Sulfuryl-Based Click Chemistry | Hot Paper

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SuFEx-Based Synthesis of Polysulfates**

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Abstract: *High-molecular-weight polysulfates are readily formed from aromatic bis(silyl ethers) and bis(fluorosulfates) in the presence of a base catalyst. The reaction is fast and proceeds well under neat conditions or in solvents, such as dimethyl formamide or N-methylpyrrolidone, to provide the desired polymers in nearly quantitative yield. These polymers are more resistant to chemical degradation than their polycarbonate analogues and exhibit excellent mechanical, optical, and oxygen-barrier properties.*

A handful of high-fidelity reactions are at the core of industrial processes producing polymers in multimillion ton quantities. Most commodity polymers are synthesized from olefins by forming carbon–carbon backbones, whereas engineering polymers are commonly prepared through condensation reactions of monomers that often contain an activated carbonyl group or its equivalent and a suitable nucleophile, thus forming carbon–heteroatom linkages. Polyesters, polyamides, polyurethanes, and polyimides are produced in this manner. Despite the variety of backbone structures, polymers containing sulfur(VI) ("-SO_2-") connectors are virtually absent from the literature and are barely used in industrial applications (with the exception of polysulfones, in which the sulfone group is already present in the monomers).[1]

Unsurprisingly, most reported attempts to synthesize sulfur(VI)-containing polymers relied on reactions mimicking carbonyl-group-based condensations, that is, reactions of sulfonyl chlorides with nucleophiles,[2] and, to a much lesser extent, Friedel–Crafts sulfonylations.[3] Although polymers obtained by those methods can have attractive properties, such as good thermal and hydrolytic stability and mechanical resilience,[2c–e] the unselective reactivity of sulfur(VI) chlorides, which are susceptible to hydrolysis and participate in redox transformations and radical chlorinations, significantly limits the utility of these methods and materials.

Sulfur(VI) fluorides, in particular sulfuryl fluoride (SO_2F_2) and its monofluorinated derivatives, sulfonyl fluorides (RSO_2–F), sulfamoyl fluorides (R_2NSO_2–F), and fluorosulfates ($ROSO_2$–F), stand in stark contrast to other sulfur(VI) halides. These sulfur oxofluorides are much more hydrolytically stable, redox-silent, and do not act as halogenating agents. Nevertheless, their selective reactivity can be revealed when an appropriate nucleophile is present under conditions in which fluoride ejection is assisted by the solvent, the pH value, or an additive. These parameters define conditions under which sulfur(VI) fluoride exchange (SuFEx) reactivity achieves click chemistry status.[4] The formation of sulfur(VI)–heteroatom bonds is described in detail in an accompanying article in this issue.[5]

In the early 1970s, Firth pioneered the synthesis of poly(aryl sulfate) polymers from fluorosulfates of bisphenol A (BPA), which he obtained from SO_2F_2 and disodium salts of the bisphenol.[6] Preparation of these monomers required prolonged heating, and the high polymer was obtained in its pure form only after repeated precipitation. Herein, we report a simple and straightforward SuFEx-based method for the synthesis of high-molecular-weight polysulfate polymers from aryl fluorosulfates and aryl silyl ethers under simple and mild reaction conditions.

Reactions of silylated and fluorinated compounds are, of course, well known in organic synthesis[7] and in polymer chemistry.[8] For example, in 1983, Kricheldorf et al. introduced the "silyl method" for the synthesis of poly(aryl ethers) taking advantage of the strength of the Si–F bond and the innocuous nature of the silyl fluoride byproducts.[9] In 2008, Gembus and co-workers demonstrated that sulfonyl fluorides react with silyl ethers in the presence of a catalytic amount of 1,8-diazabicyclo[5.4.0]undec-7-ene [DBU; Eq. (1)], producing aryl sulfonates.[10] We in turn found that fluorosulfates react with aryl silyl ethers under similar conditions to form diorganosulfates [Eq. (2)].

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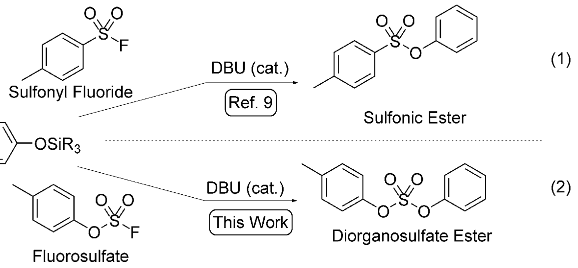
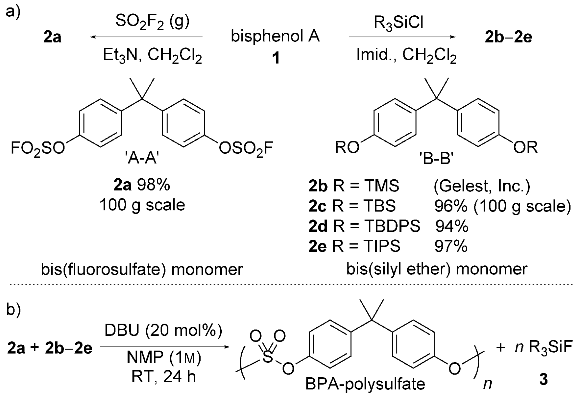


This "sulfate click reaction" is extremely efficient, and when bis(aryl fluorosulfates) **2a** and bis(aryl silyl ethers) **2b–e** are used, high-molecular-weight polymers are produced in nearly quantitative yield (Scheme 1). The reaction is catalyzed by organic bases, such as DBU or 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diaza-phosphorine (BEMP),[11] or fluoride salts, such as cesium fluoride. This transformation provides the desired products in essentially quantitative yields, it is compatible with many functional groups and does not require special equipment or precautions. The low exothermicity of this reaction facilitates scaling up, as described below.



	Yield	M_n (Da)	Dispersity	Byproduct
2a + 2b	95%	30900	1.6	**3b** (Me_3SiF)
2a + 2c	90%	24600	1.4	**3c** ($tBuMe_2SiF$)

Scheme 1. a) Preparation of fluorosulfate and silyl ether monomers from bisphenol A. b) Synthesis of polysulfates. M_n values determined in reference to polystyrene standards (by GPC). TBDPS = *tert*-butyldiphenylsilyl, TBS = *tert*-butyldimethylsilyl, TIPS = triisopropylsilyl, TMS = trimethylsilyl.

Both the fluorosulfate and the silyl ether monomers were readily obtained from BPA (Scheme 1a). Its treatment with SO_2F_2 gas in the presence of triethylamine generated bis(fluorosulfate) **2a**, which was isolated as a shelf-stable white crystalline solid in high yield on mole scale after a simple work-up that did not require chromatographic purification. The bis(silyl ether) monomers **2b–e** are either commercially available (**2b**) or were easily prepared on large scale following standard procedures (**2c–e**).

The initial examination of the reaction between monomers **2a** and **2b** in different solvents (1 M in monomers) in the presence of DBU (20 mol%) identified *N*-methylpyrrolidone (NMP) and dimethylformamide (DMF) as the optimal solvents for the preparation of polysulfates (Scheme 1b). Following precipitation with methanol, BPA-polysulfate (BPA-PS) was recovered as white powder in 95% yield ($M_n = 30900$ Da, referenced to polystyrene standards; see the Supporting Information for details). The results were similar when the TBS monomer **2c** was used ($M_n = 24600$ Da); in the latter case, liquid *tert*-butylfluorodimethylsilane (**3c**, TBSF) was generated as a byproduct, which was removed by distillation.

An investigation of different catalysts[12] revealed that compounds containing amidine, guanidine, or phosphazene moieties were active, along with fluoride [introduced through the organic fluoride source tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) or the inorganic fluoride source cesium fluoride] and potassium *tert*-butoxide (*t*BuOK). Preliminary investigations point at the involvement of hypervalent silicon intermediates, which can be formed by activation of the silyl ethers, either directly with a basic catalyst or with bifluoride $[HF_2]^-$ released from the fluorosulfate group and adventitious water. Activation of fluorosulfates with DBU, in a similar fashion to the reported interactions of sulfonyl fluorides with DBU,[13] may also provide $[HF_2]^-$. Catalytic amounts of *t*BuOK and fluoride salts gave polysulfates only with TBS monomer **2c**, suggesting that the greater stability of the TBS ethers under basic conditions[14] was critical for efficient polymerization.

The molecular weight of the polymers was proportional to the monomer concentration. Thus, polymerization of **2a** and **2b** under solvent-free conditions at 150 °C produced the polysulfates of the highest molecular weight, with decreasing M_n values as monomer concentrations were lowered.[15] At the same time, larger amounts of cyclic side products were observed under more dilute conditions. These trends mirror earlier findings for the synthesis of BPA-polycarbonate (BPA-PC).[16] Other catalysts examined under the solvent-free ("bulk") conditions included BEMP, CsF, and *t*BuOK. Similarly to the results described above, both BEMP and CsF provided polysulfates with greater M_n values than DBU. However, *t*BuOK was ineffective under the bulk conditions.

Further investigations showed that the molecular weight of the polymers depended on the nature of the catalyst, its loading, and the nature of the silyl group (Table 1 and Figure 1). The TBS monomer **2c** consistently produced the largest polymers, with M_n values surpassing 100000 Da when BEMP was used as the catalyst (Table 1, entries 4–6). DBU generally resulted in polymers of less than 70000 Da and was ineffective at low loadings (see entries 4 and 7). The M_n values of polymers obtained from the TMS monomer **2b**, in contrast to the TBS analogue, did not exceed 40000 Da regardless of the polymerization conditions. TBDPS (**2d**) and TIPS (**2e**) BPA ethers also successfully polymerized in the bulk and produced polysulfates of variable M_n values (entries 11 and 13), although higher loadings of the BEMP catalyst were required (entry 10 vs. 11). Thus, bis-TBS ether **2c** has emerged as the "Goldilocks" monomer, yielding large polymers using low catalyst loadings. Finally, several samples were subjected to multi-angle light scattering (MALS) analysis for absolute-molecular-weight determination. As

Table 1: Comparison of solvent-free polymerization conditions.[a]

Entry	Monomers	Cat. (mol%)	M_n^{MALS}	M_n^{PS}	Dispersity
1 (A)	**2a** and **2b**	BEMP (1)	2500	17000	1.2
2		BEMP (10)	8800	34000	1.4
3 (B)		DBU (20)	10600	38000	1.5
4 (D)	**2a** and **2c**	BEMP (1)	58000	120000	1.8
5		BEMP (10)	n.d.	128000	1.6
6		BEMP (20	n.d.	143000	1.5
7		DBU (1)	no polymer formation		
8 (C)		DBU (20)	19600	66000	1.5
9		CsF (20)	38300	93000	1.7
10	**2a** and **2d**	BEMP (1)	no polymer formation		
11		BEMP (10)	n.d.	118000	1.5
12	**2a** and **2e**	BEMP (1)	no polymer formation		
13		BEMP (10)	n.d.	51400	2.0

[a] Polymerization conditions: no solvent, 150°C, 2 h. Workup: dissolution in DMF followed by subsequent precipitation from methanol. GPC traces of selected polymers (A–D) are shown in Figure 1. M_n^{MALS} values determined by multi-angle light scattering. M_n^{PS} values in reference to polystyrene standards. n.d. = not determined.

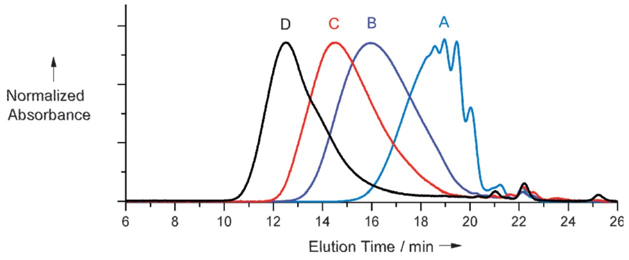


Figure 1. GPC (UV detector) traces to accompany Table 1.

was also the case for BPA-polycarbonates,[16b] polystyrene standards significantly overestimated the molecular weights of the BPA-polysulfates. This was especially noticeable for lower polymers (entries 1–3), with the error being reduced to approximately twofold for high polymers (cf. entries 4 and 9).

The bulk polymerization of **2a** and **2c** was scaled up to 0.5 mol. The reaction was performed at 120°C (internal temperature, 135°C oil bath temperature) for two hours using BEMP (1 mol%) as the catalyst. No significant elevation of the internal temperature was observed during the course of the reaction. BPA-PS with $M_n = 58000$ Da (MALS) was obtained in quantitative yield (145 g). The polymer was mildly soluble in a wide range of organic solvents, including chloroform, dichloromethane, and acetone, whereas the best solubility was observed in DMSO and DMF (ca. 1 g per 2 mL of DMF, with heating). BPA-PS was much more resistant to hydrolytic degradation than its polycarbonate analogue: Treating polysulfate with sodium hydroxide (1.3 M, 1:2 EtOH/H_2O) at ambient temperature or with a saturated solution of sodium carbonate at 80°C for 16 hours caused no observable change in M_n, whereas the analogous polycarbonate was completely hydrolyzed to low-molecular-weight materials, as indicated by gel-permeation chromatography (GPC; Figure 2).

Differential scanning calorimetry (DSC) analysis demonstrated that $T_{g,\infty}$, the temperature at which the glass transition is unaffected by an increase in molecular weight, was reached when the M_n value approached approximately 20000 Da (Figure 3).

T_g was in the range of 95 to 100°C for high-molecular-weight polymers. No crystalline melting or crystallization peaks were identified, indicating that synthesized BPA-PS was amorphous. TGA analysis showed the excellent thermal stability of the BPA-polysulfates.[17] The thermal decomposition temperature increased only slightly with M_n, but in all cases, a weight loss of 5% occurred at approximately 350°C or higher. These results are in good agreement with the data obtained by Firth.[6b]

Samples for physical and mechanical analyses were produced by pelletization and compression molding of the polymer synthesized using bulk polymerization conditions. When pressed thin, transparent and flexible, yet stiff films were obtained. Pristine thin films were used for gas permeability measurements (Figure 4). Thicker samples, like those used for tensile measurements, had an opaque tan color.

Density, tensile properties, and oxygen permeability were measured and compared to those of polycarbonate (commercially available as Lexan). As summarized in Table 2, BPA-PS was slightly more dense, had a higher tensile modulus, and a similar yield stress when compared with BPA-PC. These tensile properties, although not optimal because of compres-

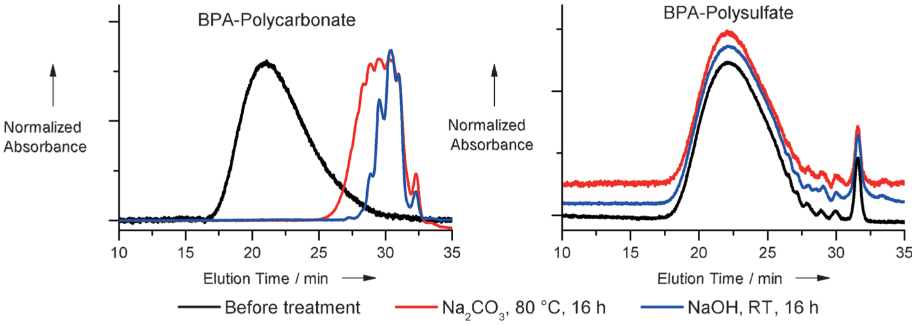


Figure 2. Hydrolytic stability of polysulfate compared to that of polycarbonate (as judged by GPC analysis).

Table 2: Average measured properties of BPA-polysulfate and BPA-polycarbonate (Lexan).

Polymer	d [g cm^{-3}]	Oxygen permeability (Barrer)	Tensile modulus (GPa)	Yield stress (MPa)
BPA-PS	1.310	0.24	2.0	50
BPA-PC	1.210	1.4	1.7	51

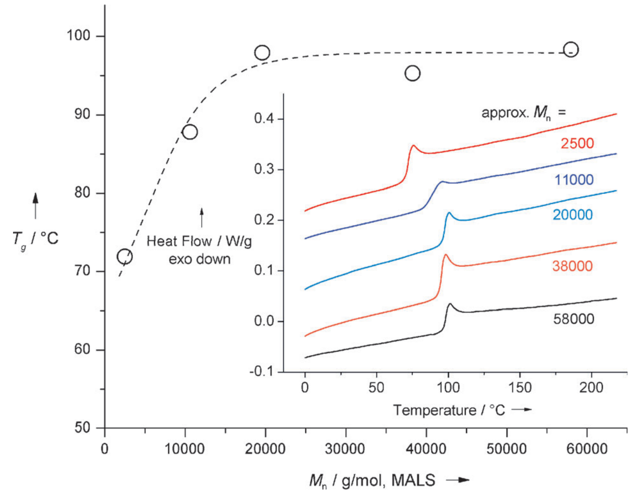


Figure 3. Relationship between T_g and M_n for representative BPA polysulfates. The inset provides DSC second heating thermograms. Line provided to guide the eye.

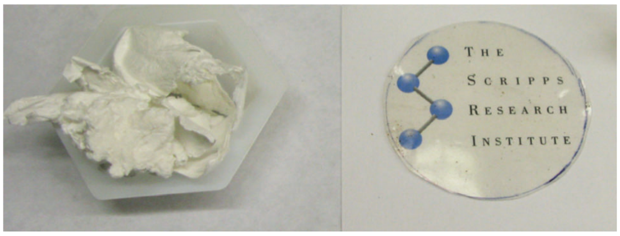


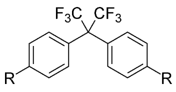
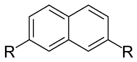
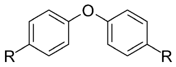
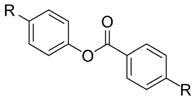
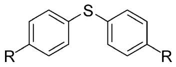
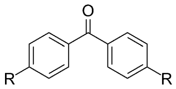
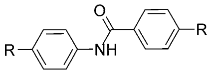
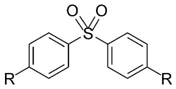
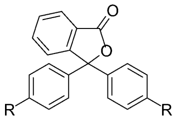
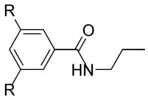
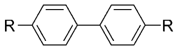
Figure 4. Left: precipitated, unprocessed BPA-polysulfate. Right: compression-molded BPA-polysulfate film.

sion-molded samples, provide a preliminary, relative comparison to the well-established structural analogue BPA-PC. Importantly, polysulfate exhibited the uncommon ductile, yet rigid mechanical behavior similar to polycarbonate. The oxygen permeability of BPA-PS was significantly lower than that of BPA-PC, suggesting that BPA-PS has a smaller free volume at room temperature.

Finally, the compatibility of the polymerization reaction with different functional groups was examined. Monomers **4**–**13** were prepared as described above and included bisphenol **AF** (**4a**/**4b**), naphthalene (**5a**/**5b**), ether (**6a**/**6c**), ester (**9a**/**9c** and **12c**), sulfide (**8a**/**8c**), ketone (**9a**/**9c**), amide (**10a**/**10c** and **13c**), and sulfone (**11a**/**11c**) derivatives. The selectivity of the reaction was demonstrated by the successful formation of co-polysulfates containing technologically useful blocks found in other engineering polymers. The polymerizations were conducted at room temperature in NMP (1 M) with 20 mol% of DBU for 48 hours. As Table 3 illustrates, a variety of homopolymers and BPA copolymers were obtained, demonstrating the compatibility of the SuFEx reaction with different functional groups.

Among BPA-copolymers of similar structure, the polymer molecular weight was sensitive to the electronic properties of the silyl monomer: Lower polymers were obtained when either electron-donating (entry 5 vs. 6, entry 11 vs. 12) or -withdrawing (entry 8 vs. 9, entry 14 vs. 15) groups were

Table 3: Preparation of polysulfate copoloymers.[a]

	Structure	Monomers		M_n^{PS}	Dispersity
1		R = OSO_2F (**4a**) R = OTMS (**4b**)			
2			**4a** + **4b**	46100	1.5
			4a + **2b**	36000	1.4
3		R = OSO_2F (**5a**) R = OTMS (**5b**)	**5a** + **5b**	52000[b]	1.6
4		R = OSO_2F (**6a**) R = OTBS (**6c**)	**6a** + **6c**	58700	1.4
5			**6a** + **2c**	67100	1.4
6			**2a** + **6c**	46600	1.4
7		R = OSO_2F (**7a**) R = OTBS (**7c**)	**7a** + **7c**	34700	1.5
8			**7a** + **2c**	37200	1.5
9			**2a** + **7c**	30600	1.5
10		R = OSO_2F (**8a**) R = OTBS (**8c**)	**8a** + **8c**	80100	1.4
11			**8a** + **2c**	52500	1.5
12			**2a** + **8c**	36900	1.4
13		R = OSO_2F (**9a**) R = OTBS (**9c**)	**9a** + **9c**	34100[c]	1.6
14			**9a** + **2c**	41100	1.6
15			**2a** + **9c**	21800[d]	1.4
16		R = OSO_2F (**10a**) R = OTBS (**10c**)	**10a** + **10c**	81100	1.4
17			**10a** + **2c**	48700	1.3
18			**2a** + **10c**	75400	1.4
19		R = OSO_2F (**11a**) R = OTBS (**11c**)	**11a** + **11c**	22100[d]	1.3
20			**11a** + **2c**	24800	1.3
21		R = OTBS (**12c**)	**2a** + **12c**	53000	1.5
22		R = OTBS (**13c**)	**2a** + **13c**	43900	1.4
23		R = SO_2F (**14**)	**14** + **2c**	46500	1.3

[a] Polymerization conditions: DBU (20 mol%), NMP (1 M), RT, 24 h. Material isolated by precipitation from methanol and analyzed by GPC. M_n^{PS} values in reference to polystyrene standards. [b] Polymerization performed at 80 °C. [c] Increasing the temperature to 100 °C gave an M_n value of 46100 Da, 1.5 PDI. [d] Oligomeric product. [e] Increasing the temperature to 100 °C gave a polymer with M_n = 43200 Da, dispersity 1.4.

introduced. Polymers were also obtained from bis(sulfonyl fluorides) (entry 23). Monomer **14** was obtained directly from 4,4′-biphenyl bis(sulfonyl chloride) using a saturated aqueous KHF_2 solution in acetonitrile at room temperature.[5]

Aside from providing a practical route to polymers with useful properties, the exceptionally facile synthesis of organosulfates described herein highlights the underappreciated potential of the sulfate connector in organic and materials chemistry as well as the unique reactivity features of sulfur(VI) oxofluorides. This new reaction should find immediate applications across a variety of disciplines. Further investigations of the mechanism of this process and its applications are now underway and will be reported shortly.

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