Pyridinium Chlorochromate Releases Quinones from Hydroquinone Silyl Ethers

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The pyridinium chlorochromate oxidation of six bis(trimethylsilyl) and six bis(*tert*-butyldimethylsilyl) ethers of *p*-hydroquinones at room temperature in methylene chloride solution gave the corresponding quinones in 60–90% yield. The bis(trimethylsilyl) ethers were slightly more reactive than the bis(*tert*-butyldimethylsilyl) ethers. High oxidation efficiency was indicated by a 1:1 molar stoichiometry; however, more convenient reaction times were obtained at a 2:1 molar ratio of pyridinium chlorochromate (PCC) to hydroquinone silyl ether. The mechanism is discussed based upon comparisons of relative reaction rates with electrochemical oxidation potentials.

The protection of hydroquinone functions as methyl ethers followed by synthetic elaboration and oxidative demethylation is an important synthetic sequence for the preparation of complex quinones. This series of reactions has proven particularly useful in the preparation of naturally occurring quinones such as ubiquinone[1] and the anticancer anthracyclines[2] as well as man-made quinone products.[3] Oxidative demethylation requires somewhat vigorous conditions and the most widely utilized oxidants have been nitric acid,[4] argentic oxide,[5] and ceric ammonium nitrate.[6] The high acidity required precludes their use with substrates containing acid labile groups.

The present report concerns chromium(VI) oxidations of the silyl ethers of hydroquinones. The general utility of mildly acidic chromium(VI) reagents, e.g., pyridinium chlorochromate, in nonaqueous media is well recognized, particularly in the case of alcohol oxidations;[7] however, there have been no reports of their use in the oxidation of siloxy functions.

A previous paper[8] described the preparative anodic oxidation of hydroquinone silyl ethers as a high-yield method for the synthesis of quinones from nonphenolic precursors. In the belief that a chemical oxidation would be a useful alternative to this electrochemical approach, several oxidants were screened. We report here on the most successful of these oxidants, pyridinium chlorochromate (PCC). Our results demonstrate the utility of silylation–oxidation as a method for the protection and deprotection of hydroquinone functions. This method may be especially useful in the synthesis of complex quinones because (a) hindered silyl ethers containing the bis(*tert*-butyldimethyl) group are stable to many reaction conditions,[9] (b) the deprotection step is not only selective but high yielding, and (c) the reaction conditions are mild.

Table I. Preparation of Hydroquinone Silyl Ethers

product	R_1	R_2	R_3	% yield[c]	mp (bp/torr), °C
1	TMS[a]	OCH_3	H	94	(117/0.25)
2	TMS	CH_3	CH_3	88	43.5-44.5
3	TMS	CH_3	H	84	(158/0.2)
4	TMS	*t*-Bu	*t*-Bu	97	130-130.5
5	TMS	H	H	91	41.5-43.5
6	TMS	Cl	H	51	(161/15)
7	*t*-BDMS[b]	OCH_3	H	81	29-31
8	*t*-BDMS	CH_3	CH_3	71	102-103.5
9	*t*-BDMS	CH_3	H	78	37-38
10	*t*-BDMS	*t*-Bu	*t*-Bu	83	148-149
11	*t*-BDMS	H	H	78	44-45
12	*t*-BDMS	Cl	H	79	45-50

[a] TMS = trimethylsilyl. [b] *t*-BDMS = *tert*-butyldimethylsilyl. [c] Yields of purified product from silylation of the hydroquinone.

Table II. Oxidation of Hydroquinone Silyl Ethers

reactant	R_1	R_2	R_3	quinone % yield[a]	k_{rel}[b]	E_p, V[c]
1	TMS	OCH_3	H	65	1.00	0.71
2	TMS	CH_3	CH_3	93	0.68	0.73
3	TMS	CH_3	H	62	0.48	0.84
4	TMS	*t*-Bu	*t*-Bu	91	0.43	0.89
5	TMS	H	H	99	0.39	1.10
6	TMS	Cl	H	no reaction		1.30
7	*t*-BDMS	OCH_3	H	50	0.14	0.88
8	*t*-BDMS	CH_3	CH_3	80	0.15	0.80
9	*t*-BDMS	CH_3	H	90	0.07	0.94
10	*t*-BDMS	*t*-Bu	*t*-Bu	99	0.26	0.78
11	*t*-BDMS	H	H	no reaction		1.03
12	*t*-BDMS	Cl	H	no reaction		1.25

[a] Products formed after 2 h at 25 °C, using 2 molar equiv of PCC. Yields quoted for TMS derivatives are isolated yields. Yields of quinones obtained from *t*-BDMS derivatives were determined by GLC using 1,4-dimethoxybenzene as an internal standard. Recrystallized yields were somewhat lower. [b] Competitive rates determined as described in the text. [c] Peak potentials from cyclic voltammetry: platinum working electrode, acetonitrile, 0.1 M tetraethylammonium fluoroborate, 1 mM substrate, scan rate 100 m V s^{-1}, $Ag|Ag^+$ reference electrode.

Results and Discussion

Preparative Aspects. The bis(trimethylsilyl) ethers were prepared by treatment of hydroquinones with trimethylsilyl chloride and hexamethyldisilazane in acetonitrile. The *tert*-butyldimethylsilyl ethers were prepared by treatment of hydroquinones with *tert*-butyldimethyl-

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(2) See, for example: Kelly, T. R.; Tsang, W.-G. *Tetrahedron Lett.* **1978**, 4457; Garland, R. B.; Palmer, J. R.; Schultz, J. A.; Sollman, P. B.; Pappo, R. *Ibid.* **1978**, 3669.
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(8) Stewart, R. F.; Miller, L. L. *J. Am. Chem. Soc.* **1980**, *102*, 4999.
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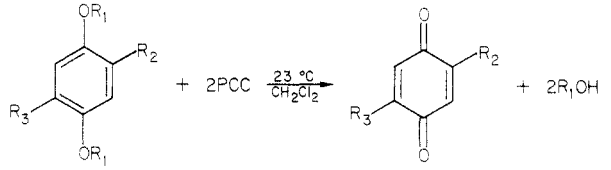
silyl triflate[8] and triethylamine in chloroform. Crystalline compounds were purified by recrystallization from acetonitrile or acetonitrile–chloroform. Liquid compounds were purified by vacuum distillation. The purity of the hydroquinone silyl ethers was determined by GLC analysis. The physical data for compounds **1–12** are summarized in Table I. No unusual precautions were taken to protect the silylated compounds from air or moisture, and over a period of several months no decomposition was apparent.

Oxidations were carried out at room temperature in lightly stoppered flasks in methylene chloride solution. The silyl ether was dissolved, with stirring, in methylene chloride followed by the addition of solid PCC. The solution was initially homogeneous, but within minutes, the reaction mixture darkened and a black, insoluble material was deposited on the walls of the flask. Similar behavior has been noted by Corey and Suggs[7c] for the oxidation of alcohols with PCC. With a 2:1 molar ratio of PCC to silyl ether, oxidation was usually complete within 2 h. Products



were isolated by chromatography on Florisil. Quinones obtained from bis(trimethylsilyl)ethers required no further purification; those products obtained from *tert*-butyldimethylsilyl ethers contained, as a byproduct, *tert*-butyldimethylsilanol[10] and were therefore recrystallized from heptane. As shown in Table II, good yields of quinones were obtained.

The PCC oxidation was unsuccessful for those compounds (**6** and **12**) containing electron-withdrawing groups in the aromatic ring as well as the nonactivated bis(*tert*-butyldimethylsilyl) ether **11**. The fact that **5** reacted much more readily than **11** suggests that, in addition to electronic effects, the ease of cleavage of the Si–O bond[8] is also important in determining overall reactivity. This is supported by the observation that the corresponding methyl ethers of **1**, **3**, and **5** also failed to react with PCC.

In order to demonstrate that the aromatic ring could be elaborated in the presence of the bis(*tert*-butyldimethylsilyl) function, the alkylation of 1,4-bis(*tert*-butyldimethylsiloxy)-2-bromobenzene (**13**) was investigated. Lithiation with *n*-butyllithium in THF and alkylation with methyl *p*-toluenesulfonate gave the corresponding methyl derivative, **9**, in 80% yield.

Mechanistic Aspects. In order to probe the stoichiometry and kinetics, the progress of the PCC oxidation of **4** was followed by periodically withdrawing samples and immediately analyzing them by GLC. Each amount of disilylhydroquinone which reacted produced an equivalent amount of quinone. Therefore, no organic intermediate built up during reaction. Indeed, no GLC evidence for hydrolyzed intermediates could be detected and hydroquinone itself was never present in detectable quantities. Thus, if PCC, acting as a Lewis acid, cleaved the O–Si bond in the first step, any resulting intermediate must be rapidly oxidized. It was established that the oxidation of hydroquinone is not so fast under these conditions, so it is not an intermediate.

With a 1:1 molar ratio of reactants it was found that oxidation proceeded to about 50% completion within 20 min and then more slowly to completion after 24 h. Similar behavior was noted for the PCC oxidation of **10**. The kinetic data for the oxidation of **4** are shown in Figure 1. The best explanation for the sharp curvature in the plot is that oxidation is occurring by two different mechanisms.[11] During the first 20 min of reaction, oxidation by Cr(VI) is rapid. This consumes 0.5 equiv of **4** and 1 equiv of Cr(VI). At this point the rate decreases and the second half of the oxidation, which requires a much longer time period, involves a different mechanism, perhaps oxidation by Cr(V).[11] At higher molar ratios of PCC to silyl ether, i.e., 2:1 or greater, oxidation proceeds rapidly to completion. Under these conditions, oxidation is presumably due almost exclusively to homogeneous Cr(VI). It has been additionally observed, as it has with PCC alcohol oxidations,[9] that an increase in solvent polarity (from methylene chloride to acetone, for example) decreases the reaction rate.

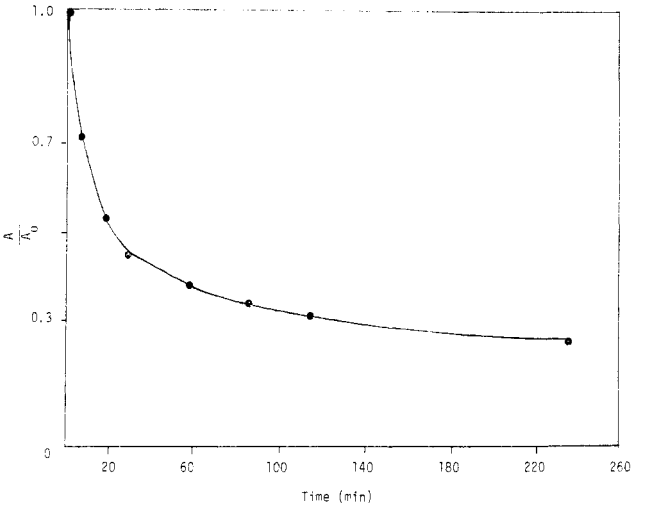


Figure 1. Disappearance of **4** by reaction with PCC. *A* equals concentration of **4** at time *t*. A_0 equals initial concentration of **4**.

The relative oxidation rates for the bis(trimethylsilyl) ethers, **1–6**, and the bis(*tert*-butyldimethylsilyl) ethers, **7–12**, were determined in a series of competitive oxidations with a less than stoichiometric amount of PCC. These data along with the electrochemical oxidation potential measurements are summarized in Table II. In the trimethylsilyl series, compound **1**, containing a ring methoxy group, reacted the fastest; while the unsubstituted compound, **5**, reacted the slowest. It will, however, be noted that the change in rate is very small. A similar ordering and insensitivity to substituent effects was observed for the *tert*-butyldimethylsilyl series. In general, these compounds reacted slightly more slowly than their trimethylsilyl counterparts. One unusual effect can be noted by comparing compounds **3** and **4**, where the relative rates are 0.48 and 0.43, with compounds **9** and **10**, where the relative rates are 0.07 and 0.26. It is proposed that the di-*tert*-butyl compound **10** reacts especially rapidly. A space-filling model of **10** reveals a large steric interaction between *tert*-butyl groups on the ring and the *tert*-butyldimethylsilyl groups. It is likely that the aromaticity of the benzene ring is diminished in **10** due to twisting of the ring out of planarity and this destabilization gives a higher reaction rate.

It was of considerable interest to compare these relative rates with electrochemical oxidation potentials obtained

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(11) Mahapatro, S. N.; Krumpolc, M.; Roček, J. *J. Am. Chem. Soc.* **1980**, *102*, 3799.

in acetonitrile. These oxidation potentials were determined by cyclic voltammetry at 100 mV s^{-1}, at a platinum electrode. The voltammograms showed chemical irreversibility and for each compound a similar peak shape was observed. The peak width at half-height was at the range 60–100 mV for every compound. This is considered to be indicative of a rate-limiting electron transfer.[12] The peak potential, E_p, is, therefore, a measure of the relative rate for loss of one electron. As shown in Table II, the electrochemical order of reactivity qualitatively shows the expected dependence on the electronic and steric character of the substituent.

Comparison of the electrochemical and chemical data requires conversion of relative potentials to relative rates by assuming $\Delta E_p = -RT \ln \Delta k_{elec}$. When this is done it is seen that the order of chemical and electrochemical reactivity for various trimethylsilyl derivatives is qualitatively parallel. A similar qualitative correlation is found for the series of *tert*-butyldimethylsilyl derivatives, even including compound **10**. There is, however, a major difference between the chemical and electrochemical relative rates. The chemical rates are much less sensitive to substituent effects. This demonstrates that less charge is built up in the ring during PCC oxidations and argues against a rate limiting one-electron transfer for the chemical mechanism. As a further test of the electron-transfer oxidizing power of PCC, it was mixed with 2,5-di-*tert*-butyl-1,4-dimethoxybenzene. GLC showed no reaction even though voltammetry on this aromatic showed a reversible one-electron couple with $E_0' = 0.85$ V. This establishes that PCC is not a good one-electron transfer oxidant. Alternative mechanisms which can accommodate the data involve formation of a reactive donor–acceptor complex between a chromium(VI) species and the aromatic.

Experimental Section

General Procedures. Melting points were obtained with open capillaries on a Mel-Temp apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Varian CFT-20 instrument using deuterated chloroform or acetone-d_6 as solvent with tetramethylsilane as internal standard. Infrared spectra were obtained on a Perkin-Elmer 727B or 297 spectrometer. Mass spectra of analytical samples were obtained on an AEI-MS30 instrument. Gas–liquid chromatographic analysis (GLC) was carried out on a Hewlett-Packard Model 5840A gas chromatograph using flame-ionization detection and a 6-ft stainless-steel column of 1:1 5% OV275 on Chromosorb W (120–140 mesh) and 3% OV17 on Chromosorb W (80–100 mesh). Quantitative analyses (GLC) were made by using 1,4-dimethoxybenzene as internal standard. Combustion analyses were obtained from M-H-W Laboratories of Phoenix, AZ. All solvents were either anhydrous or reagent grade (dried over 4-Å molecular sieves). Florisil (60–100 mesh) was obtained from Fisher Scientific. The starting materials were obtained from either Aldrich or Eastman Kodak.

Cyclic voltammetry was carried out by using a Princeton Applied Research (PAR) Model 173 potentiostat in conjucntion with a PAR Model 175 universal programmer. Voltammograms were recorded on a Houston 1000 X-Y recorder. The cyclic voltammetry cell and reference electrode have been previously described.[8]

Preparation of Hydroquinone Bis(trimethylsilyl) Ethers. General Procedure. To a stirred solution of 0.01 mol of hydroquinone in 25 mL of dry acetonitrile were added via syringe 0.022 mol of chlorotrimethylsilane and 0.022 mol of hexamethyldisilazane. The reaction mixture was stirred under argon for 18 h and filtered to remove precipitated salts and the solvent removed by rotary evaporation. The residue was dissolved in 100 mL pentane, washed with saturated aqueous bicarbonate and brine, dried over anhydrous $MgSO_4$, and evaporated to dryness. The crude product (90–100% yield) was then purified by vacuum distillation or recrystallization from acetonitrile or acetonitrile–chloroform as described below for individual compounds. The data are summarized in Table I.

1,4-Bis(trimethylsiloxy)-2-methoxybenzene (1) was obtained as a clear colorless liquid in a crude yield of 100%. Distillation in vacuo gave a 94% yield of pure product.[8] Anal. Calcd for $C_{13}H_{24}O_3Si_2$: C, 54.88; H, 8.50. Found: C, 54.67; H, 8.52.

1,4-Bis(trimethylsiloxy)-2,5-dimethylbenzene (2) was obtained after recrystallization from actonitrile–chloroform in 88% yield: mp 43.5–44.5 °C; IR (Nujol) 1255, 1210, 1180, 929, 890, 873, 842, 750, 757, 721 cm^{-1}; NMR ($CDCl_3$) δ 6.51 (s, 2 H), 2.08 (s, 6 H), 0.22 (s, 9 H), 0.20 (s, 9 H); mass spectrum, *m/e* (relative intensity) 282 (54, M^+), 267 (15), 252 (4), 193 (15), 177 (6), 91 (4), 73 (100); exact mass calcd for $C_{16}H_{20}O_2Si$ 282.1470, found 282.1468. Anal. Calcd for $C_{14}H_{26}O_2Si_2$: C, 59.52; H, 9.28. Found: C, 59.39; H, 9.30.

1,4-Bis(trimethylsiloxy)-2-methylbenzene (3) was obtained as a clear colorless liquid in a crude yield of 100%. Distillation in vacuo gave an 84% yield of pure product: bp 158 °C (0.2 torr); IR (neat) 3020–2840 (5 bands), 1600, 1585, 1490–1500 (2 bands), 1405, 1285, 1245, 1210–1220, 1150, 1100, 995, 900–915, 815–825 (2 bands), 740 cm^{-1}; NMR ($CDCl_3$) δ 6.58 (m, 3), 2.12 (s, 3), 0.22 (s, 18); mass spectrum, *m/e* (relative intensity) 268 (100, M^+), 253 (57), 237 (6), 178 (7), 163 (4), 133 (4), 119 (9), 105 (4), 73 (80); exact mass calcd for $C_{13}H_{24}O_2Si_2$ 268.1314, found 268.1320. Anal. Calcd for $C_{13}H_{24}O_2Si_2$: C, 59.52; H, 9.29. Found: C, 56.79; H, 9.02.

1,4-Bis(trimethylsiloxy)-2,5-di-*tert*-butylbenzene (4) was obtained in 97% yield after recrystallization from actonitrile.[8] Anal. Calcd for $C_{20}H_{38}O_2Si_2$: C, 65.51; H, 10.44. Found: C, 65.46; H, 10.48.

1,4-Bis(trimethylsiloxy)benzene (5) was obtained in 91% yield after recrystallization from acetonitrile–chloroform.[8] Anal. Calcd for $C_{12}H_{22}O_2Si_2$: C, 56.64; H, 8.71. Found: C, 56.36, 8.94.

1,4-Bis(trimethylsiloxy)-2-chlorobenzene (6) was obtained in a crude yield of 96%. Distillation in vacuo gave a 51% yield of the desired product: bp 161 °C (15 torr); IR (neat) 2950, 1505, 1270, 1220, 930, 860 cm^{-1}; NMR (acetone-d_6) δ 6.68 (m, 3 H), 0.25 (s, 9 H), 0.22 (s, 9 H); mass spectrum, *m/e* (relative intensity) 290 (12, M^+), 288 (29, M^+), 273 (13), 257 (12), 93 (13), 73 (100); exact mass calcd for $C_{12}H_{21}ClO_2Si_2$ 288.0768, found 288.0762. Anal. Calcd for $C_{12}H_{21}ClO_2Si_2$: C, 48.89; H, 7.33; Cl, 12.27. Found: C, 49.67; H, 7.46; Cl, 12.07.

Bis(*tert*-butyldimethylsilyl) Ethers of Hydroquinone. General Procedure. To a stirred ice cold solution of 0.010 mol of hydroquinone and 0.022 mol of triethylamine in 20 mL of chloroform, under argon, was added slowly, via syringe, 0.022 mol of *tert*-butyldimethylsilyl triflate.[8] The reaction mixture was gradually warmed to room temperature, stirred for 18 h, poured into 50 mL of ice–water, and extracted with 100 mL of chloroform. The chloroform layer was washed in turn with 100-mL portions of 1 N HCl, 1 N NaOH, and saturated aqueous bicarbonate solution and dried over anhydrous $MgSO_4$. The solvent was removed by rotary evaporation. The crude product (90–100% yield) was then purified by vacuum distillation or recrystallization as described below for individual compounds. The data are summarized in Table I.

1,4-Bis(*tert*-butyldimethylsiloxy)-2-methoxybenzene (7) was obtained in a crude yield of 100%. Distillation in vacuo [bp 169 °C (12.8 torr)] afforded an 81% yield of pure product: mp 29–31 °C; IR (neat) 3000–2800, 1585, 1500–1400 (3 bands), 1385, 1358, 1315, 1260, 1218, 1202, 1162, 1108, 1030, 1002, 970, 910, 770 cm^{-1}; NMR ($CDCl_3$) δ 6.73–6.21 (m, 3 H), 3.74 (s, 3 H), 0.97 (s, 18 H), 0.16 (s, 6 H), 0.11 (s, 6 H); mass spectrum, *m/e* (relative intensity) 368 (12, M^+), 311 (83), 296 (100), 254 (15), 239 (77), 197 (42), 182 (38), 165 (24); exact mass calcd for $C_{19}H_{36}O_3Si_2$ 368.2202, found 368.2200. Anal. Calcd for $C_{19}H_{36}O_3Si_2$: C, 61.90; H, 9.84. Found: C, 61.95; H, 9.94.

1,4-Bis(*tert*-butyldimethylsiloxy)-2,5-dimethylbenzene (8) was obtained in 84% crude yield. Recrystallization from acetonitrile–chloroform yielded pure product in 71% yield: mp 102–103.5 °C; IR (Nujol) 1510, 1500, 1400, 1250, 1205, 1175, 987, 913, 865, 830–790 (3 bands), 770 cm^{-1}; NMR ($CDCl_3$) δ 6.51 (s, 2 H), 2.09 (s, 6 H), 0.98 (s, 18 H), 0.15 (s, 12 H); mass spectrum, *m/e* (relative intensity) 366 (92, M^+), 309 (100), 251 (7), 237 (9),

(12) Nadjo, L.; Saveant, J. M. *J. Electroanal. Chem.* **1973**, *48*, 113. Ferrocene in the same solution gave $\Delta E_p = 60$ mV, so that the peak width is not due to filming.

177 (9), 163 (7), 126 (12), 73 (94); exact mass calcd for $C_{20}H_{38}O_2Si_2$ 366.2409, found 366.2401. Anal. Calcd for $C_{20}H_{38}O_2Si_2$: C, 65.51; H, 10.44; Si, 15.32. Found: C, 65.79; H, 10.63.

1,4-Bis(*tert*-butyldimethylsiloxy)-2-methylbenzene (9) was obtained in a crude yield of 100%. Recrystallization from acetonitrile–chloroform yielded 78% of pure product: mp 38–39 °C; IR (Nujol) 1500–1495 (2 bands), 1400, 1285, 1242, 1215, 1165, 990, 900, 828, 760 cm^{-1}; NMR ($CDCl_3$) δ 7.25 (s, 1 H), 6.51 (m, 2 H), 2.13 (s, 3 H) 0.99 (s, 9 H), 0.96 (s, 9 H), 0.16 (s, 6 H), 0.15 (s, 6 H); mass spectrum, *m/e* (relative intensity) 352 (50, M^+), 295 (99), 237 (7), 119 (5), 73 (45). Anal. Calcd for $C_{19}H_{36}O_2So_2$: C, 64.71; H, 10.29. Found: C, 64.59; H, 10.47.

1,4-Bis(*tert*-butyldimethylsiloxy)-2,5-di-*tert*-butylbenzene (10) was obtained in a crude yield of 97%. Recrystallization from acetonitrile gave an 83% yield of pure product.[8] Anal. Calcd for $C_{26}H_{50}O_2Si_2$: C, 69.27; H, 11.18. Found: C, 69.36; H, 11.24.

1,4-Bis(*tert*-butyldimethylsiloxy)benzene (11) was obtained in a crude yield of 98%. Recrystallization from acetonitrile–chloroform gave a 78% yield of pure product: mp 44–45 °C; IR (Nujol) 1505, 1255–1220 (3 bands), 1238, 910–920, 840, 800, 780, 740–720 (2 bands) cm^{-1}; NMR ($CDCl_3$) δ 6.68 (s, 4 H), 0.96 (s, 18 H), 0.15 (s, 12 H); mass spectrum, *m/e* (relative intensity) 338 (44, M^+), 281 (100), 223 (14), 133 (3), 112 (14), 91 (4), 73 (49); exact mass calcd for $C_{18}H_{34}O_2Si_2$ 338.2096, found 338.2096. Anal. Calcd for $C_{18}H_{34}O_2Si_2$: C, 63.84; H, 10.12. Found: 63.85; H, 10.28.

1,4-Bis(*tert*-butyldimethylsiloxy)-2-chlorobenzene (12) was obtained in a crude yield of 85%. Recrystallization from acetonitrile–chloroform gave a 79% yield of pure product: mp 48–50 °C; IR (Nujol) 1480, 1485, 1455, 1370, 1245, 1195, 1035, 900, 820, 760 cm^{-1}; NMR ($CDCl_3$) δ 6.68 (s, 3 H), 1.00 (s, 9 H), 0.95 (s, 9 H), 0.17 (s, 6 H), 0.15 (s, 6 H); mass spectrum, *m/e* (relative intensity) 374 (5, M^+), 373 (4, M^+), 372 (10, M^+), 338 (9), 315 (62), 281 (27), 279 (12), 257 (29), 199 (4), 165 (6), 149 (3), 129 (7), 93 (20), 73 (100); exact mass calcd for $C_{18}H_{33}ClO_2Si_2$ 372.1706, found 372.1718. Anal. Calcd for $C_{18}H_{33}ClO_2Si_2$: C, 57.95; H, 8.92; Cl, 9.50. Found: C, 57.55; H, 9.10; Cl, 9.34.

1,4-Bis(*tert*-butyldimethylsiloxy)-2-bromobenzene (13) was obtained in a crude yield of 85%. Recrystallization from acetonitrile–chloroform gave a 72% yield of product: mp 42–45 °C; NMR ($CDCl_3$) δ 7.03 (m, 1 H), 6.69 (m, 2 H), 104 (s, 9 H), 0.97 (s, 9 H), 0.22 (s, 6 H), 0.17 (s, 6 H). Anal. Calcd for $C_{18}H_{33}BrO_2Si_2$: C, 51.78; H, 7.97; Br, 19.14. Found: C, 51.94; H, 7.98; Br, 19.31.

Methylation of 13. Methylation of **13** was accomplished in 78% yield according to the *n*-butyllithium–methyl *p*-toluenesulfonate procedure of Syper et al.[1] The product was recrystallized from acetonitrile–chloroform and was identical in all respects with **9**.

Preparative Oxidations. To 0.001 mol of hydroquinone silyl ether dissolved in 8.0 mL of CH_2Cl_2 at 25 °C was added 0.002 mol of PCC (98%, Aldrich). The reaction mixture was stirred for 2 h or until GLC revealed the absence of starting material. The reaction mixture was evaporated to dryness and the residue extracted with 10 mL of anhydrous ether. The extract was passed through a column of Florisil (25-mL buret, 8–10 g of absorbent), eluting with anhydrous ether.

In the case of the bis(trimethylsilyl) ethers (**1–5**), evaporation of the ether elutant yielded the pure quinones. However, with the bis(*tert*-butyldimethylsilyl) ethers (**7–10**), evaporation of the ether elutant yielded a mixture of quinone and the byproduct *tert*-butyldimethylsilanol.[10] The pure quinones were obtained either by recrystallization from heptane or by washing the semisolid residue with ice-cold heptane. The results of the preparative oxidations are summarized in Table II.

Relative Reactivities (k_{rel}). Relative reactivities were determined by allowing a 1:1 molar ratio of a given pair of compounds to compete for a limited quantity of PCC. For instance, 0.5 mmol of **1** and 0.5 mmol of **2** in 8.0 mL of CH_2Cl_2 were reacted with 0.5 mmol of PCC. Prior to the addition of PCC the relative peak areas were determined by GLC analysis. After the addition of PCC the relative concentrations of the starting materials were measured by withdrawing and analyzing 0.5-μL samples at various times.

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Registry No. **1**, 73759-43-0; **2**, 78018-52-7; **3**, 78018-53-8; **4**, 18724-29-3; **5**, 2117-24-0; **6**, 67289-08-1; **7**, 78018-54-9; **8**, 78018-55-0; **9**, 78018-56-1; **10**, 73759-45-2; **11**, 78018-57-2; **12**, 78018-58-3; **13**, 78018-59-4; quinone (R_2 = OCH_3; R_3 = H), 2880-58-2; quinone (R_2 = CH_3; R_3 = CH_3), 137-18-8; quinone (R_2 = CH_3; R_3 = H), 553-97-9; quinone (R_2 = *t*-Bu; R_3 = *t*-Bu), 2460-77-7; quinone (R_2 = H; R_3 = H), 106-51-4; quinone (R_2 = Cl; R_3 = H), 695-99-8; PCC, 26299-14-9.

Assignment of Regiochemistry to Substituted Naphthoquinones by Chemical and Spectroscopic Methods. Amino-, Hydroxy-, and Bromojuglone Derivatives

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Products of the addition of hydrazoic acid to 5-methoxy-, 5-hydroxy-, and 5-acetoxy-1,4-naphthoquinone were determined. Assignment of regiochemistry resolves confusion in the literature, and a correlation between the substitution patterns and chemical shifts in the ^1H NMR spectra was noted.

A retrosynthetic analysis of the structures of the antibiotic kinamycins (**1**)[2] led us to consider a 3-aminojuglone derivative **2** (Chart I) as a building block.

A report by Thomson and co-workers[3] that 3-aminojuglone methyl ether (**2a**) was obtained from the addition of hydrazoic acid to juglone methyl ether (**3**) led us to attempt to repeat this preparation. In our hands, the procedure afforded two products which were separated by

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