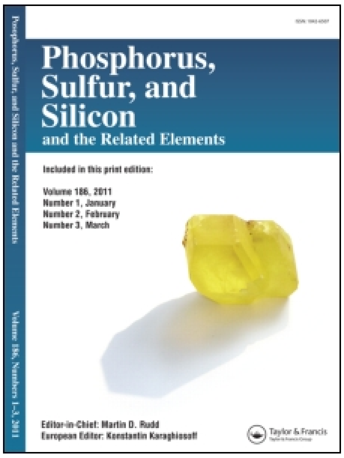

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THE AQUEOUS PERIODATE OXIDATION OF AROMATIC AND ALIPHATIC CARBOXYLIC ACID DISULFIDES

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The water-soluble carboxylic acid-functionalized aromatic disulfides, 3,3′-dithiodibenzoic acid and 5,5′-dithiodiisophthalic acid (5,5′-dithiodi(1,3-benzenedicarboxylic acid)) were prepared and their rates of periodate oxidation to the sulfonic acids were determined. The reaction is first order in each of the reactants which indicates that the slow step is the initial oxidative cleavage step. These aromatic disulfides are oxidized to the sulfonic acids 4–8 times more slowly than a typical aliphatic disulfide. In all cases, water solubility of the disulfide is of prime importance. The periodate oxidation of two aliphatic carboxylic acid analogs were also examined, however, in these cases, the reactions were multiphasic and intermediate thiosulfinates were observed by ^{1}H NMR along with the sulfonic acids.

Key words: Periodate; disulfide; thiosulfonate; sulfonic acid; carboxylic acid; ABTS.

INTRODUCTION

Recently we reported that aqueous periodate oxidatively cleaves water-soluble aliphatic amine disulfides and alcohol disulfides[1] almost as readily as it oxidizes thioethers to sulfoxides. With periodate, we also showed that a neighboring amine group facilitates the oxidation of water-soluble aliphatic disulfides but not the oxidation of thioethers. There have been no detailed studies of the oxidation of aromatic disulfides by aqueous periodate.

In an NMR-based study of the periodate oxidation of *p*-fluorobenzenethiol and *p*-fluorophenyl disulfide, this aromatic disulfide appeared to be unreactive within the brief reaction times used in the NMR experiments.[2] However, the low water solubility of *p*-fluorophenyl disulfide may have been the reason why this compound failed to react. To quantify the oxidation of water-soluble carboxylic acid-functionalized aromatic disulfides, 3,3′-dithiodibenzoic acid, **1**, and 5,5′-dithiodiisophthalic acid (5,5′-dithiodi(1,3-benzenedicarboxylic acid)), **2**, were prepared and their rates of oxidation were measured.[1]

The periodate oxidations of two aliphatic carboxylic acid analogs, 3,3′-dithiodipropanoic acid, **3**, and 4,4′-dithiodibutanoic acid, **4**, were also examined.

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RESULTS AND DISCUSSION

Preparation of Aromatic Disulfides

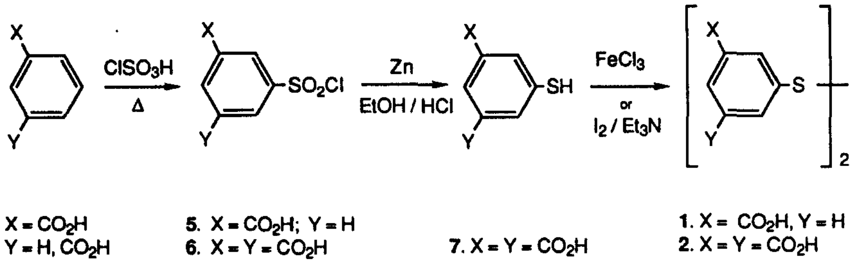
The synthesis of **1** was first attempted by preparing the diazonium salt of 3-aminobenzoic acid and treating it with sodium disulfide,[3] but this reaction gave only a crude product which could not be purified. Compound **1** was subsequently prepared by an adaptation of the method of Smiles and Stewart.[4] Benzoic acid was converted to 3-chlorosulfonylbenzoic acid, **5**, which was reduced to the thiol with Zn in EtOH/HCl and then oxidized with $FeCl_3$ to give **1** (Scheme I). Compound **2** was prepared in a similar manner from isophthalic acid by sulfonylation to give 5-chlorosulfonylisophthalic acid, **6**, reduction with Zn to 5-mercaptoisophthalic acid, **7**, and oxidation with I_2/Et_3N to give **2** (Scheme I). ($FeCl_3$ failed to oxidize **7** to the disulfide.)

meta-Substituted aromatic disulfides were selected to avoid any complications from neighboring group effects of *ortho* carboxylates. In a study of the sodium periodate oxidation of thioethers to sulfoxides,[5] periodate was shown to be an electrophilic oxidant and the enhanced reactivity of *o*-methylthiobenzoic acid was attributed to a neighboring carboxylate interaction.

Reaction Conditions. The oxidative cleavage reactions were carried out in solutions initially containing 0.50 mM of disulfide and 2.50 mM of $NaIO_4$ in pH 8.0 aqueous borate buffer at room temperature (23.0°C).[1] At pH 8, no hydrolysis of the disulfide was observed. Alkaline decomposition of disulfides has been reported to occur in aqueous 0.1 M sodium hydroxide.[6]

Kinetics. The general colorimetric method for monitoring the reaction has been previously described.[1] The rate data for disulfides **1**, **2** and 4,4′-dithiodibutanol,[7] **8**, when the concentration of the disulfide is 0.50 mM and the concentration of periodate is 2.5 mM, are listed in Table I. Plots of $1/[IO_4^-]$ vs time were linear with correlation coefficient values, r, of ≥ 0.992, indicating that under these conditions the reaction is overall second order, first order in each of the reactants. The stoichiometry of RSSR: IO_4^- of 1:5 was used to ensure that there was no loss of periodate during the long reaction time for the aromatic series, control periodate solutions were monitored. The second order rate constants were used to compare the relative reactivities of the disulfides.

Previously, we had reported that the oxidation of 4,4′-dithiobutanol, **8**, followed second order kinetics so we decided to choose **8** as our model aliphatic compound.[1]



SCHEME I Synthesis of **1** and **2**.

TABLE I
Kinetic data for the IO_4^- oxidations[a]

Compound	10^3 ($[IO_4^-]_o$: $[compound]_o$)	10^3 k_2, M^{-1} s^{-1}[b]
$[3\text{-}HO_2CC_6H_4S]_2$, **1**	2.50 : 0.500	3.89 ± 0.03
$[3,5\text{-}(HO_2C)_2C_6H_3S]_2$, **2**	2.50 : 0.500	1.90 ± 0.07
$[HO(CH_2)_4S]_2$, **8**	2.50 : 0.585[c]	17 ± 1

[a] T = 23.0 °C; 0.2 M borate buffer, pH 8.0. [b] Calculated using from 7 to 15 data points over at least 80% of the reaction. [c] Reference 1.

Although the aliphatic carboxylic acid analogs, 3,3′-dithiodipropanoic acid, **3**, and 4,4′-dithiodibutanoic acid, **4**, would have been better models, the kinetics of their reaction with periodate were multiphasic and not simply second-order so they could not be used. The periodate oxidation of 5,5′-dithiobis(2-nitrobenzoic acid) (Ellman's reagent) was also studied. However, we were unable to obtain consistent results for either the rate constant or the stoichiometry of this reaction.

Product Runs. The products of the reaction of compounds **1** and **2** were determined by treatment with 5 equiv of $NaIO_4$ in 0.2 M borate buffer at pH 8 under argon at 55–60°C. The product mixtures were lyophylized and the residual solid was analyzed by ^1H and ^{13}C NMR to reveal only the sulfonates, **9** and **10**, respectively.

The product of the oxidation of **2** was easily identified by the downfield shift of the aromatic carbon atom α to the sulfur functionality in the ^{13}C NMR spectra of the sulfonates relative to its position in the disulfides. As shown in Table II, the carbon α to the disulfide functionality and the carbon α to the carboxylate moieties in **2** both resonate at near 137 ppm. To distinguish between these carbon atoms, spectra were taken of both the carboxylate anion (NaOD in D_2O) and the carboxylic acid (in DMSO-d_6). Protonation of the carboxylate anion results in an upfield shift of signal for the ring carbon α to the carboxyl from 139 ppm to 129 ppm, whereas the signal for the ring carbon α to the disulfide or sulfonate does not change. When the disulfide is oxidized to the sulfonate, **10**, the absorption of the carbon α to the carboxylate remains about the same while the absorption for the carbon α to the sulfonate shifts downfield to 143 ppm.

The final products of the reaction of 5 equivalents of $NaIO_4$ with the aliphatic carboxylic acid disulfides, **3** and **4**, were the sulfonic acids, 3-sulfopropanoate, **11** and 4-sulfobutanoate, **12**, respectively. They were identified by the downfield triplets of the proton on the carbon α to the sulfur moiety in the ^1H NMR, as shown in Table III.

The multiphasic kinetics obtained in the oxidation of **3** and **4** might be due to the build-up of products of incomplete oxidation, such as thiosulfinates and thiosulfonates, during the course of the reaction. These products are often the major product of the reaction of disulfides by electrophilic oxidants such as H_2O_2.[12] These

TABLE II
^{13}C and ^{1}H NMR shifts (ppm)

	C–S		C–CO$_2$H	
compound	D$_2$O/NaOD	DMSO-d$_6$	D$_2$O/NaOD	DMSO-d$_6$
3,3'-dithiodibenzoic acid, **1**	137.23 or 137.88	136.30	137.88 or 137.23	132.13
5,5'-dithiodiisophthalic acid, **2**	137.45	137.00	138.64	128.99 or 131.14
5-mercaptoisophthalic acid, **5**	146.78	136.730	136.96	129.125
3-sulfobenzoic acid, **9**	143.74[a]	—	131.28[a]	—
5-sulfoisophthalic acid, **10**	143.45[b]	—	138.39[b]	—

[a] in HCl [b] in D$_2$O (pH 8)

TABLE III
^{1}H and ^{13}C NMR shifts (ppm)

	H–C–S	C–S
compound	D$_2$O	D$_2$O
$[^{-}O_2C(CH_2)_2S]_2$, **7**	2.98[a]	37.79
$[^{-}O_2C(CH_2)_3S]_2$, **8**	2.72[b]	38.61
$^{-}O_2C(CH_2)_2SO_3^{-}$, **11**	3.14	48.87
$^{-}O_2C(CH_2)_3SO_3^{-}$, **12**	2.88	51.41
$^{-}O_2C(CH_2)_2S(O)S(CH_2)_2CO_2^{-}$, **13**	3.36, 3.44	52.76
$^{-}O_2C(CH_2)_3S(O)S(CH_2)_3CO_2^{-}$, **14**	3.19, 3.21	55.61
CH_3SO_3H	—	39.6[c]
$CH_3S(O)SCH_3$	—	42.18[d]
$CH_3S(O)_2SCH_3$	—	48.63[d]

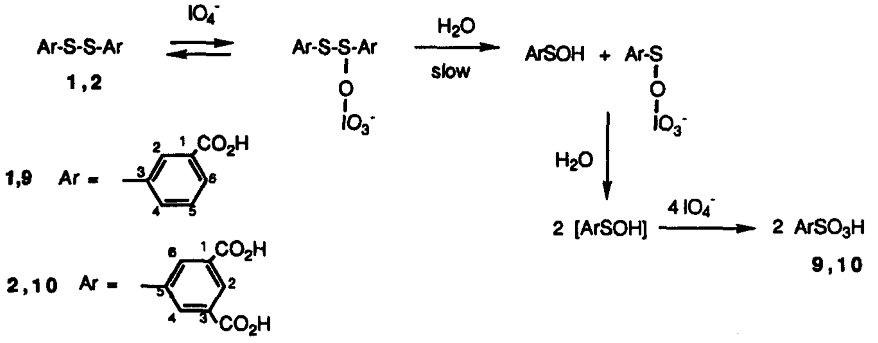
[a] ref. 7. [b] ref. 8. [c] ref. 9. [d] ref. 10.

intermediates were shown to be present by lyophylizing the reaction mixture before all 5 equivalents of $NaIO_4$ were consumed. When the sample was examined by NMR, a product of incomplete oxidation as well as the sulfonic acid, was observed. The intermediates appear to be the thiosulfinates **13** and **14** because each of them displays two downfield sets of triplets for the diastereotopic protons on the carbon α to the sulfinyl sulfur (δ 3.440 and 3.360 for **13** and δ 3.21, 3.19 for **14**). The corresponding thiosulfonates would have exhibited only one downfield triplet each due to the equivalence of both protons. Generally, the ^{13}C signals for carbons α

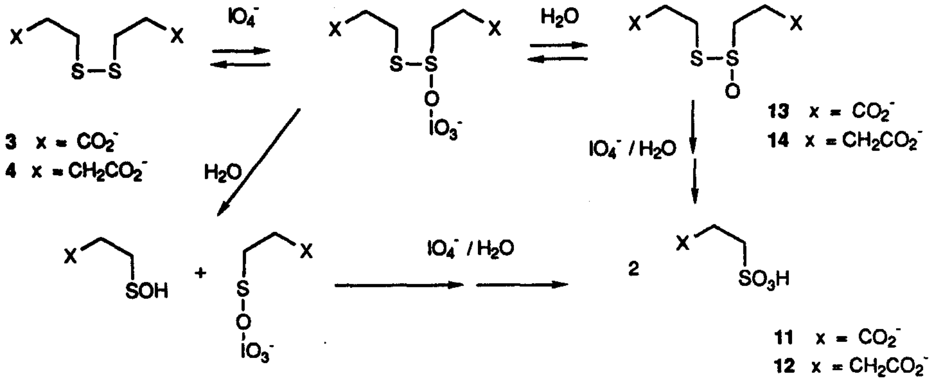
to thiosulfinates are downfield from the α carbons for the corresponding sulfonic acids as shown in Table III for CH_3SO_3H.[10] For the propanoic acid derivative, the ^{13}C absorption shifts from 52.76 ppm for thiosulfinate **13** to 48.87 ppm for the sulfonic acid **11**; for the butanoic acid derivative, the absorption shift was observed from 55.61 ppm for thiosulfinate **14** to 51.41 ppm for sulfonic acid **12**. In the presence of excess aqueous $NaIO_4$, the intermediates **13** and **14** are converted to the sulfonic acids **11** and **12**.

Mechanisms of Disulfide Cleavage. The best mechanism consistent with the second-order kinetics observed for the aqueous periodate oxidation of aromatic disulfides **1** and **2** is shown in Scheme II.[1] The rapid formation of the periodate disulfide complex is followed by rate-determining cleavage of the —S—S— bond of the complex into the sulfenic acid and the sulfeniciodic anhydride. Following the rate-determining step, rapid oxidation occurs to yield the sulfonic acid. This is the same mechanism we had proposed for the periodate oxidation of **8**.

NMR evidence reveals that the oxidation of **3** and **4** proceeds, at least in part, via the formation of the periodate-disulfide complex followed by cleavage of the —O—I— bond to give thiosulfinate (Scheme III). Further oxidation and cleavage of the thiosulfinate to the sulfonic acid proceeds at rates which are comparable to that of the original disulfide.



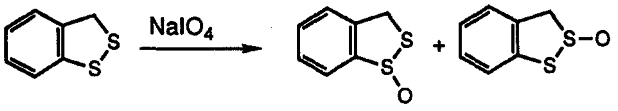
SCHEME II Periodate oxidation of **1** and **2**.



SCHEME III Periodate oxidation of **3** and **4**.

Relative Reactivities of Aliphatic and Aromatic Disulfides. Since the water-soluble aromatic carboxylic acid disulfides, **1** and **2** are oxidized by periodate in a second-order process, the rates of oxidation of the aromatic carboxylic acid disulfides can only be compared to the acyclic alcohol disulfide, **8**, which also reacts by a second-order process. The relative rates of oxidation are $[HO(CH_2)_4S]_2$:$[3\text{-}HO_2CC_6H_4S]_2$:$[3,5\text{-}(HO_2C)_2C_6H_3S]_2$ = 8.5:2:1. Thus, the difference in reactivity between aliphatic and aromatic disulfides is very small. Although **1** and **2** have carboxylate groups in *meta*-positions, the inductive effect of this group is small and the relative reactivities of **1** and **2** should be typical of water soluble aromatic disulfides.[13]

A reaction, which can be used to compare the relative reactivities of aromatic and aliphatic disulfides, is the periodate oxidation of 3H-1,2-benzodithiole, **15**.[14] Equal amounts of the two thiosulfinates, **16** and **17**, are reported indicating that the sulfur atoms α to the aliphatic and the aromatic moieties in this molecule are equally reactive.



15 **16** **17**

When thioethers are oxidized by periodate at 25°C,[15] the relative rates of oxidation of $(CH_3CH_2CH_2)_2S$:$CH_3CH_2CH_2SC_6H_5$:$C_6H_5SC_6H_5$ = 75:12:1. Thus, in thioether oxidations replacement of the aliphatic group by an aromatic group decreases the reactivity of the sulfur by a factor of 12.

EXPERIMENTAL SECTION

General. Physical measurements. Melting points were obtained uncorrected on either a Thomas-Hoover "Uni-Melt" capillary apparatus or a Nalge Polarized Hot-Stage microscopic melting point apparatus. Unless otherwise noted, all ^1H NMR are high field and were recorded on a General Electric QE-300 spectrometer at 300 MHz. Low field ^1H NMR were recorded on a Varian 390 90 MHz continuous wave spectrophotometer at 90 MHz. High field ^{13}C NMR were recorded on a General Electric QE-300 spectrometer at 75 MHz. All chemical shift values are listed in ppm referenced downfield to either internal 1,4-dioxane or DSS in the indicated deuterated solvent. Infrared spectra were obtained on an IBM FTIR-32 spectrometer and were recorded in cm^{-1}. Thin-layer chromatograms were obtained using either Eastman Kodak silica gel F_{254} TLC sheets or DC-Plastikfolien Kieselgel 60 F_{254}, both of 0.2 mm thickness using the indicated solvent systems. Elemental analyses were performed by the Microanalytical Laboratory, 20 Lewis Hall, University of California, Berkeley.

Kinetic Measurements. The method for kinetic measurements has previously been described.[1]

Reagents. All commercial solvents used were analytical reagent grade and used without further purification. Analytical grade sodium metaperiodate, boric acid, potassium phosphate monobasic, sodium phosphate dibasic, and potassium hydroxide used were from Mallinckrodt. 2,2'Azinobis(3-ethylbenzthiazoline) sulfonic acid diammonium salt was obtained from Sigma Chemical Company. 3,3'-Dithiodipropanoic acid, **3**, 97% (Aldrich Chemical Company, Inc.) was recrystallized from absolute EtOH, vigorously dried over anhydrous P_2O_5 under reduced pressure at 111°C to yield shiny white crystals: mp 155.5–157.0°C (Reference 16, mp 157–159°C). 4,4'-Dithiodibutanoic acid, **4**, 97% (Aldrich Chemical Company, Inc.) was recrystallized from absolute EtOH, vigorously dried over anhydrous P_2O_5 under reduced pressure at 65°C to yield white leaflets: mp 108.5–109.5°C (Reference 17, mp 108–110°C). Isophthalic acid and benzoic acid were obtained from Aldrich Chemical Company, Inc. Water was deionized and deoxygenated by boiling for 30 min., cooled under a stream of Ar, and kept sealed from the air.

3-Chorosulfonylbenzoic Acid, **5**. Compound **5**, was prepared by the method of Smiles and Stewart.[4] Benzoic acid and five equivalents of chlorosulfonic acid were heated for 1 h. The product was recrystallized from benzene to yield 77% of off-white crystals: mp 130–133.5°C (Reference 4, 131°C).

3,3′-Dithiodibenzoic Acid, **1**. Compound **1** was prepared by the method of Smiles and Steward[4] but was not washed with acetone before recrystallizing from gl. acetic acid and drying under reduced pressure. A yield of 47% crude solid and 27% cream colored crystals of **1** was obtained: mp 248–249°C (Reference 4, 18, 246°C, 247–248°C); TLC R_f = 0.26 (1 H_2O:2 MeOH:2 THF:5 EtOH); ^1H NMR (D_2O) δ 7.220 (dd, J^0 = 7.8 Hz, 1 H, Ar-H (H-C5)), 7.481 (ddd, J^0) = 7.2 Hz, J^m = 1.8 Hz, 1 H, Ar-H (H-C4)), 7.551 (ddd, J^0) = 7.8 Hz, J^m = 1.2 Hz, 1 H, Ar-H (H-C6)), 7.841 (dd, J^m = 1.8 Hz, 1 H, Ar-H (H-C2)); ^{13}C NMR (D_2O/NaOD) δ 128.928 (C-4, 5 or 6), 128.986 (C-4, 5 or 6), 130.097 (C-4, 5 or 6), 131.109 (C-2), 137.230 (C-3 or 1), 137.875 (C-1 or 3), 175.261 (CO_2^-); (DMSO-d_6) δ 127.487 (C-2, 5 or 6), 128.501 (C-2, 5 or 6), 129.859 (C-2, 5 or 6), 131.253 (C-4), 132.125 (C-1), 136.297 (C-3), 166.443 (CO_2H).

5-Chlorosulfonylisophthalic Acid, **6**. Compound **6** was prepared by a modification of the method by Smiles and Steward.[4] Five equivalents of freshly distilled chlorosulfonic acid (30.01 mL, 451.4 mmol, bp 147.5–148.5°C), under Ar, was added to isophthalic acid (15.00 g, 90.29 mmol) with stirring and the homogeneous solution was heated at 130°C for 2 h. The contents were poured over ice and the precipitate collected. Crude **6** was dissolved in 100 ml Et_2O, the warm solution was treated with decolorizing charcoal, hot filtered and recrystallized by adding hot benzene (50 mL) to the cloud point. The crystals were collected and retained while the mother liquor was concentrated to dryness to yield 9.77 g (41%) of crude off-white product: mp 232–248°C (Reference 19, 231–333°C); FTIR (KBr) 3088–2546 (broad), 1705 (s, C=O), 1600 and 1451 (w, aromatic C=C), 1379 (m, S=O), 1271 (m, C—O), 1192 (m, S=O), 1099 (w), (Reference 19, (KBr) 3100–2500 (broad), 1700 (s), 1450 (m), 1380 (s), 1260 (s), 1180 (s), 1095 (w).

5-Sulfoisophthalic Acid, **10**. Crystals (1.23 g (6%)) isolated from the ether/benzene solution of **6** were identified as the hydrolysis product, **10**: mp 258–260°C (Reference 20, 257–258°C); FTIR (KBr) 3069–2535 (broad), 1705 (s, C=O), 1653 and 1404 (w, aromatic C=C), 1184 and 1047 (s, S=O), 617 (s, S—O), (Reference 21, 5-potassium salt (KBr) 3300–2800 (broad), 1720 (s), 1610 and 1400 (w), 1250 (s), 1190 (s), 1050 (s), 620 (m)); ^{13}C NMR (D_2O/NaOD) δ 128.859 (C-4, 6), 132.554, (C-2), 138.394 (C-1, 3), 143.498, (C-5), 174.507 (CO_2^-), (Reference 22, 129.0 (C-4, 6), 132.8, (C-2), 138.6 (C-1, 3), 143.8, (C-5), 174.4 (CO_2^-)).

5,5′-Dithiodiisophthalic Acid, **2**. Zinc dust (4.38 g, 66.9 mmol) was added in small portions over 30 min to a vigorously stirring solution of **6**, (3.00 g, 11.3 mmol) dissolved in 20 mL of EtOH and 13 mL of conc. HCl. The mixture was stirred overnight with continuous evolution of H_2. The excess Zn was removed by filtration, the solution was concentrated, mixed with 50 mL of H_2O and adjusted to a pH of 8. The white ppt was collected, washed with H_2O, and acidified to pH 1. The off-white solid was dried under reduced pressure to yield 1.33 g (60%) of crude **7**. ^{13}C NMR (D_2O/NaOD) δ 123.490 (C-2), 136.322 (C-4, 6), 136.962 (C-1,3), 146.783 (C-5), 176.428 (CO_2^-), (DMSO-d_6) δ 129.125 (C-1, 3) 130.948 (C-2), 133.522 (C-4, 6), 136.730 (C-5), 166.106 (CO_2H).

A solution of I_2 (0.64 g, 2.5 mmol) in 10 mL of EtOH was added dropwise to a solution of **7** (1.00 g, 5.05 mmol) in 10 mL of EtOH and the reaction was simultaneously neutralized with Et_3N (2.18 mL, 15.6 mmol). Excess I_2 was decolorized with 10% aq. $Na_2S_2O_3$ and the cloudy solution concentrated. The residue was dissolved in H_2O, the pH of the aqueous solution was adjusted to ~1 with aq. HCl, and the viscous mixture was vigorously shaken to produce a white solid which was collected by filtration. Crude **2** was dried and further purified by titrating with NaOH to dissolution, filtering, and re-precipitating by adjusting the pH to ~1 to give 0.87 g (88%) of crude white product. Recrystallization from glacial acetic acid provided pure **2**: mp 333–335°C; ^1H NMR (D_2O) δ 7.986 (dd, J^m = 1.5 Hz, 2 H, Ar-H (H-C4, C6)), 8.034 (dd, J^m = 1.2 Hz, 1 H, Ar-H (H-C2)); ^{13}C NMR (D_2O/NaOD) δ 129.148 (C-2), 131.149 (C-4, 6), 137.447 (C-5), 138.641 (C-1, 3), 174.746 (CO_2^-); (DMSO-d_6) δ 128.994 (C-2 or 1, 3), 131.142 (C-1, 3 or 2), 132.618 (C-4, 6), 137.001 (C-5), 165.645 (CO_2H); Anal. Calcd for $C_{16}H_{10}O_8S_2$: C, 48.73; H, 2.56. Found: C, 49.09; H, 2.24.

3-Sulfopropanoate Salt, **11**, *from 3,3′-Dithiodipropanoic Acid*, **3**. To 100 mL of a 10 mM solution of disulfide **4** in 0.2 M borate buffer at pH 8.0 was added 100 mL of a 50 mM solution of $NaIO_4$ in 0.2 M borate buffer at pH 8.0. The mixture was stirred at room temperature for 4 days. The water was evaporated under reduced pressure to yield a white solid, which was further dried under reduced pressure to yield a hard, white crystalline solid containing **11**. NMR yield 90% referenced to potassium hydrogen phthalate: FTIR (KBr) 3300 (broad, OH), 1650 (C=O), 1450, 1200 and 1038 (S=O), 700, (S—O)

cm^{-1} (Reference 7, 23, 3400, (broad), 2900, 1550, 1380, 1175, 1030 cm^{-1}); ^1H NMR (90 MHz, D_2O) δ 2.60 (t, 2, $CH_2CO_2^-$), 3.17 (t, 2, $CH_2SO_3^-$), (Reference 7, δ 2.65 (m, 2), 3.15 (m, 2)). ^{13}C NMR (D_2O) δ 33.31 ($CH_2CO_2^-$), 48.87 ($CH_2SO_3^-$), 180.00 (CO_2^-).

3-Sulfobenzoate Salt, **9**, *from 3,3′-Dithiodibenzoic Acid,* **1**. A 50 mL solution of $NaIO_4$ (0.70 g, 3.3 mmol) in 0.2 M borate buffer at pH 8 was added to a 50 mL solution of **1** (0.20 g, 0.65 mmol) in 0.2 M borate buffer at pH 8 and heated at 60–70°C under Ar for 90 h. The solution was analyzed for the concentration of periodate using the same method as for kinetic measurements (vida supra) and no periodate remained. The solvent was removed under reduced pressure. Analysis of the cream colored mixture confirmed that it contained **9**. NMR yield 64% referenced to dioxane: ^1H NMR (D_2O/HCl) δ 7.658 (dd, J^o = 7.8 Hz, 1 H, Ar-H (H-C5)), 8.031 (δ, J^o = 7.5 Hz, Ar-H (H-C4 or C6)), 8.158 (δ, J^o = 7.2 Hz, 1 H, Ar-H (H-C4 or C6)), 8.380 (s, 1 H, Ar-H (H-C2))), (Reference 24, (D_2O) δ 7.69 (dd, Ar-H (H-C5)), 8.08 (m, Ar-H (H-C4 or C6)), 8.16 (m, Ar-H (H-C4 or C6)), 8.41 (s, Ar-H (H-C2)); ^{13}C NMR (D_2O/HCl) δ 127.400 (C-2), 130.429 (C-5), 131.139 (C-4), 131.278 (C-1), 133.341 (C-6), 143.737 (C-3), 169.188 (CO_2H) (Reference 25, (D_2O) δ 127.4 (C-2), 130.3 (C-5), 131.1 (C-1, 4), 133.1 (C-6), 143.9 (C-3), 169.9 (CO_2H).

5-Sulfoisophthalate Salt, **10**, *from 5,5′-Dithiodiisophthalic Acid,* **2**. 5,5′-dithiodiisophthalic acid, **2**, (0.05 g, 0.13 mmol) was converted to the salt by careful titration with 0.2 M KOH and was then dissolved in 10.0 mL of 0.2 M borate buffer at pH 8. To this was added $NaIO_4$ (0.14 g, 0.64 mmol) dissolved in 10.0 mL of 0.2 M borate buffer at pH 8 and the reaction mixture heated at 58°C for 97 h under Ar. The solution was analyzed for the concentration of periodate by the method used for kinetic measurements (vida supra) and no periodate remained. The solvent was then removed under reduced pressure and the white solid was found to contain **10**: NMR yield 43% referenced to dioxane. ^1H NMR (D_2O) δ 8.147 (δ, J^m = 1.5 Hz, 2 H, Ar-H (H-C4, C6)), 8.242 (t, J^m = 1.5 Hz, 1 H, Ar-H (H-C2)); ^{13}C NMR (D_2O) δ 128.815 (C-4, 6), 132.509 (C-2), 138.290 (C-1, 3), 143.451 (C-5), 174.482 (CO_2^-), (Reference 20, 129.0 (C-4, 6), 132.8, (C-2), 138.6 (C-1, 3), 143.8, (C-5), 174.4 (CO_2^-)).

Kinetics of the Oxidation of Disulfides in Aqueous Borate Buffer. The standardized plot for the colorimetric determination of periodate using 2,2′-azinobis(3-ethyl-benzthiazoline) sulfonic acid, ABTS and the method of using this indicator with aliquots of the kinetic solutions have been previously described.[1] $NaIO_4$ controls were prepared by mixing 5.0 mL of 5.00 mM $NaIO_4$ in 0.2 M borate buffer at pH 8 with 5.0 mL of 0.2 M borate buffer at pH 8 at time zero. Data points were collected at the same times for both the control and the reaction mixture. The $[IO_4^-]$ remained relatively constant.

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