Synthesis and Investigation of the Nonlinear Optical Properties of Various *p*-Aminophenyl Sulfone Oligomers

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A series of *p*-aminophenyl sulfone oligomers (monomers, dimers, and trimers) was synthesized with the purpose of studying the effect of several consecutive dipolar units on their second-order nonlinear optical (NLO) characteristics. Three classes of oligomers were synthesized, namely with a hexamethylene, dimethylene, or piperidine spacer. The dipole moments of these oligomers and the $\mu\beta_z$ value, as measured by EFISH (electric field induced second harmonic generation), are reported. The results show that these compounds, despite their head-to-tail arrangement, lack the structural features needed to display enhancement of the hyperpolarizability.

Introduction

The synthesis of novel organic polymers for use as nonlinear optical (NLO) materials has received ample attention in recent years, due to the inherent mechanical properties of polymers but also because organic polymers can be tailor-made for specific applications.[1] The required polar asymmetry for the observation of nonlinear second-order effects can be induced by applying an external dc electric field to a polymer film. To obtain more highly active NLO materials, several research groups have investigated the possible cooperative enhancement of NLO monomers when they are all incorporated in a polymer chain in head-to-tail fashion.[2-4] This would result in an efficient enhancement mechanism for $\chi^{(2)}$ at low poling field due to the cooperation of individual molecular dipole contributions in polar polymer chains.

The early work by Levine on poly(γ-benzyl-L-glutamate) showed a substantial enhancement of the average monomer susceptibility by incorporating weak NLO chromophores, in a polymer chain.[5] This increase was attributed to the polymer's large dipole moment due to the rigid α-helix structure. The question remained if this enhancement could also be observed in nonhelical polymers.

In 1988, we reported the synthesis of the first polymer in which all the NLO chromophores α-cyanocinnamate units were aligned in the same direction in the main chain of the polymer.[2] Copolymers with ω-hydroxydodecanoate had to be synthesized to achieve solubility. EFISH measurements (electric field induced second harmonic generation) in solution did show a substantial enhancement of the $\mu\beta_z$ value of the NLO units in the polymer chain over the monomeric units. However, this effect could not be observed in a poled polymer film. This was ascribed to excessive entanglements of the polymer chains in the viscous rubbery state, which would prohibit alignment of the NLO chromophores. Lindsay and co-workers reported the synthesis of a soluble homopolymer with all the NLO units aligned in the main chain, however, no conclusions were drawn on the enhancement of $\chi^{(2)}$ in the polymer film.[4]

In hopes of achieving more conclusive results, Katz and co-workers concentrated on the synthesis of specifically designed piperazine-linked oligomers.[3,6] The measured dipole moments showed a slight enhancement (8-20%) of the dimeric units over the constituent monomers. This enhancement was rationalized on the basis of conformational analysis. In a more recent paper, Katz described the synthesis of linear chromophore dimer using the imine as a difunctional acceptor linkage and showed that the dipole moment was additive.[7]

There is a great need for more information concerning the NLO enhancement in polymeric systems. The purpose of this work is to design and synthesize oligomeric head-to-tail NLO phores and to study the effect of structure on the dipole moment μ and the second-order nonlinear response $\mu\beta_z$ in model systems. The system of choice is the *p*-aminophenyl sulfone unit. The sulfone unit is used as a bifunctional acceptor moiety in the NLO-phore. It has the advantage of resulting in a larger dipole moment than the imine, and has good optical transparency.[8-10] It has previously been used to synthesize soluble main-chain polymers.[11,12] In this work the effect of several linkages

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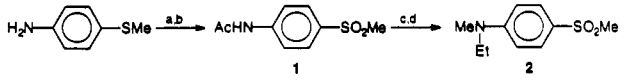
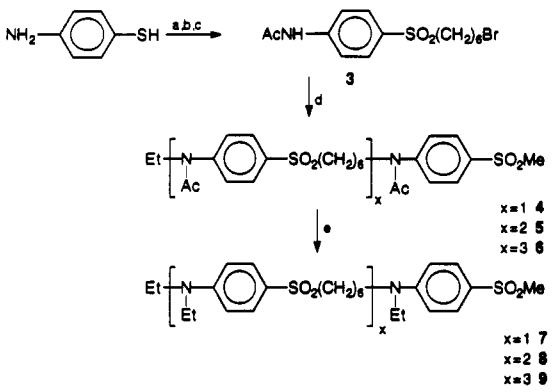
Scheme I[a]



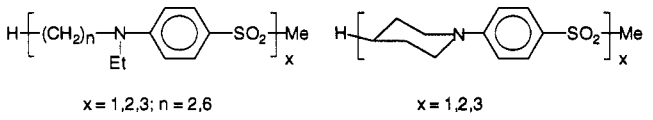
[a] (a) Ac_2O; (b) H_2O_2/AcOH; (c) MeI, KF/Al_2O_3, MeCN; (d) Me_2SBH_3.

Scheme II[a]



[a] (a) Ac_2O; (b) KF/Al_2O_3, $Br(CH_2)_6Br$; (c) H_2O_2/AcOH; (d) EtI, KF/Al_2O_3, 1; (e) $THFBH_3$.

on $\mu\beta_z$ was examined, namely hexamethylene, dimethylene, and piperidine units were used. The monomeric, dimeric, and trimeric units were synthesized and the dipole moment of each was measured, along with the hyperpolarizability by EFISH.



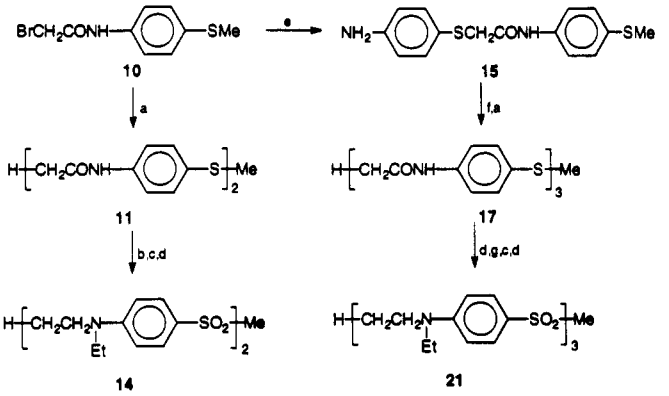
x = 1,2,3; n = 2,6 x = 1,2,3

Results

Synthesis. *Synthesis of the Monomeric NLO Chromophore.* A monomeric NLO chromophore synthesis was designed to allow extension to oligomer synthesis by the formation of consecutive alkyl amine bonds. 4-(Methylmercapto)aniline, protected as the acetamide, was oxidized to the sulfone 1,[13] as shown in Scheme I. The amide was *N*-methylated in mild conditions using 40% potassium fluoride supported on neutral alumina and methyl iodide.[14,15] Monomer **2** was prepared by borane reduction[16] and the overall yield was 60%.

Synthesis of the Oligomers with Hexamethylene Spacers. The syntheses of oligomers with hexamethylene spacers were accomplished using chemistry very similar to the monomer synthesis as shown in Scheme II. *S*-Alkylation of *p*-aminothiophenol with 1,6-dibromohexane, acetylation, and acetic acid/hydrogen peroxide oxidation led to the desired AB monomer **3** in 37% overall yield. The oligomerization of **3** was carried out by adding potassium fluoride reagent to a solution of the monomer; the amide end of the oligomers was capped using ethyl iodide, and compound **1** was used to terminate the alkyl ends of the oligomers, thus adding one additional unit to each. The formation of dimer, trimer and tetramer was observed by TLC. The oligomers **4–6** could be isolated in pure form via column chromatography and were individually reduced with tetrahydrofuran/borane complex to give the desired oligomers **7–9** in reasonable yields.

Scheme III[a]



[a] (a) *p*-AcNHPhSH, NaOMe, MeOH; (b) EtI, KF/Al_2O_3; (c) mCPBA, sulfolane; (d) $THFBH_3$; (e) *p*-NH_2PhSH, NaOMe, MeOH; (f) $BrCH_2COCl$; (g) Ac_2O.

Synthesis of the Oligomers with Dimethylene Spacers. In light of the success of the *N*-alkylation route for the hexamethylene-spaced oligomers, the same chemistry was attempted in the synthesis of the dimethylene spaced oligomers. However, this proved unsuccessful. Instead an *S*-alkylation route had to be used for these dimethylene spaced oligomers, as shown in Scheme III. *p*-(Methylmercapto)aniline was reacted with α-bromoacetyl chloride to form the α-bromoacetamide **10**, while the other half of the dimer was *N*-acetyl-*p*-aminothiophenol. These two halves were coupled using sodium methoxide to give the basic dimer skeleton **11**, which was converted to the desired dimethylene spaced dimer **14** by consecutive *N*-alkylation, oxidation to the sulfone,[17] and reduction of the acetyl functionalities. The yield of the final reduction was only 44%, the major isolated byproduct being *p*-(*N*-ethylamino)phenyl methyl sulfone. Apparently, the sulfone α to the carbonyl was the cause of the degradation of the dimer. This was also a problem in the trimer synthesis. However, the 22% yield of dimer **14** over all six steps was satisfactory.

The dimethylene spaced trimer (Scheme III) was synthesized using a reaction sequence similar to that for the dimer. The amine-terminated dimer **15** was converted to the trimer skeleton in two steps: reaction of **15** with α-bromoacetyl chloride gave a α-bromoamide which was reacted with the sodium salt of *N*-acetyl-*p*-aminothiophenol to give the basic trimer framework **17**. Originally, trimer **21** was synthesized using the same reaction sequence as described for dimer **14**. Unfortunately, the *N*-alkylation and the final borane reduction proceeded in low yields. Knowing that the cleavage was caused by the sulfone group α to the carbonyl, we were able to develop a better alternative. Borane reduction of the amide functionalities in **17** was followed by reprotection of the amine functionalities to form a triamide in excellent yield. This sequence of reactions also eliminated the need for the low-yield *N*-ethylation with the potassium fluoride reagent, and the amide protecting group was a pendant group, thus removing the problem of having the sulfone α to the amide. The sulfide groups in the protected amine were oxidized,

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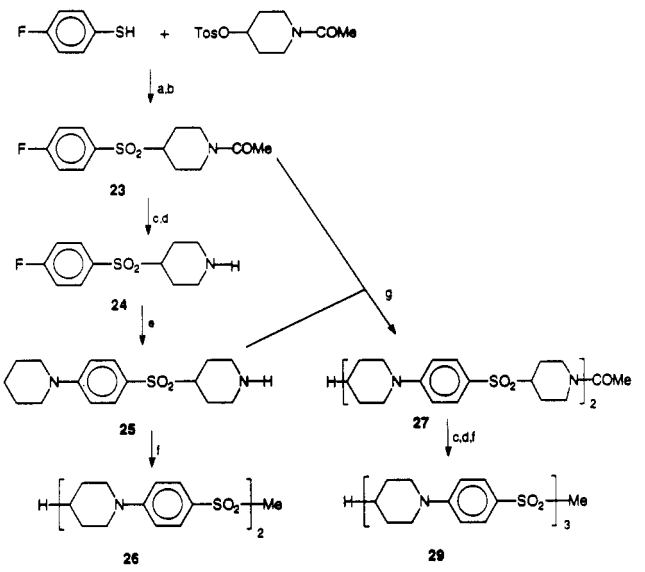
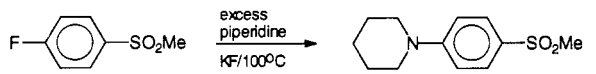
Scheme IV[a]



[a] (a) NaOMe, MeOH; (b) OXONE; (c) HCl(aq); (d) NaOH(aq); (e) excess piperidine; (f) p-FPhSO$_2$Me; (g) KF, DMSO, heat.

followed by reduction of the acetyl functions under standard borane conditions, which led to the desired dimethylene spaced trimer **21** in good yield.

Synthesis of Oligomers with Piperidine Spacers. The piperidine monomer **22** was easily synthesized in one step by heating p-fluorophenyl methyl sulfone in piperidine at 100 °C with potassium fluoride in 89% yield.



22

In a first approach to piperidine oligomers, the AB monomer **24** was made in three steps starting from 4-hydroxypiperidine, which had been acetylated and then converted to its tosylate. *N*-Acetyl-4-(tosyloxy)piperidine was reacted with sodium p-fluorothiophenolate to give 4-(p-fluorophenylmercapto)piperacetamide, which was not isolated but immediately oxidized with OXONE (50% potassium hydrogen persulfate).[18] The AB monomer **24** was then obtained by deprotection of the amine under standard conditions.

Monomer **24** was oligomerized under various conditions. Typically, the monomer was dissolved in a high-boiling polar solvent (DMSO or sulfolane) and heated at various temperatures. Anhydrous KF was always added to absorb the hydrogen fluoride evolved and to act as a catalyst.[19] In all cases, cream-to-tan colored solids were obtained, which were only soluble in trifluoroacetic acid. Attempts to create shorter oligomers by adding piperidine and p-fluorophenyl methyl sulfone still did not yield soluble oligomer. Proton NMR in deuterated trifluoroacetic acid indicated degrees of polymerization of about seven. These studies were abandoned because we could not obtain the lower oligomers soluble in solvents other than trifluoroacetic acid.

Therefore, stepwise syntheses, represented in Scheme IV, were developed for the dimers and trimers. The AB monomer **24** was used to synthesize dimer in two steps. Nucleophilic aromatic substitution of **24** by piperidine at elevated temperatures, which gave a quantitative yield of the piperidine terminated compound **25**, was followed by another nucleophilic aromatic substitution on p-fluorophenyl methyl sulfone. The piperidine spaced dimer **26** was dissolved in acetonitrile and passed through basic alumina to remove unwanted color. The yield over all seven steps was a respectable 33%.

Piperidine trimer **29** was synthesized in similar fashion. The piperidine terminated compound **25** was reacted with its precursor **23** under the usual nucleophilic aromatic substitution conditions to give compound **27** in fair yield. This dimer was deprotected to the free amine and reacted with (p-fluorophenyl)methyl sulfone for another nucleophilic aromatic substitution to give piperidine spaced trimer **29**. The total yield from compound **29** was 25%.

Measurements. *Dipole Moments.* The dipole moments for various NLO chromophores are listed in Table I. The actual and reduced values for the dipole moment based on different theories (see Experimental Section) are listed.

Electric Field Induced Second Harmonic Generation. The EFISH data obtained for the dimethylene- and piperidine-linked p-aminophenyl sulfones are summarized in Table II.

Discussion and Conclusions

Two different synthesis routes to oligomeric p-aminophenyl sulfones were investigated, one by classical stepwise synthesis procedures and one by controlled oligomerization of a monomer and subsequent separation of the oligomeric species by column chromatography. The NLO chromophores with the dimethylene and the piperidine spacers were synthesized in stepwise fashion, while the hexamethylene-spaced NLO chromophores could be most easily obtained by oligomerization.

The dipole moment μ and second-order nonlinearity $\mu\beta_z$ are listed in Tables I and II along with their reduced quantities $\mu_r = \mu/\sqrt{n}$ and $(\mu\beta_z)_r = \mu\beta_z/n$, where n is the number of repeat units. The reduced quantities are included as the macroscopic values for the ensemble and are related to the product of the total number of monomers in the entire ensemble and the reduced quantity, regardless of the degree of polymerization. For example, the nonlinear susceptibility is related to the reduced nonlinear response by $\chi^{(2)} \propto N_m(\mu\beta_z)_r$, where N_m is the monomer concentration. Another way of viewing this is that, while a polymer may have a larger value for $\mu\beta_z$ than that of the monomer, it must be larger than n monomers for there to be an increase in the overall total for the ensemble because the molecular volume of the polymer is larger than that of the monomer.

The dipole moment μ and vector component of the hyperpolarizability along the dipole moment β_z of a polymer chain composed of monomer units containing NLO groups are configuration-dependent properties. The relative orientation of the NLO groups within the polymer chain determine whether the dipole moments and hyperpolarizabilities of the individual NLO groups add constructively or destructively to produce a large or small net value for the polymer chain as a whole. In the case of freely rotating, freely jointed (uncorrelated) chains, dipole and hyperpolarizability additivity is the same as rudimentary polymer chain statistics, namely μ^2 and $\mu\beta_z$

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Table I. Actual and Reduced Values for the Dipole Moment

compound	μ			μ_r		
	Onsager	Osipov	Guggenheim	Onsager	Osipov	Guggenheim
hexamethylene spacer						
monomer	7.6	7.7	5.4	7.6	7.7	5.4
dimer	10.2	10.4	7.3	7.2	7.4	5.2
trimer	12.3	12.6	8.9	7.1	7.3	5.1
dimethylene spacer						
monomer	7.6	7.7	5.4	7.6	7.7	5.4
dimer	8.6	8.7	6.2	6.1	6.2	4.4
piperidine spacer						
monomer	7.4	7.5	5.3	7.4	7.5	5.3
dimer	10.2	10.4	7.3	7.2	7.3	5.2

Table II. Actual and Reduced Values for the Nonlinear Response

compound	$\mu\beta_z$	$(\mu\beta_z)_r$
dimethylene spacer		
monomer	26	26
dimer	67	34
trimer	92	31
piperidine spacer		
monomer	45	45
dimer	74	37
trimer	173	58

scale as the number of repeat units. In such a polymer, the reduced quantities μ_r and $(\mu\beta_z)_r$ are independent of the degree of polymerization. This should not be surprising in that the monomer dipoles act independently and therefore give the same result as that of n discrete monomers. From this aspect, flexible polymers offer no advantage (or disadvantage) in poled polymer applications. Examples of this type of polymer are the hexamethylene and dimethylene spaced *p*-aminophenyl sulfone oligomers. As predicted, the reduced dipole moments shown in Table I are largely unaffected by the degree of polymerization.

In sharp contrast, polymers in which the relative orientation of the monomer units is rigidly fixed can have dipole moments and hyperpolarizabilities that are larger (or smaller) than that of a single monomer unit. Assuming that the dipole moment and the hyperpolarizability vector are both parallel to the monomer head-to-tail vector, then for the case of dimers and trimers

$$\mu_r^2 = F\mu_m^2, \qquad (\mu\beta_z)_r = F(\mu\beta_z)_m$$

where μ_m and $(\mu\beta_z)_m$ are monomer values and the enhancement factor F is given by

$$F(\text{dimer}) = 1 + \langle\cos\theta_{1,2}\rangle$$

$$F(\text{trimer}) = 1 + {}^4/_3\langle\cos\theta_{1,2}\rangle + {}^2/_3\langle\cos\theta_{1,3}\rangle$$

where θ_{ij} is the angle between monomers i and j. As would be expected, the most advantageous polymer configuration is a rigid rod in which $\theta_{ij} = 0°$, resulting in the maximum value of $F = n$. Interestingly enough, the result for monomer dipoles with a fixed angle of $\theta_{1,2} = 90°$ and no long range correlation, i.e., $\langle\cos\theta_{1,3}\rangle \equiv 0$, is indistinguishable from that of the uncorrelated case, namely, $F \equiv 1$.

The piperidine-linked *p*-aminophenyl sulfones would be expected to display characteristics of rigidly connected oligomers.[3] However, as was the case with the methylene linkages, there appears to be very little dependence of the reduced dipole and nonlinear response on the degree of polymerization. With a rigid spacer, such as piperidine, the carbon–sulfur–carbon bond angle in the sulfone dominates the additivity effect of the dipole moment and hyperpolarizability. Results of MOPAC molecular modeling using an PM3 parametrization show that the sulfone unit introduces an angle of ~100° in the chain. The piperidine linkage is a nearly linear linkage, if we assume that the diequatorial 1,4-substitution on the ring is favored. Therefore, it should not affect the angle between neighboring monomer units. The experimental results for μ and $\mu\beta_z$ are consistent with the theoretical model in that only a small enhancement would be predicted since $\cos\theta_{1,2} \approx 0$ and $\langle\cos\theta_{1,3}\rangle = 0$ due to the unhindered bond rotation about the sulfur–carbon bonds.

In conclusion, we can state that these compounds, despite their head-to-tail arrangement, lack the structural features needed to display enhancement of the hyperpolarizability. This was not too surprising for the hexamethylene- and dimethylene-spaced oligomers, because these spacers are flexible. However, with the rigid piperidine spacers, the expected enhancement of $\mu\beta_z$ was not observed either. This is ascribed to the angle of ~100° introduced by the sulfone linkage.

Experimental Section

General Methods. Melting points were corrected and determined on a Thomas-Hoover melting point apparatus. Nuclear magnetic resonance spectra were recorded on a 250-MHz Bruker WM-250 spectrometer. Infrared spectra were recorded on a Perkin-Elmer 983 spectrometer. Elemental analyses were performed by Desert Analytics of Tucson, AZ. The chromatographic grade silica gel used was 70–230 mesh, 60 Å. The potassium fluoride reagent was prepared as described by Ando and Yamawaki;[13,14] however, it is now also commercially available from Aldrich Chemical Co.

Synthesis of the Monomeric NLO-phore. *p-Methanesulfonylacetanilide* (*1*): 4-(Methylmercapto)aniline (1 g, 7.2 mmol) and acetic anhydride (1.5 g, 14.7 mmol) were dissolved in 4 mL of acetonitrile under argon. After stirring for 0.5 h, a solution of 30% hydrogen peroxide in 3.5 mL of acetic acid was added dropwise. When the addition was complete, the reaction was warmed to 60 °C for 12 h. A trace of manganese dioxide was added and the solution was stirred for 2 h. The solvent was removed by rotary evaporation at 5 mmHg. The product was recrystallized from ethyl acetate/acetone to give a 74% yield of 1, mp 186–187 °C. IR (KBr) 3350, 1685, 1531, 1281, 1137 cm^{-1}. ^1H NMR (DMSO-d_6) δ 10.39 (s, 1H), 7.81 (dd, 4H), 3.14 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (DMSO-d_6) δ 169.2, 143.8, 134.4, 128.3, 118.7, 43.9, 24.2. Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 50.69; H, 5.20; N, 6.57; S, 15.03; O, 22.51. Found: C, 50.68; H, 5.16; N, 6.62; S, 14.91; O, 22.63.

N-Ethyl-N-methylaminophenyl methyl sulfone (*2*): Sulfone 1 (3 g, 14 mmol), 40% KF/alumina (8 g, 55 mmol of KF), and methyl iodide (5.3 g, 37 mmol) were stirred in 100 mL of dry acetonitrile under argon. After 20 h, the KF/alumina was filtered off, and the acetonitrile was evaporated. The crude product was triturated with ethyl ether to give a 95% yield of *p*-methanesulfonyl(*N*-methyl)acetanilide as a white solid, mp 125–126 °C. IR (KBr) 1653, 1300, 1150 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.93 (d, 2H),

7.37 (d, 2H), 3.26 (s, 3H), 3.03 (s, 3H), 1.93 (bs, 3H). ^{13}C NMR ($CDCl_3$) δ 169.8, 149.0, 128.8, 127.5, 44.3, 37.2, 22.5. Anal. Calcd for $C_{15}H_{15}NO_3S$: C, 52.85; H, 5.77; N, 6.16; S, 14.11; O, 21.12. Found: C, 52.74; H, 5.73; N, 6.15; S, 14.17; O, 21.21%.

The product (2.46 g, 8.5 mmol) was dissolved in 10 mL of anhydrous tetrahydrofuran under argon atmosphere. To the stirred solution, boron trifluoride etherate (1.3 g, 8.9 mmol, 1.1 mL) was added, giving a precipitate. The contents were heated to reflux. Next 10 mL of 1 M borane–methyl sulfide complex in methylene chloride was added dropwise, and the reaction was allowed to run for 6 h at reflux. The methylene chloride, ethyl ether, and dimethyl sulfide were collected by fractional distillation, and the precipitate eventually went into solution. After the 6 h, the THF was evaporated and 4 mL of 6 M aqueous HCl was added. After refluxing for 1 h, this solution was cooled in an ice bath and then neutralized with 6 M aqueous NaOH. The aqueous layer was saturated with potassium carbonate and extracted with ethyl acetate. The ethyl acetate solution was dried over anhydrous magnesium sulfate, filtered, and the solvent evaporated. The product was recrystallized from methanol/water to give an 85% yield of white crystalline **2**, mp 83–84 °C. IR (KBr) 2972, 1291, 1134 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.59 (d, 2H), 6.57 (d, 2H), 3.34 (q, 2H), 2.88 (s, 3H), 2.87 (s, 3H), 1.04 (t, 3H). ^{13}C NMR ($CDCl_3$) δ 151.8, 128.7, 124.8, 110.4, 46.2, 44.7, 37.2, 11.0. Anal. Calcd for $C_{10}H_{15}NO_2S$: C, 56.31; H, 7.09; N, 6.57; S, 15.03; O, 15.00. Found: C, 56.46; H, 7.10; N, 6.59; S, 15.11; O, 14.74.

Synthesis of the Hexamethylene Spaced Oligomers. *1-Bromo-6-(p-acetanilide sulfone) hexane (3)*: Freshly distilled 4-aminothiophenol (10.2 g, 82 mmol) was dissolved in 50 mL of anhydrous acetonitrile under argon and was added dropwise to a slurry containing KF/alumina (70 g, 6 equiv of KF), 1,6-dibromohexane (50 mL, 0.325 mol, 4 equiv), and 100 mL of anhydrous acetonitrile. After 3 h, the KF/alumina was filtered, and about 100 mL of acetonitrile evaporated off. Acetic anhydride (16 g, 160 mmol) was then added. After 1 h the solution was placed in an ice bath and filtered to remove the byproduct 1,6-bis(*p*-acetanilide sulfide)hexane (2.1 g). The acetonitrile was removed by rotary evaporation to give an oil, which was extracted with 3 × 100 mL portions of pentane to remove unreacted 1,6-dibromohexane. The crude solid dissolved in 80 mL of acetonitrile, and a mixture of 100 mL of 30% hydrogen peroxide and 100 mL of glacial acetic acid was added dropwise. After stirring at 50 °C for 15 h, the reaction was quenched and stirred for 3 h with a trace of manganese dioxide. After cooling, an oil formed, which was removed by extraction with 2 × 100 mL portions of pentane. Neutralization with 6 M aqueous sodium hydroxide solution precipitated product **3**, which was filtered and recrystallized twice from methanol to give a 37% yield of **3** as a waxy, white solid, mp 95–98 °C. IR (KBr) 3323, 1668, 1319, 1148 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 8.71 (s, 1H), 7.71 (s, 4H), 3.30 (t, 2H), 3.04 (br t, 2H), 2.13 (s, 3H), 1.70 (m, 4H), 1.33 (br t, 4H). ^{13}C NMR ($CDCl_3$) δ 169.5, 143.3, 132.7, 128.9, 119.4, 56.1, 33.5, 32.0, 27.3, 27.1, 24.4, 22.4. Anal. Calcd for $C_{19}H_{22}BrNO_3S$: C, 46.42; H, 5.56; N, 3.87. Found: C, 46.46; H, 5.66; N, 3.79.

Oligomers 4–6: To monomer **3** (5 g, 14 mmol) dissolved in 30 mL of anhydrous acetonitrile, 6 g (41 mmol of KF) of 40% KF/alumina were added under argon. This slurry was stirred for 11 hours, after which ethyl iodide (2.6 mL, 33 mmol) and 2 g additional KF/alumina were added. After stirring this mixture for another 9 h, the used KF/alumina was filtered and the solvent evaporated to remove the excess ethyl iodide. Compound **1** (3 g, 14 mmol) in 30 mL of anhydrous acetonitrile was added. To this new solution a trace of potassium iodide and KF/alumina (6 g, 41 mmol) were added, and the slurry was stirred for 22 h. The KF/alumina was then filtered away, and 20 g of column chromatographic grade silica gel (70–230 mesh) was added. The solvent was evaporated, and the silica/product was loaded on a 500-mL column of silica gel. The separation was started with 3% methanol in ethyl acetate. The first major fraction is unreacted **4** (0.92 g recovered after recrystallization). The next major fraction was 1.004 g of the dimer **4**. The solvent was switched to 5% methanol in ethyl acetate and the trimer **5** was recovered (1.026 g). Finally, the solvent was switched to 10% methanol in ethyl acetate, and 0.467 g of the tetramer **6** was recovered.

Dimer **4**: 14% yield, ^{1}H NMR ($CDCl_3$) δ 7.9 (2d, 4H), 7.3 (2d, 4H), 3.7 (q, 2H), 3.6 (t, 2H), 3.0 (br s, 5H), 1.8 (br s, 6H), 1.1–1.6 (m, 8H), 1.0 (t, 3H). ^{13}C NMR ($CDCl_3$) d 169.2, 169.0, 147.4, 147.3, 139.3, 137.9, 129.2, 128.7, 128.6, 55.6, 48.6, 44.0, 27.5, 27.1, 25.7, 22.6, 22.0, 13.0. IR (KBr) 2932, 1657, 1304, 1148 cm^{-1}.

Trimer **5**: 19% yield, ^{1}H NMR ($CDCl_3$) δ 7.9 (2d, 6H), 7.3 (m, 6H), 3.7 (q, 2H), 3.6 (t, 4H), 3.0 (br s, 7H), 1.8 (br s, 9H), 1.1–1.6 (m, 16H), 1.0 (t, 3H). ^{13}C NMR ($CDCl_3$) δ 169.4, 147.5, 139.5, 138.2, 138.0, 129.5, 129.4, 128.9, 128.7, 55.8, 48.7, 44.2, 27.6, 27.2, 25.8, 22.8, 22.1, 22.0, 13.1.

Tetramer **6**: 9% yield, ^{1}H NMR ($CDCl_3$) δ 7.9 (2d, 8H), 7.3 (m, 8H), 3.7 (q, 2H), 3.6 (t, 6H), 3.0 (br s, 9H), 1.8 (br s, 12H), 1.1–1.6 (m, 24H), 1.0 (t, 3H). ^{13}C NMR ($CDCl_3$) δ 169.3, 147.5, 139.5, 138.2, 129.4, 128.9, 128.7, 128.6, 55.8, 48.8, 44.2, 27.6, 27.3, 25.9, 22.7, 22.2, 22.1, 13.1.

Hexamethylene Spaced Oligomers 7–9: The resolved amides **4–6** were individually dissolved in 20 mL of anhydrous tetrahydrofuran under argon and 1 M THF/borane was added (4 equiv/amide unit). The tetrahydrofuran solution was refluxed for 42 h. After cooling, 5 mL of 6 M aqueous hydrochloric acid was added slowly to each reaction. The mixtures were then made basic with 6 M aqueous sodium hydroxide. The aqueous layer was separated from the ether, and each aqueous layer was extracted with ethyl acetate. The combined THF and ethyl acetate fractions were dried over anhydrous magnesium sulfate. After filtering, the solvents were evaporated and the products were each purified by column chromatography to give the pure hexamethylene spaced oligomers **7–9**.

Dimer **7**: 62% yield of a viscous white oil. IR (neat) 2930, 1589, 1296, 1135 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.6 (t, 4H), 6.6 (t, 4H), 3.3 (br q, 6H), 3.2 (t, 2H), 2.9 (m, 5H), 1.2–1.7 (m, 8H), 1.1 (t, 9H). ^{13}C NMR ($CDCl_3$ δ 151.0, 150.9, 129.6, 124.6, 122.7, 110.3, 110.1, 56.4, 49.9, 44.9, 44.3, 27.9, 26.7, 26.2, 22.6, 12.0, 11.7. Anal. Calcd for $C_{25}H_{38}N_2O_4S_2$: C, 60.70; H, 7.74; N, 5.66. Found: C, 60.77; H, 7.98; N, 5.31.

Trimer **8**: 75% yield of a white glassy solid. IR (melt) 2932, 1590, 1293, 1134 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.6 (m, 6H), 6.6 (t, 6H), 3.3 (m, 8H), 3.2 (t, 4H), 2.9 (m, 7H), 1.2–1.7 (m, 16H), 1.1 (m, 12H). ^{13}C NMR ($CDCl_3$) δ 151.1, 151.9, 129.7, 129.1, 124.7, 123.0, 122.9, 110.3, 110.2, 56.5, 50.0, 44.9, 44.4, 28.0, 26.8, 26.3, 22.7, 12.1, 11.9. Anal. Calcd for $C_{39}H_{59}N_3O_6S_3$: C, 61.47; H, 7.80; N, 5.51. Found: C, 61.77; H, 7.97; N, 5.33.

Tetramer **9**: 80% yield of a white glassy solid. IR (melt) 2931, 1590, 1295, 1133 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.6 (m, 8H), 6.6 (m, 8H), 3.3 (m, 10H), 3.2 (t, 6H), 2.9 (m, 9H), 1.2–1.7 (m, 24H), 1.1 (m, 15H). ^{13}C NMR ($CDCl_3$) δ 151.1, 151.0, 129.7, 129.0, 123.0, 122.8, 110.3, 110.2, 56.4, 50.0, 44.9, 44.4, 28.0, 26.7, 26.3, 22.7, 12.1, 11.8. Anal. Calcd for $C_{53}H_{80}N_4O_8S_4$: C, 61.84; H, 7.83; N, 5.44. Found: C, 62.07; H, 8.01; N, 5.26.

Synthesis of the Dimethylene Spaced Dimer. *p-Acetamidothiophenol*: Freshly Kugelrohr distilled *p*-aminothiophenol (1.87 g, 15 mmol) was melted and 1.7 g (1.1 equiv) of acetic anhydride was added slowly, and the solution was cooled in an ice bath as needed. Stirring for 0.5 h at room temperature was followed by Kugelrohr distillation, heating slowly to remove unreacted acetic anhydride and acetic acid. The product distilled at an oven temperature of 160 °C and 0.2 mmHg to give white crystalline *p*-acetamidothiophenol in 99% yield, mp 151–153 °C. IR (KBr) 3292, 1658, 1598, 1540 cm^{-1}. ^{1}H NMR (acetone-d_6) δ 9.18 (br s, 1H), 7.4 (dd, 4H), 4.16 (s, 1H), 2.07 (s, 3H). ^{13}C NMR (acetone-d_6) δ 168.6, 138.1, 130.4, 125.0, 120.5, 23.9. Anal. Calcd for C_8H_9NOS: C, 57.46; H, 5.42; N, 8.38. Found: C, 57.60; H, 5.34; N, 8.18.

4-(Methylmercapto)-α-bromoacetanilide (10): To freshly distilled 4-(methylmercapto)aniline (5 g, 36 mmol), 50 mL of anhydrous acetonitrile and 20 g (4 equiv) of powdered potassium carbonate under argon, a solution of 6.21 g (1.1 equiv) of α-bromoacetyl chloride in 30 mL of acetonitrile was added dropwise. After 1 h the mixture was poured into 400 mL of water. The product was filtered, dried under vacuum overnight, and recrystallized from ethyl acetate to give an 86% yield of tan colored needles **10**, mp 129–130 °C. IR (KBr) 3253, 3182, 3113, 2925, 1659, 1606, 1537, 817 cm^{-1}. ^{1}H NMR (DMSO-d_6) δ 10.4 (s, 1H), 7.4 (dd, 4H), 4.1 (s, 2H), 2.5 (s, 3H). ^{13}C NMR (DMSO-d_6) δ 164.6, 136.0, 132.6, 127.0, 119.9, 30.4, 15.4. Anal. Calcd for

$C_9H_{10}BrNOS$: C, 41.55; H, 3.87; N, 5.38. Found: C, 44.67; H, 4.18; N, 5.76.

4-Methylmercapto-α-(p-acetamidophenyl sulfide) acetanilide (11): p-Acetamidothiolphenol (2 g, 12 mmol) was dissolved in 30 mL of a freshly prepared 0.5 M sodium methoxide/methanol solution. A slurry of 3.11 g (12 mmol) of **10**, finely powdered, in 20 mL of methanol was added. This mixture was stirred for 1.5 h, and 50 mL of water was added. The product was filter dried under vacuum overnight. Recrystallization from methanol gave a 71% yield of pure **11** as white crystals, mp 200–201 °C. IR (KBr) 3289, 1659, 1601, 1536, 1493, 825 cm^{-1}. ^1H NMR (DMSO-d_6) δ 10.1 (s, 1H), 10.0 (s, 1H), 7.2–7.6 (m, 8H), 3.8 (s, 2H), 2.4 (s, 3H), 2.0 (s, 3H). ^{13}C NMR (DMSO-d_6) δ 168.4, 166.9, 138.2, 136.3, 132.1, 130.4, 128.6, 127.1, 119.9, 119.6, 24.0, 15.5. Anal. Calcd for $C_{17}H_{18}N_2O_2S_2$: C, 58.93; H, 5.24; N, 8.09. Found: C, 58.78; H, 5.33; N, 8.14.

N,N'-Diethyl-4-methylmercapto-α-(p-acetamidophenyl sulfide) acetanilide (12): To a solution of **11** (2.73 g, 8 mmol) in 90 mL of anhydrous acetonitrile under argon, 1.5 mL of ethyl iodide and 4 g of 40% KF/alumina were added, and this mixture was stirred. Every 2 h 2 g of 40% KF/alumina and 1 mL of ethyl iodide were added until the reaction appeared complete by TLC (8 h total). This mixture was allowed to stir overnight. The KF/alumina was filtered and washed with 100 mL of ethyl ether. The solvents were evaporated, and the product purified by column chromatography. An 83% yield of pure **12** was obtained as a white solid, mp 91–92 °C. IR (KBr) 2971, 1642, 1487, 1409, 1302 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.39 (d, 2H), 7.29 (d, 2H), 7.04–7.14 (m, 4H), 3.70–3.79 (m, 4H), 3.51 (s, 2H), 2.52 (s, 3H), 1.82 (s, 3H), 1.11 (q, 6H). ^{13}C NMR ($CDCl_3$) δ 169.7, 167.7, 140.9, 139.4, 138.1, 135.9, 130.1, 128.6, 128.4, 127.1, 44.5, 43.7, 36.8, 22.7, 15.3, 12.9, 12.8. Anal. Calcd for $C_{21}H_{26}N_2O_2S_2$: C, 62.66; H, 6.51; N, 6.96. Found: C, 62.53; H, 6.65; N, 6.98.

N,N'-Diethyl-4-methyl sulfone-α-(p-acetamidophenyl sulfone) acetanilide (13): To **12** (2 g, 5 mmol) in 35 mL of sulfolane, 6.87 g of 50% *m*-chloroperbenzoic acid (4 equiv) was added under argon. This solution was kept at 40 °C for 4.5 h and was then dripped into 130 mL of 5% sodium bicarbonate solution. The white product was filtered and dried under vacuum to give a 98% yield of **13**, mp 205–206 °C. IR (KBr) 2990, 1656, 1306, 1139 cm^{-1}. ^1H NMR (DMSO-d_6) δ 7.7 (2dd, 8H), 3.7 (m, 4H), 3.3 (s, 2H), 1.8 (s, 3H), 1.0 (m, 6H). ^{13}C NMR (DMSO-d_6) δ 168.5, 147.4, 145.2, 137.9, 129.7, 129.0, 128.7, 128.4, 58.9, 43.4, 22.6, 13.1. Anal. Calcd for $C_{21}H_{26}N_2O_6S_2$: C, 54.06; H, 5.62; N, 6.00. Found: C, 53.68; H, 5.52; N, 5.76.

Dimethylene spaced p-aminophenyl sulfone dimer (14): To a mixture of **13** (2 g, 4.3 mmol) and 50 mL of dry tetrahydrofuran under argon, 30 mL of 1 M THF/borane solution was added. This solution was refluxed for 18 h and then cooled, and 20 mL of 6 M hydrochloric acid were added dropwise. This solution was made basic with 6 M sodium hydroxide solution, the THF was separated and the remaining aqueous layer was extracted with 3 × 50 mL portions of ethyl acetate. After the solvent was evaporated, the product was purified by column chromatography, followed by recrystallization from methanol. A 44% yield of **14** was obtained as white crystals, mp 155–156 °C. IR (KBr) 2974, 1592, 1301, 1139 cm^{-1}. ^1H NMR (DMSO-d_6) δ 7.6 (2d, 4H), 6.6 (2d, 4H), 3.7 (t, 2H), 3.35 (m, 6H), 3.22 (t, 2H), 2.9 (s, 3H), 1.12 (m, 9H). ^{13}C NMR (DMSO-d_6 δ 151.3, 150.2, 129.7, 129.3, 126.4, 122.4, 110.8, 110.5, 52.9, 45.3, 44.9, 44.5, 44.0, 12.1. Anal. Calcd for $C_{21}H_{30}N_2O_4S_2$: C, 57.51; H, 6.89; N, 6.39. Found: C, 57.53; H, 6.88; N, 6.34.

Synthesis of the Dimethylene Spaced Trimer. *α-(p-Aminothiophenyl)-4-methylmercaptoacetanilide (15)*: p-Aminothiophenol (2.4 g, 19 mmol) was reacted with 30 mL of 0.6 M sodium methoxide/methanol solution, and a slurry of 4.9 g (1 equiv) of **10** in 20 mL of methanol was added. After 5 h the slurry was dumped in 100 mL of 0.25 M aqueous sodium hydroxide solution. The solid was isolated by filtration and recrystallized from methanol to give an 88% yield of white crystalline **15**, mp 130–131 °C. IR (KBr) 3298, 1666, 1586, 1518, 817 cm^{-1}. ^1H NMR (DMSO-d_6) δ 9.97 (s, 1H), 7.5 (d, 2H), 7.2 (2d, 4H), 6.5 (d, 2H), 5.27 (s, 2H), 3.52 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (DMSO-d_6) δ 167.3, 148.9, 136.5, 134.0, 131.9, 127.1, 119.9, 118.2, 114.3, 41.2, 15.5. Anal. Calcd for $C_{15}H_{16}N_2OS_2$: C, 59.18; H, 5.30; N, 9.20. Found: C, 59.32; H, 5.23; N, 9.18.

α-(α'-Bromo-p-acetamidothiophenyl)-4-methylmercaptoacetanilide (16): To **15** (4.5 g, 15 mmol) in 100 mL of anhydrous acetone and 3 g (2 equiv) of triethylamine under argon, 2.6 g (1.1 equiv) of α-bromoacetyl chloride in 20 mL of acetone was added while cooling with an ice bath. The resulting slurry was stirred for 0.5 h, poured into 200 mL of 0.25 M aqueous hydrochloric acid and filtered, rinsing liberally with water. After drying under vacuum a 90% yield of cream colored **16** was obtained, mp 285 °C (dec), which was used without further purification. IR (KBr) 3244, 3176, 1654, 1536, 827 cm^{-1}. ^1H NMR (DMSO-d_6) δ 10.45 (s, 1H), 10.16 (s, 1H), 7.53 (m, 4H), 7.4 (d, 2H), 7.2 (d, 2H), 4.02 (s, 2H), 3.78 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (DMSO-d_6) δ 166.8, 164.8, 137.3, 136.3, 132.1, 130.0, 129.9, 127.1, 119.9, 119.8, 30.3, 15.5.

p-Ethylmercaptoacetanilide trimer (17): To sodium hydride (98%, 0.31 g, 13 mmol) in 25 mL of anhydrous dimethyl sulfoxide, 2.2 g (13 mmol) of p-acetamidothiophenol was added, and this solution was stirred for 20 h under argon atmosphere. Then a solution of 4.98 g (12 mmol) of **16** in 30 mL of anhydrous DMSO was added. After 10 hours the product was precipitated by pouring the reaction mixture into 600 mL of 0.25 M aqueous sodium hydroxide solution. The precipitate was filtered and rinsed with 50 mL of water followed by 300 mL of methanol. After drying under vacuum, a 96% yield of tan colored **17** was obtained, mp 241–242 °C, and used without further purification. IR (KBr) 3323, 1650, 1518, 819 cm^{-1}. ^1H NMR (DMSO-d_6) δ 10.18 (s, 1H), 10.14 (s, 1H), 9.98 (s, 1H), 7.5 (m, 6H), 7.4 (m, 4H), 7.2 (d, 2H), 3.75 (s, 4H), 2.42 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (DMSO-d_6) δ 168.3, 167.0, 166.8, 138.2, 137.6, 136.3, 132.1, 130.4, 130.2, 129.3, 128.5, 127.1, 119.9, 119.8, 119.6, 38.6, 24.0, 15.5.

p-Ethylmercaptoaniline trimer (18): To compound **17** (5 g, 9.8 mmol) in 250 mL of anhydrous tetrahydrofuran under argon, 100 mL of 1 M THF/borane solution (10 equiv) was added, and the mixture was heated to reflux for 22 h. The reaction was carefully quenched with 50 mL of 6 M aqueous hydrochloric acid. The resulting solution was made basic (pH about 10) with 6 M aqueous sodium hydroxide solution. After separating the THF and aqueous phases, the aqueous phase was extracted with ethyl ether. The combined organic layers were extracted once with brine solution and dried over magnesium sulfate. After evaporation of the solvents, the product was purified by column chromatography. 87% yield of **18** was obtained as a viscous yellow oil. IR (melt) 3395, 3015, 2964, 2915, 1594, 1502, 816 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.2 (m, 6H), 6.45 (m, 6H), 3.91 (br s, 3H), 3.19 (t, 4H), 3.08 (q, 2H), 2.89 (t, 4H), 2.37 (s, 3H), 1.20 (t, 3H). ^{13}C NMR ($CDCl_3$) δ 148.1, 147.5, 146.4, 134.8, 134.7, 131.1, 124.1, 119.8, 119.2, 113.4, 113.2, 113.0, 42.2, 42.0, 38.1, 35.8, 18.8, 14.5. Anal. Calcd for $C_{25}H_{31}N_3S_3$: C, 63.93; H, 6.65; N, 8.95. Fond: C, 64.77; H, 6.79; N, 8.88.

p-Ethylmercaptoacetanilide trimer (19): At 0 °C, 3.4 g (4.5 equiv) of acetic anhydride was added dropwise to **18** (3.5 g, 7.5 mmol) in 20 mL of ethyl acetate. After 4 h at room temperature the resulting slurry was poured into 100 mL of hexane, filtered, and rinsed with 500 mL of additional hexane to remove all of the acetic acid and unreacted acetic anhydride. After drying a 97% yield of white solid, mp 196–197 °C, was obtained. The product **19** was used without further purification. IR (KBr) 2982, 1649, 1490, 1392 cm^{-1}. ^1H NMR (50% DMSO-d_6, 50% CF_3COOH) δ 7.1–7.5 (m, 12H), 4.01 (br t, 4H), 3.85 (q, 2H), 3.22 (br s, 4H), 2.48 (s, 3H), 2.03 (s, 6H), 2.00 (s, 3H), 1.18 (t, 3H). Anal. Calcd for $C_{46}H_{32}N_3O_3S_3$: C, 62.49; H, 6.26; N, 7.05. Found: C, 63.12; H, 6.27; N, 7.05.

p-Dimethylene sulfone acetanilide trimer (20): Compound **19** (4 g, 6.7 mmol) was oxidized as described for **13**. After 22 h the product was precipitated by dripping the solution in 300 mL of 0.5 M aqueous sodium hydroxide solution, filtered and rinsed with water. After drying under vacuum a 92% yield of pure **20** was obtained as a white solid, mp 203–205 °C. IR (KBr) 2976, 2928, 1664, 1299, 1151 cm^{-1}. ^1H NMR (DMSO-d_6) δ 7.9 (m, 6H), 7.55 (d, 6H), 3.95 (bt, 4H), 3.72 (q, 2H), 3.65 (bt, 4H), 3.26 (s, 3H), 1.83 (s, 3H), 1.76 (s, 6H), 0.99 (t, 3H). ^{13}C NMR (DMSO-d_6) δ 169.1, 147.5, 146.8, 146.4, 137.7, 137.2, 129.3, 129.1, 128.9, 128.5, 52.3, 43.5, 43.4, 42.5, 22.6, 22.5, 13.1. Anal. Calcd for $C_{46}H_{43}N_3O_9S_3$: C, 53.82; H, 5.39; N, 6.07. Found: C, 53.64; H, 5.32; N, 5.94.

p-Dimethylene phenyl sulfone (N-ethyl) amine trimer (21): Triamide **20** (2 g, 3 mmol) was reduced as described for **14**. After workup the crude product was purified by column chromatography to give a 75% yield of white solid **21**, mp 81 °C. IR (melt) 2970, 1590, 1299, 1138 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.63 (m, 6H), 6.65 (d, 2H), 6.54 (m, 4H), 3.75 (m, 4H), 3.38 (m, 8H), 3.22 (br q, 4H), 2.95 (s, 3H), 1.16 (m, 12H). ^{13}C NMR ($CDCl_3$) δ 151.4, 150.6, 150.2, 129.9, 129.8, 129.4, 126.7, 124.5, 122.5, 111.0, 110.8, 110.6, 53.0, 45.4, 44.9, 44.6, 44.1, 43.9, 12.2. Anal. Calcd for $C_{31}H_{43}N_3O_6S_3$: C, 57.29; H, 6.67; N, 6.47. Found: C, 56.75; H, 6.77; N, 6.20.

Synthesis of the Piperidine Monomer. *N-(4-Phenyl methyl sulfone)piperidine (22)*: To *p*-fluorophenyl methyl sulfone (1 g, 5.7 mmol) in 25 mL of piperidine under argon was added 1.65 g (5 equiv) of anhydrous potassium fluoride. The mixture was stirred at 100 °C for 22 h. After workup the product was recrystallized from ethyl acetate/hexanes. The first crop gave a 76% yield of white crystals, mp 115–116 °C. A second crop afforded an additional 13% of **22** (total yield = 89%), mp 114–116 °C. IR (KBr) 3005, 2927, 2870, 1587, 1399, 1292, 1136, 1093, 783 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.66 (d, 2H), 6.85 (d, 2H), 3.30 (br s, 4H), 2.95 (s, 3H), 1.60 (br s, 6H). ^{13}C NMR ($CDCl_3$) δ 154.3, 128.9, 127.1, 113.5, 48.4, 44.8, 25.1, 24.1. Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16; N, 5.85. Found: C, 60.55; H, 7.37; N, 5.69.

Synthesis of the Piperidine Spaced Dimer. *4-Hydroxypiperacetamide*: 4-Hydroxypiperidine was reacted with 5.6 g (1.1 equiv) of acetic anhydride at room temperature for 1 h. The product was Kugelrohr distilled to remove the acetic acid and unreacted acetic anhydride; the desired product distilled at an oven temperature of 130–135 °C at 0.05 mmHg. The product was a white crystalline solid, mp 68–69 °C, and the yield was 99%. IR (melt) 3389, 2939, 1619, 1453 cm^{-1}. ^1H NMR ($CDCl_3$) δ 4.27 (br s, 1H), 3.7–3.8 (m, 1H), 3.70 (septet, 1H), 3.5–3.6 (m, 1H), 2.9–3.1 (m, 2H), 1.90 (s, 3H), 1.6–1.8 (m, 2H), 1.2–1.4 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 168.7, 65.9, 43.4, 38.6, 34.0, 33.3, 21.0. Anal. Calcd for $C_{12}H_{15}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.77; H, 9.44; N, 9.67.

4-Tosyloxypiperacetamide: To 4-hydroxypiperacetamide (6 g, 42 mmol), dissolved in 100 mL of anhydrous tetrahydrofuran, 8 g of *p*-toluenesulfonyl chloride was added under argon. Then 4 g (1.5 equiv) of powdered potassium hydroxide was added. Over the span of 4 days a total of 4 g of additional powdered potassium hydroxide and 5 g of *p*-toluenesulfonyl chloride were added periodically. The disappearance of the alcohol was monitored by TLC. When the reaction was complete, the potassium hydroxide was filtered through a short plug of silica gel and the THF evaporated. The resulting yellow oil was purified by column chromatography, using ethyl ether as the mobile phase. The product was obtained in an 85% yield as a white solid, mp 77–82 °C. IR (melt) 2954, 2868, 1644, 1352, 1174 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.79 (d, 2H), 7.36 (d, 2H), 4.72 (septet, 1H), 3.3–3.7 (m, 4H), 2.45 (s, 3H), 2.07 (s, 3H), 1.6–1.9 (m, 4H). ^{13}C NMR ($CDCl_3$) δ 168.5, 144.7, 133.7, 129.7, 127.3, 77.1, 42.4, 37.5, 31.5, 30.5, 21.3, 21.0. Anal. Calcd for $C_{19}H_{21}NO_4S$: C, 56.55; H, 6.44; N, 4.71. Found: C, 56.60; H, 6.64; N, 4.65.

Piperacetamide 4-p-fluorophenyl) sulfone (23): *p*-Fluorothiophenol (8.6 g, 67 mmol) was mixed with 100 mL of a 0.7 M sodium methoxide/methanol solution. After 20 min a solution of 20 g (67 mmol) of *p*-(tosyloxy)piperacetamide in 50 mL of methanol was added and the reaction mixture was refluxed for 18 h. The reaction was cooled to 0 °C, and 100 mL of additional methanol added. A solution consisting of 62 g of OXONE (50% $KHSO_5$) in 250 mL of water was slowly added to the chilled reaction mixture (total time for addition was about 15 min). This slurry was stirred at room temperature for 8 h. Then 700 mL of water was added, and the resulting solution was extracted with 6 × 200 mL of chloroform. The combined chloroform extracts were dried over anhydrous sodium sulfate. After evaporating the chloroform an oil was obtained. To this oil 50 mL of ethyl ether was added, and the product quickly crystallized. After filtering and drying, 76% yield of **23** as white crystals was obtained, mp 125–126 °C. IR (melt) 3100, 2926, 1642, 1143 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.89 (m, 2H), 7.30 (m, 2H), 4.73 (br d, 1H), 3.95 (br d, 1H), 3.0–3.2 (m, 2H), 2.51 (br t, 1H), 1.9–2.2 (m, 5H), 1.5–1.7 (m, 2H). ^{13}C NMR ($CDCl_3$) δ 168.6, 167.9, 163.8, 132.3, 131.8, 131.6, 116.7, 116.3, 61.2, 44.8, 39.9, 25.3, 24.8, 21.2. Anal. Calcd for $C_{18}H_{18}FNO_3S$: C, 54.72; H, 5.65; N, 4.91. Found: C, 54.93; H, 5.68; N, 4.78.

Piperidine 4-(p-fluorophenyl) sulfone (24): Amide **23** (11 g, 35 mmol) was hydrolyzed using 1 M aqueous hydrochloric acid solution at reflux for 6 h. After workup and extraction, the product was recrystallized from water to give a 68% yield of white crystalline **23**, mp 99–100 °C. A second crop was obtained, mp 98–100 °C, total yield 79%. IR (melt) 3270, 2957, 2817, 1267, 1145 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.89 (m, 2H), 7.25 (m, 2H), 3.18 (br d, 2H), 3.02 (tt, 1H), 2.56 (td, 2H), 2.01 (br d, 2H), 1.4–1.7 (m, 3H). ^{13}C NMR ($CDCl_3$) δ 167.9, 163.8, 132.7, 132.0, 131.8, 116.6, 116.2, 62.3, 45.3, 26.2. Anal. Calcd for $C_{11}H_{14}FNO_2S$: C, 54.31; H, 5.80; N, 5.76. Found: C, 52.62; H, 5.99; N, 5.44.

Piperidine 4-(p-piperidine-N-phenyl) sulfone (25): To **24** (2 g, 8 mmol) in 35 mL of piperidine, 2 g (4 equiv) of anhydrous potassium fluoride was added under argon. The reaction mixture was stirred at 100 °C for 9 h and cooled, and the salts were filtered off and rinsed with ethyl acetate. The piperidine and ethyl acetate were evaporated and the product was dried by heating to 80 °C under vacuum (0.5 mmHg) for 2 days. The product **25** was a tan solid, mp 126–128 °C, 99% yield, which was used without further purification. IR (KBr) 3302, 2916, 1588, 1264, 1122 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.50 (d, 2H), 6.85 (d, 2H), 3.32 (br s, 4H), 3.14 (br d, 2H), 2.92 (tt, 1H), 2.52 (br t, 2H), 1.97 (br d, 2H), 1.4–1.7 (m, 9H). ^{13}C NMR ($CDCl_3$) δ 154.3, 130.6, 122.6, 113.2, 62.0, 48.2, 45.0, 26.0, 25.0, 24.0.

Piperidine-spaced dimer (26): Compound **25** (1 g, 3 mmol) and 0.72 g (1.4 equiv) of *p*-fluorophenyl methyl sulfone were dissolved in 15 mL of anhydrous dimethyl sulfoxide under argon. Anhydrous potassium fluoride (1 g, 5 equiv) was added. The mixture was stirred at 130 °C for 2 days. Precipitation in 200 mL of water yielded the crude product, which was purified on a Silica gel column using 50/50 ethyl acetate/hexanes as eluent. The pink color was removed filtering a solution of **26** in acetonitrile through basic alumina. Evaporation afforded a 64% yield of **26** as a white solid, mp 220 °C (dec). IR (KBr) 2929, 1588, 1293, 1141 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.68 (d, 2H), 7.58 (d, 2H), 6.84 (m, 4H), 3.91 (br d, 2H), 3.32 (br s, 4H), 2.9–3.1 (m, 4H), 2.81 (br t, 2H), 2.04 (br d, 2H), 1.5–1.8 (m, 8H). ^{13}C NMR ($CDCl_3$) δ 154.5, 153.5, 130.6, 129.0, 128.6, 122.3, 114.2, 113.3, 61.4, 48.2, 46.7, 44.8, 25.1, 24.6, 24.1. Anal. Calcd for $C_{23}H_{30}O_4S_4$: C, 59.71; H, 6.54; N, 6.06. Found: C, 59.68; H, 6.58; N, 5.94.

Synthesis of the Piperidine Spaced Trimer. *4-(Piperidine dimer)piperacetamide (27)*: Compound **25** (1.25 g, 4 mmol) and 1.26 g (1.1 equiv) of **23** in 20 mL of anhydrous dimethyl sulfoxide under argon were mixed with 1.18 g (5 equiv) of anhydrous potassium fluoride, and the mixture was heated to 130 °C. Precipitation in 200 mL of water and purification by column chromatography led to a 72% yield of white solid **27**, mp 208 °C (dec). IR (KBr) 2930, 1649, 1587, 1296, 1136 cm^{-1}. ^1H NMR (DMSO-d_6) δ 7.61 (d, 4H), 7.10 (m, 4H), 4.46 (br d, 1H), 4.08 (br d, 2H), 3.92 (br d, 1H), 3.42 (br s, 6H), 2.8–3.1 (m, 3H), 2.5–2.6 (m, 1H), 2.02 (s, 3H), 1.8–2.0 (br m, 4H), 1.2–1.6 (m, 10H). ^{13}C NMR (DMSO-d_6) δ 168.8, 154.2, 153.4, 130.6, 123.3, 122.3, 113.9, 113.4, 60.3, 60.2, 47.9, 45.7, 44.6, 25.7, 25.0, 24.4, 24.1, 21.4. Anal. Calcd for $C_{34}H_{41}N_3O_4S_2$: C, 60.71; H, 6.85; N, 7.32. Found: C, 59.68; H, 6.75; N, 7.01.

4-(Piperidine dimer)piperidine (28): Compound **27** (1.2 g, 2 mmol) was hydrolyzed in 10 mL of 2 M aqueous hydrochloric acid at reflux. After workup, the product was eluted through silica gel using 50/50 methanol/chloroform to give a 99% yield of compound **28** as is a tan solid, mp 155 °C (dec). IR (KBr) 3436, 2930, 1588, 1136 cm^{-1}. ^1H NMR (DMSO-d_6) δ 7.54 (m, 4H), 7.03 (d, 4H), 4.00 (br d, 2H), 3.35 (br s, 4H), 2.8–3.1 (m, 7H), 2.35 (br t, 2H), 1.87 (br d, 2H), 1.70 (br d, 2H), 1.35–1.60 (m, 8H), 1.27 (br q, 2H). ^{13}C NMR (DMSO-d_6) δ 153.9, 153.0, 130.3, 123.5, 122.2, 113.6, 113.2, 61.1, 59.9, 47.6, 45.6, 44.6, 25.9, 24.8, 24.2, 23.8.

Piperidine-spaced trimer (29): Compound **28** (0.95 g, 1.8 mmol) and 0.41 g (1.3 equiv) of *p*-fluorophenyl methyl sulfone were reacted with potassium fluoride (0.52 g, 5 equiv) as described for **26**. A 35% yield of the trimer **29** was obtained as a white solid, mp 200 °C (dec). IR (KBr) 2929, 1590, 1503, 1292, 1142, 1088 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.5–7.6 (m, 6H), 6.84 (d, 6H), 3.92 (br d, 4H), 3.32 (br s, 4H), 2.7–3.1 (m, 9H), 2.05 (br d, 4H), 1.6–1.8

(m, 10H). ^{13}C NMR ($CDCl_3$) δ 154.4, 153.5, 153.4, 130.6, 130.5, 129.0, 128.6, 123.9, 122.2, 114.2, 113.9, 113.2, 61.3, 48.2, 46.7, 46.5, 44.8, 25.1, 24.5, 24.1. Anal. Calcd for $C_{34}H_{43}N_3O_6S_3$: C, 59.54; H, 6.32; N, 6.13. Found: C, 59.57; H, 6.20; N, 5.87.

Dipole Moments. The dielectric constant ϵ and indexes of refraction n of a series of solutions containing the NLO-phores (10^{-5}–10^{-3} g/L) in chloroform were measured using a GenRad 1689 RLC Digibridge and an Abbe refractometer, respectively. All measurements were carried out at 25 °C. The dipole moments of the NLO chromophores were calculated using the above data and a modified version of the Onsager equation:[20]

$$\langle \mu^2 \rangle = \frac{9kT}{4\pi} \frac{M}{N_A \rho_s} \left(\frac{\partial f}{\partial x} + f \right)_{x=0}$$

where x is the NLO-phore weight fraction, ρ_s is the density of the solvent, M is the molecular weight of the NLO-phore, kT is the thermal energy, and N_A is Avogadro's number. The functional form of f is dependent on the particular theory used and is given by

$$f = \left\{ \frac{(\epsilon - n^2)(2\epsilon + n^2)}{\epsilon(n^2 + 2)^2} \right\} \quad \text{(Onsager)}$$

$$f = \left\{ \frac{(\epsilon - 1)(\epsilon + 2)}{8\epsilon} - \frac{(n^2 - 1)(n^2 + 2)}{8n^2} \right\} \quad \text{(Osipov)}$$

$$f = \left\{ \frac{\epsilon - 1}{\epsilon + 2} - \frac{n^2 - 1}{n^2 + 2} \right\} \quad \text{(Guggenheim)}$$

It should be noted that chloroform was used as a solvent for these measurements, due to the highly polar nature of the NLO-phores. Strictly speaking, the above equations are only applicable for dipole moments of species in dilute solution in nonpolar solvents. However, the above expressions have been shown to give adequate results for slightly polar solvents as well.[20]

EFISH. Several excellent reviews describe the electric field induced second harmonic generation technique, EFISH, which was used to determine values of $\mu\beta_z$ for NLO-phores in this study.[2,21] The measurements in this study were performed using chloroform as solvent and a fundamental wavelength of 1907 nm.

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