117708-31-3; *dl*-**16** (isomer 1), 117708-27-7; *dl*-**16** (isomer 2), 117708-32-4; *dl*-**17** (isomer 1), 117653-56-2; *dl*-**17** (isomer 2), 117708-33-5; *dl*-**18** (isomer 1), 117653-57-3; *dl*-**18** (isomer 2), 117708-34-6; *dl*-**19** (isomer 1), 117653-58-4; *dl*-**19** (isomer 2), 117708-35-7; *dl*-**20** (isomer 1), 117708-28-8; *dl*-**20** (isomer 2), 117708-36-8; *dl*-**21** (isomer 1), 117708-29-9; *dl*-**21** (isomer 2), 117708-37-9; *dl*-**22** (isomer 1), 117653-60-8; *dl*-**22** (isomer 2), 117708-39-1; *dl*-**23**, 117708-40-4; *dl*-**24** (isomer 1), 117653-59-5; *dl*-**24** (isomer 2), 117709-10-1; *dl*-**25** (isomer 1), 117708-30-2; *dl*-**25** (isomer 2), 117708-38-0; *dl*-**26**, 117653-61-9; *dl*-$THPOCH_2CH{=}CH_2$, 4203-49-0; *dl*-$(EtO)_2POCH(CH_3)COCH_3$, 117653-52-8; $CH_3OCH_2OC(Li){=}C{=}CH_2$, 117653-54-0.

Anodic Oxidation Studies of *p*-Methoxyanilides. A General Method for Preparation of Acylated Quinone Imine Ketals

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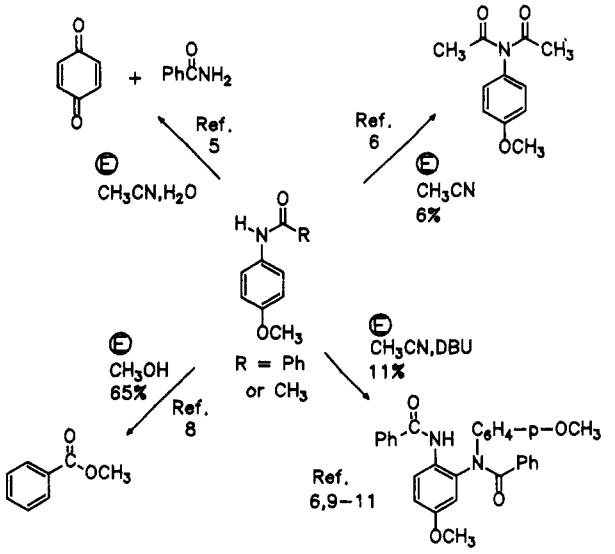
Anodic oxidation of a methanolic solution of 4-methoxybenzanilide **1a** or 4-methoxyacetanilide **1b** in a single-cell apparatus at constant current using lithium perchlorate as the supporting electrolyte afforded high yields of *N*-benzoyl- and *N*-acetyl-1,4,4-trimethoxy-1-amino-2,5-cyclohexadiene, respectively. This is the first time anodic 1,4-addition products have been characterized from anodic oxidation of anilides. When these anodic oxidations were performed in the presence of either sodium bicarbonate or 2,6-lutidine, acylated quinone imine ketals were obtained in excellent yield. The yield of acylated quinone imine ketals from these anodic oxidations is dependent upon the anode material, current density, water content of the methanol, and workup procedures. Experimental conditions have been established for conducting these reactions for a number of derivatives of **1a** and **1b** in high yield and acylated quinone imine ketals are now readily available via the anodic oxidation of *p*-methoxyanilides.

Although the anodic oxidation of anilines has been extensively studied[1-3] and preparative scale experiments were performed as long ago as 1875,[4] the electrochemical oxidation of the corresponding amides has received less attention.[5-11] Scheme I summarizes some of the results previously reported from anodic oxidations of *p*-methoxyanilide derivatives, the main theme of the present study.

Many of the products isolated from the anodic oxidation of anilides in both acetonitrile and methanol could be rationalized as arising from hydrolysis of a quinone imine formed in the reaction. For anodic oxidations in acetonitrile it was suggested that adventitious water hydrolyzed the primary oxidation product,[8] resulting in the isolation of benzoquinone and benzamide (Scheme I). However, in no case was a quinone imine intermediate isolated from these reactions. Somewhat more surprising, the product isolated from anodic oxidation in methanol (Scheme I) involved reaction of some intermediate with the solvent.

Scheme I. Selected Examples of Anodic Oxidation of *p*-Methoxyanilides



Our early experiences in conducting anodic oxidations of anilides paralleled some of the literature results: complex reaction mixtures and poor accounting of material. For example, anodic oxidation of **1a** in methanolic potassium hydroxide, conditions used for the conversion of 1,4-dimethoxybenzene to benzoquinone diketal,[12] afforded

(1) Weinberg, N. L.; Weinberg, H. R. *Chem. Rev.* **1968**, *68*, 449.
(2) Kyriacou, D. K. *Basics of Electroorganic Synthesis*; John Wiley & Sons, Inc.: New York, 1981.
(3) Ross, S. D.; Finkelstein, M.; Rudd, E. F. *Anodic Oxidation*; Academic Press: New York, 1975.
(4) Goppelsroeder, F. *C.R. Acad. Sci.* **1875**, 228; **1876**, 1392.
(5) Ikenoya, S.; Masui, M.; Ohmori, H.; Sayo, H. *J. Chem. Soc., Perkin Trans. 2* **1974**, 571. See also ref 8. This basic chemistry has recently been employed as a deprotection method for *N*-(*p*-methoxyphenyl)-2-azetidinones: Corley, E. G.; Karady, S.; Abramson, N. L.; Ellison, D.; Weinstock, L. M. *Tetrahedron Lett.* **1988**, *29*, 1497.
(6) Hess, U.; Gross, T. *Z. Chem.* **1978**, *18*, 405.
(7) Masui, M.; Ohmori, H.; Sayo, H.; Ueda, A.; Ueda, C. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1180.
(8) Ohmori, H.; Ueda, C.; Nobushe, Y.; Saitou, N.; Yokota, T.; Masui, M. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1599.
(9) Sainsbury, M.; Wyatt, J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 661.
(10) Sainsbury, M.; Wyatt, J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 108.
(11) Ueda, C.; Ohmori, H.; Ueno, K.; Hamada, Y.; Tatsumi, S.; Masui, M. *Chem. Pharm. Bull.* **1985**, *33*, 1407. Cech, I.; Kopke, W.; Hess, U.; Thadewald, I. *Z. Chem.* **1976**, *16*, 191.

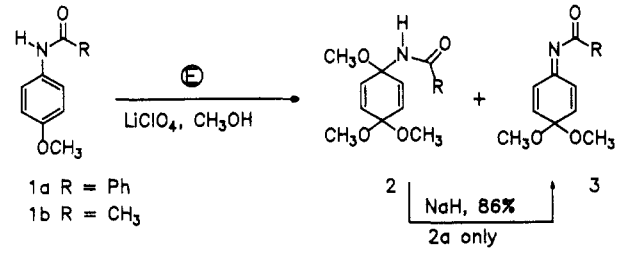
(12) For reviews, see: Swenton, J. S. *Acc. Chem. Res.* **1983**, *16*, 74. Swenton, J. S. *Chemistry of Quinones, Volume 2*; Rappoport, Z., Patai, S., Eds.; John Wiley: New York, 1988; p 899.

0022-3263/89/1954-0051$01.50/0

a mixture of products which were not characterized. *However, electrochemical oxidation of* **1a** *in methanol using lithium perchlorate as electrolyte followed by careful workup gave the 1,4-addition product* **2a** *as a white solid* (86%).[13] Although **2a** is the nitrogen analogue of a hemiacetal, it can be isolated as a crystalline solid, but it is slowly converted to the acylated quinone imine ketal **3a** upon standing at room temperature.

Anodic oxidation of the *N*-acetyl derivative **1b** in a manner similar to that described above gave the corresponding 1,4-addition product **2b** in 89% crude yield (>95% pure by ^{1}H NMR spectroscopy). Although the lability of the product complicated preparation of analytically pure material, the IR, ^{1}H NMR, and ^{13}C NMR data of **2b** strongly support the structure assignment. Thus, the NH stretch in the IR occurs at 3550–3330 cm^{-1}, the ^{1}H NMR shows four vinyl hydrogens as a broad singlet at δ 6.14, and the ^{13}C NMR shows eight signals (methoxy carbons overlapping) in agreement with the plane of symmetry present in **2b**. The exact mass measurement affirmed the elemental composition of **2b**. *This is the first time 1,4-addition products have been obtained in high yields from anodic oxidation of p-methoxyanilides.*

The chemistry of the 1,4-adducts of **1a** and **1b** has not been extensively studied; however, reaction of **2a** with sodium hydride resulted in liberation of hydrogen and formation of the acylated quinone imine ketal **3a** (86%). These same reaction conditions when applied to **2b** gave a much more complex mixture of products. Since analogues of **3** were deemed to have interesting synthetic possibilities, direct electrochemical conversion of **1a,b** to **3a,b** was examined. Electrochemical oxidation of **1a,b** in methanol containing suspended sodium bicarbonate gave crude **3a,b** in yields of 92% and 88%, respectively.



Although not appreciated initially, detailed studies have shown that the product ratios and yields in these oxidations are a function of a number of experimental variables. During larger scale anodic oxidations of **1a** and **1b** the yield and ratio of the anodic oxidation products **2** and **3** was found to be dependent upon the scale, current density, anode material, and bottle of sodium bicarbonate. Although a platinum gauze anode was always employed in the oxidations, different cathodes were examined. Using a copper wire as cathode, it was difficult to completely consume the starting material when the reaction was performed at currents higher than 0.5 A even when 2–3 equiv of current were passed through the solution. This undoubtedly arises from partial reduction of **3a,b** to the starting anilide at the cathode. When pure **3a** in methanol was subjected to the electrochemical conditions (copper cathode, 2–3 equiv of current passed), a mixture of **1a**, **2a**, and **3a** was formed in the ratio 2:1:4. The formation of **1a** in this reaction could come only from reduction of **3a** at the cathode. This reduction process appeared to be minimal when platinum, which has a lower overvoltage for hydrogen evolution, was used as the cathode; thus, a platinum cathode is preferred for the oxidative conversion of **1** to **3**.

(13) For a preliminary report dealing with some of this chemistry, see: Chen, C.-P.; Chou, C.-T.; Swenton, J. S. *J. Am. Chem. Soc.* **1987**, *109*, 946.

Table I. Effects of Current upon the Anodic Oxidation of 1b Using $NaHCO_3$ as Base

$NaHCO_3$, g	1b, g	solvent (mL)	current,[a] A (min)	ratio 2b/3b
1.0	0.1	5% H_2O/CH_3OH (150)	0.1 (20)	<1:99
1.0	0.1	5% H_2O/CH_3OH (150)	0.2 (10)	<1:99
1.0	0.1	5% H_2O/CH_3OH (150)	0.5 (4)	3:97
1.0	0.1	5% H_2O/CH_3OH (150)	1.0 (2)	16:84
1.8	1.0	3% H_2O/CH_3OH (250)	0.1 (194)	5:95
1.8	1.0	3% H_2O/CH_3OH (250)	0.5 (40)	25:75
5	4.0	CH_3OH (100)	0.3 (280)	12:88
18[b]	10.0	CH_3OH (250)	0.4 (685)	44:56

[a] Oxidations conducted with a 0.5 × 3 cm Pt cathode and a 5 cm diameter × 5 cm 45-mesh Pt anode using 1.5% $LiClO_4$ in methanol. [b] Initially 8 g was added, and 2.5 g was added every 2 h thereafter.

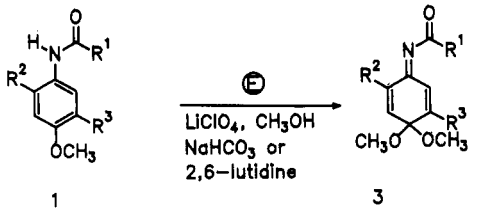
A second complication in preparative electrolyses leading to **3** was the occasional formation of appreciable amounts of the 1,4-addition products **2a** and **2b**. Variable amounts of water in different batches of methanol would effect the solubility of sodium bicarbonate in the reaction medium; this could partly account for the variability of the ratio of products **2** and **3**. In addition, the sodium bicarbonate appeared to become coated with material during some of the oxidations, and this would hinder dissolution of the base as the reaction progressed. Although using 2,6-lutidine as a homogeneous base for the reaction minimized this problem in small scale reactions, the removal of the lutidine under vacuum on larger scale electrolyses was inconvenient. *A more satisfactory solution was to use 5% aqueous methanol as the reaction solvent and to add freshly ground sodium bicarbonate during the course of preparative reactions.* The increased water content in the reaction medium increases the solubility of the base and the addition of fresh sodium bicarbonate minimizes the coating problem as the reaction proceeds.

Interestingly, the ratio of **2b** to **3b** was a function not only of the water content of the methanol but also of the current as shown in Table I. These results are a function of the current density; therefore, the data in Table I apply quantitatively only to the electrodes employed here. However, this does establish that *current density* is a variable in the ratio of **2** to **3** formed in the reaction.

A final experimental variable that became very apparent during large scale oxidations involves the workup of the reaction. The acylated quinone imine linkage can be hydrolyzed during concentration of the methanolic sodium bicarbonate solution, giving the much more labile quinone imine ketal. A similar deacylation probably accounts for the formation of methyl benzoate noted in Scheme I. Thus, if the temperature for solvent removal is not kept near room temperature during concentration of the reaction mixture, a decreased yield of product results. This can be avoided if the crude reaction mixture is poured into a 5-fold volume of water and the product extracted with chloroform. Many of the reactions listed in Table II were conducted before these optimum conditions were established; however, the procedure detailed in the Experimental Section for oxidation of **1a** and **1b** incorporates the above considerations and would be most appropriate for all these compounds.

Table II lists the results from anodic oxidation of a number of anilide derivatives at constant current in a single cell. The current efficiencies (typically 80–90%) and chemical yields (usually >75%) for the oxidation of the anilides to their respective acylated quinone imine ketals

Table II. Anodic Oxidations of Anilides



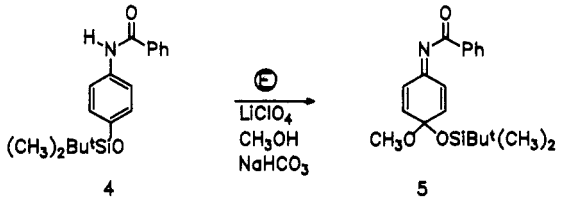
1 3

entry	compd	R^1	R^2	R^3	current efficiency, %	yield,[a] %
1	**1a**	Ph	H	H	60, 90	92, 74[b,c]
2	**1b**	CH_3	H	H	—, 87	89, 79[c,d]
3	**1c**	Ph	H	OCH_3	92	92
4	**1d**	OBu^t	H	OCH_3	55	79
5	**1e**	OCH_3	H	OCH_3	98	54
6	**1f**	Ph	CH_2CO_2Et	OCH_3	91	97
7	**1g**	CH_3	CH_2CO_2Et	H	94	80
8	**1h**	Ph	CH_2CO_2Et	H	95	94
9	**1i**	Ph	CH_2CH_2Cl	OCH_3	64	90
10	**1j**	OCH_3	CH_2CH_2Cl	OCH_3	64	80
11	**1k**	OBu^t	CH_2CH_2Cl	OCH_3	81	73
12	**1l**	OBu^t	CH_2CH_2F	OCH_3	87	86

[a] Yield of material of >95% purity by ^1H NMR spectroscopy from 0.1–1.0-g oxidation isolated by chromatography or crystallization. [b] Yield of crystalline material from a 10-g oxidation. [c] Sodium bicarbonate was used as base. [d] Yield of distilled material from a 5-g oxidation.

are good. Ester, chloro, and fluoro substituents are stable under the electrochemical oxidation conditions. Only for the chloro systems **3i–k** were the acylated quinone imine ketals noticeably unstable on standing. Possibly some intramolecular cyclization of the amide to the chloroethyl side chain is occurring with these compounds, and the hydrogen chloride generated catalyzes the decomposition of these acylated quinone imine ketals. Simple acylated quinone imine ketals appear to be more thermally stable than quinone monoketals[14] since both **3a** and **3b** were purified in preparative runs by vacuum distillation and samples of crystalline **3a** have been stored for greater than a month at room temperature with no appreciable decomposition. However, samples of acylated quinone imine ketals containing minor impurities should be stored at 0 °C in ammonia-washed containers to prevent acid-catalyzed decomposition.

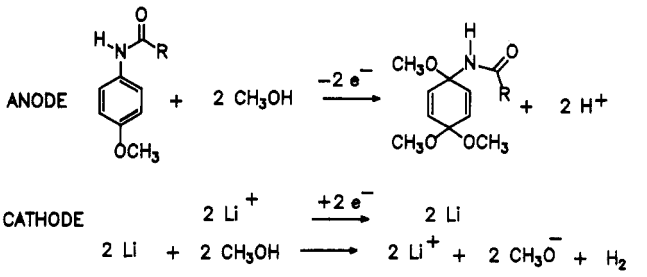
These single cell, constant current oxidation conditions should be applicable for the conversion of other anilides to acylated quinone imine ketals provided the compounds do not have oxidizable or reducible substituents. One example of a *tert*-butyldimethylsilyl-protected system, **4**,



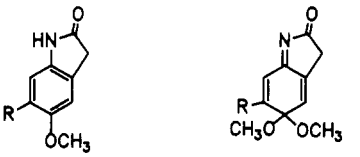
4 5

was also studied; in this case, the acylated quinone imine mixed ketal, **5**, was formed in 50% yield.[15] The only *p*-methoxyanilide derivatives that failed to give isolable acylated quinone imine ketals under our standard conditions were **6a**[16] and **6b**.[17] Instead, complex mixtures were

Scheme II. Anodic and Cathodic Reactions for Anilide Oxidation in Methanol



obtained from the oxidation of these compounds. It was not established whether the acylated quinone imine ketals, i.e. **7**, were formed and decomposed under the reaction conditions or other electrochemical processes dominated the chemistry.



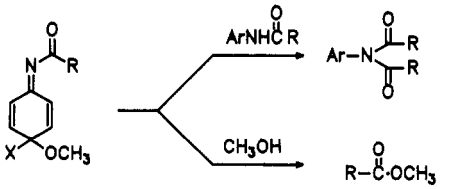
6a R = H
6b R = OCH_3

7

Discussion

The products isolated from electrooxidation of amides derived from *p*-alkoxyanilines are markedly dependent upon the reaction conditions and isolation procedures. The results presented here demonstrate that the anodic oxidation of these compounds at platinum, using lithium perchlorate as supporting electrolyte, gives primarily the 1,4-addition compounds **2**, which slowly eliminate methanol to give the acylated quinone imine ketals **3**. The overall electrochemical reaction should not result in a decrease in the pH of the solution (Scheme II). However, in practice the reaction mixture from anodic oxidations in methanol using lithium perchlorate as supporting electrolyte (no base present) becomes slightly acidic. The formation of a slightly acidic solution during the oxidation together with the presence of adventitious water could account for some of the products previously reported from reactions performed under similar conditions.

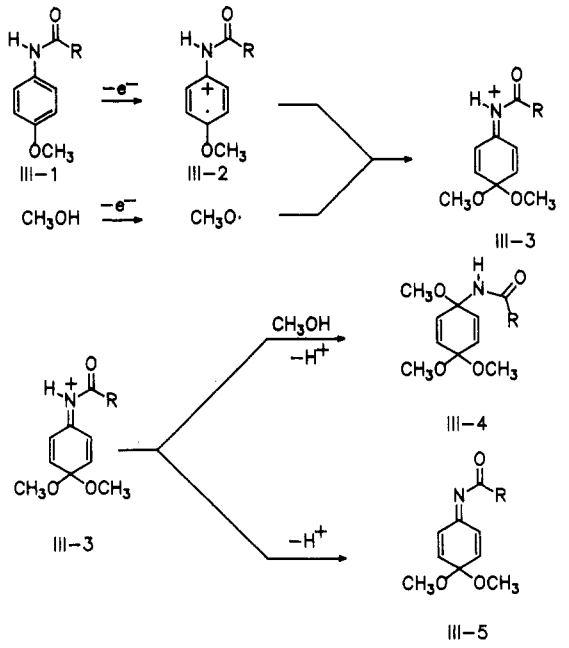
The isolation of methyl benzoate from anodic oxidation of the *p*-methoxybenzanilide in methanol (Scheme I) reasonably arises from deacylation of acylated quinone imine ketal **8a**. Furthermore, anodic oxidations in acetonitrile could be leading to 1,4-addition products such as **8b**, which could serve as acylating agents for unreacted amide or undergo hydrolysis to furnish benzoquinone and benzamide (Scheme I).[18]



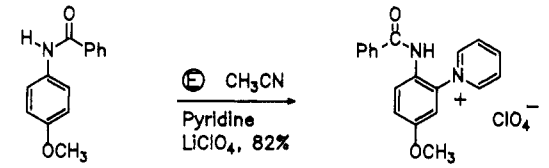
8a X = OCH_3
8b X = $^+N{\equiv}CCH_3$

(14) Capparelli, M. P.; Swenton, J. S. *J. Org. Chem.* **1987**, *52*, 5360.
(15) We thank Alan Stern for allowing inclusion of this result.
(16) Beckett, A. H.; Daisley, R. W.; Walker, J. *Tetrahedron* **1968**, *24*, 6093.
(17) Kametani, T.; Nemoto, H. *Chem. Pharm. Bull.* **1971**, *19*, 1325.
(18) Anodic amidation of certain aromatic compounds involves addition of acetonitrile to the oxidized aromatic compound followed by hydrolysis. For leading references, see: Yoshida, K. *Electrooxidation in Organic Chemistry*; John Wiley & Sons: New York, 1985; pp 233–236.

Scheme III. EEC_rC_p Mechanism Applied to Anilide Oxidation



Anodic oxidation of anilide derivatives in the presence of sodium bicarbonate has not been previously reported. However, anodic oxidation of anilides in pyridine does yield pyridinium compounds such as **10**.[5] In our studies,



analogous pyridinium compounds were not observed as products when the more hindered 2,6-lutidine was employed as a base with methanol as solvent. The favored reaction sequence[19,20] for the anodic oxidation of 1,4-dimethoxybenzene to benzoquinone bis(dimethyl ketal) is the EEC_rC_p mechanism.[20] For this brief discussion, the *p*-methoxyanilide to acylated quinone imine ketal conversion is conveniently viewed in the same mechanistic framework (Scheme III), although further work is required to fully support this viewpoint.

The EEC_rC_p mechanism involves two electrochemical steps (EE) forming an aromatic radical cation, III-2, and a methoxy radical at the platinum anode. Reaction of the radical cation with the methoxy radical (C_r, the radical combination step) at the electrode surface forms III-3 (Scheme III). The preference for addition of methoxy radical at C-4 relative to C-2 may be related to the thermodynamic benefit of having two oxygen atoms bonded to the same carbon.[21] This step is followed by either proton removal from III-3 to give III-5 or addition of methanol to III-3 to afford III-4 (C_p, the polar step). Since the 1,4-addition product does not undergo facile elimination with sodium bicarbonate in methanol, it cannot be responsible for the major amounts of acylated quinone imine ketals (III-4) formed in anodic oxidations having sodium bicarbonate present. The dependence of the ratio of 1,4-addition product (III-4) to the acylated quinone imine ketal (III-5) on current density suggests that there may be yet another mechanism for the formation of the 1,4-addition product, perhaps involving direct addition of methanol to the oxidized aromatic substrate.

While further research is needed to fully define the mechanism of this electrochemical oxidation, the reaction does afford a simple, reasonably general, preparative route to acylated quinone imine ketals. These compounds serve as interesting intermediates for the preparation of substituted anilide derivatives and have potential for the facile construction of a number of alkaloid ring systems.[22] The chemistry of acylated quinone imine ketals will be described in future papers.

Experimental Section

General. Melting points were taken in capillaries on a Thomas-Hoover Unimelt apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer Model 283B spectrometer. ^1H and ^{13}C nuclear magnetic resonance spectra (NMR) were recorded on an IBM NR 80 Model spectrometer. All NMR spectra were recorded in $CDCl_3$ (stored over anhydrous potassium carbonate) and are reported in parts per million (ppm) relative to TMS ($\delta = 0.0$) or $CHCl_3$ ($\delta = 7.26$) unless otherwise noted. Mass spectral and exact mass measurements were obtained by Richard Weisenberger on a Kratos MS-30 spectrometer. Neutral alumina and silica gel (230–400 mesh) were obtained from E. Merck Co. Throughout the experimental, the following abbreviations are used: petroleum ether, bp 35–60 °C (PE), tetrahydrofuran (THF), acetic acid (AcOH). The more standard preparations of anilides are detailed in the supplementary material section. Unless noted otherwise all preparative anodic oxidations were performed in a single-cell apparatus in reagent grade methanol using a circular platinum gauze anode (33 mm diameter × 28 mm high) and platinum sheet cathode (8 × 8 mm). Standard workup refers to extraction of the product with Et_2O or CH_2Cl_2, washing with brine solution (Et_2O extractions only), drying over sodium sulfate or Drierite, concentration in vacuo, and drying at <1.0 Torr until constant weight was recorded.

Ethyl 2-Nitro-4,5-dimethoxyphenylacetate. To 3,4-dimethoxyphenylacetic acid (13.12 g, 66.9 mmol) was added thionyl chloride (20 mL). The resulting dark solution was allowed to stir at room temperature for 5 h, and excess thionyl chloride was removed in vacuo. To the dark residue was added EtOH (35 mL), resulting in an exothermic reaction. After bubbling ceased, the mixture was heated on a steam bath for 1 h. The majority of the ethanol was removed in vacuo and the residue was taken up in CH_2Cl_2 (150 mL). Workup gave a dark residue, which was passed through a plug of silica gel (CH_2Cl_2 as eluant). This crude material was dissolved in AcOH (80 mL), the solution was cooled to 0 °C, and concentrated HNO_3 (10 mL) was added in portions over 30 min. The solution was allowed to stir at 0 °C for 1 h. Crushed ice was added, and the resulting solid was filtered and recrystallized from $EtOAc/Et_2O$ to give 10.2 g (58%) of the title ester: mp 110–112 °C; mass spectrum, exact mass calcd for $C_{12}H_{15}NO_6$ *m/e* 269.0889, obsd *m/e* 269.0889.

Ethyl 2-Benzamido-4,5-dimethoxyphenylacetate (1f). A mixture of ethyl 2-nitro-4,5-dimethoxyphenylacetate (3.19 g, 11.9 mmol) and 5% Pd/C (220 mg) in dry THF (100 mL) was hydrogenated at 70 psi overnight. After 10 h, the mixture was filtered through Celite. To the light yellow filtrate was added NEt_3 (6 mL), followed by benzoyl chloride (1.5 mL), resulting in the precipitation of a solid. The mixture was allowed to stir for 4 h, water (ca. 15 mL) was added, and THF was removed in vacuo. Water (ca. 200 mL) was added, and the resulting white precipitate was collected by filtration. Recrystallization from CH_3OH gave **1f** (2.6 g, 64%) as a white solid: mp 127.5–129.5 °C; mass spectrum, exact mass calcd for $C_{19}H_{21}NO_5$ *m/e* 343.1420, obsd *m/e* 343.1427.

(19) Nilsson, A.; Palmquist, U.; Pettersson, T.; Ronlan, A. *J. Chem. Soc., Perkin Trans. 1* **1978**, 708.
(20) Dolson, M.; Swenton, J. S. *J. Am. Chem. Soc.* **1981**, *103*, 2361.
(21) (a) Hine, J. *Structural Effects on Equilibria in Organic Chemistry*; John Wiley: New York, 1975; p 9. (b) Cox, J. D.; Pilcher, G. *Thermochemistry of Organic and Organometallic Compounds*; Academic Press: New York, 1970; pp 593–595.
(22) Chou, C.-T.; Swenton, J. S. *J. Am. Chem. Soc.* **1987**, *109*, 6898.

Ethyl 2-Acetamido-5-methoxyphenylacetate (1g). To a solution of ethyl 2-nitro-5-methoxyphenylacetate[23] (1.1 g, 4.6 mmol) in AcOH (20 mL) were added 5% Pd/C (200 mg) followed by addition of Ac_2O (4.5 mL, 47.7 mmol). The mixture was hydrogenated at an initial pressure of 68 psi for 5 h. No pressure drop was noticed; therefore, Raney Ni (200 mg) was added, and hydrogenation was continued for another 10 h. The solution was filtered, and the filtrate was dissolved in water (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were dried over Na_2SO_4 and concentrated to give a pink solid (0.95 g), which was recrystallized from PE/CH_2Cl_2 to give **1g** (0.89 g, 77%) as a colorless solid: mp 98–100 °C; mass spectrum, exact mass calcd for $C_{13}H_{17}NO_4$ *m/e* 251.1157, obsd *m/e* 251.1163.

Ethyl 2-Benzamido-5-methoxyphenylacetate (1h). To ethyl 2-nitro-5-methoxyphenylacetate[23] (1.88 g, 7.9 mmol) and benzoic anhydride (3.81 g, 16.9 mmol) in a hydrogenation bottle were added EtOAc (30 mL) followed by Pd/C (0.5 g). The mixture was hydrogenated at an initial pressure of 79 psi. The solution was filtered through a pad of Celite to give a very light yellow solution, which was washed with saturated Na_2CO_3 solution. Removal of solvent gave a light brown oil, which gradually solidified on standing. Recrystallization from EtOH gave a white solid (1.24 g). The filtrate was concentrated to give more solid, which was recrystallized from EtOAc/Et_2O to give a second crop as a white solid (0.54 g, combined yield 1.78 g, 72%): mp 130–131.5 °C.

2-Nitro-4,5-dimethoxyphenethyl Alcohol. To a −78 °C solution of 2-nitro-4,5-dimethoxyphenylacetic acid[24] (45.02 g, 0.19 mol) in dry THF (500 mL) was added 1.0 M BH_3·THF (215 mL, 0.22 mmol). Comparable results were obtained when similar reductions were performed at 0 °C. The dry ice bath was removed, and the solution was allowed to stir at room temperature for 24 h. To the now homogeneous solution were slowly added H_2O (10 mL) and 10% KOH (10 mL). Workup gave a solid, which was recrystallized from CH_2Cl_2 to give 2-nitro-4,5-dimethoxyphenethyl alcohol (39.2 g, 92%) as a yellow solid: mp 104–106 °C; mass spectrum, exact mass calcd for $C_{10}H_{13}NO_5$ *m/e* 227.0793, obsd *m/e* 227.0794.

2-Nitro-4,5-dimethoxyphenethyl Chloride. A solution of 2-nitro-4,5-dimethoxyphenethyl alcohol (18.8 g, 82.8 mmol), triphenylphosphine (32 g, 122 mmol), carbon tetrachloride (100 mL), and CH_2Cl_2 (50 mL) was heated at reflux for 4 h. After cooling, 30% H_2O_2 (6 mL) was added to the dark solution. The resulting yellow solution was washed with 10% $NaHSO_3$ (100 mL). After drying over Na_2SO_4, concentration gave a yellow solid. Most of the triphenylphosphine oxide was removed by recrystallization, and the residue was passed through a silica gel column to give 2-nitro-4,5-dimethoxyphenethyl chloride (19.3 g, 95%) as a bright yellow solid: mp 105–106 °C; mass spectrum, exact mass calcd for $C_{10}H_{12}ClNO_4$ *m/e* 247.0426, obsd *m/e* 247.0416.

***N*-Benzoyl-2-(2-chloroethyl)-4,5-dimethoxyaniline (1i).** A mixture of 2-nitro-4,5-dimethoxyphenethyl chloride (3.92 g, 16.0 mmol) and 5% Pd/C (0.4 g) in dry THF (100 mL) was hydrogenated for 4 h with an initial pressure of about 60 psi. The mixture was filtered through Celite, and to the filtrate were added NEt_3 (5 mL) followed by benzoyl chloride (3.5 mL). After stirring for 2 h, the THF was removed in vacuo. The residue was dissolved in CH_2Cl_2 (100 mL) and was washed with water (100 mL). Workup gave a brown solid, which was filtered through a plug of silica gel to give **1i** (3.93 g, 77%) as a colorless solid: mp 148–150 °C; mass spectrum, exact mass calcd for $C_{17}H_{18}ClNO_3$ *m/e* 321.0946, obsd *m/e* 321.0933.

2-(2-Chloroethyl)-4,5-dimethoxyphenyl Isocyanate. A mixture of 2-nitro-4,5-dimethoxyphenethyl chloride (7.47 g, 30.4 mmol) and 5% Pt/C (0.94 g) in EtOAc (130 mL) was hydrogenated for 4 h at an initial pressure of 60 psi (final pressure 53 psi). The reaction mixture was filtered through a pad of Celite, and to the filtrate was added a solution of phosgene (25 g) in EtOAc (70 mL). The resulting dark solution was heated at reflux for 2 h. After distillation of the EtOAc, the residue was vacuum distilled to give 2-(2-chloroethyl)-4,5-dimethoxyphenyl isocyanate (5.13 g, 70%) as a colorless oil, which solidified on standing: bp 175–189 °C/1 mm; mp 70–72.5 °C; mass spectrum, exact mass calcd for $C_{11}H_{12}ClNO_3$ *m/e* 243.0476, obsd *m/e* 243.0477.

***N*-(Methoxycarbonyl)-2-(2-chloroethyl)-4,5-dimethoxyaniline (1j).** A solution of 2-(2-chloroethyl)-4,5-dimethoxyphenyl isocyanate (2.5 g, 10.4 mmol) in dry CH_3OH (60 mL) was heated at reflux for 1 h, after which time the IR showed no isocyanate band. The CH_3OH was distilled off, and the residue was dissolved in Et_2O/CH_2Cl (1:2) and was passed through a plug of silica gel (0.8 in. × 5 in.) to give **1j** (2.41 g, 85%) as a white solid: mp 101–102.5 °C; mass spectrum, exact mass calcd for $C_{12}H_{16}ClNO_4$ *m/e* 275.0739, obsd *m/e* 275.0756.

***N*-(*tert*-Butoxycarbonyl)-2-(2-chloroethyl)-4,5-dimethoxyaniline (1k).** A mixture of 2-(2-chloroethyl)-4,5-dimethoxyphenyl isocyanate (4.70 g, 19.5 mmol) in dry *t*-BuOH (150 mL) was heated at reflux for 3 h. After cooling, the solution was filtered, the filtrate was concentrated (ca. 50 mL), and water was added. The resulting solid was collected by filtration to give **1k** (5.43 g, 89%) as white needles: mp 88–90 °C; mass spectrum, exact mass calcd for $C_{15}H_{22}ClNO_4$ *m/e* 317.1208, obsd *m/e* 317.1229.

3,4-Dimethoxyphenethyl Fluoride. To a 0 °C solution of 3,4-dimethoxyphenethyl alcohol (5.62 g, 30.9 mmol) in CH_2Cl_2 (30 mL) was added a solution of (diethylamino)sulfur trifluoride (5.0 mL, 31.1 mmol) in dry CH_2Cl_2 (20 mL). The resulting orange solution was allowed to stir at room temperature for 5 h. Concentration gave a residue that was dissolved in CH_2Cl_2 (100 mL) and was washed with saturated Na_2CO_3 and water. After drying over Na_2SO_4, concentration gave an orange oil, which was filtered through a silica gel column (0.8 in. × 6 in., CH_2Cl_2 as eluant). The filtrate was collected and concentrated to give 3,4-dimethoxyphenethyl fluoride (3.98 g, 70%) as a yellow oil. Part of this was crystallized from Et_2O/PE to give a white solid: mp 34–35 °C; mass spectrum, exact mass calcd for $C_{10}H_{13}FO_2$ *m/e* 184.0990, *m/e* obsd 184.0894.

2-(2-Fluoroethyl)-4,5-dimethoxynitrobenzene. To 3,4-dimethoxyphenethyl fluoride (1.04 g, 5.7 mmol) in AcOH (6 mL) in an ice bath was added concentrated HNO_3 (1 mL). After stirring for 15 min, water (40 mL) was added. The yellow precipitate was collected by filtration to give 2-(2-fluoroethyl)-4,5-dimethoxynitrobenzene (1.07 g, 83%) as a yellow solid: mp 66.5–67.5 °C; ^{19}F NMR ($CDCl_3$) −216.13 (tt, J = 47.2, 25.6 Hz); mass spectrum, exact mass calcd for $C_{10}H_{12}FNO_4$ *m/e* 229.0750, obsd *m/e* 229.0762.

2-(2-Fluoroethyl)-4,5-dimethoxyphenyl Isocyanate. To a solution of 2-(2-fluoroethyl)-4,5-dimethoxyphenylnitrobenzene (7.1 g, 31 mmol) in EtOAc (150 mL) was added 5% Pd/C (1 g). This was hydrogenated at an initial pressure of 53 psi for 4.5 h (final pressure 46 psi). This solution was filtered, and the filtrate was added to a solution of phosgene (40 g) in EtOAc (150 mL). After heating at reflux for 3.5 h, EtOAc was distilled off. The residue was vacuum distilled to give the isocyanate (5.3 g, 76%) as a light yellow solid: bp 142–145 °C/0.4 Torr; mp 95–97 °C; mass spectrum, exact mass calcd for $C_{11}H_{12}FNO_3$ *m/e* 225.0801, *m/e* obsd 225.0809.

***N*-(*tert*-Butoxycarbonyl)-2-(2-fluoroethyl)-4,5-dimethoxyaniline (1l).** To 2-(2-fluoroethyl)-4,5-dimethoxyphenyl isocyanate (2.97 g, 13.2 mmol) was added dry *t*-BuOH (80 mL). The heterogeneous mixture was heated to reflux for 4 h, during which time the solid dissolved. The solid was filtered off, and the filtrate was concentrated in vacuo to give a thick oil, which was recrystallized from EtOAc/PE to give **1l** (2.11 g, first crop, and 0.77 g, second crop, 73% overall) as a white solid: mp 77–79 °C; mass spectrum, exact mass calcd for $C_{15}H_{22}FNO_4$ *m/e* 299.1533, obsd *m/e* 299.1571.

***N*-[4-(*tert*-Butyldimethylsiloxy)phenyl]benzamide.** To a solution of THF (50 mL), imidazole (2.0 g, 29 mmol), and *p*-aminophenol (2.0 g, 18.3 mmol) was added *tert*-butyldimethylsilyl chloride (3.6 g, 24 mmol) with rapid stirring. A heavy white precipitate formed immediately. After 0.5 h, the mixture was poured into water (150 mL) and extracted with Et_2O (2 × 50 mL). The Et_2O portions were washed with water (2 × 100 mL) and brine (50 mL), dried through a cone of $CaSO_4$, and concentrated to afford a brown oil (4.45 g). A small amount, purified by preparative GC, showed the following characteristics: IR (neat) 2960 (m), 2930 (m), 1510 (s), 1245 (s), 920 (s), 910 (s), 835 (s) cm^{-1}; ^1H NMR δ 6.61 (s, 2 H), 6.58 (s, 2 H), 3.12 (br, 2 H), 0.95 (s, 9

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(24) McDonald, E.; Wylie, R. D. *Tetrahedron* **1979**, *35*, 1415.

H), 0.13 (s, 6 H); mass spectrum, exact mass calcd for $C_{12}H_{21}NOSi$ m/e 223.1392, obsd m/e 223.1379.

To the oil were added THF (70 mL), triethylamine (2.42 g, 24 mmol), and benzoyl chloride (2.81 g, 20 mmol). The addition of benzoyl chloride caused an exothermic reaction and precipitated a white solid. After 1 h, the mixture was poured into water (250 mL) and extracted with Et_2O (100 mL). The Et_2O solution was washed with water (2 × 50 mL) and brine (50 mL), dried over $CaSO_4$, and concentrated in vacuo. Upon removal of all solvent, the remaining light brown oil solidified. The crude amide (7.09 g) was dissolved in boiling Et_2O (20 mL), PE (20 mL) was added, and the mixture was allowed to crystallize, affording a white solid (4.67 g), mp 107–110 °C, sufficiently pure for further use. A second crop of the amide was obtained from the mother liquor (0.45 g) to afford a total yield of 5.12 g (86% for two steps). A small portion of the amide was recrystallized twice more, affording white fibers, mp 112–113 °C, used for analysis: IR (KBr) 1645 (s), 1535 (m), 1512 (m), 1261 (m), 1253 (m), 920 (m), 840 (m) cm^{-1}; ^1H NMR δ 7.89–7.77 (m, 3 H), 7.50–7.44 (m, 2 H), 7.47 (d, J_{AB} = 8.8 Hz, 2 H), 6.82 (d, J_{AB} = 8.8 Hz, 2 H), 0.97 (s, 9 H), 0.18 (s, 6 H); mass spectrum, exact mass calcd for $C_{19}H_{25}NO_2Si$ m/e 327.1654, obsd m/e 327.1658.

Anodic Oxidation of 1a To Form the 1,4-Addition Product 2a. A magnetically stirred solution of **1a** (300 mg, 1.32 mmol) in a 2% $LiClO_4/CH_3OH$ solution (120 mL) was electrolyzed (0.1 A) at 0 °C for 60 min (71% current efficiency). The resulting solution was concentrated in vacuo at ca. 10 °C, and the residue was extracted with CH_2Cl_2 (3 × 40 mL)/H_2O (40 mL). The organic phase was worked up to give a white solid. Recrystallization (PE/CH_2Cl_2) of this material gave **2a** (0.30 g, 80%) in two crops. The material decomposed on standing to give primarily **3a**. The freshly prepared material showed the following: mp 113–114 °C; IR (KBr) 3290, 1650, 1530, 1110, 1080, 1045, 960 cm^{-1}; ^1H NMR δ 7.8–7.65 (m, 2 H), 7.5–7.25 (m, 3 H), 6.55–6.8 (br s, 1 H), 6.24 (s, 4 H), 3.37 (s, 3 H), 3.34 (s, 3 H), 3.22 (s, 3 H); mass spectrum, only M – CH_3 (15) peak present.

Anodic Oxidation of 1b To Form the 1,4-Addition Product 2b. A magnetically stirred solution of **1b** (1.5 g, 9.1 mmol) in 2% $LiClO_4/CH_3OH$ (150 mL) at 0 °C was electrolyzed (3.9 V, 0.15 A) for 4.9 h (67% current efficiency). The resulting solution was concentrated in vacuo at ca. 10 °C, extracted with CH_2Cl_2 (3 × 40 mL)/H_2O (40 mL), and washed with brine (40 mL). Drying (Na_2SO_4) and concentration in vacuo gave **2b** (1.84 g, 89%) as a very light yellow oil, the crude NMR spectrum of which showed the material to be >95% pure. Further attempts at purification resulted in less pure material: IR (neat) 3550–3300 (br), 1665 (br), 1535 (br), 1460, 1405, 1370, 1270, 1100, 1050, 1035 (sh), 955 cm^{-1}; ^1H NMR δ 6.14 (s, 4 H), 6.1–5.8 (br s, 1 H), 3.29 (s, 3 H), 3.25 (s, 3 H), 3.12 (s, 3 H), 1.9 (s, 3 H); ^{13}C NMR δ 169.6, 130.4 (2 C), 129.3 (2 C), 92.1, 78.9, 49.9, 49.2 (2 C), 23.1; mass spectrum, exact mass calcd for $C_{11}H_{17}NO_4$ m/e 227.1012, obsd m/e 227.1076.

Preparation of 3a from 2a by Reaction with Sodium Hydride. To a magnetically stirred solution of **2a** (187 mg, 0.65 mmol) in THF (20 mL) at room temperature under nitrogen was added NaH (31.2 mg, 60% oil dispersion, 1.2 equiv). After stirring for 2 h, the reaction was quenched by the addition of $NaHCO_3$. Workup gave a light brown oil, which was purified by flash column chromatography (CH_2Cl_2 as eluant) to give **3a** (140 mg, 86%) as a light yellow oil, showing identical spectroscopic properties to those reported below.

General Comments Concerning Anodic Oxidation of Anilides To Form Acylated Quinone Imine Ketals. Three procedures are described in detail. Two procedures are for the preparative anodic oxidation of the benzoyl, **1a**, and acetyl, **1b**, derivatives of *p*-methoxyaniline using sodium bicarbonate as base. These were performed under optimized conditions. The third procedure is for the anodic oxidation conducted by using 2,6-lutidine as base. For the other anodic oxidations of 1 g of anilide or less, the product was isolated by flash column chromatography on silica gel. For other oxidations, the data are given as follows: g (mol); CH_3OH (mL); base (g or mL); current (A); isolation method; substrate (g, mol); (% yield); and spectroscopic data.

***N*-Benzoyl-*p*-benzoquinone Imine Dimethyl Ketal (3a).** A sample (3.00 g, 13.2 mmol) of *N*-(4-methoxyphenyl)benzamide (**1a**) was dissolved in a 2% solution of $LiClO_4/CH_3OH$ (300 mL), the mixture was cooled to 0 °C, and freshly ground $NaHCO_3$ (6.0 g) was added. This rapidly stirred mixture was anodically oxidized (3.5 cm diameter × 5 cm Pt screen anode/3 cm Pt wire cathode) at a constant current (0.3 A) for 140 min. The oxidation was stopped, additional benzamide **1a** (3.0 g) was added and allowed to dissolve (15 min), and the oxidation was resumed. After an additional electrolysis time of 280 min, **1a** (3.0 g) and $NaHCO_3$ (4.0 g) were added. After 420 min, **1a** (1.0 g, 10.0 g total) and $NaHCO_3$ (4.0 g) were added. After a total of 9 h of electrolysis (87% current efficiency) the starting benzamide could no longer be detected by TLC. The electrolysis mixture was poured into water (1500 mL) and extracted with $CHCl_3$ (5 × 100 mL). The combined extracts were washed with water (100 mL) and brine (100 mL) and filtered through Na_2SO_4, and the solvent was removed in vacuo to yield a brown oil (11.22 g, 99%), which solidified under vacuum and was predominantly (by ^1H NMR spectroscopy) the desired **3a**. Light petroleum ether (100 mL) and Et_2O (35 mL) were added to the crude oil, leaving a dark brown oil at the bottom of the flask. After ca. 10 min, petroleum ether (50 mL) was added, and the mixture was allowed to settle for 30 min. The light yellow upper layer was decanted from the red oil (2.25 g), and this solution was clarified by adding Et_2O (4 mL). Crystallization at −20 °C yielded **3a** (6.074 g, 54%) as tan crystals, mp 48–50 °C. The combined residues were distilled under vacuum with a short path distillation head to give a light brown oil: bp 148–158 °C (2.7 × 10^{-3} Torr), which was crystallized from Et_2O/light PE at −20 °C to yield light brown crystals (2.807 g, total yield 79%), mp 44–47 °C, which exhibited only a trace of impurity by ^1H NMR spectroscopy and would be of sufficient purity for most subsequent chemistry. The product can also be isolated by flash chromatography on silica gel (20:1 CH_2Cl_2/acetone as eluant). The analytically pure material had the following: mp 51–53 °C; IR (film) 1680, 1665, 1605, 1250, 1110, 1060, 1040, 1005, 710 cm^{-1}; ^1H NMR δ 8.0–7.8 (m, 2 H), 7.6–7.26 (m, 3 H), 6.53 (AB q, J_{AB} = 11 Hz, 2 H), 6.44 (AB q, J_{AB} = 11 Hz, 2 H), 3.32 (s, 6 H); ^{13}C NMR δ 179.0, 154.6, 139.0 (2 C), 132.8, 132.2, 128.6 (2 C), 128.0 (2 C), 125.6 (2 C), 92.1, 49.1 (2 C). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.87. Found: C, 70.09; H, 5.96.

***N*-Acetyl-*p*-benzoquinone Imine Dimethyl Ketal (3b).** The *N*-(4-methoxyphenyl)acetamide **1b** (2 g, 12.1 mmol) was dissolved in a solution of 5% water/2% $LiClO_4/CH_3OH$ (250 mL) and cooled to 0 °C, and freshly ground $NaHCO_3$ (10 g) was added. This rapidly stirred mixture was anodically oxidized (3.5 cm diameter × 5 cm Pt screen anode/3 cm Pt wire cathode) at a constant current (0.25 A) for 1 h after which the electrodes were cleaned with water (this cleaning was repeated every hour). After 2 h the electrolysis was stopped, **1b** (2.0 g) was added, the mixture was allowed to mix for 5 min, and the electrolysis was resumed. After 4 h of electrolysis, additional **1b** (1.0 g, 5.0 g total) amide was added. After 6 h of total electrolysis time no starting material could be detected by TLC. This mixture was added to water (1.0 L) and extracted with $CHCl_3$ (7 × 100 mL). The organic phase was washed with brine (50 mL) and dried over Na_2SO_4, and the solvent was removed in vacuo to yield a brown oil (5.57 g, 94%) as an 87:13 mixture of the *N*-acetyl-*p*-benzoquinone imine dimethyl ketal (**3b**) product and the 1,4 methanol addition product **2b**. Isolation of pure **3b** can also be conducted by chromatography on silica gel (20:1 $CH_2Cl_2/(CH_3)_2CO$ as eluant). For this preparative run distillation on a Kugelrohr apparatus at 80–90 °C (1–2 × 10^{-3} Torr) yielded **3b** (4.34 g, 74%, >98% pure by ^1H NMR spectroscopy), which showed the following: IR (film) 1695, 1670, 1605, 1220, 1110, 1080, 1060, 1035, 955 cm^{-1}; ^1H NMR δ 6.54 (AB q, J_{AB} = 11 Hz, 2 H), 6.35 (AB q, J_{AB} = 11 Hz, 2 H), 3.33 (s, 6 H), 2.23 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 185.3, 151.1, 138.8 (2 C), 125.7 (2 C), 92.3, 49.4 (2 C), 24.8; mass spectrum, exact mass calcd for $C_{10}H_{13}NO_3$ m/e 195.0895, obsd m/e 195.0907.

***N*-Acetyl-*p*-benzoquinone Imine Dimethyl Ketal (3b) Employing 2,6-Lutidine as Base.** A solution of **1b** (282.3 mg, 1.71 mmol), $LiClO_4$ (1.9 g), and 2,6-lutidine (0.2 mL, 1.71 mmol) in CH_3OH (140 mL) was anodically oxidized (0.2 A). After 35 min, TLC showed no starting material. The CH_3OH was removed, and the residue was slurried with water (180 mL) and extracted with CH_2Cl_2 (3 × 40 mL). The combined extracts were washed with brine (40 mL). After drying over Na_2SO_4, the solvent was removed in vacuo to give a light brown oil. The ^1H NMR spectrum showed it to be a mixture of **3b** and lutidine. The lutidine was removed in vacuo (<0.1 Torr) overnight to give **3b** (301 mg, 90%),

which showed spectroscopic data identical with those reported above.

***N*-Benzoyl-3-methoxy-*p*-benzoquinone imine dimethyl ketal (3c)**: **1c** (0.58 g, 2.3 mmol); $LiClO_4$ (1.3 g); 2,6-lutidine (0.27 mL) in CH_3OH (140 mL); 0.1 A, 0 °C, 80 min. Chromatography on silica gel gave **3c** (0.60 g, 92%): mp 66–69 °C; IR (KBr) 1665, 1647, 1582, 1242, 1123, 1104, 1057, 968, 743 cm^{-1}; ^1H NMR δ 8.02–7.92 (m, 2 H), 7.60–7.29 (m, 3 H), 6.57 (dd, J_{AB} = 10.2 Hz, J = 1.7 Hz, 1 H), 6.41 (d, J_{AB} = 10.2 Hz, 1 H), 5.70 (d, J = 1.7 Hz, 1 H), 3.76 (s, 3 H), 3.31 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 180.0, 164.9, 157.1, 137.2, 133.1 (2 C), 129.3, 128.9 (2 C), 128.4 (2 C), 98.9, 94.2, 55.7, 51.2 (2 C); mass spectrum, exact mass calcd for $C_{16}H_{17}NO_4$ m/e 287.1157, obsd m/e 287.1129.

***N*-(*tert*-Butoxycarbonyl)-3-methoxy-*p*-benzoquinone imine dimethyl ketal (3d)**: **1d** (0.46 g, 1.8 mmol); $LiClO_4$ (1.5 g); 2,6-lutidine (0.25 mL) in CH_3OH (120 mL); 0.1 A, 0 °C, 2 h. Chromatography on silica gel gave a light yellow oil (0.42 g, 79%): IR (neat) 2985, 2950, 1720, 1670, 1610, 1468, 1377, 1250 (br), 1150 (br), 1110 (br), 988 cm^{-1}; ^1H NMR δ 6.67–6.27 (m, 2 H), 5.74 (d, J = 1.4 Hz, 1 H), 3.80 (s, 3 H), 3.29 (s, 6 H), 1.57 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 164.7, 161.5, 158.9, 137.2, 132.0 (br s), 96.4 (bs), 94.4, 82.0, 55.5, 51.3 (2 C), 27.8 (3 C); mass spectrum, exact mass calcd for $C_{14}H_{21}NO_5$ m/e 283.1420, obsd m/e 283.1438.

***N*-(Methoxycarbonyl)-3-methoxy-*p*-benzoquinone imine dimethyl ketal (3e)**: **1e** (0.52 g, 2.5 mmol); $LiClO_4$ (1.1 g), lutidine (0.3 mL) in CH_3OH (120 mL); 0.1 A, 0 °C, 82 min. Crude product was recrystallized from Et_2O to give **3e** (0.32 g, 54%): mp 91–91.5 °C; IR (KBr) 1735, 1670, 1618, 1599, 1250 (br), 1138, 1090, 1065 cm^{-1}; ^1H NMR δ 6.6–6.3 (m, 2 H), 5.76 (d, J = 1.4 Hz, 1 H), 3.87 (s, 3 H), 3.83 (s, 3 H), 3.29 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 165.3, 162.7, 160.2, 137.6, 131.1 (br), 97.8 (br), 94.1, 55.6, 53.0, 51.0; mass spectrum, exact mass calcd for $C_{11}H_{15}NO_5$ m/e 241.0950, obsd m/e 241.0952.

***N*-Benzoyl-2-(carbethoxymethyl)-5-methoxy-*p*-benzoquinone imine dimethyl ketal (3f)**: **1f** (0.5764 g, 1.7 mmol); $LiClO_4$ (1.5 g); 2,6-lutidine (0.2 mL, 1.7 mmol) in CH_3OH (130 mL); 0.1 A, 0 °C, 1 h. Workup gave a red oil (0.6063 g, 97%): IR (NaCl) 1732, 1654, 1612, 1248, 1212, 1155, 1055 (br) cm^{-1}; ^1H NMR δ 7.95–7.83 (m, 2 H), 7.47–7.38 (m, 3 H), 6.33 (s, 1 H), 5.54 (s, 1 H), 4.13 (q, J = 7.2 Hz, 2 H), 3.64 (s, 3 H), 3.50 (s, 2 H), 3.28 (s, 6 H), 1.20 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 180.4 (s), 170.7 (s), 164.8 (s), 156.5 (s), 136.6 (d), 135.4 (d), 133.1 (d), 133.0 (s), 129.4 (2C, d), 128.4 (2C, d), 97.0 (d), 94.9 (s), 60.8 (t), 55.8 (q), 51.4 (2 C, q), 36.3 (t), 14.0 (q); mass spectrum, exact mass calcd for $C_{20}H_{23}NO_6$ m/e 373.1525, m/e obsd 373.1520.

***N*-Acetyl-2-(carbethoxymethyl)-*p*-benzoquinone imine dimethyl ketal 3g**: **1g** (0.27 g, 1.1 mmol); $LiClO_4$ (1.7 g), 2,6-lutidine (0.12 mL) in CH_3OH (150 mL); 0.22 A, 0 °C, 17 min. Chromatography on flash silica gel (0.4 in. × 9 in. column, 75% PE/Et_2O as eluant) gave an oil (0.22 g, 80%): IR (NaCl) 1740, 1696, 1603, 1210, 1177, 1124, 1075, 1030, 957 cm^{-1}; ^1H NMR δ 6.2–6.3 (m, 3 H), 4.15 (q, J = 7 Hz, 2 H), 3.39 (d, J = 0.8 Hz, 2 H), 3.34 (s, 6 H), 2.20 (s, 3 H), 1.25 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 185.9, 170.4, 151.3, 139.6, 138.1, 133.8, 123.1, 93.6, 60.9, 50.4 (2C), 36.4, 25.5, 14.2; mass spectrum, exact mass calcd for $C_{14}H_{19}NO_5$ m/e 282.1263, obsd m/e 282.1249.

***N*-Benzoyl-2-(carbethoxymethyl)-*p*-benzoquinone imine dimethyl ketal (3h)**: **1h** (0.62 g, 2.0 mmol); 2,6-lutidine (0.250 mL, 2.1 mmol); $LiClO_4$ (1.6 g, 15 mmol); in CH_3OH; 0.08 A, 0 °C, 80 min. Chromatography on silica gel (0.4 in. × 3 in. column, 50% PE/CH_2Cl_2 through 5% EtOAc/CH_2Cl_2 as eluant) gave an oil (0.64 g, 95%): IR (NaCl) 1732, 1674 (sh), 1659, 1628, 1601, 1343, 1174, 1123, 1071 (sh), 1058, 1031 cm^{-1}; ^1H NMR δ 7.95–7.83 (m, 2 H), 7.42–7.54 (m, 3 H), 6.54 (br s, 1 H), 6.41–6.31 (m, 2 H), 4.27 (q, J = 7.2 Hz, 2 H), 3.52 (s, 2 H), 3.35 (s, 6 H), 1.25 (t, J = 7.1 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 179.7, 170.3, 154.5, 139.3, 138.2, 133.5, 133.1 (2 C), 132.4 (2 C), 129.1, 128.2, 123.2, 93.2, 60.5, 49.8 (2 C), 36.2, 13.7; mass spectrum, exact mass calcd for $C_{19}H_{21}NO_5$ m/e 343.1420, obsd m/e 343.1388.

***N*-Benzoyl-2-(2-chloroethyl)-5-methoxy-*p*-benzoquinone imine dimethyl ketal (3i)**: **1i** (0.94 g, 2.9 mmol); $LiClO_4$ (1.5 g); 2,6-lutidine (0.35 mL) in CH_3OH (120 mL); 0.1 A, 0 °C, 100 min. Chromatography on flash silica gel (0.4 in. × 8 in. column) gave an oil (0.93 g, 90%): IR (NaCl) 1655, 1602, 1595, 1252, 1214, 1072, 1060 cm^{-1}; ^1H NMR δ 8.0–7.74 (m, 2 H), 7.62–7.42 (m, 3 H), 6.39 (s, 1 H), 5.57 (s, 1 H), 3.87 (t, J = 6.4 Hz, 2 H), 3.69 (s, 3 H), 3.34 (s, 6 H), 3.02 (t, J = 6.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 180.3, 164.9, 156.5, 136.7, 136.3, 133.1, 132.9, 129.1 (2 C), 128.4 (2 C), 96.7, 94.5, 55.7, 51.3 (2 C), 43.1, 33.7; mass spectrum, exact mass calcd for $C_{18}H_{20}ClNO_4$ m/e 349.1081, obsd m/e 349.1088.

***N*-(Methoxycarbonyl)-2-(2-chloroethyl)-5-methoxy-*p*-benzoquinone imine dimethyl ketal (3j)**: **1j** (0.50 g, 1.8 mmol); $LiClO_4$ (1.2 g); lutidine (0.2 mL) in CH_3OH (140 mL); 0.1 A, 0 °C, 90 min. Chromatography on flash silica gel (0.4 in. × 3 in. column) gave an oil (0.45 g, 80%), which was recrystallized from CH_2Cl_2/PE to give a white solid: mp 75–77.5 °C; IR (KBr) 1722, 1670, 1620, 1600, 1433, 1230 (br), 1178, 1088 cm^{-1}; ^1H NMR δ 6.32 (s, 1 H), 5.64 (s, 1 H), 3.87 (s, 3 H), 3.81 (s, 3 H), 3.76 (t, J = 6.3 Hz, 2 H), 3.30 (s, 6 H), 2.90 (t, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$) δ 164.9, 162.8, 158.8, 136.4, 136.3, 96.1, 94.0, 55.3, 52.7, 50.8 (2 C), 49.4, 42.5, 33.0. This product was unstable, and an exact mass measurement was not attempted.

***N*-(*tert*-Butoxycarbonyl)-2-(2-chloroethyl)-5-methoxy-*p*-benzoquinone imine dimethyl ketal (3k)**: **1k** (1.03 g, 3.25 mmol); $LiClO_4$ (1.4 g); 2,6-lutidine (0.4 mL) in CH_3OH (120 mL); 0.1 A, 0 °C, 130 min. The crude product was recrystallized from CH_2Cl_2/PE to give a solid (0.82 g): mp 98–100 °C dec; IR (KBr) 1712, 1612, 1597, 1255, 1240, 1155, 1088 cm^{-1}; ^1H NMR δ 6.3 (s, 1 H), 5.6 (s, 1 H), 3.8–3.6 (m, 5 H), 3.3 (s, 6 H), 2.8 (t, J = 10 Hz, 2 H), 1.55 (s, 9 H); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 164.4, 162.3, 157.6, 137.2, 126.0, 96.5, 94.7, 82.1, 55.5, 51.4 (2 C) 43.2, 33.6, 28.0 (3 C); mass spectrum, exact mass calcd for $C_{16}H_{24}ClNO_5$ m/e 345.1343, obsd m/e 345.1307.

***N*-(*tert*-Butoxycarbonyl)-2-(2-fluoroethyl)-3-methoxy-*p*-benzoquinone imine dimethyl ketal (3l)**: **1l** (1.13 g, 3.8 mmol); $LiClO_4$ (1.3 g); lutidine (0.43 mL) in CH_3OH (120 mL); 0.2 A, 0 °C, 70 min. Concentration gave a residue that was dissolved in CH_2Cl_2 (100 mL) and the crude product was recrystallized from CH_2Cl_2 to give a solid (1.07 g, 86%): mp 72.5–75 °C; IR (KBr) 1710, 1618, 1599, 1369, 1255, 1240, 1224, 1187, 1150, 1093, 1069, 1004 cm^{-1}; ^1H NMR δ 6.28 (s, 1 H), 5.60 (s, 1 H), 4.58 (dt, J = 47.2, 5.7 Hz, 2 H), 3.75 (s, 3 H), 3.26 (s, 6 H), 2.82 (dt, J = 26.4, 5.7 Hz, 2 H), 1.55 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 164.3, 162.2, 157.6, 136.8 (d, J = 3.1 Hz), 135.3, 96.2, 94.5, 81.8, 81.5 (d, J = 167.3 Hz), 55.3, 51.1 (2 C), 31.1 (d, J = 20.5 Hz), 27.8; mass spectrum, exact mass calcd for $C_{16}H_{24}FNO_5$ m/e 329.1638, obsd m/e 329.1641.

***N*-Benzoylbenzoquinone Imine Methyl *tert*-Butyldimethylsilyl Ketal (5)**. To a chilled (6 °C) solution of CH_3OH (100 mL) and $LiClO_4$ (1.7 g) in a single-cell electrolysis apparatus equipped with a cylindrical platinum gauze anode and an 8-cm 20 gauge platinum wire cathode was added *p*-(*tert*-butyldimethylsiloxy)benzanilide (1.50 g, 4.59 mmol). A current (0.1 A) was passed through the cell for 2.75 h, completely consuming the silyl ether (89% current efficiency). The methanol solution was poured into water (500 mL) and extracted with Et_2O (4 × 100 mL). The combined Et_2O portions were washed with water (200 mL) and brine (100 mL), dried through a cone of $CaSO_4$, and concentrated to afford the crude acylimine (1.36 g). The crude acylimine was purified by MPLC [Lobar pre-packed column, size B (310-25), LiChroprep Si 60 (40–63 μm, 5% Et_2O/hexane to 20% Et_2O/hexane as eluant], affording a clear oil (0.82 g, 50%) that solidified upon standing at 20 °C. A small amount was recrystallized from hot hexane, mp 65–66 °C: IR (neat) 1678 (m), 1660 (m), 1600 (m), 1250 (s), 1110 (m), 1070 (m), 1055 (s), 1035 (m), 820 (m) cm^{-1}; ^1H NMR δ 7.96–7.84 (m, 2 H), 7.57–7.41 (m, 3 H), 6.44 (d, J_{AB} = 10.4 Hz, 2 H), 6.34 (d, J_{AB} = 10.4 Hz, 2 H), 3.26 (s, 3 H), 0.87 (s, 9 H), 0.11 (s, 6 H); mass spectrum, exact mass calcd for $C_{20}H_{27}NO_3Si$ m/e 357.1761, obsd m/e 357.1791.

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Registry No. **1a**, 7472-54-0; **1b**, 51-66-1; **1c**, 39078-05-2; **1d**, 102421-43-2; **1e**, 106107-52-2; **1f**, 117559-76-9; **1g**, 106501-76-2; **1h**, 117559-77-0; **1i**, 110934-61-7; **1j**, 117559-78-1; **1k**, 110934-60-6; **1l**, 117559-79-2; **2a**, 106501-68-2; **2b**, 106501-75-1; **3a**, 106501-69-3; **3b**, 106501-77-3; **3c**, 117559-80-5; **3d**, 117559-81-6; **3e**, 117559-82-7; **3f**, 117559-83-8; **3g**, 106501-79-5; **3h**, 106501-80-8; **3i**, 110934-59-3; **3j**, 117559-84-9; **3k**, 110905-14-1; **3l**, 117559-85-0; **4**, 117559-86-1; **5**, 117559-87-2; ethyl 2-nitro-4,5-dimethoxyphenylacetate, 5415-

53-2; 3,4-dimethoxyphenylacetic acid, 93-40-3; ethyl 2-nitro-5-methoxyphenylacetate, 117559-88-3; 2-nitro-4,5-dimethoxyphenethyl alcohol, 73357-23-0; 2-nitro-4,5-dimethoxyphenylacetic acid, 73357-18-3; 2-nitro-4,5-dimethoxyphenethyl chloride, 90869-96-8; 2-(2-chloroethyl)-4,5-dimethoxyphenyl isocyanate, 110905-13-0; 3,4-dimethoxyphenethyl fluoride, 117559-89-4; 3,4-dimethoxyphenethyl alcohol, 7417-21-2; 2-(2-fluoroethyl)-4,5-dimethoxynitrobenzene, 117559-90-7; 2-(2-fluoroethyl)-4,5-dimethoxyphenyl isocyanate, 117559-91-8; *p*-aminophenol, 59000-01-0.

Supplementary Material Available: Table of infrared, ^1H NMR, and ^{13}C NMR spectral data for compounds not given in the Experimental Section, preparations of **1c–e**, and the ^1H NMR spectra of **2a**, **2b**, and **3b** (8 pages). Order information is given on any current masthead page.

Stereochemistry in the Michael Addition of Silylcuprate to α,β-Unsaturated Sulfoxide

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Lithium bis(dimethylphenylsilyl)cuprate (**2**), in contrast to dialkylcuprates, reacted with α,β-unsaturated sulfoxides **1** to give Michael products **3** and **4** in good yields. The *E* and *Z* sulfoxides **1** afforded predominantly **3** and **4**, respectively. When the reaction was quenched with deuterium oxide, four α-deuteriated sulfoxides **5–8** were obtained. While the ratio of **5** to **6** was 90:10 from (*E*)-**1** and 70:30 from (*Z*)-**1**, **7** and **8** were formed in equal amounts irrespective of the starting sulfoxides.

α,β-Unsaturated sulfoxides have been utilized in many asymmetric syntheses as Michael acceptors[1] since the pioneering works of Stirling[2] and Ogura.[3] But a problem in this methodology is the difficulty in predicting the stereochemistry of the β-carbon, that is, which diastereomeric face a nucleophile comes from. This problem is complicated particularly in the acyclic sulfoxides because there is no definite information on the conformer to participate in the reaction. The most reliable system studied has been an α-keto α,β-unsaturated sulfoxide reported by Posner,[4] in which metal chelation between the carbonyl and sulfoxide oxygens fixed the conformation and the nucleophile approached from a less crowded face. Recently Hehre[5] reported a theoretical study on the model reaction of methyl vinyl sulfoxide with hydride, suggesting that the nucleophilic attack was anti to the sulfur lone pair and syn to the methyl of the reacting conformer in which S=O was cis and coplanar to the C=C bond. He pointed out simultaneously that this prediction was in accord with the electronic factor but contrary to steric considerations, and not valid in the systems where chelation occurred.

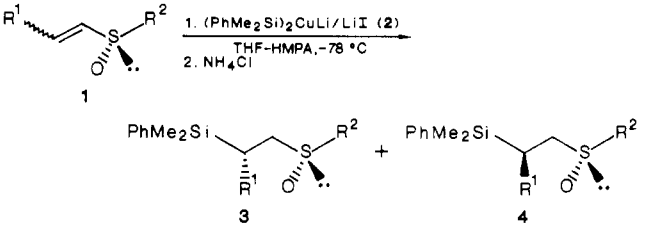
With respect to the stereochemistry of the α-carbon, little has been known in the Michael addition. The only definite example was the α-sulfinylcyclopentenone system,[6] but the direction of electrophilic attack was controlled by the ring. On the other hand, the stereochemistry and reactivity of α-sulfinyl carbanion itself prepared by the proton abstraction from benzylic sulfoxide have been in controversy for a long period, and recently, the original work by Durst was reinvestigated by Ohno.[7] However, the carbanion formed by the Michael addition would be different from that in many respects, particularly because a new chiral center (β-carbon) is adjacent to it.

Insight into this question is disturbed by the limitations of nucleophiles. The sulfoxide having no carbonyl group on the α-position has reacted only with malonic esters[3] and protic substrates such as amines[2] and alcohols.[8] The exceptional example other than this category was the reaction of *p*-chlorophenyl vinyl sulfoxide with dialkylcuprates under special conditions.[9]

In this paper we report a new reaction of α,β-unsaturated sulfoxide with silylcuprate and discuss the stereochemistry of the Michael addition.

Results and Discussion

A reaction of phenyl vinyl sulfoxide (**1a**) with lithium bis(dimethylphenylsilyl)cuprate (**2**)[10] at −78 °C in THF–HMPA[11] followed immediately by quenching with ammonium chloride gave 2-(dimethylphenylsilyl)ethyl phenyl sulfoxide (**3a**) in 70% yield. A longer reaction time caused a decrease of the yield and formation of undefined materials. Similarly, racemic (**1a–d**) and R_s chiral (**1e,f**) α,β-unsaturated sulfoxides reacted with **2** to afford the Michael adducts **3** and **4** in good yields (Table I). The two diastereomers **3** and **4** were easily separated from each other by column chromatography: **4** eluted first.



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