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# Novel Trifunctional Building Blocks for Fluorescent Polymers

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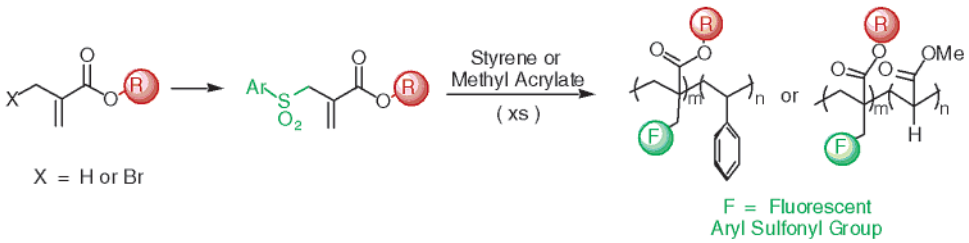
## ABSTRACT

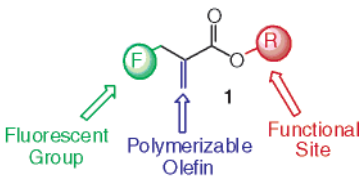



**Herein, we describe the synthesis of fluorescent 2-(arylsulfonyl)methacrylates and its polymers. These novel trifunctional monomers, possessing a fluorescent arylsulfonyl ($ArSO_2$) group, an alkyl group (R), and a polymerizable olefin, serve as useful building blocks for functionalized fluorescent polymers.**

Fluorescent probes have played an important role in the elucidation of physical properties of polymers.[1,2] The introduction of the fluorescent probe can be achieved either by incorporating the probe in a polymerizable monomer or by uptake following polymerization, either by physical absorption or covalent attachment. We are developing general strategies for the introduction of fluorescent diagnostics in molecularly imprinted network polymers (MIPs). An important goal of this strategy is to locate the probe in proximity to the MIP binding site.

An application of these MIPs would be as chemical sensors, where the fluorescent probe would serve as a transducer for the binding event.[3] In two recent examples, the fluorescent molecule was incorporated into the polymer matrix[4] or the binding site[5] by a polymerizable fluorescent probe. In both of these approaches, however, considerable background fluorescence was observed as a result of the noncovalent interaction between the fluorescent monomer and the template. This resulted in significant *nonspecific* fluorescence not associated with analyte binding. A key design element to a successful MIP fluorescent sensor is to locate the fluorescent probe *only* at the binding site.

To that goal, we have designed a new family of polymerizable *trifunctional* monomers **1** that contain a polymerizable double bond, a functional group to covalently bind the imprint molecule (R), and a fluorescent probe (F) fragment. Covalent linking of probe (F) and template (R) would achieve proximity of the diagnostic *only* at the binding site. The monomers described in this report are compatible with radical copolymerizations, and the imprint molecule (R) can be cleaved following incorporation into a suitable polymer.




We chose aryl sulfonyl groups such as 5-(dimethylamino)-1-naphthalenesulfonyl (dansyl), 2-anthracenesulfonyl, and 1-pyrensulfonyl as the fluorescent moieties because of the

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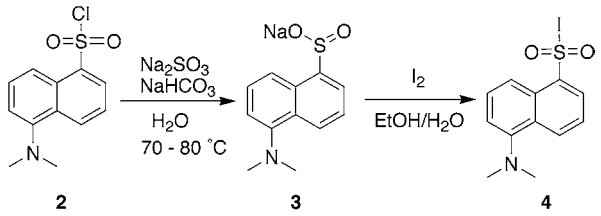
ready availability of their sulfonyl chloride derivatives and their application as microenvironment diagnostics in polymer systems.[6,7]

Monomers bearing the dansyl group[8,9] were synthesized by a modified procedure based on the work of Najera et al.[10,11] Dansyl iodide (**4**) was synthesized from the chloride (**2**) by a $Na_2SO_3$/$NaHCO_3$ reduction,[12] followed by an iodine oxidation[13] in 70% overall yield (Scheme 1). This conversion

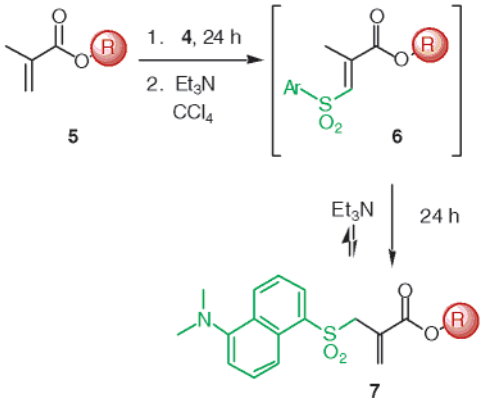
**Scheme 1**




to the iodide was necessary because the subsequent halosulfonylation of methacrylates does not proceed with sulfonyl chlorides.

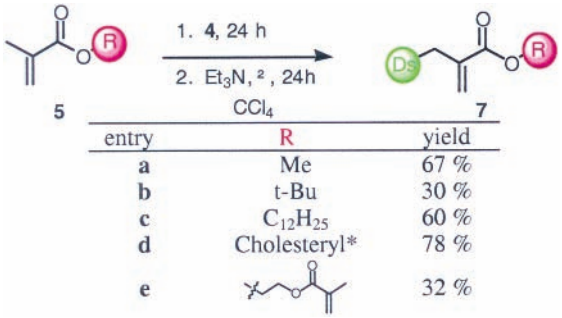
Condensation of dansyl iodide (**4**) with methacrylate **5** was achieved in a one-pot procedure by the addition of triethylamine. The reaction involves a tandem iodosulfonylation−dehydroiodination to afford the vinylic sulfone **6**, which is equilibrated to the thermodynamically more stable allylic sulfone **7** under reflux in the presence of base (Scheme 2).

**Scheme 2**




This methodology was applicable for the conversion of methacrylates **5a**−**e** to the corresponding (2-dansyl)-methacrylates **7a**−**e** (Table 1). The reaction proceeded in moderate 60−78% yields for most R groups. The fluorescent

**Table 1.** Synthesis of Monomers **7**

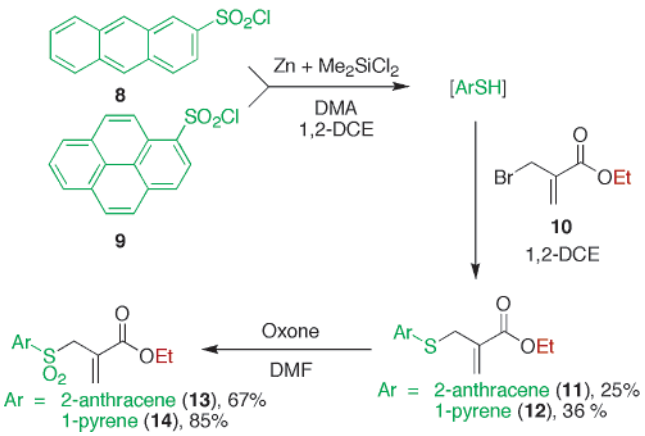



| entry | R | yield |
|---|---|---|
| a | Me | 67 % |
| b | t-Bu | 30 % |
| c | $C_{12}H_{25}$ | 60 % |
| d | Cholesteryl* | 78 % |
| e |  | 32 % |

probe could also be incorporated into the cross-linking monomer, ethylene glycol dimethacrylate (EGDMA), and bulky functional monomer, *tert*-butyl methacrylate, albeit in modest yield (30−32%).

Fluorescent monomers bearing a 2-anthracenesulfonyl or 1-pyrenesulfonyl group were targeted next. However, the conversion of commercially available anthracenesulfonyl chloride (**8**) and pyrenesulfonyl chloride (**9**) to the corresponding iodides was not successful because of the insolubility of the arylsodium sulfinate intermediates. To overcome this difficulty, 2-anthracenesulfonyl chloride (**8**) and 1-pyrenesulfonyl chloride (**9**) were reduced to the corresponding aryl thiols under anhydrous conditions using dichlordimethylsilane, zinc, and dimethylacetamide (Scheme 3).[14] In situ

**Scheme 3**




addition of 2-bromomethacrylate **10** to the reaction mixture gave the aryl sulfides **11** and **12** in 25−36% overall yield.


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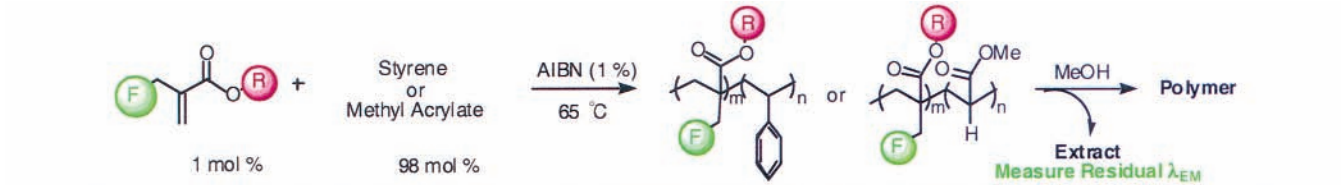
**Table 2:** Synthesis and Analysis of Polymers Derived from Fluorescent Monomers **7d**, **13**, and **14**




| polymer | fluorescent monomer | fluorescent probe | R group | co-monomer | yield | $M_w$[a] | $M_n$[a] | PDI[a] | % probe incorporation[b] |
|---|---|---|---|---|---|---|---|---|---|
| **P1** | **7d** | Dansyl | Cholesteryl | Styrene | 83% | 70k | 30k | 2.3 | 99% |
| **P2** | **13** | Anthracene Sulfonyl | Ethyl | Styrene | 99% | *c* | *c* | *c* | >99% |
| **P3** | **14** | Pyrene Sulfonyl | Ethyl | Styrene | 99% | 168k | 44k | 3.8 | >99% |
| **P4** | **7d** | Dansyl | Cholesteryl | Methyl Acrylate | 87% | 64k | 34k | 1.9 | 80% |
| **P5** | **13** | Anthracene Sulfonyl | Ethyl | Methyl Acrylate | 91% | 88k[d] | 34k[d] | 2.6[d] | >99% |
| **P6** | **14** | Pyrene Sulfonyl | Ethyl | Methyl Acrylate | 84% | 103k | 41k | 2.5 | 77% |
| **P7** | – | – | – | Styrene | quant. | 145k | 49k | 3.0 | – |
| **P8** | – | – | – | Methyl Acrylate | quant. | 128k | 49k | 2.6 | – |

[a] Determined by GPC analysis (THF, 35 °C, polystyrene standard). [b] Calculated from residual fluorescence of the MeOH extraction of the polymers. [c] Molecular weight could not be determined because of the insolubility of the polymer. [d] Determined for the soluble portion of the polymer (~5%). Remaining portion of the polymer was insoluble and its molecular weight could not be determined.

Although low yielding, this methodology offers a rapid one-pot procedure for attaching the pyrene and anthracene moieties to methacrylates. The sulfides can subsequently be oxidized to the desired sulfones **13** and **14** using oxone in good yield.

2-Substituted methacrylates have been successfully homopolymerized.[15−18] Template loading in molecularly imprinted polymers, however, is typically 1−2%. For diagnostic applications, loadings can be substantially less. Therefore, to demonstrate the efficacy of these fluorescent molecules as reactive polymerizable monomers, one monomer from each fluorescent derivative, dansyl (**7d**), 2-anthracenesulfonyl (**13**) and 1-pyrenesulfonyl (**14**) was copolymerized with an excess of styrene or methyl acrylate (Table 2).[19]

The resulting polymers were precipitated with MeOH and analyzed by GPC (THF, 35 °C, polystyrene standard, Table 2). The polymers were high molecular weight (30−168 k), and the PDI ranged from 1.9−3.8. These materials compared well with the molecular weight and PDI of polymers synthesized in the absence of fluorescent monomer, i.e., polystyrene **P7** and polyacrylate **P8**. Two polymers, **P2** and **P5**, which incorporated the 2-anthracenesulfonyl monomer **13**, gave insoluble polymers that swelled in organic solvents. Although the fluorescence spectra of the swollen polymers showed the presence of the anthracene moiety, the peaks were significantly shifted compared to the monomer **13**. This change could have been caused by the polymer microenvironment[8] but could also show evidence of the anthracene group reacting under the thermal, radical polymerization conditions and resulting in a cross-linked polymer. The mechanism for this cross-linking is currently under investigation.

The labeled polymers were analyzed for fluorescent monomer incorporation by measuring the residual fluorescence of the MeOH extracts from the polymer precipitations. This was done from Beer's law plots of the fluorescence emission maxima of monomers **7d**, **13**, and **14** at various concentrations. The plots were then used to determine the residual fluorescence in the MeOH extracts.

All three fluorescent monomers were incorporated quantitatively (>99%) into the polystyrenes (**P1**−**P3**, Table 2). These results agreed with the comparable reactivity ratios found for styrene ($r_1 = 0.52$) with methacrylate ($r_2 = 0.46$).[20]

As for the polyacrylates, the dansyl and 1-pyrenesulfonyl derivatives were found to be incorporated at 80% and 77% within the polymers **P4** and **P6**, respectively. This lower incorporation agrees with the *mismatched* reactivity ratios of methacrylates ($r_1 = 1.91$) with acrylates ($r_2 = 0.50$).[20] The anthracenesulfonyl monomer **13** seemed to be an exception, proving to be very reactive with methyl acrylate and giving more than 99% incorporation in polymer **P5**. This higher reactivity may be due to the reactivity of the anthracene group under the free radical polymerization conditions, giving a cross-linked polymer (vide supra).

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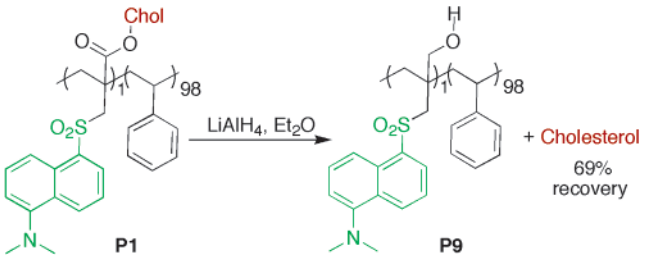
(19) The monomers **7d**, **13**, and **14** were copolymerized at 1 mol %. The polymers were initiated thermally (65 °C) by AIBN (1 mol %). Styrene polymerizations were carried out neat. Acrylate polymerizations required solvent (1:1, $CH_3CN/CHCl_3$) for solubility of the fluorescent monomers in the reaction mixture.
(20) Reactivity ratios calculated from Alfrey-Price Q-e values at 60 °C. See Allcock, H. R.; Lampe, F. W. In *Contemporary Polymer Chemistry*; Prentice Hall: Englewood Cliffs, 1990; pp 309−311.

Finally, the use of these labeled functional monomers in imprinted polymers requires the template molecule to be selectively cleaved after polymerization without loss of fluorescence. This can be performed in the styrene polymers, as the ester moiety is only present at the functional site. The ester group can be cleaved from the polymer under a variety of conditions.[21] We chose to reductively cleave the template with $LiAlH_4$,[22] which removed the cholesterol group from the polymer **P1**, leaving the fluorescent dansyl group in tact. The resulting polymer **P9** showed the same fluorescent properties as **P1**, and 69% of the theoretical amount of cholesterol present in polymer **P1** was recovered (Scheme 4).

**Scheme 4**




In conclusion, the methodologies described above offer convenient syntheses of trifunctional monomers where the incorporation of a fluorescent diagnostic at a MIP binding site is necessary. We are currently incorporating these monomers in cross-linked imprinted polymers and analyzing their ability to behave as chemosensors for steroids and marine toxins. In addition to various MIPs, these monomers can also be incorporated into other functionalized polymers where a fluorescent probe (F) and an amenable functional group (R) are required in a polymerizable monomer. For styrene-based polymers, the R group can be successfully cleaved under reducing conditions.

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**Supporting Information Available:** Experimental procedures and characterization data for all compounds; experimental procedures for the synthesis and analysis of all fluorescent polymers is also available. This material is available free of charge via the Internet at http://pubs.acs.org.

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