

A soluble fluororous phase polymer support

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The synthesis of fluororous phase soluble fluoropolymer supports that readily covalently bind amine-containing reagents and that react with and separate from reagents in aqueous and hydrocarbon solvents is described.

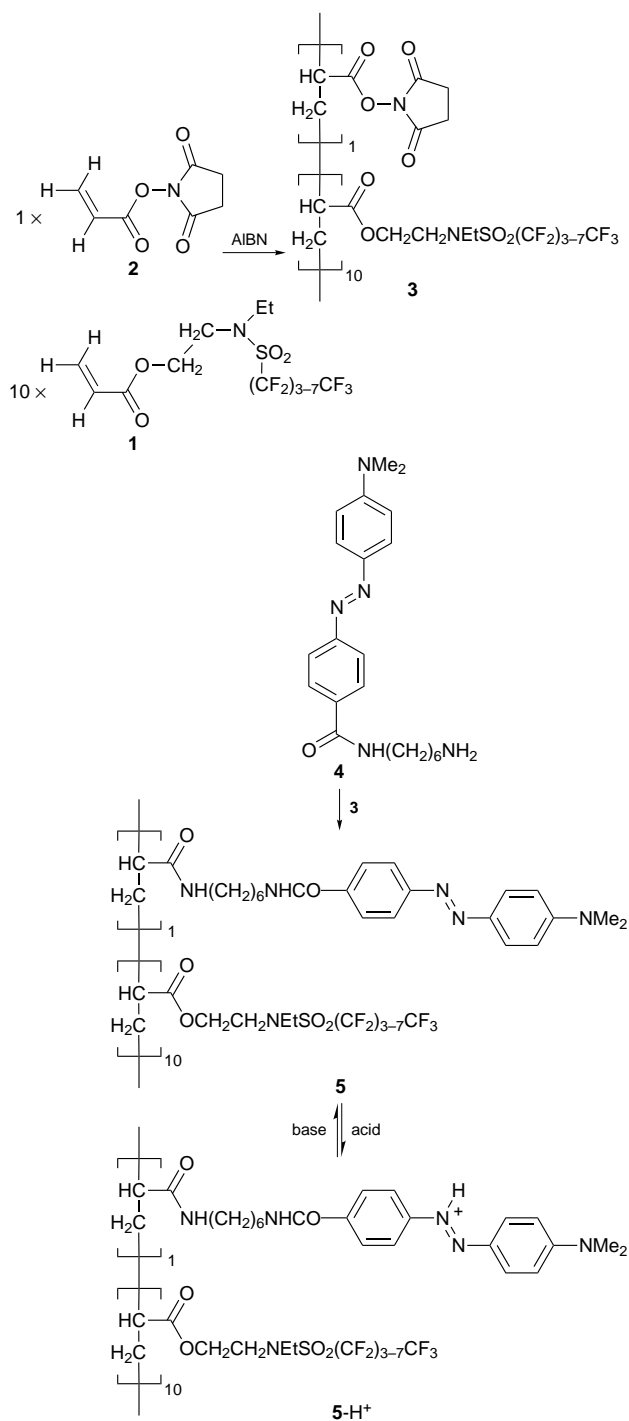
Fluororous phase chemistry is the most recent of several strategies that have been developed to facilitate separation of catalysts or reagents from products or one another.^{1–5} Such separation processes are of increasing interest for environmental reasons and as a basis for the recovery, separation and processing of intermediates or products in synthetic chemistry.^{2,6} As originally described by Horváth,¹ this chemistry consists of essentially three elements; a fluorocarbon solvent, a hydrocarbon solvent and a fluororous tag that renders something fluororous phase soluble. Here we describe an alternative approach to synthesis of fluororous labels. The idea was to prepare a soluble fluorocarbon polymer that has reactive sites that can be used to covalently bind reagents and to render them soluble in the fluororous phase as a polymer-bound reagent.

A soluble polymer support for fluororous phase chemistry has several requirements beyond those generally expected in a polymer support. Such a polymer should be selectively soluble in a fluororous phase as opposed to an aqueous or hydrocarbon solvent phase. It should be easy to attach or remove reagents, catalysts or ligands. Moreover, if a fluoropolymer support were to be practically useful, emulsions formed by shaking a hydrocarbon solution with the fluoropolymer in the fluororous phase should quickly and easily phase separate. Finally, a fluororous phase soluble fluoropolymer supported reagent has to react readily with species in a non-fluorocarbon aqueous or hydrocarbon phase. The preliminary experiments outlined here show that these goals can be achieved with simple fluorocarbon polymers derived from acrylic acid.

To test our ideas, we prepared a fluoropolymer-bound dye as shown in Scheme 1. The requisite fluoropolymer-bound dye is prepared in two steps. First, we prepared a fluoroacrylate–*N*-acryloyloxysuccinimide (NASI) copolymer **3**. The active ester in this copolymer was in turn used to attach an amino-containing *p*-Methyl Red derivative **4** to yield a highly coloured pH-sensitive fluoropolymer-bound dye **5**.

The copolymerization of the fluorinated acrylate **1** and the *N*-acryloyloxysuccinimide **2** was accomplished using AIBN as the initiator in *tert*-butyl alcohol. After 48 h, the copolymer precipitated. After decantation of the remaining reaction solution, any residual monomers in the fluoropolymer were removed by THF extraction. The product was characterized by IR spectroscopy (imide peaks at 1818 and 1788 cm⁻¹, an intense but broad carbonyl peak at 1746 cm⁻¹ and C–F peaks in the 1150–1250 cm⁻¹ region). The absence of vinyl peaks at δ 5.8–6.8 in the ¹H NMR spectrum of the polymer confirmed that there was no monomer in the polymeric product. The polymer's molecular weight was measured by end group titration for samples of the homopolymer of **1** and for 1–NASI copolymers produced using 4,4'-azobis(4-cyanovaleric acid) as the initiator. These *M_n* values were 120 345 and 107 705 Da, respectively. Viscometry was also carried out and the intrinsic viscosity of the 1–NASI copolymer produced with AIBN initiation was 1.56 dl g⁻¹ in Cl₂CFCClF₂ at 29 °C (*K* and *a* values for this polymer are not available) (a structurally similar fluorinated polyacrylate

of reasonably high molecular weight had a reported intrinsic viscosity of 0.25–0.49 dl g⁻¹).⁷



Scheme 1

Derivatization of this active ester-containing polymer with functional amines was carried out in a biphasic reaction mixture. For example, reaction of **3** with the Methyl Red derivative **4** was carried out by dissolving **3** in a fluorocarbon solvent (FC77, 3M Co., a fluorinated cyclic ether, C₈F₁₆O) and vigorously mixing this solution with a THF solution of the amine-containing Methyl Red derivative **4**. The yield in this reaction was high (>90%) based on the observed complete disappearance of the broad CH₂ singlet of the succinimide at δ 2.9. The product copolymer **5** was isolated by simple separation of fluorocarbon phase and removal of the FC77 solvent. The product polymer's IR spectrum showed a complete loss of the active ester imide peaks (confirming the NMR results, *vide supra*) and a new amide carbonyl peak at 1638 cm⁻¹. The loading of Methyl Red on this polymer was estimated to be 0.075×10^{-3} equiv. of Methyl Red per gram of polymer.

The Methyl Red-containing fluoropolymer **5** was not soluble in ordinary organic solvents (THF, alcohols, chloroform, DMSO, toluene) but **5** like **3**, was soluble in fluorinated solvents such as FC77 or PhCF₃.^{8,9} Solutions of **5** or **5**-H⁺ in FC77 were immiscible with water and organic solvents. Separation of this fluoropolymer-bound dye from these solvents appeared visually to be quantitative. A more quantitative estimate of >99.9% of **5** being retained in the fluororous phase was obtained by UV-visible spectroscopy of the THF or water layer, which showed no Methyl Red present in this second phase.

Shaking solutions of **5** in FC77 with THF produces emulsions that separate within 10 min. In the case of mixtures of **5**-FC77 and water, the emulsion of **5**-H⁺-FC77 and water required up to 60 min to separate on standing.

Reaction of the fluoropolymer-bound Methyl Red with aqueous HCl or with HCl that had been added to an immiscible THF phase led to an immediate protonation of the fluoropolymer-bound dye as evidenced by the instantaneous change in the fluororous phase colour from yellow to red. Similarly, addition of a base to the THF or water solution produced a change back to yellow. Bases like NaOH-H₂O or Et₃N in THF were equally effective.

Another advantage of this fluorocarbon polymer support is that the so-called 'Teflon pony-tails' are well insulated from the reacting group. However, it is worth noting that this alone is not sufficient to make ionic chemistry in a fluororous phase

equivalent to that in an aqueous phase. Equilibration of **5** in FC77 with buffer solutions of varying pH and with THF solutions of **4** show that **5** is a weaker base than **4**. We estimate that the pK_a of the fluororous phase Methyl Red **5** is between 1.0 and 1.5 based on the colour change for fluorocarbon solutions of **5** equilibrated with aqueous buffer solutions. This greater than one hundred-fold decrease in the acidity of **4** on covalent binding to **3** is most likely due to decreased solvation of the cation in the fluororous phase.

In summary, vinyl fluoropolymers copolymerize with other vinyl monomers that contain reactive groups to form starting materials for synthesis of polymer-supported reagents that will be fluororous phase soluble. The product polymer-supported species can easily be separated from organic or aqueous solutions but still have excellent reactivity as judged by the fast protonation/deprotonation experiments described here. Continuing work will explore other fluoropolymer supports and exploit this reactivity in catalytic chemistry.

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Footnotes and References

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