Use of 4-piperidones in one-pot syntheses of novel, high-molecular-weight linear and virtually 100%-hyperbranched polymers†

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4-Piperidone and 4-alkyl piperidones react selectively with aromatic hydrocarbons in a mixture of trifluoromethanesulfonic acid (TFSA) and CH_2Cl_2 to give linear polymers, while *N*-(2-phenethyl)-piperidone undergoes self-polymerization to yield virtually 100%-hyperbranched polymer.

Piperidones and their derivatives are an important class of heterocyclic compounds which are used widely in organic syntheses, manufacture of chemicals, and pharmaceutical drugs.[1,2] Numerous reactions of piperidones involving carbonyl and secondary amine reactive centers have been described. However, there are surprisingly few reports concerning the preparation of aryl-substituted piperidines by acid-catalyzed reactions of piperidones with aromatic compounds.[3]

Recently, it was shown that diaryl piperidines may be prepared in good to excellent yields by the reaction of piperidones with benzene in the presence of trifluoromethanesulfonic acid.[4,5] We have performed calculations of the TFSA-catalyzed reaction of piperidone with biphenyl and found that the high reactivity of the carbonyl group is due to the inductive effect of a protonated heteroatom rather than through-space electrostatic effects.[6] Besides, the results obtained also indicated that the Gibbs free activation energy of the first reaction step (carbinol formation) is higher than that of the second (diaryl derivative), which makes this process potentially applicable for the design of long linear structures.

Therefore, it seemed plausible that piperidones would react with aromatic compounds more nucleophilic than benzene in electrophilic aromatic substitution reactions. One may expect that reactions of piperidones with aromatic compounds capable of disubstitution would lead to the highly regioselective polymer-forming polyhydroxyalkylation. One such compound is 4,4′-diphenoxybenzophenone. High nucleophilicity of the terminal phenyl groups and very low reactivity of phenylene fragments adjacent to the carbonyl make 4,4′-diphenoxybenzophenone a very convenient monomer for Friedel–Crafts polymerizations. Indeed, we have found that stirring an equimolar mixture of 4,4′-diphenoxybenzophenone with 4-piperidone monohydrate hydrochloride in a TFSA medium at room temperature for 4.5 h followed by precipitation into an aqueous solution of K_2CO_3, washing successively with water, and drying, affords a linear, soluble, film-forming, high-molecular-weight polymer **2aA** (Scheme 1, Table 1).

Measurements of inherent viscosity (0.2% solution in NMP, 25 °C) gave a value of 0.24 dL g^{-1}, proton and ^{13}C NMR (Bruker Avance 400, operating at 400.13 and 100 MHz for ^{1}H and ^{13}C, respectively) spectra were well-resolved and the aromatic resonances anticipated for diphenoxybenzophenone and side piperidine groups are all evident.

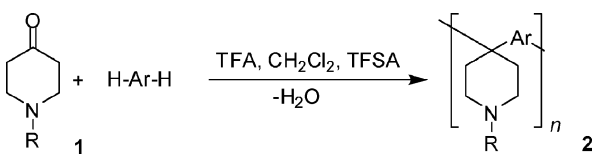
Generally, biphenyl is considered to be a monomer of low reactivity for traditional Friedel–Crafts polymerizations, such as polyacylation or polysulfonations. Despite this, a white, elastic, solid substance was obtained from the polymerization of **1a** with biphenyl. The product obtained was insoluble in common organic solvents; however, the quaternization of **2aB** by methyl iodide in NMP medium at room temperature gave a solution, which indicated formation of a linear polymer.

Polymer **2aB** is readily alkylated with *tert*-butyl bromoacetate in NMP with K_2CO_3 as base at room temperature for 24 h. One can predict that polymer **2aB** would also react with other alkylating reagents.

N-Alkyl piperidones **1b** and **1c** smoothly reacted with biphenyl and terphenyl to yield soluble, high-molecular-weight polymers. The ^{1}H NMR spectra revealed highly selective *para* substitution in the main chain.

Piperidones **1d** and **1e** also reacted with aromatic compounds to give polymers. However, the viscosity of the polymers was not very high. It is very likely that acylation of amino groups leads to the reduction of the nitrogen basicity. It is well known that the oxygen atom, not the nitrogen atom, is the first protonation site in amides; therefore, activation (and reactivity) of carbonyl groups decreases for acylated monomers.

Surprisingly, reaction of **1f** with aromatic hydrocarbons also gave a linear polymer. This monomer contains a phenyl group, which can potentially react with the piperidone carbonyl group in the presence of superacids. One can expect that the increase of aliphatic spacer length between



Scheme 1 Reactions of piperidones with aromatic hydrocarbons.

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Table 1 Polymer-forming reactions of piperidones

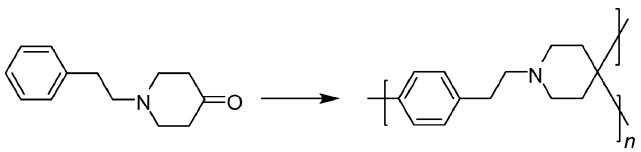
Entry	Piperidone	Hydrocarbon[a]	Polymer[c]	η_{inh}/dl g^{-1}[d]	T_g/°C
1	**1a** (R = H·HCl)	**A** (PhOPC$_6$H$_4$COC$_6$H$_4$OPh)	**2aA**	0.24	187
2	**1a** (R = H·HCl)	**B** (Ph–Ph)	**2aB**	Insol.	Nd
3	**1b** (R = CH_3)	**B** (Ph–Ph)	**2bB**	0.65	167
4	**1c** (R = $CH_2CH_2CH_3$)	**C** (Ph–C$_6$H$_4$–Ph)[b]	**2cB**	0.65	Nd
5	**1d** (R = $COCH_3$)	**A** (PhOPC$_6$H$_4$COC$_6$H$_4$OPh)	**2dA**	0.08	146
6	**1e** (R = $COOCH_2CH_3$)	**A** (PhOPC$_6$H$_4$COC$_6$H$_4$OPh)	**2eA**	0.07	111
7	**1f** (R = CH_2Ph)	**A** (PhOPC$_6$H$_4$COC$_6$H$_4$OPh)	**2fA**	0.21	178
8	**1g** (R = CH_2CH_2Ph)	—	**2g**	0.58	140

[a] **A** = 4,4′-Diphenoxybenzophenone. [b] **C** = *p*-terphenyl. [c] Polymer yield exceeds 95%. [d] NMP, 25 °C. *Conditions*: Entry 1: **1a**, **A** (2.6 mmol), TFSA (2.5 ml), TFA (0.2 ml), 4.5 h. Entry 2: **1a**, **B** (6.87 mmol), TFSA (5 ml), TFA (0.4 ml), CH_2Cl_2 (1.1 ml), 5 h. Entry 3: **1b**, **B** (6.87 mmol), TFSA (5 ml), TFA (0.4 ml), CH_2Cl_2 (1.1 ml), 3 h. Entry 4. **1c**, **C** (2.7 mmol), TFSA (2.5 ml), TFA (0.2 ml), CH_2Cl_2 (1.4 ml), 7 h. Entry 5: **1d**, **A** (2.97 mmol), TFSA (2.5 ml), TFA (0.2 ml), 7 h. Entry 6: **1e**, **A** (2.73 mmol), TFSA (2.5 ml), TFA (0.2 ml), 7 h. Entry 7: **1f**, **A** (2.16 mmol), TFSA (2.5 ml), TFA (0.2 ml), 6 h. Entry 8: **1g** (1.35 mmol), TFSA (1.8 ml), TFA (0.2 ml), 41 h.

the nitrogen atom and the phenyl group would decrease the electron-withdrawing effect of the protonated amino group, which would thereby make the phenyl group more nucleophilic in electrophilic aromatic substitution reactions. If so, a monomer such as *N*-(2-phenethyl)piperidone (which is, in fact, an AB_2 type monomer) should be capable of self-polymerization to give hyperbranched polymers. Hyperbranched polymers are a relatively new class of macromolecules which have gained significant attention from both academia and industry due to their unique chemical and physical properties as well as their potential applications in coatings, additives, drug and gene delivery, macromolecular building blocks, nanotechnology, and supramolecular science.[7–9]

Taking into account recent reports on the preparation of 100%-hyperbranched polymers from superacid-catalyzed polyhydroxyalkylation reactions,[10–15] a hyperbranched polymer with perfect branching should be expected from self-polymerization of *N*-(2-phenethyl)piperidone (Scheme 2). Exploratory reactions were carried out treating **1g** with various quantities of TFSA at room temperature. We have found that stirring of **1g** in a TFSA medium at room temperature for 41 h followed by the precipitation into Na_2CO_3 aqueous solution, washing, and drying gave a white fibrous powder. The product thus obtained was completely soluble in NMP, DMF and DMSO. The precipitation of the reaction solution into water gave a polymer containing amine-triflate complexes in 93% yield. This product, after drying in air, was soluble in methanol. The high solubility of polymer **2g** allowed us to perform reliable spectral studies to delineate its structure.

2D NMR and the ^{13}C NMR spectroscopy with DEPT 135 allowing for differentiation between C, CH, and CH_2 groups turned out to be most informative methods to reveal the characteristic signals from dendritic units, dendritic units adjacent to terminal units, and terminal units themselves (Fig. 1).



Scheme 2 Synthesis of hyperbranched polymer **2g**.

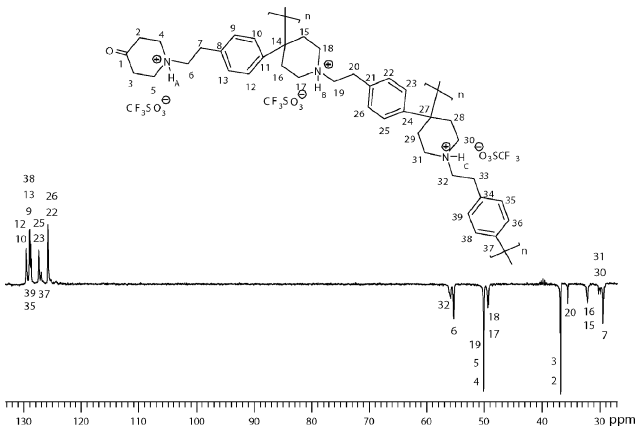


Fig. 1 ^{13}C NMR spectrum with DEPT 135 of polymer **2g** (solution of amine-triflate complex in DMSO-d$_6$).

The resulting hyperbranched polymer was found to contain no linear units. It is noteworthy that only half of the carbonyl groups react with the aromatic rings; the rest of the groups present are located at the terminal units. The presence of the groups was confirmed by ^{13}C NMR and FT-IR spectroscopy. Molecular weights M_w and M_n were found to be 67 719 and 54 490, respectively (SEC-MALS). Although the terminal units are not necessarily located at the periphery of the molecule, the feature of the degree of the branching of 100% could facilitate a more selective functionalization of the periphery. Indeed, **2g** reacted with hydroxylamine quantitatively to give the corresponding oxime. No carbonyl group signals were detected in the IR spectrum of the product. This modification increased the T_g of the polymer from 140 to 190 °C, which is in line with the existing concept of the strong effect of the nature of terminal functional groups of hyperbranched polymers on their thermal behavior.

It is well known that progress in the area of hyperbranched polymers depends on such factors as new synthesis strategies and approaches allowing for synthesis simplification and better structural control. In this respect, self-polymerization of commercially available *N*-phenethyl piperidones presents a promising challenge.

We have demonstrated a novel and facile one-pot procedure for the syntheses of linear, high-molecular-weight aromatic

polymers with side *N*-H, *N*-alkyl- and *N*-alkylaryl piperidines *via* superacid-catalyzed reactions of piperidones with non-activated aromatic hydrocarbons. Although the superacid-catalyzed reactions of piperidones were carried out with only a few hydrocarbons, it is evident that a large variety of aromatics can react with piperidones to give polymers. Besides, piperidones also can be used as coupling agents for different aromatic blocks.

Homopolymerization of *N*-(2-phenethyl)piperidone gave rise to a virtually 100%-hyperbranched polymer with a high T_g. This polymer allows easy and extensive functionalization at the periphery which opens up a number of possibilities, their mechanical and physical properties, and to gain insight into structure–property correlations. It is to be noted that we used commercially available monomer in contrast to tediously synthesized monomers in so far reported hyperbranched syntheses *via* superacid-catalyzed polyhydroxyalkylation.[10–15]

Low-cost and well-defined hyperbranched polymers synthesized with multifunctional terminal groups can offer their interior or peripheral functional groups to covalently fix bioobjects or, depending on their core–shell architecture, to sequester guest molecules.

Novel, highly branched polymeric materials with hybrid architectures (*e.g.*, linear-hyperbranched) might be obtained by combinations of syntheses of linear and hyperbranched piperidone based polymers. Cheaper, commercially available monomers and the promising properties of polymers that might be obtained from them would stimulate interest in that field.

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