of $Me_4NOH·5H_2O$ (Fluka). The water contained in the solid sample was removed by repeated azeotropic distillations with benzene under vacuum.[1] The residue was then repeatedly taken up with anhydrous ethanol, evaporated to dryness, and eventually dissolved in a calculated amount of dry ethanol. All operations were carried out under argon. *p*-Nitrophenylacetate (Fluka) was used without further purification.

Kinetics. Rate measurements were carried out by using either conventional or stopped flow spectrophotometry. Solutions were prepared and handled under argon to prevent contamination by atmospheric carbon dioxide. The kinetic runs were started by adding a calculated amount of an ethanolic solution of the *p*-NO_2-aryl acetate to an ethanolic solution of base and added salt. On standing, a white crystalline material precipitated from the more concentrated solutions of alkaline-earth metal bromides and Me_4NOEt. The nature of the solid material was not investigated. Solutions for kinetic runs were prepared immediately before use. Occasional checks showed strictly reproducible results in all cases.

Fitting of k_{obs} to eq 4 was carried out by a nonlinear least-squares procedure.[1]

Acknowledgment. Work carried out in the frame of EC joint projects, contracts no. ST2J-0215 and no. SC1*-0359. Thanks are due to EC for financial support, as well as to the Italian Ministry of University and Scientific Research (MURST) and to the Deutsche Forschungsgemeinschaft (DFG) for the part of work carried out in Rome and Mainz respectively.

Registry No. **3a**, 137794-10-6; **3b**, 137794-11-7; **3c**, 137794-12-8; **3d**, 137794-13-9; **3e**, 137794-14-0; **4**, 2150-52-9; **7a**, 6315-52-2; **7b**, 7460-82-4; **7c**, 19249-03-7; **7d**, 37860-51-8; **7e**, 42749-27-9; **8a**, 137794-15-1; **8b**, 137794-16-2; **8c**, 137794-17-3; **8d**, 137794-18-4; **8e**, 137794-19-5; **9a**, 137794-20-8; **9b**, 137794-21-9; **9c**, 137794-22-0; **9c** alcohol, 137794-23-1; **9d**, 137794-24-2; **9e**, 137794-25-3; **10a**, 137794-26-4; **10b**, 137794-27-5; **10c**, 137794-28-6; **10d**, 137794-29-7; **10e**, 137794-30-0; **11c**, 137822-75-4; **12a**, 41973-43-7; **12b**, 74882-32-9; **12c**, 137794-31-1; **13a**, 137794-32-2; **13b**, 137794-33-3; **13c**, 137794-34-4; **14a**, 137794-35-5; **14b**, 137794-36-6; **14c**, 137794-37-7; triethylene glycol monoethyl ether tosylate, 62921-74-8; 1,5-bis-(2'-(2,4,7,10-tetraoxaundecanyl)phenyl)-3-hydroxypentane, 137794-38-8; 2-nitromalondialdehyde sodium salt, 34461-00-2.

Supplementary Material Available: First order rate constants k_{obs} (s^{-1}) at various metal-bound ethoxide concentrations, tables of positional and thermal parameters, bond distances and angles, and ^{13}C NMR data (23 pages). Ordering information is given on any current masthead page.

The Regioselective Cleavage of Aryl Tosylates by Electrochemical Reduction

Edgar R. Civitello and Henry Rapoport*

Department of Chemistry, University of California, Berkeley, California 94720

Received July 19, 1991 (Revised Manuscript Received October 4, 1991)

The electrochemical reductions of eight bis(tosyloxy)benzenoid compounds were studied as a method for the regioselective cleavage of aryl tosylates. For the methyl bis(tosyloxy)benzoate isomers, a strong preference was observed for cleavage of the tosyl group in conjugation with the electron-withdrawing ester moiety. Thus it was possible to selectively cleave tosyl groups to the ortho or para positions over tosyl groups at the meta positions. The bis(tosyloxy)anisole isomers displayed the opposite regioselectivity favoring cleavage of tosyl groups that were meta to the electron-donating methoxy substituent. The general electrochemical process for the reduction of aryl tosylates has been shown to be selective, high yielding, and reproducible on gram quantities.

Introduction

Background. The cleavage of arenesulfonates and sulfonamides by electrochemical reduction was originally observed in 1965,[1] and although it has been the subject of several studies,[2] it has not found widespread application in synthesis as a deprotection method. The existing literature can be organized into the following two categories: the selective cleavage of different arenesulfonyl derivatives from the same type of functional group and the selective cleavage of the same arenesulfonyl from two different functional groups. With respect to the former category, different ring substituents in the para position of both alkyl and aryl benzenesulfonates have been shown to have a dramatic effect on the half-wave potential.[3] Selectivity in the electrochemical reduction of two differently substituted benzenesulfonates was possible when the difference between their half-wave potentials was sufficiently large. The following trend among para substituents was observed going toward more negative $E_{1/2}$ values:

$$EtO_2C \gg Cl > CH_3CONH > CH_3O$$

The difference in $E_{1/2}$ between the two extremes was approximately 800 mV. The second category deals with selectivity between different functional groups protected with the same arenesulfonyl group. For example, the *O,N*-bis(toluenesulfonyl)-protected methyl ester of serine has been shown to be regiospecifically deprotected at oxygen, preserving the toluenesulfonamide.[4] For the electrochemical cleavage of the tosyl group, the ease of S–X bond cleavage has been shown to decrease in the following sequence:[5]

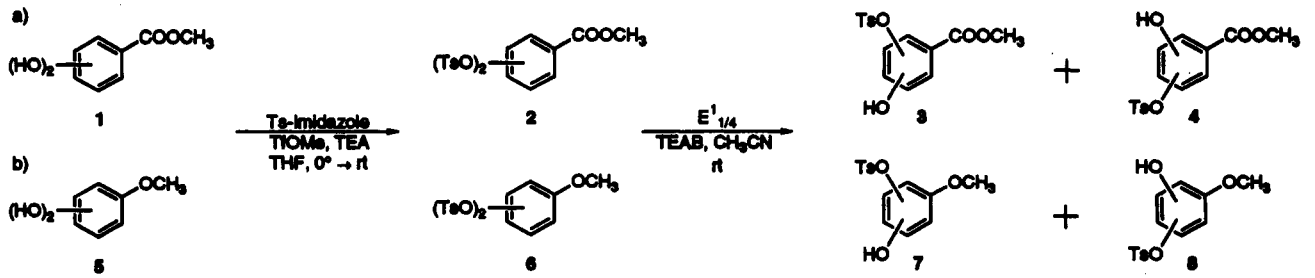
Ts-O-aryl > Ts-O-alkyl, Ts-NH-aryl > Ts-NH-alkyl > Ts-NH-CH(alkyl)-COOR

Conspicuously missing from the existing literature is a study of the selective monocleavage of tosylated poly-

(1) Horner, L.; Neuman, N. *Chem. Ber.* **1965**, *98*, 1715, 3462.
(2) For a general review, see: Horner, L.; Lund, H. In *Organic Electrochemistry*, 2nd ed.; Baizer, M. M.; Lund, H., Ed.; Marcel Dekker: New York, 1983; Chapter 22.
(3) Horner, L.; Schmitt, R. *Phosphorus Sulfur* **1978**, *5*, 223. Horner, L.; Schmitt, R. *Phosphorus Sulfur* **1982**, *13*, 189.
(4) Maia, H. L. S.; Medeiros, M. J.; Montenegro, M. I.; Court, D.; Pletcher, D. *J. Electroanal. Chem.* **1984**, *164*, 347.
(5) Mairanovsky, V. G. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 281.

0022-3263/92/1957-0834$03.00/0

Scheme I. General Synthesis and Electrochemical Reduction of Methyl Bis(tosyloxy)benzoate and Bis(toxyloxy)anisole Regioisomers



1a, 5a: 2,3-dihydroxy-
1b, 5b: 2,4-dihydroxy-
1c, 5c: 2,5-dihydroxy-
1d, 5d: 3,4-dihydroxy-

2a, 6a: 2,3-bis(tosyloxy)-
2b, 6b: 2,4-bis(tosyloxy)-
2c, 6c: 2,5-bis(tosyloxy)-
2d, 6d: 3,4-bis(tosyloxy)-

3a, 7a: 2-hydroxy-3-tosyloxy-
3b, 7b: 2-hydroxy-4-tosyloxy-
3c, 7c: 2-hydroxy-5-tosyloxy-
3d, 7d: 3-hydroxy-4-tosyloxy-

4a, 8a: 3-hydroxy-2-tosyloxy-
4b, 8b: 4-hydroxy-2-tosyloxy-
4c, 8c: 5-hydroxy-2-tosyloxy-
4d, 8d: 4-hydroxy-3-tosyloxy-

hydroxybenzenoid compounds, which would constitute a third category in which the same protecting group is cleaved from the same type of functionality with regioselectivity. Polyoxygenated aromatic functionality, such as that found in the aflatoxin family, is frequently encountered in natural product synthesis, and a simple method for the regioselective deprotection of polyphenols would be advantageous. In our concurrent work toward the synthesis of (−)-aflatoxin B_1, we found it necessary to develop a viable methodology for the selective monodeprotection of bis(tosyloxy)-substituted aromatic compounds. Herein we report just such a synthetic method utilizing a facile electrochemical reduction process. In all cases high regioselectivity was observed in good to excellent yield.

Synthesis of Eight Model Compounds

Methyl Bis(tosyloxy)benzoates and Bis(tosyloxy)-anisoles. We have chosen for our investigations eight model compounds representing all possible orientations of an unsymmetrically substituted diphenol with both an electron-withdrawing group (compounds **2a–d**) and an electron-donating group (compounds **6a–d**) (Scheme I). All eight compounds were synthesized from their corresponding dihydroxybenzoate (**1a–d**) or dihydroxyanisole isomers (**5a–d**) using the tosylimidazolium methodology.[6] In all cases a near quantitative yield of the ditosylated product was obtained. An aqueous alkali wash during the isolation followed by column chromatography of the crude product ensured that all model compounds were free of any monotosylated material. Precursors **1a–d** and **5a–d** are reported in the literature and were either purchased from commercial suppliers or synthesized by known methods (see the Experimental Section).

Electrochemistry

Methodology. The preparative electrochemical apparatus used in this study closely resembles that described in a previous publication from our research group dealing with the removal of *N*-arenesulfonyl groups from α-amino acids.[7] Several modifications were made which are discussed in detail here, but the basic cell design and the general procedure are the same. All electrochemical reductions were carried out in acetonitrile with tetraethylammonium bromide (TEAB) as the electrolyte. For reasons of simplicity, a plain silver wire was used as the reference electrode. Although it is well-known that silver wire does not provide a stable reference, we found it to be reproducible and reliable within the confines of our study. In our experiences with self-contained reference systems, such as the saturated sodium chloride calomel electrode, it was necessary to replace the Vycor tip after nearly every bulk reaction presumably because it had become clogged with organic matter. This would result in a sharp increase in the cell voltage which led to substantial decomposition of solvent and substrate at the cathode.

The amount of electrolyte present in solution was found to be crucial in the large-scale electrochemical reduction. In our apparatus, TEAB serves as both the electrolyte and as the source of electrons for the reduction. At the anode, bromide ion is oxidized to bromine, giving the solution a light orange color. Consequently, enough TEAB must be added to complete the reaction and still support the flow of electrons through the solution. If an insufficient amount of TEAB was used, the cell voltage increased drastically during the course of the reaction as the electrolyte was consumed. In all such cases, a significant amount of product decomposition resulted. For all reactions, a saturated solution of TEAB in acetonitrile in an approximate ratio of ~100 mL per gram of substrate was found to be sufficient. However, it was possible to increase the rate of reaction by increasing the concentration of substrate; to compensate for the corresponding decrease in the relative amount of electrolyte present in solution, it was possible to add excess solid TEAB to each chamber during the course of the reaction.

The rate of electrochemical reduction is known to depend upon three major factors: (a) the volume of the solution, (b) the surface area of the working electrode, and (c) the effectiveness of stirring.[8] Minimizing the solution volume increases the reaction rate; however, this is regulated by the amount of electrolyte that can be carried in solution, as was discussed above. Increasing the surface area of the working electrode also serves to increase the rate of reaction. The use of a mercury pool cathode not only provides a large surface but also one that is constantly cleaned of decomposition byproducts. Efficient stirring can be achieved by a nitrogen bubbler which also serves to remove oxygen from the cathode chamber. The exclu-

(6) Use of the tosylimidazolium reagent as a versatile method for controlled tosylation of alcohols and phenols has been developed in our laboratories with J. F. O'Connell and will be reported in detail shortly.
(7) Roemmele, R. C.; Rapoport, H. *J. Org. Chem.* 1988, *53*, 2367.
(8) Cauquis, G. In *Organic Electrochemistry*, 2nd ed.; Baizer, M. M., Lund, H., Eds.; Marcel Dekker: New York, 1983; Chapter 2. Lund, H. In *Organic Electrochemistry*, 2nd ed.; Baizer, M. M., Lund, H., Eds.; Marcel Dekker: New York, 1983; Chapter 5.

Table I. Summary of Electrochemical Reductions

starting material	major product	minor product	ratio[a]	% yield[b]	% conversion[a]
2a	3a	4a	91/9	85	89
2b	4b	3b	66/34	90	85
2c	3c	4c	95/5	86	95
2d	4d	3d	99/1	93	89
6a	8a	7a	69/31	74 (94)[c]	>98 (96)[c]
6b	7b	8b	94/6	96	78
6c	8c	7c	77/23	-	-
6d	7d	8d	99/1	82[d]	96

[a] From NMR analysis of the crude product mixture. [b] Crude yield of major product based on unreacted starting material. [c] Small-scale reaction, 104 mg. [d] Pure isolated yield.

sion of O_2, as well as water, was found to be essential since they can generate hydroxide anion at the potentials used in this study. If O_2 was allowed to enter the cathode compartment, the solution slowly darkened to a deep red-black color, the cell voltage increased, and significant loss of material resulted.

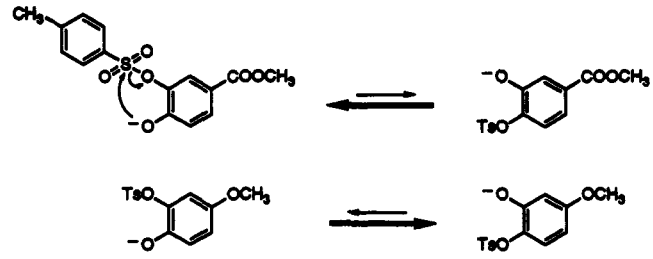
All model compounds were reduced at their first quarter-wave potential, $E^1_{1/4}$, which we define as the potential corresponding to one-fourth the height of the first reduction wave seen in the cyclic voltammogram (CV). This value was chosen as a compromise between maximum regioselectivity and minimum reaction time; typical reaction times for 1 g of substrate at 85% conversion were 10–12 h. All attempts to push the electrochemical reduction beyond 85–90% conversion led to a noticable decrease in yield.

The CV of all model compounds showed two irreversible reduction waves that were separated by 300–500 mV. Mechanistic studies on the reduction of aryl tosylates have shown that each wave corresponds to a two-electron reduction of a single tosyl group.[4,9] The relatively large distance between the two reduction waves observed in the cyclic voltammograms (300–500 mV) was due to the fact that the formation of a phenoxide anion upon cleavage of one tosyl group made the reduction of the second tosyl group substantially more difficult. Thus, it was possible to be completely selective for monocleavage, and with all compounds studied we have not seen any evidence of di-reduction. All cyclic voltammograms were measured with a silver wire reference electrode under conditions identical to the bulk electrolysis reaction.

Results and Discussion

The results for the electrochemical reduction of compounds **2a–d** and **6a–d** are summarized in Table I. For the methyl benzoate series, a strong preference was observed for reduction at the tosyl group in conjugation with the electron-withdrawing methyl ester. Hence it was possible to achieve excellent regioselectivity toward tosyloxy substituents at the ortho and para positions versus the meta position. The driving force for the high selectivity toward ortho/para substituent is thought to be due to the activation of the sulfonyl moiety and formation of the more stable phenoxide product, both as a result of conjugation with the electron-withdrawing methyl ester. In the reduction of compound **2d** complete regiospecificity was observed, resulting in only one regioisomeric product, compound **4d**. For compound **2b**, which has electronically equivalent tosyloxy substituents, a modest preference for reduction at the 4-position was observed. This relatively low selectivity is believed to be due to the steric influence of the methoxy substituent on the adjacent tosyl group, thereby slightly favoring reduction at the 4-position.

Scheme II

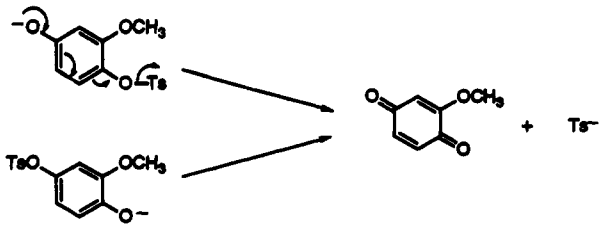


As expected, the anisole series **6a–d** demonstrated the opposite regioselectivity. By an extension of the previous argument, the electronic effect of the electron-donating methoxy group deactivates the ortho and para positions. It should be noted that the methoxy group displays electron-withdrawing character at the meta positions through an inductive effect, and this also contributed to the observed selectivity. However, for the anisole derivatives **6a** and **6c**, only modest regioselectivity was seen for meta reduction. It appeared that the electron-withdrawing effect of the methyl ester was stronger than the electron-donating effect of the methyl ether. Compounds **6b** and **6d**, however, demonstrated excellent regioselectivity, and it was reasonable to assume that other factors are influencing these results. Although both tosyloxy substituents in **6b** are considered electronically equivalent, there was a high degree of selectivity for reduction at the ortho position despite the increased steric hindrance. One possible explanation is that the phenoxide salt of **7b** is stabilized by coordination of the *o*-methoxy group with the tetraethylammonium cation, despite the fact that we would not expect the large cation to form a stable complex in a polar solvent such as CH_3CN. If this is indeed the case, it suggests that the transition state for the reductive cleavage of bis-tosylates is influenced more by the difference in energies of the two phenoxide products than by any difference between the two tosyl groups in the starting material. Although both **7a** and **7c** can form the same type of complex, it is overshadowed by the relative stability of having the phenoxide anion meta to the electron-donating methoxy group. This phenomenon would explain, in part, the relatively low degree of regioselectivity seen with **6a** and **6c**.

For compound **6d**, in which ortho complexation was not a possibility, complete regiospecificity for meta reduction was observed, and, similar to its benzoate counterpart **2d**, only one regioisomer was detected by NMR analysis. This complete and opposite regiospecificity seen with the 3,4-bis(tosyloxy)benzenoid derivatives **2d** and **6d** was a puzzling observation. It is possible that conjugation with para substituents is a more significant factor than with ortho substituents in either favoring or discouraging reductive cleavage. It is also possible that the corresponding products, **4d** and **7d**, were undergoing tosyl migration during the course of the reaction (Scheme II). If this were the case, then compounds **3a** and **7a** would also be expected to undergo this process, but the migration might be tempered by the proximity of the electron-withdrawing or -donating group. Although we offer no direct evidence for tosyl migration, we have investigated the product composition of **6d** at various reaction times. At conversions as low as 16% the reaction was still found to be completely regiospecific, suggesting that, if tosyl migration was indeed occurring, the rate of migration was much faster than the rate of the electrochemical reduction.

(9) Yousefzadeh, P.; Mann, C. K. *J. Org. Chem.* **1968**, *33*, 2716.

Scheme III. *p*-Benzoquinone Formation



It was not possible to develop a preparative process for the electrochemical reduction of **6c** due to the decomposition of both hydroxyanisole products **7c** and **8c**. The reduction of **6c**, if allowed to go to completion, resulted solely in the formation of highly polar black material. The obvious explanation was the conversion of the products **7c** and **8c** to methoxy-*p*-benzoquinone by the elimination of the toluenesulfinate anion (Scheme III). That neither **6a** nor **6d** displayed this behavior was attributed to the fact that *p*-benzoquinones are more readily formed than their corresponding *o*-benzoquinones. This phenomenon was also not observed with compound **2c**, presumably because the electron-withdrawing ester disfavors oxidation. It was possible to isolate small quantities of **7c** and **8c** by quenching the reduction with an excess of 1 M KH_2PO_4 approximately midway through the reaction. As phenols, **7c** and **8c** are surprisingly stable and could be isolated pure from preparative TLC, albeit in very low yield. The ratio of products reported in Table I was measured from this partial reaction, and it presumes that the rates of oxidation of **7c** and **8c** are equal. Because of rapid decomposition, this reduction could not be reproduced reliably, and consequently, no percent yield is reported.

Regiochemical Assignments. Hydrogen Bonding. The regiochemistry of the major products from the reduction of all eight model compounds was established by one of three methods: (a) hydrogen bonding, (b) deoxygenation, or (c) NOESY correlation. By far the simplest method was hydrogen bonding since it required only routine ^1H NMR in a nonhydroxylic solvent such as $CDCl_3$. Due to hydrogen bonding with the ester moiety, the hydroxylic protons in **3a–c** were seen as a sharp singlets between 10 and 11 ppm. Conversely, in compounds **4a–c** the hydroxyl signals appeared as a broad lump between 5 and 6 ppm. This distinction between hydroxyl signals, also seen in the NMR of dihydroxybenzoates **1a–c**, was significant enough to form a basis for the regiochemical assignment of compounds **3a–c** and **4a–c**.

Deoxygenation. The removal of the phenolic hydroxyl group provided an unambiguous method for the regiochemical assignment of compounds **4b** and **8a** (Scheme IV). Following the reported procedure,[10] phenols **4b** and **8a** were coupled with 1-chloro-2-phenyltetrazole. Neither reaction gave a high yield; for **8a** (27%) this was attributed to steric hindrance of the adjacent tosyloxy group, and **4b** (43%) was thought to be deactivated by the para methyl ester. The reductive cleavage of the tetrazolyl ethers **9** and **11** could only be accomplished with Raney nickel. Both palladium on carbon and platinum dioxide were found to be completely ineffective at rt and 60 psi of H_2. The reductions, however, were not clean, and most of the material was lost presumably due to the overreduction of the aromatic rings. However, enough of both **10** and **12** were isolated to confirm their ortho substitution pattern by NMR analysis.

(10) Entwistle, I. D.; Hussey, B. J.; Johnstone, R. A. W. *Tetrahedron Lett.* **1980**, *21*, 4747.

NOESY Correlation. The NMR signals of the aromatic protons for nearly all compounds reported here were found to be first-order, and by analysis of the coupling constants, it was possible to accurately assign all of them. Being able to identify the aromatic signals would allow us to establish the regiochemistry of the remaining phenol products, hopefully, through an NOE correlation between the phenolic substituent and one of the aromatic protons. However, the phenols had to be methylated first because the phenolic protons are known to undergo rapid chemical exchange making it impossible to observe any NOE correlation with them. Previous experience with anisole derivatives had shown it was possible to observe an NOE between the methoxy group and the ortho aromatic protons. Thus compounds **4d**, **7b**, and **7d** were methylated under standard conditions and analyzed with 2D phase-sensitive NOE spectroscopy (NOESY) (Scheme V).[11] Compound **13** was the simplest case—a single cross-peak was seen between the methoxy group and the aromatic proton H_5. Proton H_5 could be identified by large ortho J coupling (9 Hz) while H_6 showed large ortho coupling and weak meta coupling (2 Hz), and H_2 showed just weak meta coupling. These assignments were also supported by the NOESY data. For compound **14**, the two methoxy signals were clearly distinguishable, and the aromatic signals could also be assigned by a coupling-constant analysis. Cross-peaks were clearly seen between H_6 and one of the methoxy signals, and H_3 and the other methoxy signal. If the regiochemistry shown for **7b** was reversed, we would then expect to seen a cross-peak between one of the methoxy groups and H_5. Compound **15** was assigned in a completely analogous fashion. Cross-peaks were seen between the methoxy groups and protons H_6 and H_2, and not with H_5.

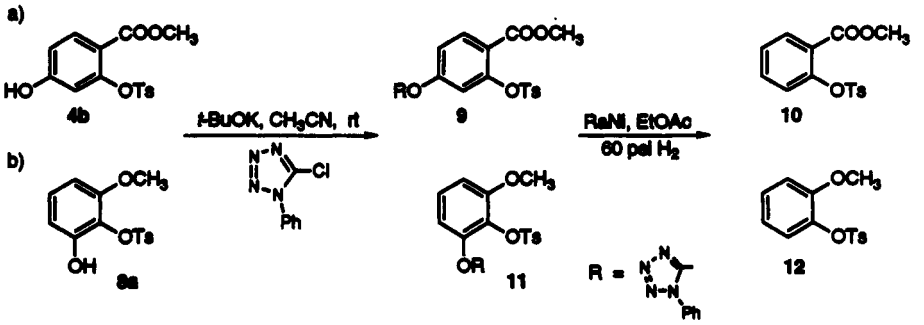
Assigning regiochemistry for the products from the electrochemical reduction of **6c** was not straightforward. Direct methylation of **7c** or **8c** was unsuccessful presumably due to their rapid conversion to the corresponding quinones upon deprotonation as discussed previously. It was discovered that small quantities of the methyl ethers of **7c** and **8c** could be obtained by quenching the electrochemical reduction of **6c** with a large excess of methyl iodide after partial reduction had occurred. It was not possible to continue the reduction of **6c** in the presence of methyl iodide because the reagent was quickly consumed by reduction. Due to symmetry, methylation of **7c** and **8c** afforded compounds **14** and **15**, respectively, and thus their regiochemistry was established. This reaffirmed our assignments for **7b** and **7d** since neither of their regioisomers would have given products identical to those of **7c** or **8c** upon methylation.

Conclusions

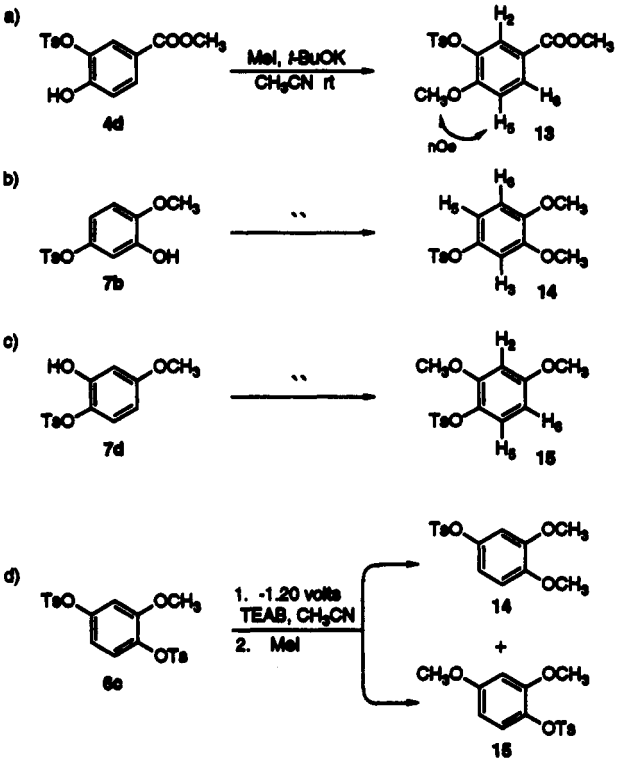
We have developed a simple method for the regioselective cleavage of aryl tosylates by electrochemical reduction. An electron-withdrawing substituent (methoxycarbonyl) was found to favor cleavage of ortho and para tosylates while an electron-donating substituent (methoxy) favored cleavage of meta tosylates. For most of the compounds tested, the process has been shown to be high yielding and reproducible on a gram scale. The regiochemistry of all major products from the electrochemical

(11) NOESY spectra were collected on a Bruker AM-500 spectrometer in the phase-sensitive TPPI mode. Data were aquired using 256 1K FIDs of 16 or 32 scans over a sweep width of approximately 3000 Hz. The mixing time was 1.0 s and the recycle delay was 2 s. Data were processed in each dimension with 90°-shifted sine-bell apodization, zero-filled to 1K × 1K prior to Fourier transformation, and phase corrected.

Scheme IV. Deoxygenation of Phenols



Scheme V. Regiochemical Assignment of Methoxybenzene Derivatives by 2D NOE Spectroscopy



reduction study were established by either hydrogen bonding, deoxygenation, or NOE correlation.

Experimental Section

General. Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran (THF) was distilled from sodium/benzophenone prior to use; triethylamine (TEA) was distilled from CaH_2 and stored over 4-Å sieves; acetonitrile was distilled from CaH_2 directly before use in electrochemistry; tetraethylammonium bromide (TEAB) was recrystallized from EtOH and dried at ~110 °C overnight before use. Methyl trifluoromethanesulfonate ($TfOCH_3$) and *N*-(toluenesulfonyl)imidazole were prepared following literature procedures.[12,13] Potassium *tert*-butoxide (*t*-BuOK) was prepared by dissolving potassium metal in *tert*-butyl alcohol. The solution was concentrated to dryness, and the crude residue was then sublimed at ~140 °C (0.10 mmHg). Concentrations were done by rotary evaporation under aspirator pressure (~25 mmHg) followed by static evaporation with an oil pump (0.05 mmHg). Preparative low-pressure chromatography (LPC) was done on 230–400-mesh silica gel (E. Merck). Preparative thin-layer chromatography (prep plate TLC) was done on pre-coated 1000 μm silica G60/F_{254} glass-backed plates (E. Merck). Melting points (Pyrex capillary) were determined on a Büchi melting point apparatus and are uncorrected. Preparative electrochemistry was done using a Princeton Applied Research Model 173 potentiostat/galvanostat. ^1H NMR spectra were determined in $CDCl_3$ on Bruker AM-400 or AM-500 superconducting FT spectrometers; chemical shifts are reported in ppm with respect to internal TMS; coupling constants, *J*, are in hertz. Elemental analyses were performed by the Microanalytical Laboratory, operated by the College of Chemistry, University of California, Berkeley, CA.

Bis-tosylation of Methyl Dihydroxybenzoates and Dihydroxyanisoles. General Procedure. A 250-mL single-neck round-bottom flask, equipped with stir bar and N_2 balloon, was charged with 1-tosylimidazole (250 mol %) in 100 mL of THF. The solution was cooled in an ice/water bath, and methyl triflate (250 mol %) was added by syringe. After 15 min the solution became cloudy. Methyl dihydroxybenzoate or dihydroxyanisole (0.5–1.0 g) was then added in a solution of THF (2 × 5 mL) followed immediately by TEA (250 mol %). After 20 min the ice bath was removed, and the solution was stirred at rt under N_2 overnight. The reaction was then quenched with 10 mL of 1 M KH_2PO_4. Approximately 75% of the THF was removed by rotary evaporation, and the residue was partitioned between EtOAc (50 mL) and H_2O (75 mL). The aqueous layer was separated and extracted with EtOAc (2 × 30 mL), and the combined EtOAc layers were washed with 0.5 M KOH (2 × 40 mL), 0.5 M HCl (2 × 40 mL), saturated $NaHCO_3$ (30 mL), and brine (30 mL). The organic solution was then dried and evaporated. The crude product was purified by LPC (60 g SiO_2, hexanes/EtOAc, 3/1 → 2/1).

Methyl 2,3-Bis(tosyloxy)benzoate (2a). Starting materials were methyl 2,3-dihydroxybenzoate (**1a**)[14] (0.80 g, 4.76 mmol), 1-tosylimidazole (2.17 g, 9.76 mmol, 205 mol %), $TfOCH_3$ (1.10 mL, 9.72 mmol, 204 mol %), and TEA (1.35 mL, 9.73 mmol, 204 mol %). The pure crystalline solid obtained was characterized as **2a** (2.21 g, 97%): mp 130–131 °C; ^1H NMR (400 MHz) δ 7.81 (dd, 1 H, J_1 = 7.9, J_2 = 1.8), 7.56–7.61 (m, 4 H), 7.42 (dd, 1 H, J_1 = 8.2, J_2 = 1.7), 7.22–7.34 (m, 5 H), 3.84 (s, 3 H), 2.46 (s, 3 H), 2.44 (s, 3 H). Anal. Calcd for $C_{22}H_{20}O_8S_2$: C, 55.4; H, 4.2. Found: C, 55.2; H, 4.1.

Methyl 2,4-Bis(tosyloxy)benzoate (2b). Starting materials were methyl 2,4-dihydroxybenzoate (**1b**)[15] (887 mg, 5.28 mmol), 1-tosylimidazole (2.40 g, 10.8 mmol, 205 mol %), $TfOCH_3$ (1.25 mL, 11.0 mmol, 209 mol %), and TEA (1.50 mL, 10.8 mmol, 205 mol %). The pure white solid obtained was characterized as **2b** (2.41 g, 96%): mp 62–65 °C; ^1H NMR (500 MHz) δ 7.82 (d, 1 H, *J* = 8.6), 7.69 (d, 2 H, *J* = 8.5), 7.68 (d, 2 H, *J* = 8.5), 7.34 (d, 2 H, *J* = 8.2), 7.33 (d, 2 H, *J* = 8.3), 6.98 (dd, 1 H, J_1 = 8.6, J_2 = 2.3), 6.81 (d, 1 H, *J* = 2.3), 3.79 (s, 3 H), 2.47 (s, 3 H), 2.46 (s, 3 H). Anal. Calcd for $C_{22}H_{20}O_8S_2$: C, 55.4; H, 4.2. Found: C, 55.2; H, 4.3.

Methyl 2,5-Bis(tosyloxy)benzoate (2c). Starting materials were methyl 2,5-dihydroxybenzoate (**1c**)[16] (1.00 g, 5.95 mmol), 1-tosylimidazole (2.72 g, 12.2 mmol, 206 mol %), $TfOCH_3$ (1.40 mL, 12.4 mmol, 208 mol %), and TEA (1.70 mL, 12.2 mmol, 206

(12) Beard, C. D.; Baum, K.; Grakauskas, V. *J. Org. Chem.* **1973**, *38*, 3673.
(13) Staab, H. A.; Wendel, K. *Chem. Ber.* **1960**, *93*, 2902.
(14) Columbia Organic Chemical Co. Inc., Camden, SC.
(15) Aldrich Chemical Co. Inc., Milwaukee, WI.
(16) Indofine Chemical Co. Inc., Somerville, NJ.

mol %). The white solid obtained was characterized as pure **2c** (2.34 g, 83%): mp 92–94 °C; ^{1}H NMR (500 MHz) δ 7.70 (d, 4 H, J = 8.2), 7.51 (d, 1 H, J = 3.0), 7.34 (d, 2 H, J = 7.9), 7.33 (d, 2 H, J = 8.1), 7.10 (dd, 1 H, J_1 = 8.9, J_2 = 3.0), 7.03 (d, 1 H, J = 8.9), 3.77 (s, 3 H), 2.46 (s, 6 H). Anal. Calcd for $C_{22}H_{20}O_8S_2$: C, 55.4; H, 4.2. Found: C, 55.4; H, 4.1.

Methyl 3,4-Bis(tosyloxy)benzoate (2d). Starting materials were methyl 3,4-dihydroxybenzoate (**1d**)[17] (1.00 g, 5.95 mmol), 1-tosylimidazole (2.71 g, 12.2 mmol, 205 mol %), $TfOCH_3$ (1.40 mL, 12.4 mmol, 208 mol %), and TEA (1.70 mL, 12.2 mmol, 206 mol %). Pure **2d** was isolated as a cloudy white oil (2.70 g, 95%): ^{1}H NMR (500 MHz) δ 7.93 (dd, 1 H, J_1 = 8.5, J_2 = 2.1), 7.91 (d, 1 H, J = 2.0), 7.65 (d, 2 H, J = 8.4), 7.62 (d, 2 H, J = 8.4), 7.35 (d, 1 H, J = 8.5), 7.29 (t, 4 H, J = 8.2), 3.91 (s, 3 H), 2.46 (s, 3 H), 2.45 (s, 3 H). Anal. Calcd for $C_{22}H_{20}O_8S_2$: C, 55.4; H, 4.2. Found: C, 55.4; H, 4.1.

2,3-Bis(tosyloxy)anisole (6a). Starting materials were 3-methoxycatechol (**5a**)[15] (500 mg, 3.57 mmol), 1-tosylimidazole (1.66 g, 7.47 mmol, 209 mol %), $TfOCH_3$ (850 μL, 7.51 mmol, 211 mol %), and TEA (1.0 mL, 7.2 mmol, 202 mol %). The crystals (from $CHCl_3$/hexanes) were characterized as **6a** (1.31 g, 82% yield): mp 156–157.5 °C; ^{1}H NMR (500 MHz) δ 7.77 (d, 2 H, J = 6.7), 7.49 (d, 2 H, J = 6.8), 7.32 (d, 2 H, J = 8.0), 7.19 (d, 2 H, J = 8.1), 7.19 (t, 1 H, J = 8.5), 6.98 (dd, 1 H, J_1 = 8.5, J_2 = 1.4), 6.83 (dd, 1 H, J_1 = 8.5, J_2 = 1.3), 3.70 (s, 3 H), 2.47 (s, 3 H), 2.41 (s, 3 H). Anal. Calcd for $C_{21}H_{20}O_7S_2$: C, 56.2; H, 4.5. Found: C, 56.2; H, 4.3.

2,4-Bis(tosyloxy)anisole (6b). Starting materials were 4-methoxyresorcinol (**5b**)[18] (636 mg, 4.54 mmol), 1-tosylimidazole (2.52 g, 11.3 mmol, 250 mol %), $TfOCH_3$ (1.30 mL, 11.5 mmol, 253 mol %), and TEA (1.60 mL, 11.5 mmol, 254 mol %). Pure **6b** was obtained as a clear colorless oil (1.53 g, 75% yield): ^{1}H NMR (400 MHz) δ 7.67 (d, 2 H, J = 8.4), 7.65 (d, 2 H, J = 8.4), 7.34 (d, 2 H, J = 8.3), 7.31 (d, 2 H, J = 8.2), 6.90 (dd, 1 H, J_1 = 9.0, J_2 = 2.8), 6.76 (d, 1 H, J = 2.8), 6.72 (d, 1 H, J = 9.0), 3.52 (s, 3 H), 2.46 (s, 3 H), 2.45 (s, 3 H). Anal. Calcd for $C_{21}H_{20}O_7S_2$: C, 56.2; H, 4.5. Found: C, 56.2; H, 4.3.

2,5-Bis(tosyloxy)anisole (6c). Starting materials were methoxyhydroquinone (**5c**)[19] (565 mg, 4.03 mmol), 1-tosylimidazole (2.24 g, 10.1 mmol, 250 mol %), $TfOCH_3$ (1.15 mL, 10.2 mmol, 252 mol %), and TEA (1.40 mL, 10.1 mmol, 250 mol %). The solid obtained was pure **6c** (1.30 g, 72% yield): mp 126–128.5 °C; ^{1}H NMR (400 MHz) δ 7.71 (d, 2 H, J = 8.1), 7.69 (d, 2 H, J = 8.0), 7.32 (d, 2 H, J = 8.1), 7.29 (d, 2 H, J = 7.9), 7.02 (d, 1 H, J = 8.8), 6.55 (d, 1 H, J = 2.6), 6.41 (dd, 1 H, J_1 = 8.8, J_2 = 2.7), 3.45 (s, 3 H), 2.46 (s, 3 H), 2.45 (s, 3 H). Anal. Calcd for $C_{21}H_{20}O_7S_2$: C, 56.2; H, 4.5. Found: C, 55.9; H, 4.4.

3,4-Bis(tosyloxy)anisole (6d). Starting materials were 4-methoxycatechol (**5d**)[20] (396 mg, 2.83 mmol), 1-tosylimidazole (1.58 g, 7.11 mmol, 251 mol %), $TfOCH_3$ (810 μL, 7.16 mmol, 253 mol %), and TEA (1.0 mL, 7.2 mmol, 255 mol %). The white solid obtained was pure **6d** (968 mg, 76% yield): mp 93–95 °C; ^{1}H NMR (400 MHz) δ 7.64 (d, 2 H, J = 8.4), 7.59 (d, 2 H, J = 8.4), 7.27 (d, 2 H, J = 8.5), 7.25 (d, 2 H, J = 8.4), 7.11 (d, 1 H, J = 9.0), 6.77 (d, 1 H, J = 2.9), 6.73 (dd, 1 H, J_1 = 9.0, J_2 = 2.9), 3.75 (s, 3 H), 2.44 (s, 3 H), 2.43 (s, 3 H). Anal. Calcd for $C_{21}H_{20}O_7S_2$: C, 56.2; H, 4.5. Found: C, 56.3; H, 4.3.

Controlled-Potential Electrochemical Reduction. General Procedure. A standard H-cell (length, 15.0 cm; o.d. 3.2 cm)[6] was equipped with a platinum foil anode, mercury pool cathode, silver wire reference electrode, and nitrogen bubbler. Both chambers were charged with CH_3CN saturated with TEAB (30–35 mL). The apparatus was preelectrolyzed at −1.50 V for 15–30 min to a background current in the range of 0.1–0.3 mA. Voltage to the cell was then shut off while the bis(tosyloxy) starting material (0.50–1.00 g) was added to the cathode chamber, and it was dissolved with the help of bubbling nitrogen. The solution was reduced at the quarter-wave potential ($E^1_{1/4}$) of the starting material, determined from its cyclic voltammogram, and the reaction was stopped after approximately 85–90% conversion (usually 8–16 h), estimated by TLC (aliquot workup: EtOAc and 1 M KH_2PO_4). The contents of each chamber were poured simultaneously into two beakers side by side. The cathode solution was quenched with 0.25 M KH_2PO_4 (~200 mL) and extracted with EtOAc (3 × 30 mL). The combined EtOAc layers were washed with H_2O (30 mL), saturated $NaHCO_3$ (2 × 30 mL), and brine (30 mL), dried, and evaporated. The crude material was analyzed directly by high-resolution NMR to determine the ratio of regioisomeric products. Unless otherwise specified, the reaction yields were extrapolated to account for unreacted starting material. In most cases, the two regioisomeric products could be isolated pure by either LPC or prep plate TLC (hexanes/EtOAc, 3/1).

Methyl 2-Hydroxy-3-(tosyloxy)benzoate (3a) and Methyl 3-Hydroxy-2-(tosyloxy)benzoate (4a). Starting material was **2a** (552 mg, 1.16 mmol); $E^1_{1/4}$ ~ −1.15 V. The crude material obtained was identified as a mixture of **3a** and **4a** in a ratio of 91/9 (282 mg, 85% based on 61 mg of unreacted **2a**). Compound **3a**: light yellow oil; ^{1}H NMR (500 MHz) δ 10.75 (s, OH, sharp), 7.81 (d, 2 H, J = 8.3), 7.73 (dd, 1 H, J_1 = 8.0, J_2 = 1.6), 7.37 (dd, 1 H, J_1 = 8.1, J_2 = 1.7), 7.31 (d, 2 H, J = 8.4), 6.82 (t, 1 H, J = 8.1), 3.92 (s, 3 H), 2.44 (s, 3 H). Anal. Calcd for $C_{15}H_{14}O_6S$: C, 55.9; H, 4.4. Found: C, 55.9; H, 4.3.

Methyl 2-Hydroxy-4-(tosyloxy)benzoate (3b) and Methyl 4-Hydroxy-2-(tosyloxy)benzoate (4b). Starting material was **2b** (816 mg, 1.71 mmol); $E^1_{1/4}$ ~ −1.13 V. The crude solid obtained was identified as a mixture of **3b** and **4b** in a ratio of 34/66 (422 mg, 90% based on 122 mg of unreacted **2b**). Compound **3b**: white solid mp; 86–88 °C; ^{1}H NMR (500 MHz) δ 10.86 (s, OH, sharp), 7.78 (d, 1 H, J = 8.7), 7.73 (d, 2 H, J = 8.3), 7.32 (d, 2 H, J = 8.1), 6.62 (dd, 1 H, J_1 = 8.7, J_2 = 2.3), 6.59 (d, 1 H, J = 2.3), 3.93 (s, 3 H), 2.45 (s, 3 H). Anal. Calcd for $C_{15}H_{14}O_6S$: C, 55.9; H, 4.4. Found: C, 55.8; H, 4.4. Compound **4b**: white solid; mp 176–178.5 °C; ^{1}H NMR (400 MHz) δ 7.76 (d, 1 H, J = 8.7), 7.73 (d, 2 H, J = 8.3), 7.32 (d, 2 H, J = 8.1), 6.76 (dd, 1 H, J_1 = 8.7, J_2 = 2.4), 6.61 (d, 1 H, J = 2.4), 3.72 (s, 3 H), 2.44 (s, 3 H). Anal. Calcd for $C_{15}H_{14}O_6S$: C, 55.9; H, 4.4. Found: C, 55.8; H, 4.4.

Methyl 2-Hydroxy-5-(tosyloxy)benzoate (3c) and Methyl 5-Hydroxy-2-(tosyloxy)benzoate (4c). Starting material was **2c** (925 mg, 1.94 mmol); $E^1_{1/4}$ ~ −1.12 V. The crude solid obtained was identified as a mixture of **3c** and **4c** in a ratio of 95/5 (510 mg, 86% based on 46 mg of unreacted **2c**). Compound **3c**: white powder; mp 106.5–107.5 °C; ^{1}H NMR (500 MHz) δ 10.39 (s, OH, sharp), 7.70 (d, 2 H, J = 8.3), 7.54 (d, 1 H, J = 2.9), 7.36 (t, 2 H, J = 8.3), 6.97 (dd, 1 H, J_1 = 9.0, J_2 = 2.9), 6.85 (d, 1 H, J = 9.0), 3.94 (s, 3 H), 2.44 (s, 3 H). Anal. Calcd for $C_{15}H_{14}O_6S$: C, 55.9; H, 4.4. Found: C, 56.3; H, 4.3.

Methyl 3-Hydroxy-4-(tosyloxy)benzoate (3d) and Methyl 4-Hydroxy-3-(tosyloxy)benzoate (4d). Starting material was **2d** (766 mg, 1.61 mmol); $E^1_{1/3}$ ~ −1.05 V. The resulting crude solid was identified as **4d**; compound **3d** was not found (429 mg, 93% based on 84 mg of unreacted **2d**). Compound **4d**: light yellow solid; mp 132–134.5 °C; ^{1}H NMR (500 MHz) δ 7.84 (dd, 1 H, J_1 = 8.5, J_2 = 2.0), 7.78 (d, 2 H, J = 8.3), 7.54 (d, 1 H, J = 2.0), 7.36 (d, 2 H, J = 8.1), 7.02 (d, 1 H, J = 8.6), 6.6–6.8 (s, OH, broad), 3.84 (s, 3 H), 2.447 (s, 3 H). Anal. Calcd for $C_{15}H_{14}O_6S$: C, 55.9; H, 4.4. Found: C, 56.2; H, 4.3.

2-Hydroxy-3-(tosyloxy)anisole (7a) and 3-Hydroxy-2-(tosyloxy)anisole (8a). Starting material was **6a** (462 mg, 1.03 mmol); $E^1_{1/4}$ ~ −1.25 V. The crude oil obtained was identified as a mixture of **7a** and **8a** in a ratio of 31/69 (225 mg, 74%, only traces of unreacted **6a** were seen). Compound **7a**: white crystalline solid; mp 124–126 °C; ^{1}H NMR (400 MHz) δ 7.80 (d, 2 H, J = 8.0), 7.31 (d, 2 H, J = 8.0), 6.75 (m, 2 H), 6.67 (dd, 1 H, J_1 = 6.5, J_2 = 2.5), 5.60 (s, OH, broad), 3.86 (s, 3 H), 2.45 (s, 3 H). Anal. Calcd for $C_{14}H_{14}O_5S$: C, 57.1; H, 4.8. Found: C, 57.0; H, 4.5. Compound **8a**: white crystalline solid; mp 137–138.5 °C; ^{1}H NMR (400 MHz) δ 7.83 (d, 2 H, J = 8.4), 7.32 (d, 2 H, J = 8.1), 7.05 (t, 1 H, J = 8.3), 6.66 (dd, 1 H, J_1 = 8.4, J_2 = 1.5), 6.4–6.6 (s, OH, broad), 6.33 (dd, 1 H, J_1 = 8.3, J_2 = 1.4), 3.46 (s, 3 H), 2.46 (s, 3 H). Anal. Calcd for $C_{14}H_{14}O_5S$: C, 57.1; H, 4.8. Found: C, 56.9; H, 4.7.

2-Hydroxy-4-(tosyloxy)anisole (7b) and 4-Hydroxy-2-(tosyloxy)anisole (8b). Starting material was **6b** (0.500 g, 1.11 mmol); $E^1_{1/4}$ ~ −1.30 V. The crude solid obtained was identified as a mixture of **7b** and **8b** in a ratio of 94/6 (244 mg, 93% based

(17) Fairfield Chemical Co. Inc., Blythewood, SC.
(18) Camps, F.; Colomina, O.; Coll, J.; Messeguer, A. *Tetrahedron* **1982**, *38*, 2955. Crosby, D. G. *J. Org. Chem.* **1961**, *26*, 1215. Shamma, M.; Stiver, L. D. *Tetrahedron* **1969**, *25*, 3887.
(19) Fluka Chemical Corp., Ronkonkoma, NY.
(20) Carr, J. B. U.S. Patent 4,208,424, June 17, 1980.

on 111 mg of unreacted **6b**). Compound **7b**: white crystalline solid; mp 108.5–111 °C; ^{1}H NMR (400 MHz) δ 7.69 (d, 2 H, J = 8.2), 7.30 (d, 2 H, J = 8.0), 6.69 (d, 1 H, J = 8.8), 6.53 (d, 1 H, J = 2.8), 6.48 (dd, 1 H, J_1 = 8.8, J_2 = 2.8), 5.83 (s, OH, broad), 3.83 (s, 3 H), 2.43 (s, 3 H). Anal. Calcd for $C_{14}H_{14}O_5S$: C, 57.1; H, 4.8. Found: C, 57.4; H, 4.9.

2-Hydroxy-5-(tosyloxy)anisole (7c) and 5-Hydroxy-2-(tosyloxy)anisole (8c).[21] Starting material was **6c** (530 mg, 1.18 mmol); $E^1_{1/4} \sim -1.25$ V. From the resulting crude oil was isolated small amounts of **7c** and **8c** in a ratio of 23/77 with significant decomposition. Compound **7c**: ^{1}H NMR (400 MHz) δ 7.74 (d, 2 H, J = 8.4), 7.29 (d, 2 H, J = 8.1), 6.98 (d, 1 H, J = 8.6), 6.33 (d, 1 H, J = 2.8), 6.29 (dd, 1 H, J_1 = 8.6, J_2 = 2.8), 4.90 (s, OH, broad), 3.49 (s, 3 H), 2.44 (s, 3 H). Compound **8c**: ^{1}H NMR (400 MHz) δ 7.70 (d, 2 H, J = 8.2), 7.31 (d, 2 H, J = 8.1), 6.73 (d, 1 H, J = 8.7), 6.61 (d, 1 H, J = 2.6), 6.33 (dd, 1 H, J_1 = 8.7, J_2 = 2.6), 5.50 (s, OH, broad), 3.80 (s, 3 H), 2.45 (s, 3 H).

3-Hydroxy-4-(tosyloxy)anisole (7d) and 4-Hydroxy-3-(tosyloxy)anisole (8d). Starting material was **6d** (250 mg, 0.557 mmol); $E^2_{1/4} \sim -1.15$ V. The crude oil obtained was identified as compound **7d**; compound **8d** was not found. Purification by LPC gave pure **7d** as a light yellow oil (129 mg, 82%). An estimated 11 mg of unreacted **6d** was extrapolated from the NMR of the crude product (96% conversion): ^{1}H NMR (500 MHz) δ 7.74 (d, 2 H, J = 8.4), 7.33 (d, 2 H, J = 8.4), 6.62 (d, 1 H, J = 9.0), 6.53 (d, 1 H, J = 3.0), 6.27 (dd, 1 H, J_1 = 9.0, J_2 = 3.0), 6.06 (s, OH, broad), 3.74 (s, 3 H), 2.46 (s, 3 H). Anal. Calcd for $C_{14}H_{14}O_5S$: C, 57.1; H, 4.8. Found: C, 56.9; H, 4.8.

Methylation. General Procedure. To a 10-mL flask equipped with a stir bar and N_2 balloon was added the phenolic starting material (75–150 g) in CH_3CN (6 mL). To this solution was added t-BuOK (110 mol %). The deep red solution was allowed to stir for 15 min, and then MeI (1000 mol %) was added. A precipitate immediately developed. The reaction was stirred at room temperature under N_2 for 1 day and then poured into a 60-mL solution of 0.5 M KOH and EtOAc, 1/1. The aqueous layer was separated and extracted with EtOAc (1 × 30 mL). The combined organic layers were washed with brine (20 mL), dried, and evaporated, and the crude product was purified by prep plate TLC (hexanes/EtOAc, 2/1).

Methyl 4-Methoxy-3-(tosyloxy)benzoate (13). Starting materials were **4d** (78 mg, 0.24 mmol), t-BuOK (34 mg, 0.30 mmol, 125 mol %), and MeI (155 μL, 2.5 mmol, 1030 mol %). The white powder obtained was **13**: mp 91–92.5 °C; ^{1}H NMR (500 MHz) δ 7.92 (dd, 1 H, J_1 = 8.7, J_2 = 2.1), 7.81 (d, 1 H, J = 2.1), 7.75 (d, 2 H, J = 8.3), 7.31 (d, 2 H, J = 8.2), 6.87 (d, 1 H, J = 8.7), 3.88 (s, 3 H), 3.63 (s, 3 H), 2.45 (s, 3 H). Anal. Calcd for $C_{16}H_{16}O_6S$: C, 57.1; H, 4.8. Found: C, 57.0; H, 4.5.

2-Methoxy-4-(tosyloxy)anisole (14). Starting materials were **7b** (152 mg, 0.516 mmol), t-BuOK (60 mg, 0.535 mmol, 104 mol %), and MeI (1000 μL, 16.1 mmol, 3110 mol %). The light yellow oil obtained was **14**: ^{1}H NMR (500 MHz) δ 7.70 (d, 2 H, J = 8.3), 7.31 (d, 2 H, J = 8.3), 6.70 (d, 1 H, J = 8.7), 6.51 (d, 1 H, J = 2.7), 6.48 (dd, 1 H, J_1 = 8.7, J_2 = 2.7), 3.84 (s, 3 H), 3.74 (s, 3 H), 2.45 (s, 3 H). Anal. Calcd for $C_{15}H_{16}O_5S$: C, 58.4; H, 5.2. Found: C, 58.4; H, 5.3.

3-Methoxy-4-(tosyloxy)anisole (15). Starting materials were **7d** (156 mg, 0.530 mmol), t-BuOK (66 mg, 0.588 mmol, 111 mol %), and MeI (500 μL, 2.5 mmol, 1520 mol %). The light yellow solid obtained was **15**: mp 89–91.5 °C; ^{1}H NMR (500 MHz) δ 7.71 (d, 2 H, J = 8.3), 7.27 (d, 2 H, J = 8.3), 7.03 (d, 1 H, J = 9.0), 6.34–6.37 (m, 2 H, AB), 3.75 (s, 3 H), 3.48 (s, 3 H), 2.42 (s, 3 H). Anal. Calcd for $C_{15}H_{16}O_5S$: C, 58.4; H, 5.2. Found: C, 58.6; H, 5.2.

Registry No. **1a**, 2411-83-8; **1b**, 2150-47-2; **1c**, 2150-46-1; **1d**, 2150-43-8; **2a**, 137668-91-8; **2b**, 137668-92-9; **2c**, 137668-93-0; **2d**, 137668-94-1; **3a**, 137668-95-2; **3b**, 137668-96-3; **3c**, 94033-94-0; **4a**, 137668-97-4; **4b**, 137668-98-5; **4d**, 137668-99-6; **5a**, 934-00-9; **5b**, 6100-60-3; **5c**, 824-46-4; **5d**, 3934-97-2; **6a**, 137669-00-2; **6b**, 137669-01-3; **6c**, 137669-02-4; **6d**, 137669-03-5; **7a**, 137669-04-6; **7b**, 137669-05-7; **7c**, 137669-06-8; **7d**, 137669-07-9; **8a**, 137669-08-0; **8b**, 137669-09-1; **8c**, 137669-10-4; **9**, 137669-11-5; **10**, 51207-44-4; **11**, 137669-12-6; **12**, 4416-67-5; **13**, 137669-13-7; **14**, 137669-14-8; **15**, 137669-15-9; 5-chloro-1-phenyltetrazole, 14210-25-4.

Supplementary Material Available: ^{1}H NMR spectra for compounds **10** and **12**, cyclic voltammograms for compounds **2a–d** and **6a–d**, and NOESY spectra for compounds **13–15** (13 pages). Ordering information is given on any current masthead page.

(21) Phenols **7c** and **8c** were characterized fully as their corresponding methyl ethers **14** and **15**, respectively.

Radical Reactions of Epoxides. Chlorine Atom Abstraction from α- and β-Chloro Epoxides by the Triphenyltin Radical[1]

Kevin W. Krosley, Gerald Jay Gleicher,* and Gary E. Clapp

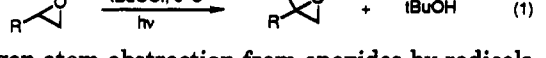
Department of Chemistry, Oregon State University, Corvallis, Oregon 97331-4003

Received August 1, 1991 (Revised Manuscript Received October 7, 1991)

The four isomers of chloroepoxypropane have been prepared, and their relative reactivities with triphenyltin hydride have been determined. The three α-chloroepoxypropanes react at a much slower rate than does epichlorohydrin, the only β-chloro epoxide of the four. The nature of the increased reactivity for the β-chloro epoxides has been investigated by studying two pair of diastereomeric β-chloro epoxides, and a single acyclic β-chloro ether. The results are discussed in terms of the inductive, resonance, and stereoelectronic effects of the epoxide.

Introduction

The first studies of the free-radical chemistry of epoxides in solution were reported by Walling and co-workers in 1962.[2] They found that the photoinitiated reactions of epoxides with *tert*-butyl hypochlorite formed α-chloro epoxides as the major products (eq 1). Subsequent studies



(1)

of hydrogen atom abstraction from epoxides by radicals including bromine atom,[3] chlorine atom,[4] and *tert*-butoxyl radical[5] have appeared. In nearly every case, abstraction of an α-hydrogen atom from the epoxide can account for

(1) Initial presentation of results at the 201st National Meeting of the American Chemical Society, Atlanta, GA, April 16, 1991.

(2) (a) Walling, C.; Fredricks, P. S. *J. Am. Chem. Soc.* **1962**, *84*, 3326. (b) Walling, C.; Mintz, M. J. *J. Am. Chem. Soc.* **1967**, *89*, 1515.

(3) Calò, V.; Lopez, L.; Valentino, D. S. *Synthesis* **1978**, 139.

(4) Etlis, V. S.; Trofimov, N. N.; Razuvaev, G. A. *Zh. Obsh. Khim.* **1964**, *34*, 2784.

(5) Wallace, T. J.; Gritter, R. J. *Tetrahedron* **1963**, *19*, 657.

0022-3263/92/1957-0840$03.00/0