Substituted Azole Derivatives as Nonlinear Optical Chromophores

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A series of nonlinear optical chromophores containing a single substituted thiazole ring has been synthesized and characterized. Selected imidazole, oxazole, and phenyl analogues have also been prepared and characterized for comparison. All experimental hyperpolarizabilities have been extrapolated to zero frequency for purposes of comparison using the well-established two-level model. The thiazoles are superior to oxazoles and imidazoles from a nonlinear point of view. The reasons for their superiority and the implications for their use in optoelectronic devices are discussed.

Introduction

The ideal chromophore for nonlinear optical applications has a large value of the projection of the hyperpolarizability along the dipole moment ($\mu\beta$) and is also thermally robust.[1-4] The former criterion is satisfied by long, delocalized molecules with strong electron donors and acceptors at opposite ends of a π-conjugated network. The latter criterion is best satisfied by aromatic derivatives.

Marder et al.[5,6] have suggested that, to some extent, these criteria are mutually incompatible. For most nonlinear chromophores in a nonlinear process, the electric field of the incident radiation couples the ground state with an excited state that exhibits substantial charge transfer. In the electron transfer from donor to acceptor, each aromatic ring along the conjugation pathway becomes quinodal, thus losing aromatic stabilization. This phenomenon leads to spectrally blue-shifted absorption maxima for aromatic derivatives relative to conjugated polyenes and reduced nonlinearities.

For organic nonlinear optical (NLO) chromophores to be practical, the trade-off between thermal stability and nonlinearity must be minimized. One possible compromise is the use of five-membered heterocyclic rings in place of classical aromatic and/or heteroaromatic substituents. Five-membered heterocyclic rings such as furans, thiophenes, pyrazoles, and azole derivatives still constitute fully conjugated six-π-electron systems, a condition often associated with aromaticity, but are less aromatic than classical aromatic derivatives.[7,8] Consequently, the formation of quinodal structures in five-membered heterocycles is not quite as energetically costly. The heterocycles are often more electron-rich than classical six-membered aromatic carbocyclics, since the six π-electrons are distributed over only five atoms.

Although the five-membered heterocyclics are all clearly aromatic by most accepted criteria,[7] bond localization and reactivity arguments suggest that the oxygen-containing derivatives (e.g., furan, oxazole, etc.) are less so, showing more dienic character.[8,9] Despite this, recent studies on 1,4,5-triaryl-substituted azole derivatives[10] showed that the order of nonlinearities was in fact thiazoles > oxazoles > imidazoles, although the measured differences were not very great. Other nonlinear studies on a variety of heterocycles have been reported including pyrazoles,[11,12] thiophenes,[13-15] and thiazoles.[16-20] Dirk et al.[16-18] have suggested that thiazole derivatives are good candidates as NLO chromophores and have tested this hypothesis in a limited number of cases. They conclude that replacing a benzene ring in a NLO chromophore by a thiazole ring can increase $\mu\beta$ by up to a factor of 3, although much of the increase has been attributed to dispersion effects. Accordingly, we have synthesized and characterized a large number of 2,5-disubstituted thiazoles together with a

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smaller number of imidazoles and oxazoles for direct comparison.

Experimental Section

Synthesis. The proton and carbon NMR spectra were recorded on a IBM-Bruker AF-250 machine operating at 250 MHz for proton and 62.9 MHz for carbon, and the chemical shifts are referenced relative to TMS. The fluorine NMR spectra were recorded on an IBM-AC-300 machine operating at 282.4 MHz and the chemical shifts are referenced relative to fluorotrichloromethane. IR spectra were measured using an IBM IR/32 Fourier transform instrument. UV-visible spectra were recorded using a Hewlett-Packard 8450A diode array spectrometer. Elemental analyses were performed by Galbraith Microanalytical Laboratory in Knoxville, TN. The thermal gravimetric analyses and differential scanning calorimetry studies were conducted using a Perkin-Elmer TGA-7 thermogravimetric analyzer and a DuPont Instruments Inc. Model 910 differential scanning calorimeter, respectively.

2-(Triethylstannyl)oxazole, 1. A solution of *n*-BuLi (23 mL, 1.6 M, 36.8 mmol) in hexane was added dropwise to solution of oxazole (2.5 g, 36.2 mmol) in 50 mL of THF stirring at −70 °C under nitrogen. The mixture was maintained at this temperature for 45 min, and a solution of triethyltin bromide (10.6 g, 39 mmol) in 20 mL of THF was slowly added. After 40 min, the reaction was allowed to warm to room temperature. Solvent was removed under reduced pressure, and pentane was added to the residue. The white precipitate was filtered off and the filtrate was concentrated. Distillation of the residue at 68–74 °C (1 mTorr) afforded a colorless liquid (8.1 g, 82% yield): ^{1}H NMR δ ($CDCl_3$) 7.86 (s, 1H), 7.20 (s, 1H), 1.34–1.09 (m, 15H); ^{13}C NMR δ ($CDCl_3$) 172.1, 140.9, 126.2, 10.6, 1.8; IR (film) 3150, 2948, 2912, 2870, 2825, 1465–1446, 1422, 1379, 1190, 1063, 1052, 961, 911, 753, 674 cm^{-1}.

2-Bromoxazole, 2b. To a solution of 2-triethylstannyl oxazole (6.1 g, 22 mmol) in 50 mL of dichloromethane stirred at 0 °C, bromine (3.6 g, 22 mmol) dissolved in 20 mL of dichloromethane was added dropwise. After 45 min, the reaction was allowed to warm up to room temperature, and the solution turned clear. Solvent was removed and the colorless product was distilled at 65–70 °C (10 mTorr), 2.1 g, 63% yield: ^{1}H NMR δ ($CDCl_3$) 7.72 (s, 1H), 7.13 (s, 1H); ^{13}C NMR δ ($CDCl_3$) 142.6, 133.7, 129.8; IR (NaCl) 3167, 3134, 2959, 2932, 2871, 1539, 1485, 1312, 1160, 1092, 1052, 927, 908, 854, 752, 669 cm^{-1}.

2-Bromo-*N*-methylimidazole, 2c. *n*-Butyllithium (1.6 M, 21 mL, 32 mmol) was added dropwise to *N*-methylimidazole (2.5 g, 30 mmol) in 80 mL of THF cooled at −70 °C. After 30 min, a solution of 1,2-dibromoethane (8 mL, 93 mmol) in 20 mL of THF was added slowly. The mixture was allowed to warm slowly to room temperature and then heated to a gentle reflux for 20 min. Dilute aqueous ammonium chloride was added, and the reaction mixture was extracted with of ethyl acetate. The combined organic extracts were dried over sodium sulfate, filtered, and concentrated. The residue was distilled under reduced pressure (54–57 °C, 1 mTorr, lit. 101–102 °C, 12 mTorr),[21] to give 4.1 g of clear liquid (82% yield): ^{1}H NMR δ ($CDCl_3$) 6.96 (s, 1H), 6.94 (s, 1H), 3.60 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 129.6, 122.9, 119.9, 34.4; IR (NaCl) 3135, 3112, 2952, 1513, 1475, 1416, 1364, 1352, 1276, 1119, 1081, 909, 740, 681, 660, 625 cm^{-1}.

2-(*p*-Methoxyphenyl)imidazole, 4a. This material was prepared from *p*-methoxybenzaldehyde, tartaric acid dinitrate, and ammonia using a similar procedure as that described for the preparation of imidazole:[22] mp 162–164 °C (lit. 160–161 °C);[23] ^{1}H NMR δ (acetone-d_6) 7.91 (d, J = 8.9 Hz, 2H), 7.08 (s, 2H), 6.96 (d, J = 8.9 Hz, 2H), 3.81 (s, 3H); ^{13}C NMR δ (acetone-d_6) 160.4, 146.9, 127.1, 124.7, 123.3, 114.6, 55.4; IR (KBr) 3450, 3181–2862, 1610, 1572, 1578, 1560, 1517, 1455, 1444, 1439, 1402, 1386, 1307, 1253, 1179, 1101, 1028, 954, 848, 818, 763, 737, 708, 618 cm^{-1}.

2-(*p*-Methoxyphenyl)thiazole, 5a. To a solution of *p*-bromoanisole (3.8 g, 20 mmol) in 70 mL of THF stirred at −100 °C under nitrogen, a 1.7 M pentane solution of *t*-BuLi (24 mL, 40.8 mmol) was added dropwise. The resulting yellow solution was stirred for 30 min at −100 °C and 30 min at −60 °C. In another three-neck flask, 2.76 g of zinc chloride (20 mmol) was fused under vacuum, dissolved in 30 mL of THF, and then cooled to −60 °C. The (*p*-methoxyphenyl)lithium solution was cannulated into the zinc chloride solution, and the mixture was slowly warmed to room temperature and then heated to reflux for 30 min. The solution was recooled to −10 °C, where tetrakis(triphenylphosphine)palladium(0) (0.74 g, 0.6 mmol) and 2-bromothiazole (2.2 g, 13 mmol) were added in one portion. After refluxing for 4 h, the resulting dark mixture was filtered through Celite, diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude residue was flash chromatographed[24] on silica gel eluting with 10% acetone–hexane to give a colorless oil (1.7 g, 68% yield): ^{1}H NMR δ ($CDCl_3$) 7.91 (d, J = 8.9 Hz, 2H), 7.81 (d, J = 3.3 Hz, 1H), 7.25 (d, J = 3.3 Hz, 1H), 6.69 (d, J = 8.9 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 168.2, 161.0, 143.3, 127.9, 126.5, 117.8, 114.2, 55.3; IR ($CDCl_3$) 3137, 3094, 3018, 2950, 2938, 2925, 2831, 1610, 1577, 1521, 1487, 1463, 1430, 1414, 1323, 1305, 1304, 1254, 1174, 1144, 1110, 1058, 1035, 975, 834, 633 cm^{-1}.

2-(*p*-Methoxyphenyl)oxazole, 5b. (*p*-Methoxyphenyl)-lithium was metathesized with zinc chloride and coupled with 2-bromoxazole following the procedure described above for **5a**. The crude product was purified by flash chromatography on silica gel eluting with 15% acetone–hexane. Further purification by Kugelrohr distillation at 110 °C (0.1 mTorr) gave a colorless oil in 75% yield: ^{1}H NMR δ ($CDCl_3$) 7.98 (d, J = 9.0 Hz, 2H), 7.66 (s, 1H), 7.18 (s, 1H), 6.96 (d, J = 9.0 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 161.9, 161.2, 137.9, 128.0, 127.9, 120.2, 114.0, 55.2; IR ($CDCl_3$) 3175, 3137, 3031, 2994, 2969, 2937, 2925, 1615, 1588, 1526, 1496, 1464, 1443, 1424, 1366, 1304, 1257, 1174, 1142, 1104, 1077, 1060, 1028, 839, 790 cm^{-1}.

2-(*p*-Methoxyphenyl)-*N*-methylimidazole, 5c. In an oven-dried flask under nitrogen, sodium hydride 60% dispersion in oil (0.12 g, 3 mmol) was suspended in pentane. The pentane was decanted and the solids were dispersed in 80 mL of THF. A solution of 2-(*p*-methoxyphenyl)imidazole (0.35 g, 2 mmol) in 40 mL of THF was added slowly at −15 °C and stirred for 1 h. Excess iodomethane (0.6 g, 4 mmol) was added in one portion, and the reaction was stirred at room temperature for 2 h. The reaction mixture was diluted with ether and extracted with brine. The organic layer was dried over sodium sulfate and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography on silica gel eluting with 20% acetone–hexane and recrystallized from ether–hexane to give a white solid (0.35 g, 92% yield): mp 198–199 °C; ^{1}H NMR δ ($CDCl_3$) 7.56 (d, J = 8.9 Hz, 2H), 7.10 (d, J = 1.2 Hz, 1H), 6.98 (d, J = 8.9 Hz, 2H), 6.95 (d, J = 1.2 Hz, 1H), 3.86 (s, 3H), 3.72 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 159.6, 148.0, 129.9, 128.0, 123.0, 121.8, 113.8, 55.2, 34.3; IR ($CDCl_3$) 3162, 3131, 3018, 2975, 2950, 2919, 1614, 1578, 1548, 1510, 1475, 1464, 1451, 1440, 1295, 1280, 1251, 1177, 1139, 1110, 1088, 1037, 1025, 837, 610 cm^{-1}.

2-(*p*-Methoxyphenyl)-5-bromo-*N*-methylimidazole, 6. Bromine (0.68 g, 4.25 mmol) in 20 mL of dichloromethane was added dropwise to 2-(*p*-methoxyphenyl)-*N*-methylimidazole (**5c**, 0.8 g, 4.25 mmol) dissolved 40 mL in dichloromethane stirring at 0 °C. After 2 h, the mixture was diluted with 10% aqueous sodium thiosulfate and extracted with dichloromethane. The organic layer was dried over sodium sulfate and the solvent was removed under reduced pressure. The crude product was flash chromatographed on silica gel eluting with 20% acetone–hexane and recrystallized from petroleum ether to give a white solid (0.71 g, 62% yield): mp 113–134 °C; ^{1}H NMR δ ($CDCl_3$) 7.51 (d, J = 8.9 Hz, 2H), 7.09 (s, 1H), 6.98 (d, J = 8.9 Hz, 2H), 3.92 (s, 3H), 3.64 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 160.1, 148.6, 129.9, 128.4, 123.0, 113.9, 104.4, 55.2, 33.2; IR 9$CDCl_3$) 3156, 3137, 3025, 2962, 2950, 2931, 2856, 1613, 1579, 1538, 1502, 1460, 1440, 1381, 1294, 1252, 1178, 1132, 1111, 1082, 1029, 837, 815, 617 cm^{-1}.

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2-(*p*-Methoxyphenyl)-5-(perfluorobutylsulfonyl)thiazole, 7a. A solution of 1.6 M *n*-BuLi (2.8 mL, 4.5 mmol) in hexane was added dropwise to a solution of 2-(*p*-methoxyphenyl)-thiazole (**5a**, 0.86 g, 4.5 mmol) in 60 mL of THF at −70 °C under nitrogen. The mixture was stirred for 45 min, and perfluorobutylsulfonyl fluoride (1.6 g, 5.4 mmol) was slowly added, maintaining the reaction temperature at −70 °C. The reaction was allowed to warm to room temperature and quenched with dilute aqueous ammonium chloride. The mixture was extracted with portions of ether and dried over sodium sulfate. The solution was filtered, the solvent was evaporated under reduced pressure, and the residue was flash chromatographed on silica gel eluting with 10% acetone–hexane. Recrystallization from ethanol–hexane afforded white needles in 41% yield: mp 117–118 °C; ^{1}H NMR δ ($CDCl_3$) 8.45 (s, 1H), 7.96 (3, *J* = 8.9 Hz, 2H), 7.01 (d, *J* = 8.9 Hz, 2H), 3.91 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 180.0, 163.4, 154.8, 129.2, 124.8, 124.3, 114.7, 55.5; IR ($CDCl_3$) 3150, 3025, 2950, 2925, 2850, 1606, 1525, 1474, 1393, 1378, 1351, 1307, 1290, 1261, 1241, 1216, 1174, 1156, 1142, 1067, 1031, 836, 615, 858 cm^{-1}. Anal. Calcd for $C_{14}H_8F_9NO_3S_2$: C, 35.52; H, 1.70; F, 36.12; N, 2.96; S, 13.55. Found: C, 35.27; H, 1.75; F, 35.68; N, 2.92; S, 13.87.

2-(*p*-Methoxyphenyl)-5-(perfluorobutylsulfonyl)-oxazole, 7b. 2-(*p*-Methoxyphenyl)oxazole (**5b**) was metalated and quenched as described above. The product was flash chromatographed on silica gel eluting with 15% acetone–hexane followed by recrystallization from petroleum ether giving white needles in 61% yield: mp 96–97 °C; ^{1}H NMR δ ($CDCl_3$) 8.12 (s, 1H), 8.10 (d, *J* = 9.0 Hz, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 3.91 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 168.5, 163.6, 143.1, 138.8, 129.9, 117.2, 116.6, 114.6, 114.3, 110.6, 108.4, 55.5; ^{19}F NMR δ ($CDCl_3$) −80.9 (m, 2F), −112.1 (m, 2F), −121.4 (m, 2F), −126.2 (m, 3F); IR ($CDCl_3$) 3162, 3137, 3025, 2975, 2944, 2906, 2862, 1611, 1520, 1479, 1441, 1425, 1392, 1351, 1308, 1270–1200, 1176, 1161, 1142, 1111, 1028, 841, 625, 570 cm^{-1}. Anal. Calcd for $C_{14}H_8F_9NO_4S$: C, 36.77; H, 1.76; F, 37.39; N, 3.06; S, 7.01. Found: C, 36.83; H, 1.78; F, 37.07; N, 2.93; S, 6.80.

2-(*p*-Methoxyphenyl)-5-(perfluorobutylsulfonyl)-*N*-methylimidazole, 7c. 2-(*p*-Methoxyphenyl)-5-bromo-*N*-methylimidazole (**6**) was metalated with 2 equiv of *t*-BuLi and at −100 °C and reacted with (perfluorobutyl)sulfonyl fluoride following the procedure described above. The product was flash chromatographed on silica gel eluting with 20% acetone–hexane mixture and recrystallized from ether–petroleum ether mixture to afford 0.25 g (40% yield) of white solid: mp 122–123 °C; ^{1}H NMR δ ($CDCl_3$) 8.08 (s, 1H), 7.61 (d, *J* = 8.9 Hz, 2H), 7.05 (d, *J* = 8.9 Hz, 2H), 3.91 (s, 3H), 3.89 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 161.4, 156.4, 144.6, 130.9, 121.2, 120.1, 114.3, 55.4, 33.8; IR ($CDCl_3$) 3156, 3131, 3018, 2975, 2937, 2843, 1613, 1472, 1461, 1449, 1375, 1333, 1351, 1328, 1296, 1255, 1240, 1226, 1175, 1142, 1028, 838, 568 cm^{-1}. Anal. Calcd for $C_{15}H_{11}F_9N_2O_3S$: C, 38.31; H, 2.36; F, 36.35; N, 5.96; S, 6.82. Found: C, 38.50; H, 2.61; F, 35.96; N, 5.69; S, 6.99.

2-((*p*-Methoxyphenyl)ethynyl)thiazole, 9a. A mixture containing 2-bromothiazole (3.28 g, 20 mmol), triethylamine (28 mL, 200 mmol), dichlorobis(triphenylphosphine)palladium (0.70 g, 1.0 mmol), cuprous chloride (50.0 mg, 0.5 mmol) in 10 mL of benzene was degassed and stirred under nitrogen. This mixture was heated in an oil bath maintained at 80 °C while (*p*-methoxyphenyl)acetylene 8 (2.6 g, 20 mmol) in 10 mL of benzene was added dropwise. The reaction mixture was heated at reflux for 1.5 h. The dark solution was filtered through Celite, rinsed with ethyl acetate, and the combined filtrates were extracted with water. The organic layer was dried over sodium sulfate and concentrated under reduced pressure. The crude oil was flash chromatographed on silica gel with 10% ethyl acetate–hexane. A slight yellow oil was obtained (3.9 g, 90% yield): ^{1}H NMR δ ($CDCl_3$) 7.83 (d, *J* = 3.3 Hz, 1H), 7.53 (d, *J* = 8.86 Hz, 2H), 7.35 (d, *J* = 3.3 Hz, 1H), 6.90 (d, *J* = 8.85 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 160.4, 149.1, 143.4, 133.5, 120.2, 114.1, 113.3, 94.2, 81.2, 55.2; IR ($CDCl_3$) 3130, 3002, 2950, 2895, 2840, 2210, 1606, 1570, 1516, 1476, 1465, 1441, 1294, 1269, 1251, 1180, 1175, 1161, 1094, 1057, 1031, 833 cm^{-1}.

2-((*p*-Methoxyphenyl)ethynyl)oxazole, 9b. 2-Bromooxazole (**2b**) was coupled with (*p*-methoxyphenyl)acetylene (**8**) as described above. After extraction, the crude product was flash chromatographed on silica gel eluting with 12% ethyl acetate–hexane and recrystallized from hexane to give colorless needles (70% yield): mp 65–66 °C; ^{1}H NMR δ ($CDCl_3$) 7.66 (s, 1H), 7.54 (d, *J* = 8.9 Hz, 2H), 7.20 (s, 1H), 6.89 (d, *J* = 8.9 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 160.8, 147.2, 139.2, 133.7, 128.3, 114.1, 112.4, 91.6, 75.9, 55.2; IR ($CDCl_3$) 3125, 3025, 2962, 2937, 2841, 2228, 1608, 1550, 1515, 1495, 1464, 1441, 1294, 1252, 1252, 1181, 1161, 1109, 1078, 1032, 834 cm^{-1}.

2-((*p*-Methoxyphenyl)ethynyl)-*N*-methylimidazole, 9c. 2-Bromo-*N*-methylimidazole (**2c**) was coupled with (*p*-methoxyphenyl)acetylene as described. After extraction, the crude product was flash chromatographed on silica gel eluting with 25% acetone–hexane and recrystallized from ether–hexane to give colorless needles (59% yield): mp 95–96 °C; ^{1}H NMR δ ($CDCl_3$) 7.49 (d, *J* = 8.7 Hz, 2H), 7.07 (d, *J* = 1.25 Hz, 1H), 6.92 (d, *J* = 1.25 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 2H), 3.82 (s, 3H), 3.76 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 160.1, 133.2, 132.7, 129.5, 121.0, 114.0, 113.8, 92.6, 77.3, 55.2, 33.4; IR ($CDCl_3$) 3144, 3125, 3012 2950–2930, 2840, 2221, 1607, 1570, 1524, 1506, 1467, 1438, 1407, 1305, 1289, 1250, 1178, 1158, 1138, 1032, 834 cm^{-1}.

2-((*p*-Methoxyphenyl)ethynyl)-5-(perfluorobutylsulfonyl)thiazole, 10a. A solution of 1.6 M *n*-BuLi (1.4 mL, 2.3 mmol) in hexane was added dropwise to a solution of 2-((*p*-methoxyphenyl)ethynyl)thiazole (**9a**, 0.41 g, 1.9 mmol) in 50 mL of THF at −70 °C under nitrogen. The mixture was stirred for 45 min and perfluorobutylsulfonyl fluoride (0.57 g, 1.9 mmol) was slowly added, maintaining the reaction temperature at −70 °C. The reaction was allowed to warm to room temperature and quenched with dilute aqueous ammonium chloride. The mixture was extracted with portions of ether and dried over sodium sulfate. The solution was filtered, the solvent was evaporated under reduced pressure, and the residue was flash chromatographed on silica gel eluting with 10% ethyl acetate–hexane mixture. Recrystallization from acetone–hexane afforded 0.43 g (46% yield) of light yellow needles: mp 201–202 °C; ^{1}H NMR δ ($CDCl_3$) 8.45 (s, 1H), 7.60 (d, *J* = 8.9 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 161.9, 154.1, 134.3, 126.9, 114.4, 111.3, 102.1, 80.9, 55.4, 55.2; IR ($CDCl_3$) 3150, 3050–2920, 2850, 2203, 1605, 1515, 1467, 1406, 1382, 1351, 1297, 1242, 1171, 1144, 1092, 1065, 842, 594 cm^{-1}. Anal. Calcd for $C_{16}H_8F_9NO_3S_2$: C, 38.64; H, 1.62; F, 34.38; N, 2.82; S, 12.89. Found: C, 38.59; H, 1.53; F, 33.55; N, 2.58; S, 12.75.

2-((*p*-Methoxyphenyl)ethynyl)-5-(perfluorobutylsulfonyl)oxazole, 10b. 2-((*p*-Methoxyphenyl)ethynyl)oxazole (**9b**) was metalated and quenched as described above. The product was flash chromatographed on silica gel eluting with 90% toluene–hexane followed by recrystallization from ether–hexane to afford white needles (32% yield): mp 104–105 °C; ^{1}H NMR δ ($CDCl_3$) 8.11 (s, 1H), 7.62 (d, *J* = 8.8 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 161.9, 152.8, 141.9, 139.7, 134.6, 114.5, 110.5, 97.9, 75.0, 55.4; IR ($CDCl_3$) 3144, 3000–2906, 2850, 2219, 1607, 1544, 1513, 1487, 1397, 1352, 1297, 1254, 1241, 1208, 1175, 1144, 1030, 835 cm^{-1}. Anal. Calcd for $C_{16}H_8F_9NO_4S$: C, 39.93; H, 1.67; F, 35.53; N, 2.91; S, 6.66. Found: C, 40.36; H, 1.52; F, 35.00; N, 3.06; S, 6.50.

2-((*p*-Methoxyphenyl)ethynyl)-5-(perfluorobutylsulfonyl)-*N*-methylimidazole, 10c. 2-((*p*-Methoxyphenyl)ethynyl)-*N*-methylimidazole (**9c**) was metalated and quenched as described. The product was flash chromatographed on silica gel eluting with 20% acetone–hexane followed by recrystallization from hexane to afford light yellow crystals in 15% yield: mp 147–148 °C; ^{1}H NMR δ ($CDCl_3$) 8.00 (s, 1H), 7.60 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 3.99 (s, 3H), 3.86 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 161.3, 144.3, 133.8, 133.6, 114.3, 114.2, 111.7, 98.1, 75.6, 55.3, 33.3; IR ($CDCl_3$) 3187, 3144, 3031–2950, 2856, 2220, 1605, 1521, 1463, 1380, 1351, 1333, 1295, 1240, 1218, 1170, 1142, 1029, 834, 570 cm^{-1}. Anal. Calcd for $C_{17}H_{11}F_9N_2O_3S$: C, 41.30; H, 2.24; F, 34.59; N, 5.67; S, 6.48. Found: C, 40.90; H, 2.25; F, 36.51; N, 5.57; S, 6.48.

4-Methoxy-4′-(perfluorobutylsulfonyl)biphenyl, 11. (*p*-Methoxyphenyl)lithium was metathesized with zinc chloride and coupled with *p*-(perfluorobutylsulfonyl)bromobenzene following the procedure described for the preparation of **5a**. Pure product was obtained by flash chromatography on silica gel eluting with 5% acetone–hexane followed by recrystallization from petroleum ether to give white needles in 90% yield: mp 91–92 °C; ^{1}H NMR δ ($CDCl_3$) 8.52 (d, *J* = 8.6 Hz, 2H), 7.83 (d, *J* = 8.6 Hz, 2H), 7.62

(d, J = 8.8 Hz, 2H), 7.04 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 160.7, 149.1, 131.5, 130.4, 129.3, 128.7, 127.4, 114.6, 55.3; IR ($CDCl_3$) 3169, 3019, 2968, 2931, 2919, 2844, 1609, 1592, 1521, 1487, 1368, 1351, 1420, 1217, 1205, 1171, 1142, 1123, 1084, 1038, 824, 618 cm^{-1}. Anal. Calcd for $C_{17}H_{11}F_9O_3S$: C, 43.79; H, 2.38; F, 36.67; S, 6.87. Found: C, 43.76; H, 2.12; F, 36.66; S, 6.93.

4-Methoxy-4′-(perfluorohexylsulfonyl)tolane, 12. (*p*-Methoxyphenyl)acetylene and *p*-(perfluorohexylsulfonyl)bromobenzene were coupled as described for the preparation of **9a** using diisopropylethylamine in place of triethylamine. A 2-fold excess (*p*-methoxyphenyl)acetylene (8) and a longer reaction time of 4 h were necessary to drive this reaction to completion. The product was purified by flash chromatography on silica gel eluting with 8% ethyl acetate–hexane and recrystallized from hexane to give colorless crystals in 62% yield: mp 144–145 °C; ^{1}H NMR δ ($CDCl_3$) 8.00 (d, J = 8.7 Hz, 2H), 7.75 (d, J = 8.7 Hz, 2H), 7.52 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 160.5, 133.5, 132.7, 132.1, 130.9, 130.1, 114.1, 113.7, 96.3, 86.3, 55.3; IR ($CDCl_3$) 3156, 3000–2906, 2838, 2215, 1606, 1587, 1514, 1369, 1289, 1243, 1211, 1174, 1151, 1138, 1114, 1081, 1031, 837 cm^{-1}. Anal. Calcd for $C_{21}H_{11}F_{13}O_3S$: C, 42.72; H, 1.88; F, 41.84; S, 5.43. Found: C, 42.71; H, 1.98; F, 42.03; S, 5.39.

2-Bromo-5-methanesulfonylthiazole, 14. 2-Amino-5-methanesulfonylthiazole was diazotized and halogenated following the literature procedure.[25] Recrystallization from ethanol–hexane afforded a white solid (58% yield): mp 96–97 °C (lit. 90–91 °C);[26] ^{1}H NMR δ ($CDCl_3$) 8.10 (s, 1H), 3.23 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 147.5, 143.6, 140.9, 46.1; IR ($CDCl_3$) 3105, 2927, 1489, 1369, 1334, 1184, 1154, 1010, 957, 592, 554, 536 cm^{-1}.

2-Phenyl-5-nitrothiazole, 16. In a three-neck flask, zinc chloride (0.85 g, 6.2 mmol) was fused under vacuum, purged with nitrogen, dissolved in 30 mL of THF, and then cooled to −60 °C. Phenyllithium (2 M, 2.6 mL, 5.2 mmol) was added dropwise to the above solution and the mixture was heated to reflux for 30 min. After cooling to 0 °C, tetrakis(triphenylphosphine)-palladium(0) (0.25 g, 0.22 mmol), 2-bromo-5-nitrothiazole (1.1 g, 5.2 mmol) were added in one portion, and the mixture was refluxed for 4 h. The resulting mixture was filtered through Celite, diluted with ethyl acetate, and washed with brine. The organic layer was dried over sodium sulfate and filtered, and the solvent was removed under reduced pressure. The product was purified by flash chromatography on silica gel eluting with 5% ethyl acetate–hexane and recrystallized from acetone–hexane to give light tan needles (81% yield): mp 157–158 °C; ^{1}H NMR δ ($CDCl_3$) 8.58 (s, 1H), 7.99 (d, J = 7.5, J = 1.8 Hz, 2H), 7.58–7.48 (m, 3H); ^{13}C NMR δ ($CDCl_3$) 173.2, 148.5, 144.2, 132.4, 131.9, 129.3, 126.9; IR ($CDCl_3$) 3117, 3075, 1524, 1452, 1408, 1351, 1319, 1246 1151, 817 cm^{-1}. Anal. Calcd for $C_9H_6N_2O_2S$: C, 52.42; H, 2.93; N, 13.58; S, 15.54. Found: C, 52.41; H, 2.67; N, 13.72; S, 15.51.

2-(*p*-Methoxyphenyl)-5-nitrothiazole, 17. (*p*-Methoxyphenyl)lithium was metathesized with zinc chloride and coupled with 2-bromo-5-nitrothiazole following the procedure described for the preparation of **16**. The product was purified by flash chromatography on silica gel eluting with 10% ethyl acetate–hexane and recrystallized from ethanol–hexane to give yellow crystals (40% yield): mp 148–149 °C; ^{1}H NMR δ ($CDCl_3$) 8.63 (s, 1H), 8.46 (d, J = 8.5, 1H), 7.57–7.50 (m, 1H), 7.18–7.08 (m, 2H), 4.12 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 166.5, 157.0, 142.8, 133.1, 128.7, 121.3, 111.2, 55.7; IR (KBr) 3110, 2950, 2860, 1598, 1506, 1474, 1355, 1317, 1281, 1259, 1225, 1161, 1015, 816, 757 cm^{-1}. Anal. Calcd for $C_{10}H_8N_2O_3S$: C, 50.84; H, 3.41; N, 11.86; S, 13.57. Found: C, 51.33; H, 3.30; N, 12.28; S, 13.33.

2-(Phenylethynyl)-5-nitrothiazole, 18. Phenylacetylene and 2-bromo-5-nitrothiazole were coupled as described in the preparation of **9a** using diisopropylethylamine in place of triethylamine and stirring at room temperature for 16 h. The product was flash chromatographed eluting with 40% chloroform–hexane and recrystallized from ether–hexane to give pale yellow crystals (36% yield): mp 131–132 °C; ^{1}H NMR δ ($CDCl_3$) 8.75 (s, 1H), 7.65 (m, 2H), 7.47 (m, 3H); ^{13}C NMR δ ($CDCl_3$) 153.2, 143.8, 132.3, 130.8, 128.7, 119.8, 100.9, 99.0, 82.0; IR ($CDCl_3$) 3156, 2206, 1525, 1472, 1350, 1308, 1172, 1125, 842 cm^{-1}. Anal. Calcd for $C_{11}H_6N_2O_2S$: C, 57.38; H, 2.63; N, 12.17; S, 13.92. Found: C, 57.63; H, 2.55; N, 11.94; S, 13.84.

2-((*p*-Methoxyphenyl)ethynyl)-5-nitrothiazole, 19. (*p*-Methoxyphenyl)acetylene and 2-bromo-5-nitrothiazole were coupled as described for **9a** using diisopropylethylamine in place of triethylamine, stirring at room temperature for 60 h. The product was flash chromatographed eluting with 40% chloroform–hexane and recrystallized from ether–hexane to give yellow needles (70% yield): mp 159–160 °C; ^{1}H NMR δ ($CDCl_3$) 8.54 (s, 1H), 7.58 (d, J = 9.1 Hz, 2H0, 6.94 (d, J = 9.1 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 161.6, 153.6, 148.1, 143.8, 134.2, 114.4, 111.7, 100.0, 81.4, 55.3; IR ($CDCl_3$) 3155, 3020–2907, 2850, 2205, 1605, 1516, 1411, 1352, 1296, 1257, 1176, 1095, 1026, 834, 817 cm^{-1}. Anal. Calcd for $C_{12}H_8N_2O_3S$: C, 55.38; H, 3.10; N, 10.76; S, 12.32. Found: C, 56.26; H, 2.89; N, 10.72, S, 12.33.

4-Amino-1-ethynylbenzene, 20. Trimethylsilylacetylene and *p*-iodoaniline were coupled as described for **9a** in a pressure bottle at room temperature for 16 h. Solvent was evaporated under reduced pressure and the crude residue was hydrolyzed in a 1:1 mixture of 1 M KOH–MeOH at 50 °C for 2 h. After extraction, the crude product was flash chromatographed on silica gel eluting with 15% ethyl acetate–hexane to give a light sensitive white solid (24% yield): mp 103–105 °C (lit. 103–104 °C);[26] ^{1}H NMR δ ($CDCl_3$) 7.30 (d, J = 8.5 Hz, 2H), 6.60 (d, J = 8.5 Hz, 2H), 3.82 (s, 2H), 2.97 (s, 1H); ^{13}C NMR δ ($CDCl_3$) 146.9, 133.4, 114.5, 111.2, 84.3, 74.8; IR ($CDCl_3$) 3496, 3407, 3316, 3302, 3100, 2975, 2937, 2248, 2105, 1622, 1512, 1289, 1174, 829, 596, 538 cm^{-1}.

2-((*p*-Aminophenyl)ethynyl)-5-nitrothiazole, 21. (*p*-Aminophenyl)acetylene and 2-bromo-5-nitrothiazole were coupled as described for the preparation of **9a** using diisopropylethylamine in place of triethylamine and stirring at room temperature for 16 h. The product was flash chromatographed eluting with 30% ethyl acetate–hexane and recrystallized from acetone–hexane to give tan crystals (38% yield): mp 220 °C (dec); ^{1}H NMR δ (acetone-d_6) 8.65 (s, 1H), 7.40 (d, J = 8.8 Hz, 2H), 6.74 (d, J = 8.8 Hz, 2H), 5.56 (s, 2H); ^{13}C NMR δ (acetone-d_6) 154.5, 152.4, 145.1, 134.9, 120.9, 114.7, 106.4, 102.7, 81.8; IR (KBr) 3485–3360, 3225, 3107, 2184, 1623, 1601, 1521, 1416, 1351, 1305, 1263, 1239, 1185, 1091, 833, 817, 734, 622 cm^{-1}. Anal. Calcd for $C_{11}H_7N_3O_2S$: C, 55.38; H, 2.88; N, 17.13; S, 13.07. Found: C, 53.83; H, 2.80; N, 16.35; S, 13.13.

2-((*p*-Methoxyphenyl)ethynyl)-5-methanesulfonylthiazole, 22. (*p*-Methoxyphenyl)acetylene and 2-bromo-5-methanesulfonylthiazole[25] were coupled as described for **9a** using diisopropylethylamine in place of triethylamine at 60 °C for 2 h. The product was flash chromatographed on silica gel eluting with 30% ethyl acetate–hexane and recrystallized from ethanol–hexane affording pale yellow plates (80% yield): mp 133–134 °C; ^{1}H NMR δ ($CDCl_3$) 8.29 (s, 1H), 7.57 (d, J = 6.9 Hz, 2H), 6.93 (d, J = 6.9 Hz, 2H), 3.86 (s, 3H), 3.26 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 161.7, 155.8, 148.2, 137.1, 134.0, 114.3, 112.0, 98.9, 80.6, 55.3, 46.3; IR (KBr) 3080, 3010, 2900, 2830, 2203, 1603, 1515, 1487, 1412, 1313, 1293, 1268, 1252, 1187, 1163, 1139, 1091, 1067, 1022, 965, 836, 769, 635, 578, 534 cm^{-1}. Anal. Calcd for $C_{13}H_{11}NO_3S_2$: C, 53.23; H, 3.78; N, 4.77; S, 21.86. Found: C, 53.36; H, 3.64; N, 4.60; S, 21.67.

2-(β-Styryl)-5-nitrothiazole, 23. To a solution of β-iodostyrene (2.0 g, 8.7 mmol) in 40 mL of the THF stirred at −100 °C under nitrogen, a 1.8 M pentane solution of *t*-BuLi (9.7 mL, 17.8 mmol) was added dropwise. The resulting yellow solution was stirred for 30 min at −100 °C and 30 min at −60 °C. In another three-neck flask, 1.2 g of zinc chloride (9.0 mmol) was fused under vacuum, dissolved in 30 mL of THF, and then cooled to −60 °C. The β-styryllithium solution was cannulated into the zinc chloride solution and the mixture was slowly warmed to room temperature then heated to reflux for 30 min. The solution was recooled to −10 °C, where tetrakis(triphenylphosphine)palladium(0) (0.5 g, 0.4 mmol) and 2-bromo-5-nitrothiazole (1.9 g, 9 mmol) were added in one portion. After refluxing for 4 h, the resulting dark mixture was filtered through Celite, dilute with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure. The product

(25) Balli, H.; Low, R. *Helv. Chim. Acta* **1976**, *59*, 155.

(26) Henry, D. W. *J. Med. Chem.* **1969**, *12*, 304.

was purified by flash chromatography on silica gel eluting with 25% ethyl acetate–hexane followed by recrystallization from ethanol–hexane to give yellow needles (35% yield): mp 166–167 °C)lit. 164–166 °C;[26] ^{1}H NMR δ ($CDCl_3$) 8.55 (s, 1H), 7.68 (d, J = 16.1 Hz, 1H), 7.63–7.58 (m, 2H), 7.48–7.44 (m, 3H), 7.23 (d, J = 16.1 Hz, 1H); ^{13}C NMR δ (THF-d_8) 172.3, 148.8, 145.3, 139.8, 135.9, 130.8, 129.7, 128.7, 121.1; IR ($CDCl_3$) 3030–3115, 1622, 1521, 1485, 1452, 1405, 1351, 1303, 1207, 1087, 956, 817 cm^{-1}. Anal. Calcd for $C_{11}H_8N_2O_2S$: C, 56.88; H, 3.47; N, 12.06; S, 13.80. Found: C, 57.00; H, 3.47; N, 12.06; S, 13.80. Found: C, 57.00; H, 3.24; N, 12.28; S, 13.72.

2-(β-*p*-Methoxystyryl)-5-nitrothiazole, 24. Following the procedure described above, *p*-methoxy-β-styryllithium was methathesized with zinc chloride and coupled with 2-bromo-5-nitrothiazole. The product was purified by flash chromatography on silica gel eluting with 25% ethyl acetate–hexane followed by recrystallization from ethanol to give orange needles (57% yield): mp 167–168 °C; ^{1}H NMR δ ($CDCl_3$) 8.47 (s, 1H), 7.58 (d, J = 16.0 Hz, 1H), 7.50 (d, J = 8.7 Hz, 2H), 7.04 (d, J = 16 Hz, 1H), 6.92 (d, J = 8.8 Hz, 2H), 3.83 (s, 3H); ^{13}C NMR δ (THF-d_8) 173.0, 162.6, 148.1, 145.4, 139.7, 130.4, 128.5, 118.7, 115.2, 55.6; IR ($CDCl_3$) 3025–2947, 2855, 1602, 1513, 1351, 1307, 1292, 1252, 1196, 1083, 1033, 819 cm^{-1}. Anal. Calcd for $C_{12}H_{10}N_2O_3S$: C, 54.95; H, 3.84; N, 10.68; S, 12.22. Found: C, 55.26; H, 3.86; N, 10.53; S, 12.23.

β-Bromo-4-(*N,N*-dimethylamino)styrene, 25. This material was prepared from *p*-(dimethylamino)benzaldehyde using a procedure similar to that described in the literature.[27] The crude product was flash chromatographed on silica gel, using 8% ethyl acetate–hexane and recrystallized from petroleum ether to give a white solid (65% yield): mp 49–51 °C; ^{1}H NMR δ ($CDCl_3$) 7.68 (d, J = 8.9 Hz, 2H), 6.96 (d, J = 8.0 Hz, 1H), 6.72 (d, J = 8.9 Hz, 2H), 6.19 (d, J = 8.0 Hz, 1H), 3.00 (s, 6H); ^{13}C NMR δ ($CDCl_3$) 150.1, 131.7, 130.1, 122.9, 111.4, 101.5, 40.2; IR (KBr) 3075, 3000–2869, 2812, 1672, 1610, 1521, 1429, 1360, 1335, 1321, 1234, 1198, 1159, 1131, 1062, 948, 820, 645, 571, 528 cm^{-1}.

2-(*p*-Dimethylamino-β-styryl)-5-nitrothiazole, 26. Following the procedure described for the preparation of **23**, *p*-(dimethylamino)-β-styryllithium (1.13 g, 5 mmol) was methathesized with zinc chloride and coupled with 2-bromo-5-nitrothiazole 91.06 g, 5.1 mmol). The product was purified by flash chromatography on silica gel eluting with 15% ethyl acetate–hexane followed by recrystallization from ethanol to give red crystals (0.6 g, 44% yield): mp 206–208 °C; ^{1}H NMR δ ($CDCl_3$) 8.47 (s, 1H), 7.58 (d, J = 15.86 Hz, 1H), 7.47 (d, J = 8.8 Hz, 2H), 6.98 (d, J = 15.85 Hz, 1H), 6.70 (d, J = 8.8 Hz, 2H), 3.06 (s, 6H); ^{13}C NMR δ ($CDCl_3$) 173.5, 151.8, 145.8, 144.8, 140.3, 129.7, 122.0, 114.8, 111.8, 40.0; IR ($CDCl_3$) 3100, 3031, 2994, 2925, 2875, 2812, 1593, 1527, 1435, 1403, 1349, 1308, 1287, 1256, 1207, 1185, 1170, 1149, 1120, 1081, 813 cm^{-1}. Anal. Calcd for $C_{13}H_{13}N_3O_2S$: C, 56.71; H, 4.76; N, 15.26; S, 11.64. Found: C, 56.54; H, 4.86; N, 15.19; S, 11.58.

β-Bromo-4-(*N,N*-diphenylamino)styrene, 27. This material was prepared as described for **25** using *p*-(diphenylamino)-benzaldehyde. The product was flash chromatographed on silica gel, eluting with 5% ethyl acetate–hexane to give a pale yellow oil (62% yield): ^{1}H NMR δ ($CDCl_3$) 7.62 (d, J = 8.8 Hz, 2H), 7.39–7.25 (m, 6H), 7.15–7.02 (m, 7H), 6.31 (d, J = 8.1 Hz, 1H); ^{13}C NMR δ ($CDCl_3$) 147.2, 132.9, 131.4, 129.9, 129.2, 126.8, 124.7, 123.2, 122.1, 104.1; IR (KBr) 3288, 3069, 3051, 1591, 1504, 1492, 1331, 1317, 1280, 1193, 1173, 1118, 1065, 1020, 945, 902, 838, 755, 721, 695, 621, 572 cm^{-1}.

2-(*p*-(*N,N*-Diphenylamino)-β-styryl)-5-nitrothiazole, 28. *p*-(Diphenylamino)-β-styryllithium was metathesized with zinc chloride and coupled with 2-bromo-5-nitrothiazole as described above. The product was flash chromatographed on silica gel eluting with 10% ethyl acetate–hexane and recrystallized from ethanol to give red crystals (14% yield): mp 180–181 °C; ^{1}H NMR δ ($CDCl_3$) 8.50 (s, 1H0, 7.59 (d, J = 16.0 Hz, 1H), 7.42 (d, J = 8.8 Hz, 2H), 7.36–7.28 (m, 4H), 7.17–7.10 (m, 6H), 7.09–7.00 (m, 3H); ^{13}C NMR δ (THF-d_8) 173.1, 150.8, 148.0, 147.9, 145.5, 139.6, 130.3, 130.0, 129.0, 126.3, 124.9, 122.3, 118.6; IR (KBr) 3088, 3062, 3031, 1586, 1557, 1509, 1489, 1428, 1404, 1351, 1327, 1285, 1251, 1190, 1177, 1147, 1122, 1081, 964, 815, 754, 700, 542, 520 cm^{-1}. Anal. Calcd for $C_{23}H_{17}N_3O_2S$: C, 69.15; H, 4.29; N, 10.52; S, 8.02. Found: C, 68.99; H, 4.29; N, 10.28; S, 8.11.

2-((*p*-Methoxyphenyl)ethynyl)-6-nitrobenzothiazole, 29. (*p*-Methoxyphenyl)acetylene and 2-bromo-6-nitrobenzothiazole[28] were coupled as described for the preparation of **9a**. The product was flash chromatographed on silica gel eluting with 20% acetone–hexane and recrystallized from ethanol to yield yellow needles (70% yield): mp 211–212 °C; ^{1}H NMR δ ($CDCl_3$) 8.81 (d, J = 2.3 Hz, 1H), 8.39 (dd, J = 2.3, J = 9.0 Hz, 1H), 8.14 (d, J = 9.1 Hz, 1H), 7.60 (d, J = 8.86, 2H), 6.94 (d, J = 8.86, 2H); ^{13}C NMR δ ($CDCl_3$) 161.4, 156.6, 154.4, 145.3, 135.4, 134.1, 123.4, 122.0, 117.8, 114.3, 112.0, 99.9, 81.6, 55.3; IR (KBr) 3100, 2925, 2837, 2201, 1603, 1568, 1518, 1338, 1300, 1253, 1176, 1087, 1027, 910, 835, 753, 748, 677 cm^{-1}. Anal. Calcd for $C_{16}H_{10}N_2O_3S$: C, 61.93; H, 3.25; N, 9.03; S, 10.33. Found: C, 61.87; H, 2.94; N, 8.89; S, 10.42.

2-(*p*-(*N,N*-Diphenylamino)-β-styryl)-6-nitrobenzothiazole, 30. β-(*p*-Diphenylamino)styryllithium was metathesized with zinc chloride and coupled with 2-bromo-6-nitrobenzothiazole[28] as described for the preparation of **23**. The product was flash chromatographed on silica gel eluting with 15% ethyl acetate–hexane and recrystallized from ethanol to give red plates (14% yield): mp 184–186 °C; ^{1}H NMR δ (THF-d_8) 8.89 (d, J = 2.3 Hz, 1H), 8.32 (dd, J = 2.3 Hz, J = 8.9 Hz, 1H), 8.01 (d, J = 8.9 Hz, 1H), 7.73 (d, J = 16.0 Hz, 1H), 7.58 (d, J = 8.8 Hz, 2H), 7.41 (d, J = 6.0 Hz, 1H), 7.33–7.27 (m, 4H), 7.15–7.00 (m, 8H); ^{13}C NMR δ (THF-d_8) 173.7, 159.0, 150.6, 148.0, 147.9, 145.6, 140.4, 135.8, 130.2, 129.9, 129.3, 126.2, 124.8, 123.2, 122.5, 122.4, 119.7, 119.0; IR (KBr) 3068, 3062, 3038, 1588, 1557, 1509, 1493, 1477, 1440, 1334, 1278, 1252, 1195, 1188, 1128, 1100, 972, 912 892, 818, 757, 724, 700 cm^{-1}. Anal. Calcd for $C_{27}H_{19}N_3O_2S$: C, 72.14; H, 4.26; N, 9.35; S, 7.13. Found: C, 72.16; H, 4.47; N, 9.39; S, 7.36.

2-(*p*-Methoxyphenyl)azo-5-nitrothiazole, 33. Diazotization of 2-amino-5-nitrothiazole and coupling with anisole was performed as described in the preparation of **35**. The crude product was flash chromatographed on silica gel eluting with 30% ethyl acetate–hexane and recrystallized from ethanol to give red needles (68% yield): mp 202–203 °C; ^{1}H NMR δ ($CDCl_3$) 8.68 (s, 1H), 8.06 (d, J = 9.1 Hz, 2H), 7.07 (d, J = 9.1 Hz, 2H), 3.96 (s, 3H); ^{13}C NMR δ ($CDCl_3$) 181.7, 153.9, 148.8, 146.4, 143.2, 127.6, 115.0, 55.9; IR ($CDCl_3$) 2936, 1602, 1521, 1372, 1356, 1289, 1250, 1139, 1120, 1073 cm^{-1}. Anal. Calcd for $C_{10}H_8N_4O_3S$: C, 45.45; H, 3.05; N, 21.20; S, 12.13. Found: C, 45.67; H, 3.02; N, 20.86; S, 12.08.

***N*-Ethyl-*N*-(ω-hydroxyhexyl)aniline, 34.** Into a flask was placed *N*-ethylaniline 93.3 g, 27 mmol), 6-bromo-1-hexanol (5.0 g, 27 mmol), sodium bicarbonate 92.8 g, 33 mmol), and 40 mL of DMF. The mixture was stirred and heated to reflux for 2.5 h. After cooling, the reaction mixture was diluted with brine and extracted with ethyl ether. The combined organic extracts were dried over sodium sulfate, filtered, and concentrated. The residue was flash chromatographed on silica gel using 20% acetone–hexane to give a clear oil (4.2 g, 69% yield): ^{1}H NMR δ ($CDCl_3$) 7.27–7.18 (m, 2H), 6.70–6.62 (m, 3H), 3.66 (t, 2H), 3.37 (q, 2H), 3.27 (t, 2H), 1.78–1.55 (m, 4H), 1.48–1.38 (m, 4H), 1.16 (t, 3H); ^{13}C NMR δ ($CDCl_3$) 147.8, 128.1, 115.2, 111.7, 62.8, 50.2, 44.8, 32.7, 27.4, 26.9, 25.6, 12.2; IR ($CDCl_3$) 3069, 3062, 3012, 2937, 2860, 1598, 1571, 1467, 1397, 1372, 1354, 1271, 1194, 1072, 1050, 1037, 997 cm^{-1}.

2-(*p*-*N*-Ethyl-*N*-(ω-hydroxyhexyl)aniline)azo-5-nitrothiazole, 35. To a solution of 2-amino-5-nitrothiazole (1.4 g, 9.5 mmol) dissolved in 20 mL of 85% phosphoric acid, sodium nitrite (0.65 g, 9.5 mmol) in 2.5 mL of water was added slowly maintaining the reaction temperature at 0–5 °C. After stirring for 1.5 h, the diazotized mixture was poured slowly into a vigorously stirring solution of *N*-ethyl-*N*-(ω-hydroxyhexyl)aniline (1.75 g, 7.9 mmol) in a HCl–water mixture (70:1) maintained at 0 °C. The reaction mixture was stirred for another 1.5 h and then diluted with ice water and extracted with portions of ethyl acetate. The combined organic extracts were dried over magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel eluting with 30% acetone–hexane. Recrystallization from ether–hexane afforded

(27) Matsumoto, M.; Kuroda, K. *Tetrahedron Lett.* **1980**, *21*, 4021.

(28) Erlenmeyer, H.; Ueberwasser, H. *Helv. Chim. Acta* **1942**, *25*, 515.

a dark green solid (0.8 g, 27% yield): mp 115–116 °C; ^{1}H NMR δ ($CDCl_3$) 8.57 (s, 1 H), 7.91 (d, J = 9.0 Hz, 2H), 6.73 (d, J = 9.3 Hz, 2H), 3.67 (t, 2H), 3.52 (q, 2H), 3.45 (t, 2H), 1.69–1.59 (m, 4H), 1.45–1.43 (m, 4H), 1.28 (t, 3H); ^{13}C NMR δ ($CDCl_3$) 181.7, 153.9, 146.4, 144.3, 143.8, 142.5, 112.1, 62.5, 50.9, 45.9, 32.4, 27.6, 26.7, 25.5, 12.5; IR ($CDCl_3$) 2936, 1602, 1521, 1372, 1356, 1289, 1250, 1139, 1120, 1073 cm^{-1}. Anal. Calcd for $C_{17}H_{23}N_5O_3S$: C, 54.09; H, 6.14; N, 18.55; S, 8.49. Found: C, 54.50; H, 6.11; N, 18.73; S, 8.69.

2-((*N,N*-Diphenylamino)phenyl)azo-5-nitrothiazole, 36. To a flask equipped with mechanical stirrer was added triphenylamine (2.0 g, 8.2 mmol), sodium dodecylphenyl sulfonate (0.28 g, 0.82 mmol), 100 mL of dichloromethane, and 80 mL of water. After the mixture was cooled to 0 °C, a diazotized solution of 2-amino-5-nitrothiazole (1.4 g, 9.5 mmol) in 25 mL of phosphoric acid was added, maintaining the reaction temperature at 0 °C for 2.5 h. The resulting mixture was diluted, extracted and dried over magnesium sulfate. The crude product was purified by flash chromatography on silica gel eluting with 10% acetone–hexane. Recrystallization from ethanol afforded dark crystals (1.2 g, 31% yield): mp 208–209 °C; ^{1}H NMR δ ($CDCl_3$) 8.63 (s, 1H), 7.8 (d, J = 9.2 Hz, 2H), 7.44–7.37 (m, 4H), 7.30–7.23 (m, 6H), 7.00 (d, J = 9.2 Hz, 2H); ^{13}C NMR δ ($CDCl_3$) 180.3, 154.4, 147.7, 145.1, 145.0, 143.5, 129.9, 127.6, 126.7, 126.2, 118.8; IR ($CDCl_3$) 3144, 3106, 3062, 3031, 1607, 1586, 1556, 1519, 1490, 1368, 1336, 1286, 1264, 1245, 1209, 1138, 1123, 844, 815, 791 cm^{-1}. Anal. Calcd for $C_{21}H_{15}N_5O_2S$: C, 62.83; H, 3.77; N, 17.44; S, 7.99. Found: C, 62.46; H, 3.96; N, 17.43; S, 8.16.

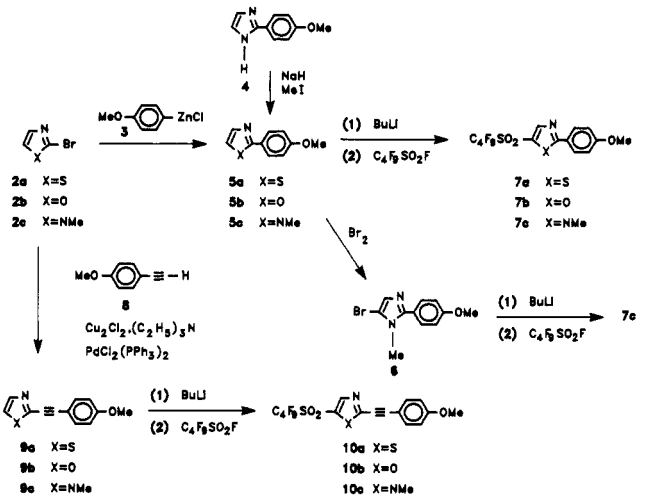
2-(*p*-[*N*-Ethyl-*N*-(ω-hydroxyhexyl)amino]phenyl)azo-6-nitrobenzothiazole, 37. Diazotization of 2-amino-6-benzothiazole and coupling with *N*-ethyl-*N*-(ω-hydroxyhexyl)aniline was carried out as described for **35**. The product was flash chromatographed on silica gel eluting with ethyl acetate–hexane–ethanol mixture (1:1:0.1). Recrystallization from ethanol afforded dark violet crystals (41% yield): mp 150–151 °C; ^{1}H NMR δ ($CDCl_3$) 8.68 (d, J = 2.3 Hz, 1H), 8.26 (dd, J = 9.0, J = 2.3 Hz, 1H), 8.04 (d, J = 9.0 Hz, 1H), 7.92 (d, J = 9.2 Hz, 2H), 6.85 (d, J = 9.3 Hz, 2H), 3.67 (m, 2H), 3.51 (q, 2H), 3.41 (t, 2H), 1.71–1.59 (m, 4H), 1.47–1.39 (m, 4H), 1.26 (t, 3H); ^{13}C NMR δ ($CDCl_3$) 182.3, 158.8, 153.5, 144.7, 142.7, 134.3, 123.3, 121.4, 118.3, 111.7, 62.5, 50.8, 45.7, 32.5, 27.5, 26.7, 25.5, 12.4; IR ($CDCl_3$) 3131, 3087, 2984, 2931, 2862, 1601, 1572, 1550, 1520, 1414, 1331, 1311, 1273, 1238, 1195, 1145, 1120, 1074, 993, 827 cm^{-1}. Anal. Calcd for $C_{21}H_{25}N_5O_3S$: C, 59.00; H, 5.83; N, 16.38; S, 7.50. Found: C, 58.46; H, 6.08; N, 15.97; S, 7.67.

2-((*N,N*-Diphenylamino)phenyl)azo-6-nitrobenzothiazole, 38. Diazotization of 2-amino-6-benzothiazole and coupling with triphenylamine was carried out using the phase-transfer procedure as described for **36**. The product was flash chromatographed on silica gel eluting with 25–35% acetone–hexane and recrystallized from ethanol to afford dark violet crystals (27% yield): mp 209–211 °C; ^{1}H NMR δ ($CDCl_3$) 8.75 (d, J = 2.3 Hz, 1H), 8.33 (dd, J = 8.9, J = 2.3 Hz, 1H), 8.15 (d, J – 8.9 Hz, 1H), 7.92 (d, J = 9.2 Hz, 2H), 7.44–7.37 (m, 4H), 7.28–7.23 (m, 6H), 7.02 (d, J = 9.2 Hz, 2H); ^{13}C NMR δ ($CDCl_3$) 181.3, 156.4, 154.1, 145.4, 145.3, 145.2, 134.4, 129.8, 127.2, 126.7, 125.9, 124.1, 121.6, 118.8, 118.5; IR ($CDCl_3$) 3143, 3078, 3056, 1603, 1586, 1559, 1522, 1493, 1377, 1330, 1307, 1301, 1276, 1248, 1184, 1143, 1120 cm^{-1}. Anal. Calcd for $C_{25}H_{17}N_5O_2S$: C, 66.51; H, 3.79; N, 15.51; S, 7.10. Found: C, 66.21; H, 4.04; N, 15.49; S, 7.41.

Characterization

Molecular hyperpolarizabilities were determined by electric-field-induced second harmonic generation (EFISH)[29,30] as previously described.[11] Briefly, solutions of each compound were subjected to high-voltage electrical pulses and focused laser pulses simultaneously, and the resulting frequency-doubled light pulses were monitored as a function of path length through the experimental cell. From these data, signal amplitudes and coherence

Scheme 1. Synthetic Route to 2-Substituted 5-(Perfluorobutylsulfonyl)imidazoles, -oxazoles, and -thiazoles



lengths were extracted, and referenced to a quartz sample. The concentration dependence of the nonlinear susceptibility and the dielectric constant (uncertainties 0.1 D) were used to determine the molecular hyperpolarizability β at the experimental laser wavelength. The uncertainties in the β_ω values are less than 10% in every case. Absorption spectra were taken with a diode array spectrophotometer, and the λ_{max} values (accuracy 2 nm) were used to extrapolate β to zero frequency (β_0) according to the two-level model of Oudar and Chemla:[31,32]

$$\beta_0 = \beta_\omega\left(1 - \frac{\lambda_{max}^2}{\lambda^2}\right)\left(1 - 4\frac{\lambda_{max}^2}{\lambda^2}\right) \quad (1)$$

Many of the thiazoles were characterized at 1064 nm, but some were characterized using 1907-nm light, the output of a hydrogen Raman shifter cell.

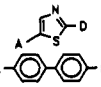
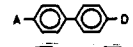
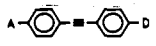
Results

The synthesis of the desired 2,5-disubstituted azole and 2,6-disubstituted benzoazole derivatives are described in Schemes 1–3. In general, the desired materials were prepared by palladium-catalyzed carbon–carbon bond formation from the appropriately substituted 2-bromothiazoles or benzothiazoles. The azo derivatives were all prepared from the substituted 2-aminothiazoles or benzothiazoles via diazotization and subsequent azo coupling reactions.[33]

A direct comparison of the linear and nonlinear properties of some comparably substituted *N*-methylimidazoles, oxazoles, and thiazoles was performed, and the results are reported in Table 1. The EFISH results were obtained in *p*-dioxane at 1.064 μm and extrapolated to zero frequency as described above. The quantity in the last column of Table 1 ($\mu\beta_{1300}^{EO}$) is relevant to potential poled polymer electrooptic applications. It was determined as follows: β_0 values were multiplied by 3 to correct for convention

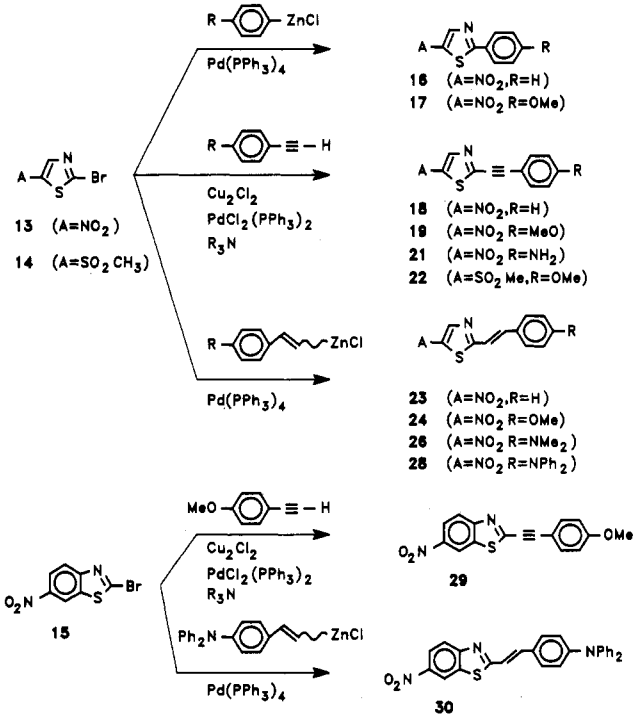
(29) Bethea, C. G.; Levine, B. F. *J. Chem. Phys.* **1975**, *63*, 2660.
(30) Bethea, C. G. *Appl. Opt.* **1975**, *14*, 1477.
(31) Oudar, J. L. *J. Chem. Phys.* **1977**, *67*, 446.
(32) Oudar, J. L.; Chemla, D. S. *J. Chem. Phys.* **1977**, *66*, 2664.
(33) Dickey, J. B.; Torone, E. B.; Bloom, M. S.; Moore, W. H.; Hill, H. M.; Heynemann, H.; Hedberg, D. G.; Sievers, D. C.; Otis, M. V. *J. Org. Chem.* **1959**, *24*, 187.

Table 1. Nonlinearities of Some Substituted Thiazoles, Oxazoles, and *N*-Methylimidazoles

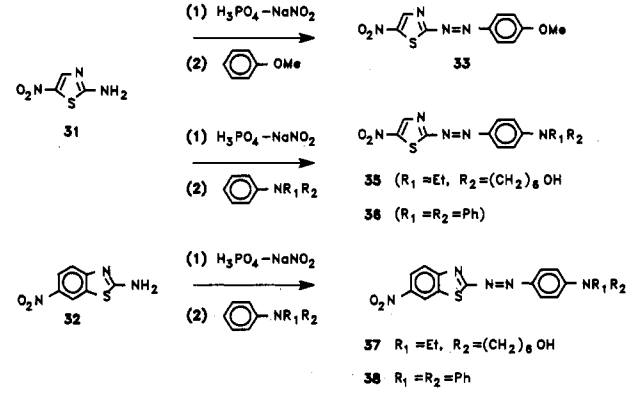
entry	structure	A	D	μ (D)	λ_{max}[a] (nm)	$\beta_\omega \times 10^{30}$ (esu)[b]	$\beta_0 \times 10^{30}$ (esu)	$\mu\beta_{1300}^{EO} \times 10^{30}$ (cm^5 D esu^{-1})[c]
1		$SO_2C_4F_9$	MeOPh	6.0	282	2.7	1.8	21
2			MeOPhC≡C—	7.6	312	9.9	5.9	89
3		$SO_2C_4F_9$	MeOPh	5.1	312	11.8	7.1	71
4			MeOPhC≡C—	6.2	328	21.4	12.0	150
5		$SO_2C_4F_9$	MeOPh	6.0	338	15.0	8.0	97
6			MeOPhC≡C—	7.4	358	26.9	13.1	198
7		$SO_2C_4F_9$	MeO	6.3	310	13.6	8.2	102
8		$SO_2C_6F_{13}$	MeO	6.8	334	19.6	10.7	146

[a] Recorded in *p*-dioxane. [b] Measured in *p*-dioxane at 1.064 μm. [c] Dipole moment (D) × quadratic hyperpolarizability for the electrooptic effect ($\beta(-\omega; \omega, 0)$) extrapolated to 1300 nm as described in the text.

Scheme 2. Synthetic Route to a Variety of Donor–Acceptor-Substituted Thiazoles and Benzothiazoles



Scheme 3. Synthetic Route to a Variety of 2-Azo-Substituted Thiazoles and Benzothiazoles



inconsistencies[34] and were then reduced to reference them to the preferred value of the quartz standard[35,36] (7.2 × 10^{-10} esu at 1.064 μm). The corrected β_0 values were extrapolated to 1300 nm using the dispersion expression appropriate for the electrooptic effect.[37] The β_0 values in Tables 1–3 are *not* adjusted in this fashion to facilitate direct comparison with similar values reported in the literature. In one case (compound **12**), the acceptor group contains a perfluorohexyl substituent instead of a perfluorobutyl group and is therefore not an exact analogue. We expect its behavior to be sufficiently similar to the (perfluorobutyl)sulfonyl substituent to warrant its inclusion in Table 1 for comparison. The corresponding substituted biphenyl **11** and the tolane **12** (entries 7 and 8) are included in this table for direct comparison with the heterocyclic derivatives.

We have collected the pertinent linear and nonlinear data for a variety of thiazole derivatives substituted with moderate electron donors (i.e., Ph, MeOPh—, PhCH=CH—, MeOPhCH=CH—, MeOPhC≡C—) in Table 2. Also included in this table are data for one substituted benzothiazole derivative (entry 3). All of the materials in Table 2, with the exception of the azo derivative (entry 2), were studied in *p*-dioxane at 1.064 μm.

Finally, we have prepared and studied a variety of thiazole and benzothiazole derivatives substituted with strongly electron donating amino substituents, and these data are collected in Table 3. The EFISH and spectroscopic measurements for these materials were performed in chloroform at 1.907 μm. Also included with the spectroscopic data is the onset decomposition temperature (T_d) of the neat chromophore. This value, which is defined as the intercept between the decomposition exotherm and the base line, was determined by differential scanning colorimetry (DSC) analysis at heating rate of 20 °C/min[38] and provides a crude estimate of the thermal stability of the NLO chromophore. Lower heating rates result in lower values for T_d, sometimes by as much as 25–50 °C.

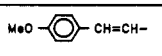
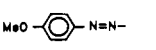
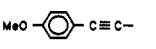
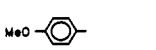
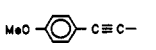
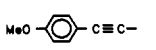
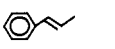
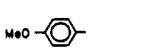
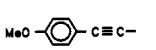
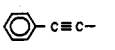
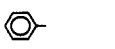
Discussion

We have recently described the thermal and nonlinear optical studies of a variety of donor–acceptor-substituted 2,4,5-triaryl-substituted imidazole, oxazole, and thiazole derivatives.[10] Unfortunately, the triaryl substitution pattern, while imparting impressive thermal and oxidative stability, causes severe steric crowding of the aromatic substituents in positions 4 and 5 which causes them to

(34) (a) Moylan, C. R.; Swanson, S. A.; Walsh, C. A.; Thackara, J. I.; Twieg, R. J.; Miller, R. D.; Lee, V. Y. *Proc. SPIE* **1993**, *2025*, 192. (b) Willetts, A.; Rice, J. E.; Burland, D. M.; Shelton, D. P. *J. Chem. Phys.* **1992**, *97*, 7590.

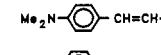
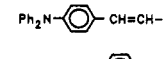
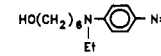
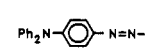
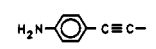
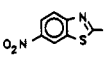
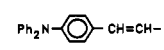
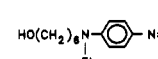
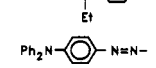
(35) Jerphagnon, J.; Kurtz, S. K. *Phys. Rev. B* **1970**, *1*, 739.
(36) Roberts, D. A. *IEEE J. Quantum Electron.* **1992**, *28*, 2057.
(37) Singer, K. D.; Kuzyk, M. G.; Sohn, J. E. *J. Opt. Soc. Am. B* **1987**, *4*, 968.
(38) Miller, R. D.; Betterton, K. M.; Burland, D. M.; Lee, V. Y.; Moylan, C. R.; Twieg, R. J.; Walsh, C. A.; Volksen, W. *Proc. SPIE*, in press.

Table 2. Nonlinearities of Thiazole Derivatives Substituted with Moderate Electron Donors

entry	structure	donor	acceptor	μ (D)	λ_{max}[a] (nm)	$\beta_\omega \times 10^{30}$ (esu)[b]	$\beta_0 \times 10^{30}$ (esu)[c]	$\mu\beta_{1300} \times 10^{30}$ (cm^5 D esu^{-1})[d]
1			NO_2	6.0	406	67.7	24.2	310
2			NO_2	6.2	424[e]	29.7[e]	22.7	328
3			NO_2	6.0	362	46.9	22.3	276
4			NO_2	5.4	378	41.2	17.8	199
5			NO_2	5.9	382	33.7	14.2	175
6			$SO_2C_4F_9$	7.4	358	26.9	13.1	198
7			NO_2	4.9	372	26.0	11.7	119
8			$SO_2C_4F_9$	6.0	338	15.0	8.0	97
9			SO_2Me	6.0	334	13.2	7.2	87
10			NO_2	5.5	354	10.9	5.4	60
11			NO_2	4.1	346	8.1	4.2	35

[a] Measured in *p*-dioxane. [b] Measured in *p*-dioxane at 1.064 μm. [c] Calculated according to the two-state model. [d] Dipole moment (D) × quadratic hyperpolarizability for the electrooptic effect ($\beta(-\omega; \omega, 0)$) extrapolated to 1300 nm. [e] Measured at 1.907 μm.

Table 3. Nonlinearities of Some Nitrothiazole and -benzothiazole Derivatives Substituted with Amino Electron Donors

entry	structure	donor	T_d (°C)[a]	μ (D)	λ_{max}[b] (nm)	$\beta_\omega \times 10^{30}$ (esu)[c]	$\beta_0 \times 030$ (esu)[d]	$\mu\beta_{1300} \times 10^{30}$ (cm^5 D/esu)[d]
1			253	8.2	478[f]	93.8[f]	65.8	1320
2			325	5.2	492	83.0	56.8	737
3			233	9.0	582	91.7	52.2	1320
4			298	6.9	582	120	68.2	1320
5			NA	7.1	426[f]	71.9[f,g]	21.7	360
6			367	5.5	458	78.8	57.2	756
7			248	9.5	548	97.8	60.1	1530
8			356	7.2	550	117	71.8	1390

[a] Onset decomposition temperature measured by DSC at 20 °C min. [b] Measured in chloroform. [c] Measured in chloroform at 1.907 μm. [d] Calculated using the two-level approximation. [e] Dipole moment (D) × quadratic hyperpolarizability for the electro-optic effect ($\beta(-\omega; \omega, 0)$) extrapolated to 1300 nm. [f] Measured in *p*-dioxane. [g] Measured at 1.06 μm.

twist from coplanarity with the heterocyclic ring, thus affecting both the linear and nonlinear optical properties. Such steric interactions are not present in 2,5-disubstituted thiazoles or 2,6-disubstituted benzothiazoles, rendering such derivatives potentially attractive for NLO studies.

The first question to be answered in such a study in which particular heterocyclic azole ring is intrinsically the most nonlinear. We have tried to answer this for a number of simple 2,5-disubstituted *N*-methylimidazoles, oxazoles, and thiazoles where the electron-attracting substituent is directly bonded to the heterocyclic ring at position 5 and the donor group is located in position 2. For the purpose of initial screening, we have selected the perfluoroalkylsulfonyl substituent as an appropriate electron acceptor and a variety of alkoxyaryl moieties as electron donors. Perfluoroalkylsulfonyl substituents are strongly electron attracting, are thermally and oxidatively stable, and have respectable group dipole moments directed near the main charge-transfer axis of the NLO molecule.[39] We have therefore developed a general synthetic procedure applicable to the preparation of 2,5-disubstituted *N*-methylimidazoles, oxazoles, and thiazoles containing a perfluoroalkylsulfonyl acceptor substituent at position 5 which is based on the anionic chemistry shown in Scheme 1. The key intermediates in each case are the 2-substituted *p*-methoxyphenyl- and (*p*-methoxyphenyl)ethynyl-*N*-methylimidazoles, -oxazoles, and -thiazoles. Each class of starting materials is readily available from the 2-haloazole derivative by palladium-catalyzed carbon–carbon bond-formation reactions: zinc reagents[40,41] for the 2-aryl derivatives and Hagahira[42,43] coupling conditions for the 2-arylethynyl derivatives. Treatment of the 2-arylazole derivatives with *n*-BuLi generally results in the regiospecific formation of the lithium anion at ring position 5 on

(39) Cheng, L.-T.; Tam, W.; Feiring, A. C. *Mol. Cryst. Liq. Cryst. Sci. Technol., Sect. B* **1992**, *3*, 69.
(40) Amatore, C.; Jutland, A.; Negri, S.; Fauvarque, J.-F. *J. Organomet. Chem.* **1990**, *390*, 389.
(41) Negishi, E. I.; Hayashi, T.; King, A. O. *Org. Synth.* **1987**, *66*, 67.
(42) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467.
(43) Takahashi, S.; Kuroyama, K.; Sonogashira, N.; Hagihara, N. *Synthesis* **1980**, 627.

the heterocyclic ring which can be subsequently functionalized by quenching with perfluorobutylsulfonyl fluoride to produce the desired perfluorosulfonyl-substituted azole derivatives. Because of the complexity of the resonances associated with carbons bound to fluorine and reduced sensitivities, these carbons were usually not detected under normal conditions. These resonances may be identified by comparison of the ^{13}C spectra recorded with no decoupling with those measured with only ^{19}F decoupling. For some reason, the attempted sulfonation of the species generated by the treatment of *N*-methyl-2-(*p*-methoxyphenyl)imidazole (**5c**) with *n*-BuLi gave an unusually low yield of the desired product (<10% even in the presence of 1.5 equiv of HMPTA) despite the fact that the same reaction was successful for functionalizing corresponding 2-(*p*-methoxyphenyl)ethynyl derivative **9c**. In the case of **7c**, it proved more expedient to first generate 5-bromo-1-methyl-2-(*p*-methoxyphenyl)imidazole (**6**) by direct bromination of the starting material **5c**. This product was readily converted to the desired anion with *tert*-butyllithium and subsequently sulfonated with perfluorobutylsulfonyl fluoride to yield **7c**.

The linear and nonlinear properties of **7a–c** and **10a–c** are shown in Table 1 in comparison with the comparably substituted biphenyl and tolane derivatives (entries 7 and 8). For the simple substitution patterns studied, the order of nonlinearity was thiazole > oxazole ≫ *N*-methylimidazole, although the difference between thiazoles and oxazoles is not great. For electrooptic poled polymer applications, the substituted thiazoles are viewed as somewhat superior by virtue of the combination of their substantial dipole moments, red-shifted absorption maxima, and somewhat enhanced nonlinearities. For these reasons, we concentrated our subsequent studies on substituted thiazole derivatives.

The synthetic procedures used for the preparation of a variety of thiazole derivatives substituted with moderately strong electron donors are shown in Scheme 2. The key intermediates for the preparation of the materials listed in Table 2 are the 2-bromothiazoles and benzothiazoles **13–15** prepared from the diazonium derivatives available by diazotization of the corresponding readily available 2-amino derivatives.[25,28] Palladium-catalyzed coupling of organozinc derivatives prepared from the corresponding lithium reagents proved to be the simplest and most consistent procedure for the preparation of 2-aryl and 2-β-styryl thiazoles. The lithium reagents were prepared by metal–halogen exchange of the aryl or β-styryl iodides or bromides using 2 mol of *tert*-butyllithium. The preferred route to the latter was via the Wittig reaction between the corresponding aldehyde and the ylide prepared from triphenyl(bromomethyl)phosphonium bromide.[27] This procedure usually generates a mixture of isomers in which the *Z* isomer predominates. In our hands, using THF as the solvent, we apparently isolate the pure *Z* isomer **25** based on the observed vinylic proton coupling constants of 8.9 Hz. The pure *E* isomer of **25** (mp 124 °C) could be prepared in low yield by the bromination of *p*-(dimethylamino)cinnamic acid followed by treatment with sodium carbonate.[44] The diphenyl derivative **27** is isolated as a mixture of *E,Z* isomers. In the subsequent coupling reactions to produce **26, 28,** and **31** only the *E* isomers are isolated as evidenced by the large vinylic coupling constants (J = 15.9, 16.0, and 16.0 Hz respectively) of the products. The use of *p*-methoxy-*trans*-β-iodostyrene, obtained by the sequential hydroboration–iodination of (*p*-methoxyphenyl)acetylene with catecholborane–iodine,[45] for the formation of the vinyllithium reagent was successful but offered no competitive advantage over the Wittig procedure route.

From Table 2 it is obvious that the progression of donor substituents from phenyl, *p*-methoxyphenyl, (*p*-methoxyphenyl)ethynyl to *p*-methoxy-β-styryl results both in red-shifted absorption maxima and enhanced nonlinearities (see Table 2) as anticipated from the increased conjugation length and donor strengths of the substituents. In this respect, the nonlinearity of 2-(methoxyphenyl)-5-nitrothiazole (**17**, entry 4) seems anomalously high. The error bars for this measurement are also unusually large (β_0 = $(17.8 \pm 6.6) \times 10^{-30}$ esu) suggesting that the order of ranking in the table (i.e., entry 4 > entry 5) may need to be reinvestigated. For the thiazoles listed in Table 2, the nonlinearities decrease for the acceptor groups: NO_2 > $SO_2C_4F_9 \gg SO_2CH_3$ as expected. Comparison of a stilbene derivative **24** versus the comparably substituted azo benzene **33** (entry 1 versus entry 2) suggests that the dipole moments and nonlinearities are comparable even though the absorption maximum of the latter is red-shifted by 18 nm (1046 cm^{-1}). The data for a single 6-nitrobenzothiazole included in this table (entry 3) suggest that the measured nonlinearity is unexpectedly large based on its blue-shifted absorption maximum (compare entries 3 and 5 in Table 2). This trend was also observed for other benzothiazole derivatives (vide infra).

A number of conclusions can be drawn regarding the thermal stabilities of the materials listed in Table 3. First and foremost is the greatly improved thermal stability of materials substituted with diphenylamino substituents. This seems to be a general phenomenon that is independent of both the nature of the acceptor group or the conjugating bridge substituent.[46] Second, the measured stabilities of the benzothiazoles derivatives **30, 37,** and **38** (entries 6–8) all appear to be significantly better than those of simple 5-nitrothiazole derivatives with comparable substitution. As a result, maximum thermal stabilities are achieved for the diphenylamino-substituted 6-nitrobenzothiazole derivatives. For the materials surveyed here, there seems to be little difference in the thermal stabilities for comparably substituted stilbene and azo derivatives as determined by thermal analysis techniques.

The intrinsic nonlinearities of the thiazole derivatives listed in Table 3, as defined by β_0, are quite large. For comparison, β_0 for 4-(dimethylamino)-4′-nitrostilbene (DANS) measured at 1.907 in chloroform is $\sim 40 \times 10^{-30}$ esu.[34a] The nonlinearity of the only amino-substituted derivative studied containing an acetylenic linkage **21** (entry 5) is significantly lower than the others. Although this is also the only derivative containing a NH_2 donor, it seems unlikely that either alkyl or aryl substitution on nitrogen will boost the nonlinearity into the range of the other materials discussed. This conclusion is also consistent with the substantially lower intrinsic nonlinearities of tolane derivatives in comparison with comparably substituted stilbenes and azo derivatives.[34a] The effect

(44) Barbieri, P. *C. R. Acad. Sci. C* **1950**, *231*, 57.

(45) Brown, H. C.; Hamaoka, T.; Ravindran, N. *J. Am. Chem. Soc.* **1973**, *95*, 5786.

(46) Moylan, C. R.; Twieg, R. J.; Lee, V. Y.; Swanson, S. A.; Betterton, K. M.; Miller, R. D. *J. Am. Chem. Soc.* **1993**, *115*, 12599.

on the nonlinearities of *N,N*-diphenyl versus *N,N*-dialkyl substitution is less clear cut. For the azo derivatives, the nonlinearities of the diaryl substituted derivatives seem somewhat larger than for dialkyl substitution (entries 3, 4 and 7, 8). This relationship is true for both the thiazole and benzothiazole derivatives. The conclusions are more ambiguous for those derivatives containing an ethylenic spacer. In the case of 5-nitrothiazole pair (entries 1 and 2), the nonlinearities are comparable with those of the dialkyl-substituted derivatives, although the former is slightly more nonlinear. A simple dialkylamino substituted analogue of the corresponding 6-nitrobenzothiazole was not available for study.

The nonlinearity for poled polymer applications, which we define for convenience as $\mu\beta_{1300}^{EO}$ in Table 3, is sometimes slightly lower for diphenyl versus dialkyl substitution, primarily due to the lower dipole moments of the diphenylamino-substituted derivatives. This ordering may change with the attachment of appropriate tether functionality necessary for bonding to appropriate high temperature polymers. In general, it can be stated that for comparable substitution, the dipole moments are larger and the absorption maxima red-shifted for the azo derivatives relative to the corresponding stilbenes. As a result, the measured nonlinearities are often larger for the azo derivatives, but exceptions should not be surprising (see, for example, entries 1 versus 3, although the substitution in this comparison is not identical). Finally, a comment concerning the efficacy of 6-nitrobenzothiazoles versus 5-nitrothiazoles, where the nitro substituent is bonded directly to the thiazole ring, is in order. For comparable substitution, the thermal stability of the former is always significantly greater, the dipole moments are larger and the absorption maxima are significantly blue-shifted. Despite the spectral blue-shifts, the extrapolated nonlinearities (β_0) of the benzo derivatives are comparable to or larger than those measured for the 5-nitrothiazole derivatives with similar substitution.

For both electrooptical and frequency doubling applications, it is important to know how much additional nonlinearity is achieved with a given red shift, because absorptive loss concerns place an upper limit on λ_{max}. The traditional way to measure this tradeoff is by taking the slope of a log–log plot of hyperpolarizability vs absorption maximum.[47] Such a plot for 12 simple thiazoles is shown in Figure 1. The least-squares slope of the dashed line is 6.2 ± 0.7. The thiazoles therefore show the same nonlinearity-transparency tradeoff as do pyrazoles,[11] within experimental error (the latter exhibited a slope of 6.5 ± 1.0). Not included on this plot are the data for the azo derivatives and the benzothiazoles (**29, 30, 33,** and **35–38**). A preliminary examination of the data for these compounds suggests that most points would lie significantly off the least-squares line in Figure 1. Such a result is not too unexpected given the significant differences in electronic structure.

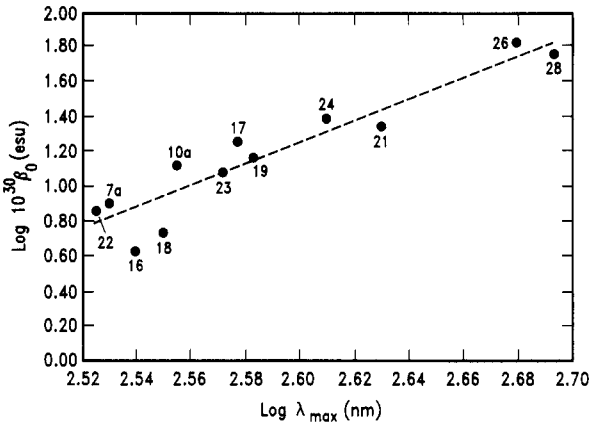


Figure 1. Nonlinearity vs transparency plot for a number of donor–acceptor-substituted thiazole derivatives.

Conclusions

In summary, we have prepared and characterized a variety of NLO chromophores containing five-membered heterocyclic azole rings. These examples include 2,5-donor–acceptor-substituted *N*-methylimidazoles, oxazoles, and thiazoles as well as a number of 2,6-disubstituted benzothiazole derivatives. The substitution patterns were chosen in an effort to maintain maximum conjugative interaction between the donor and acceptor substituents while minimizing unfavorable steric interactions which could result in twisting of the substituents, thus effecting both the linear and nonlinear spectroscopic properties. For simple 2,5-donor–acceptor monocyclic substitution, the order of nonlinearity is thiazole > oxazole ≫ *N*-methylimidazole. This is the same order found previously for a variety of 2,4,5-triaryl-substituted azole derivatives except that the imidazoles in the current study are relatively less nonlinear. For comparable substitution, the thiazole derivatives are found to be somewhat more nonlinear than oxazoles (by comparison of the zero-field quadratic molecular hyperpolarizabilities). This is despite the fact that the oxazole ring is believed to be the least aromatic of the heterocyclic rings studied. Even though the differences in the nonlinearities between the thiazoles and oxazoles are not large for the examples studied, the former are preferred for electrooptic applications such as modulation and switching due to their larger dipole moments and red-shifted absorption maxima. As expected, amino donor substitution results in greatly enhanced nonlinearities. For these materials, diaryl substitution on nitrogen also leads to much improved thermal stabilities without compromising the resulting nonlinearities. Similarly 6-nitro-substituted benzothiazoles were more thermally stable than the corresponding 5-nitrothiazole derivatives. The former were also more nonlinear in spite of the fact that the long wavelength absorption maxima were significantly blue-shifted. The combination of thermal stability and high nonlinearities present in appropriately substituted thiazoles and benzothiazoles suggests potential utility in host–guest and tethered poled polymer electrooptic applications. These applications are currently under investigation.

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(47) Cheng, L. T.; Tam, U.; Feiring, A.; Rikken, G. *Proc. SPIE Int. Soc. Opt. Eng.* **1990**, *1337*, 203.