entropically favored process to form a new polyisobutyl tertiary carbocation that is energetically equivalent to the first formed polyisobutyl tertiary carbocation. Reaction of this cation with isobutylene or reaction of the isobutylene formed in this process with protons formed in situ could then form *tert*-butyl carbocations that are presumably the

source of the *tert*-butylarene byproducts. Further complicating the picture is the fact that the alkylation of the arene can be reversible as shown in Scheme 1. Thus even if a PIB arene is formed, it can protonate to form a  $\sigma$ -complex that can dealkylate under the reaction conditions to reform the polyisobutyl tertiary carbocation that can depolymerize.

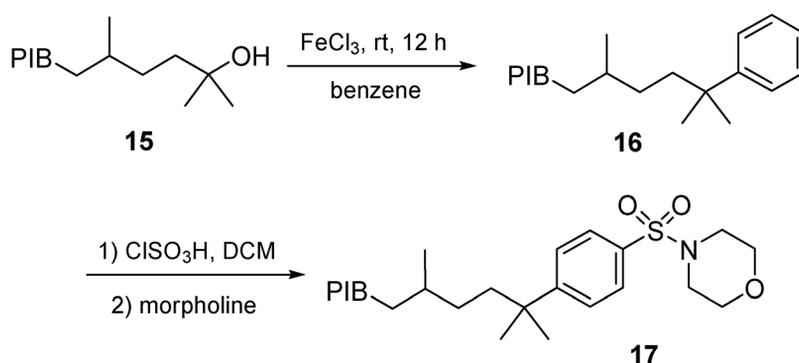
To test this hypothesis, we prepared a PIB-bound tertiary alcohol that would in situ form a tertiary carbocation under Friedel–Crafts conditions that could not decompose to form a stable tertiary carbocation by loss of isobutylene. Our expectation was that this PIB derivative could alkylate simple arenes. This alcohol **15** was formed by the multistep synthesis shown in Scheme 2. In this synthesis, the alkene **1** was first converted into a primary alcohol **10**.



**Scheme 2** Synthesis of a tertiary alcohol-terminated PIB that does not terminate in a diisobutylene group. The overall yield of **15** in this sequence varied between 28–34 %.

Subsequent mesylate formation and a Finkelstein reaction formed a primary bromide **11** that served as an electrophile in a malonic ester synthesis. Hydrolysis and decarboxylation of the product diethylmalonate **12** formed in this synthesis and subsequent esterification of the carboxylic acid **13** produced by decarboxylation produced the ethyl ester **14**. A Grignard reaction of this ester **14** with CH<sub>3</sub>MgBr then formed the tertiary alcohol **15**. Since this PIB derivative does not contain oligoisobutylene repeat units adjacent to the tertiary alcohol, loss of isobutylene from the tertiary carbocation formed from **15** would form an unstable primary carbocation instead of a tertiary carbocation like **9** that is formed in Scheme 1. If this analysis is correct, an alkyl chloride formed from **15** in situ should successfully alkylate arenes.

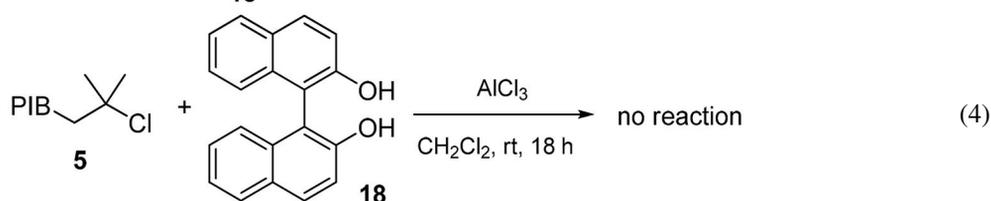
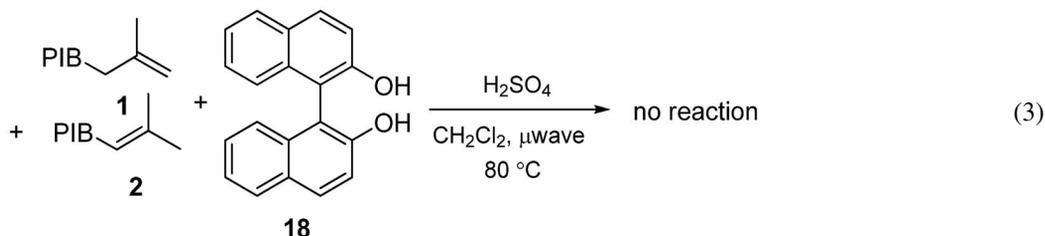
This supposition proved correct. Alkylation of benzene with **15** in the presence of FeCl<sub>3</sub> afforded the phenyl-terminated PIB derivative **16**, which was characterized by <sup>1</sup>H NMR spectroscopy. This phenyl-terminated PIB derivative **16** was subsequently chlorosulfonated with chlorosulfonic acid to form a 4-polyisobutylphenylsulfonyl chloride that could be modified to form a sulfonamide **17** on reaction with morpholine to show that this arene could be converted into sulfonamide derivatives (Scheme 3). This reaction sequence provides a route to simpler arene-terminated PIB derivatives and shows that such species can be further modified for synthesis of other ligands if desired.



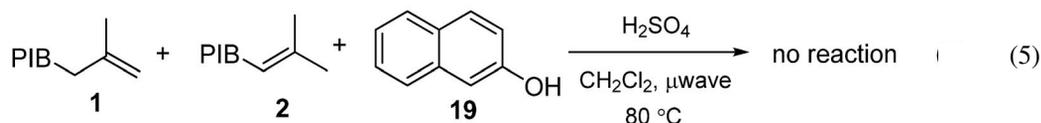
**Scheme 3** Synthesis of PIB derivatives that serve as precursors for electrophilic aromatic substitution of unactivated arenes.

### POLYISOBUTYL DERIVATIVES OF 2,2'-BINAPHTHOL

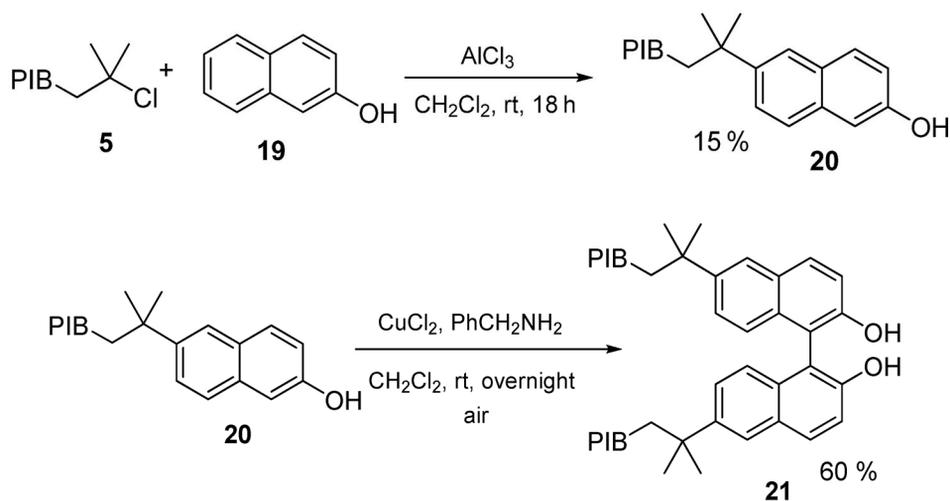
Given that phenol is a suitable substrate for electrophilic aromatic substitution, we also pursued formation of Friedel–Crafts alkylation of 2,2'-binaphthol (BINOL) by the PIB-terminated alkenes **1** and **2**. However, both under the conditions that worked for the synthesis of the PIB-phenol **3** and under a variety of other conditions (e.g., microwave irradiation), formation of a PIB derivative of BINOL was not successful (eqs. 3 and 4). The reaction of a preformed PIB-terminated tertiary chloride with BINOL using  $\text{AlCl}_3$  was also unsuccessful. However, some 6-*tert*-butyl-2,2'-binaphthol was formed, suggesting that in the case of BINOL substitution, depolymerization like that seen in simple unactivated arenes is competitive with BINOL alkylation by a polyisobutyl cation. These arenes **18** are presumably less reactive than phenol because of complexation of the binaphthol by the aluminum Lewis acid.



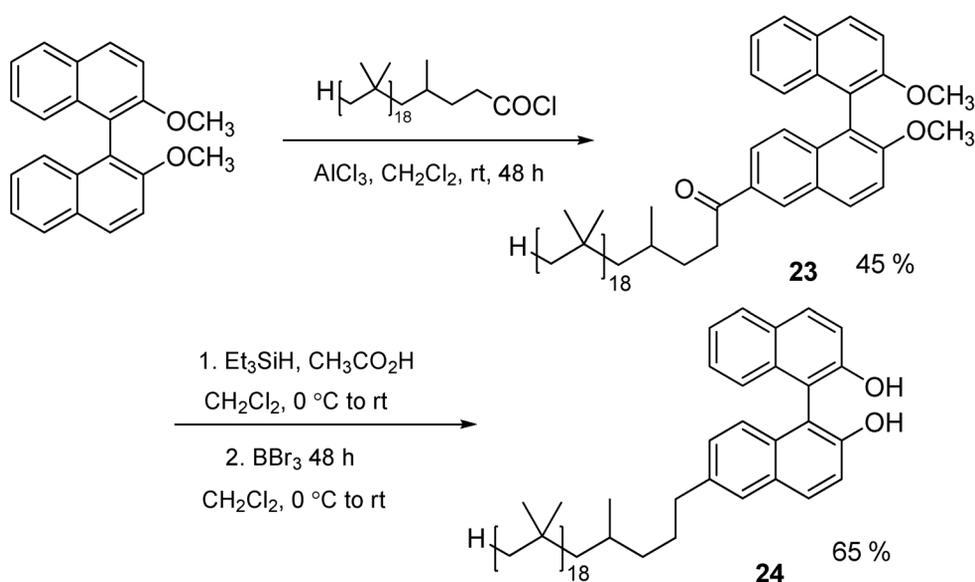
To deal with this issue, we examined Friedel–Crafts polyisobutylation of 2-naphthol. The expectation was that this product could be a precursor to a PIB derivative of BINOL if the PIB derivative of 2-naphthol could be oxidatively coupling to itself. Unfortunately, this reaction too proved unsuccessful even under microwave conditions with a mixture of **1** and **2** in the presence of  $\text{H}_2\text{SO}_4$  (eq. 5).



Successful Friedel–Crafts alkylation of 2-naphthol in the 6 position is known using *tert*-butylchloride and  $\text{AlCl}_3$  [19]. This chemistry was also marginally successful with **5** and 2-naphthol. However, only low yields of the 6-polyisobutyl-2-naphthol product **20** arising from the Friedel–Crafts reaction were observed. These low yields (ca. 15 %) seen at room temperature could not be increased by increasing temperature and reaction times as harsher conditions simply led to formation of larger amounts of 6-*tert*-butyl-2-naphthol. While the product **20** could be separated by hexane extraction from the 6-*tert*-butyl-2-naphthol byproduct, the low yields of the 6-polyisobutyl-2-naphthol would be problematic in any large-scale synthesis of PIB-bound BINOL ligands for catalysis, we did briefly explore the oxidative coupling of the PIB-bound 2-naphthol with itself using  $\text{CuCl}_2$  and benzyl amine to determine if oxidative coupling could afford the desired binaphthol product. This reaction did afford the desired PIB-bound BINOL **21** in moderate yield as shown below.



Because of the low yields in direct functionalization of both BINOL or even of 2-naphthol, we examined an alternative route to PIB derivatives using Friedel–Crafts acylation. It is known that BINOL derivatives undergo  $\text{AlCl}_3$ -mediated Friedel–Crafts acylation and the intermediate acylium ions formed from an acid chloride derivative of an  $-\text{COCl}$ -terminated PIB should not undergo the depolymerization process that appeared to complicate the alkylation reaction [20]. To carry out this process, an acid chloride-terminated PIB derivative was prepared from the acid **13** using  $\text{SOCl}_2$  treatment. This acid chloride was then allowed to react under Friedel–Crafts conditions with the bismethyl ether of BINOL in the presence of  $\text{AlCl}_3$  (Scheme 4). The desired aryl-polyisobutyl ketone **23** was obtained in 45 % yield. Subsequent reduction of ketone and deprotection then afforded the desired PIB-bound BINOL product **24** on a multigram scale. The products of this synthesis were phase-selectively soluble in heptanes. Further development of more direct routes to this class of privileged ligands, especially to chiral variants of these ligands, thus warrants further attention as polyisobutylated versions of catalysts derived from species like **21** or **24** should be recoverable reusable catalysts.



**Scheme 4** Synthesis of a PIB-bound binaphthol via a Friedel–Crafts acylation sequence.

## SUMMARY

The studies described above show that a variety of functional arenes can be coupled to phase-selectively soluble polyisobutyl polymers to prepare ligands or ligand precursors for homogeneous transition-metal catalysts. Complications due to depolymerization of the intermediate carbocations formed from commercially available PIB derivatives can be minimized by modification of the PIB terminal groups. Both Friedel–Crafts alkylation and acylation are suitable reactions for formation of these PIB arene derivatives.

## ACKNOWLEDGMENTS

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