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Formation of reactive *o*-quinone methides from the reaction of trimethylsilyl(methyl)-substituted 1,4-benzoquinones with nucleophiles

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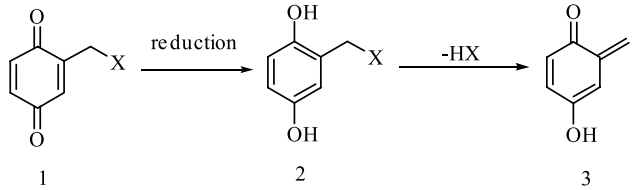
Abstract—*o*-Quinone methides are formed from the reaction of nucleophiles with trimethylsilyl(methyl)-1,4-benzoquinones. These reactive intermediates are trapped by excess nucleophile to form substituted quinones following oxidation. In addition, varying amounts of a symmetrical dimer and a xanthen derivative were observed. The influence of different nucleophiles and ring substituents on the rate of reaction have been studied, and are consistent with rate-limiting formation of a vinylogous enolate initiated by attack of the nucleophile on the silyl group.

1. Introduction

The formation of *o*-quinone methides as reactive intermediates in biologically-active natural products has been reviewed.[1] For example, a proposed reactive quinone methide intermediate generated from the naturally occurring antitumor antibiotic, mitomycin C, is believed to be responsible for DNA alkylation.[2] Similarly, a quinone methide has been detected to arise from daunomycin and shown to function as an alkylating agent.[3] Apart from their involvement in biological processes, *o*-quinone methides have proven useful as synthetic intermediates. For example, electrophilic *o*-quinone methides of structural type **3** react with a variety of nucleophiles (Michael addition), resulting in substituted hydroquinones.[4] They also function as efficient heterodienes in Diels–Alder reactions and undergo a variety of self dimerization reactions.[5]

A common method for the generation of *o*-quinone methides **3** from appropriately substituted quinones, **1**, is initiated by their reduction to the corresponding hydroquinone **2** followed by intramolecular elimination of an equivalent of HX to form the *o*-quinone methide (Scheme 1). Variations of this method include the thermal dehydration of *o*-hydroxybenzyl alcohols and the fluoride-induced desilylation of silylated *o*-hydroxybenzyl bromide (X=Br) and bis-silylated *o*-hydroxybenzyl alcohol (X=OH).[6] Other methods of note involve oxidation of *o*-alkyl-substituted phenols and the thermal ring expansion of 4-allenyl-4-hydroxycyclobutenones.[7,8] Reported herein is a new method for the generation of *o*-quinone methides from (trimethylsilylmethyl or triarylsilylmethyl)-1,4-benzoquinones. This involves treatment of (trialkylsilylmethyl or triarylsilylmethyl)-1,4-benzoquinones with oxygen-nucleophiles such as alcohols or water. The reaction conditions are mild and the transformation can be accomplished under neutral conditions.[9]

A generalized mechanistic paradigm to account for the reaction is outlined in Scheme 2. The appropriately substituted quinone **4** reacts with nucleophiles to generate vinylogous enolate **5**, which provides *o*-quinone methide **6** upon silylation. The resulting *o*-quinone methide reacts further with the nucleophile to form substituted hydroquinone **7**, which is readily oxidized to the corresponding substituted quinone. Details of this study including synthetic applications and mechanistic details are now provided.



Scheme 1.

Keywords: *o*-Quinone methide; 1,4-benzoquinones; Trimethylsilyl; Michael addition; Diels–Alder; Dimerization.

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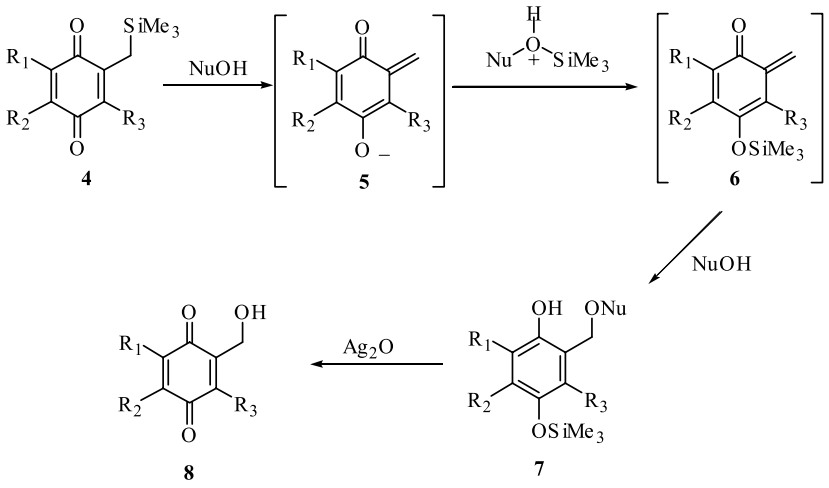
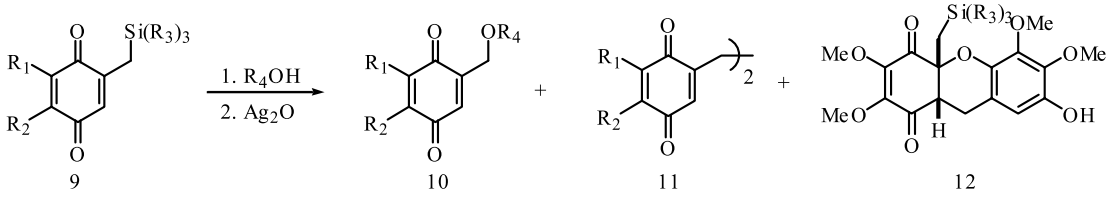


Scheme 2.

2. Results and discussion

A set of reactions illustrating the intermediacy of the *o*-quinone methides is outlined below (Scheme 3). When an ethanolic solution of quinone **9a** ($R_1=R_2=OMe$, $R_3=Me$) was refluxed for 45 min then worked up under oxidative conditions (Ag_20), the corresponding ethoxymethyl quinone **10a** ($R_1=R_2=OMe$, $R_4=Et$) was isolated in 82% yield along a minor amount (5%) of the symmetrical dimer **11a** ($R_1=R_2=OMe$). The symmetrical dimer **11a** may be envisaged to arise via a number of possible pathways. For example Diels–Alder dimerization of two *o*-quinone methides would result in a spiropyran. Subsequent ring opening would then provide the dimer in its half reduced form. Oxidative work up leads to **11a**. An alternate route would provide the half reduced dimer via Michael addition



a) $R_1=R_2=OMe$, $R_3=Me$
b) $R_1=OMe$, $R_2=n$Bu, $R_3=Me$
c) $R_1=n$Bu, $R_2=OMe$, $R_3=Me$
d) $R_1=R_2=OMe$, $R_3=Ph$

Compound	Conditions	9 (%)	10 (%)	11 (%)	12 (%)
9a	EtOH, reflux 45 min	0	82	5	0
9a	EtOH, RT 24 h	0	45	22	0
9a	10% EtOH/CH_3CN, reflux 44 h	44	trace	0	37
9a	10% H_2O/CH_3CN, reflux 1.5 h	0	18	67	trace
9a	5% H_2O/CH_3CN, reflux 8 h	0	12	46	22
9a	HOAc, reflux 4 h	10	54	0	0
9a	6 eq. NaOAc/HOAc, reflux 0.5 h	0	79	<2	0
9a	0.1 eq. NaOAc/HOAc, reflux 0.5 h	50	30	0	0
9b	EtOH, reflux 6 h	11	63	5	0
9c	EtOH, reflux 45 min	13	67	7	0
9d	EtOH, reflux 32 h	0	70	0	0

Scheme 3.

of the enolate to the *o*-quinone methide. At ambient temperature the reaction required 24 h and the above products were realized in 45 and 22%, respectively. In comparison, when the amount of ethanol was reduced to 10% in a solvent of acetonitrile, only a trace of **10a** was observed after refluxing for 44 h. The major product was the xanthene-1,4-dione **12** (37%), and a significant amount (44%) of starting material was recovered. In related studies ethanolic solutions of the quinones **9b** (R_1=OMe, R_2=*n*-Bu, R_3=Me) and **9c** (R_1=*n*-Bu, R_2=OMe, R_3=Me) gave the corresponding **10b** (R_1=OMe, R_2=*n*-Bu, R_4=Et) and **10c** (R_1=*n*-Bu, R_2=OMe, R_4=Et) in respective yields of 63 and 67% along with 5 and 7% of the dimers **11b** (R_1=OMe, R_2=*n*-Bu) and **11c** (R_1=*n*-Bu, R_2=OMe) after reaction times of 6 h for **9b** and 45 min for **9c** at reflux temperature. Quinone **9d** (R_1=R_2=OMe, R_3=Ph) also gave **10a** in 70% yield. However, the bulkier triphenylsilyl group significantly retarded the reaction rate; 32 h in refluxing ethanol was required as compared to 45 min for the trimethyl analogs, **9a**,**c** and 6 h for **9b**.

The steric bulk of the alcohol also influences the reaction course. For example, when solutions of **9a** in *iso*-propanol and *tert*-butanol were refluxed, the reaction times increased to 9 and 44 h, respectively. Also, the yields of the corresponding alkoxymethyl-substituted quinones decreased and the yield of the symmetrical dimer increased. In *iso*-propanol the quinone **10d** (R_1=R_2=OMe, R_4=*i*-Pr) and the dimer **11a** were obtained in 65 and 10%, respectively, as compared to yields of **10e** (R_1=R_2=OMe, R_4=*t*-Bu) (45%) and **11a** (16%) in *tert*-butanol.

In a related study a solution of **9a** in 5% aqueous acetonitrile was refluxed for 8 h followed by subsequent oxidation (Ag_2O). Here, the quinone **10f** (R_1=R_2=OMe, R_4=H) (12%), the symmetrical dimer **11a** (46%) and the xanthene-1,4-dione **12** (22%) were realized. Interestingly, the amount of water had a significant effect on the product distribution. For example, when 10% aqueous acetonitrile was employed, the dimer **11a** and quinone **10f** were realized in respective yields of 67 and 18%, and the xanthene-1,4-dione **12** was detected in only trace amounts.

Further data were obtained when a solution of **9a** in glacial acetic acid containing 6 equiv of sodium acetate was heated to reflux for 0.5 h. The major product detected was the quinone **10g** (R_1=R_2=OMe, R_4=Ac) (79%) along with $<$2% of dimer **11a**. When the amount of sodium acetate was reduced to 0.1 equiv the observed products were the quinone **10g** (30%) and recovered starting material. In acetic acid alone quinone **10g** was realized in 54% along with 10% recovered starting material. Dimer **11a** was not detected from the reactions containing 0.1% NaOAc or in pure acetic acid.

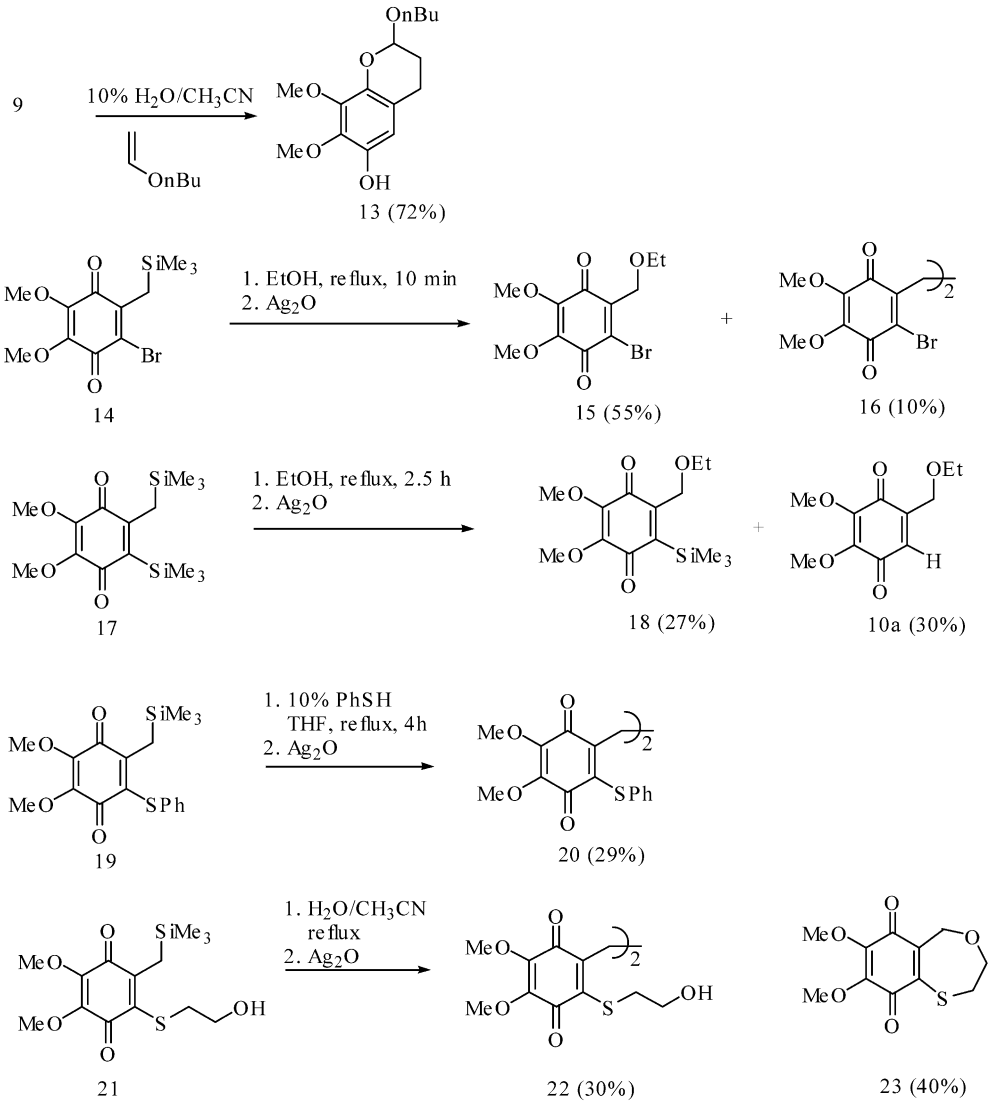
Additional examples are presented in Scheme 4. Treatment of **9a** with 10% aqueous acetonitrile in the presence of excess *n*-butyl vinyl ether gave the chromanol **13** in 72% yield. Quinone **14** was found to readily react with ethanol. After only 10 min at reflux followed by an oxidative (Ag_2O) workup, quinone **15** along with dimer **16** were realized in 55 and 10%, respectively. Under analogous conditions **17** was converted to **18** in 27% yield along with quinone **10a** in 30% yield.

Quinone **19** was found to be stable in dry refluxing THF after 7 h. However, addition of a catalytic amount (10 mol%) of thiophenol resulted in the formation of the symmetrical dimer **20** (29%) along with recovered starting material after an additional 4 h at reflux. Similar behavior was observed with the mercaptoethanol-substitued quinone **21**. Heating solutions of this quinone in refluxing THF for 5 h or toluene for 8 h failed to induce any reaction. However, heating a dilute aqueous acetonitrile solution of **21** for 3 h induced the formation of symmetrical dimer **22** and the annelated quinone **23** in respective yields of 30 and 40%.

The reaction rates of a variety of quinones with ethanol were studied to determine the influence of ring substitution. The reactions of **9a** as well as the regioisomeric *n*-butyl-substituted quinones **9b**, and **9c** were measured in ethanol-d_6 at 70° by ^{1}H NMR. The disappearance of the methylene group resonance as a function of time was monitored using the methyl group resonance of *p*-xylene as an internal standard. Due to the limited solubility of triphenylsilyl-substituted quinone **9d** in ethanol, the reaction rate of this quinone was followed by HPLC. In all cases, the reactions exhibited clean pseudo first-order kinetic behavior. The half lives of **9a**,**b**,**c**,**d** at 70 °C were calculated to be, respectively, 21 min, 85 min, 28 min and 15 h. The reaction of the bromoquinone **14** with ethanol was much too fast to be measured accurately at 70 °C. Therefore, the rate of reaction was studied by ^{1}H NMR at 30 °C in ethanol-d_6, revealing a half life of 13 min.

The data outlined above are consistent with the mechanism provided in Scheme 2. In this regard, the following points are of particular note:

1. The rate-limiting step is nucleophilic attack on the silyl group of quinone **4** to produce the enolate anion **5**. The difference in the reaction rates of **9a** and **9d** is particularly revealing in this regard. The data show the less bulky quinone **9a** to react approximately 43 times faster than its more hindered analog **9d** at 70 °C. The difference in rate between the other quinones is also noteworthy. For example, the half-life of the bromoquinone **14** is 13 min at 30 °C while that of **9a** is 21 min at 70 °C. Here again, the data suggest enolate anion formation in the rate-limiting step, that is, the electronegative bromine adds stability to the enolate and thus increases the reaction rate. The observed rate differences between the other quinones are less remarkable, but even here the data suggest the importance of enolate stability. Note, for example, the rate difference between the regioisomeric quinones, that is, **9b**/**9c**=1:3. This would be consistent with anion stabilization in **5**. Thus **9b** (R_1=OMe) would result in a vinylogous ester enolate while **9c** (R_1=*n*-Bu) would give a more stable keto enolate.[10]
2. Unambiguous data for the silyloxy quinone methide **6** as opposed to the protio analog was not obtained. However, the silyl analog is favored on the basis of the results obtained when **9a** was treated with acetic acid or acetic



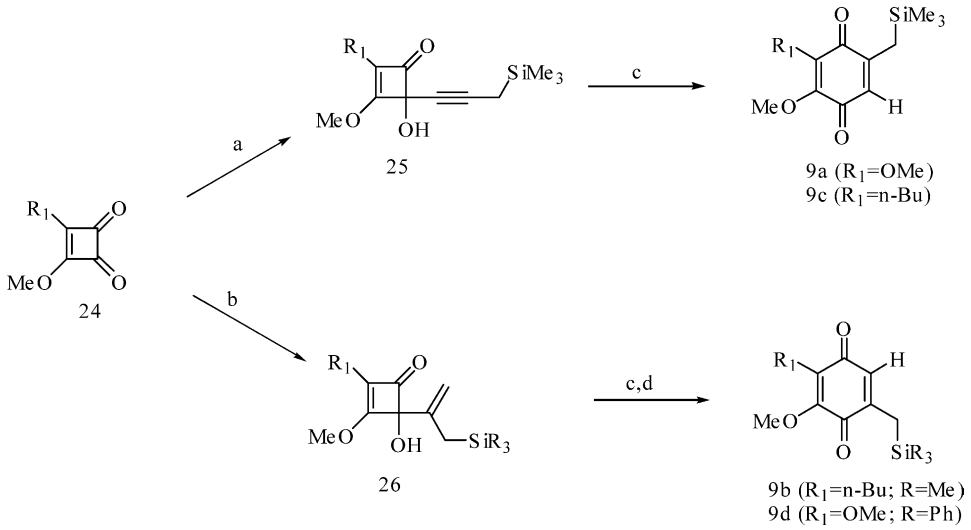
Scheme 4.

acid/sodium acetate. Under these acidic conditions no simple protio desilylated product (e.g., 2,3-dimethoxy-5-methyl-1,4-benzoquinone) was detected. These data are in agreement with the mechanistic paradigm outlined in Scheme 2, that is, *O*-silylation of the enolate **5** to give the quinone methide **6** is presumably favored over *O*-protonation. This intermediate then functions as the key precursor to the observed reaction products.

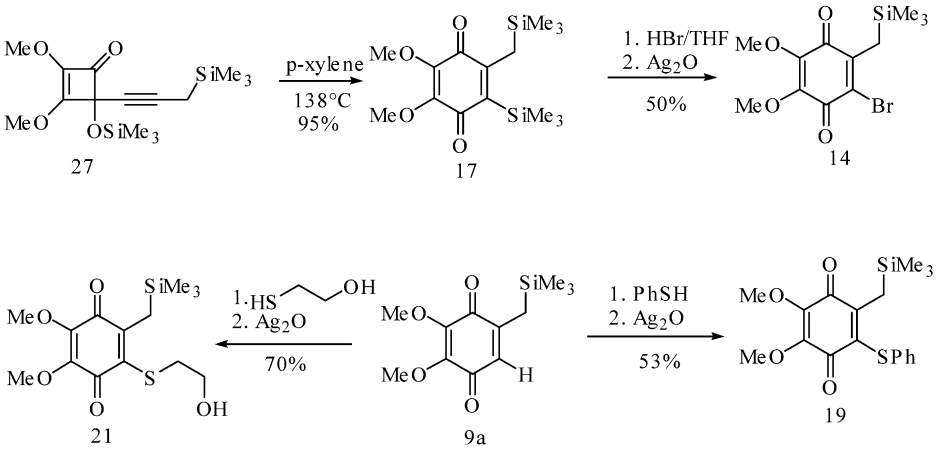
3. The above reactions are in agreement with an *o*-quinone methide precursor. Selected examples are noted below. Quinones of general structure **10** are envisaged to arise via Michael additions of ROH to the enone of the *o*-quinone methide followed by oxidation of the resulting silylated hydroquinone.[4g,11] As the concentration of ROH decreases (see, for example, entry b in Scheme 3) the *o*-quinone methide is competitively trapped by the starting quinone in a Diels–Alder reaction to give the xanthene-1,4-dione **12**. Analogously, the *o*-quinone methide can be intercepted to give **13** when generated in the presence of excess *n*-butylvinyl ether. The dimers of general structure **11** may arise via an initial Diels–Alder dimerization of the quinone methides, a known reaction pathway for such intermediates.[12] Alternatively, dimers **11** may be formed by Michael addition of enolate **5** to *o*-quinone methide **6**.

Quinones **9a**,**b**,**c**,**d**, **14**, **17**, **19** and **21**, needed for the study reported herein, find their synthetic genesis in the previously reported thermal rearrangement of 4-alkynyl and 4-alkenylcyclobutenones (Scheme 5).[13] For example, 3-*n*-butyl-4-methoxycyclobuten-1,2-dione (**24**) was converted to the corresponding adducts **25** and **26** (R_1 = *n*-Bu, R = Me) upon treatment with the appropriate alkynyl or vinyl lithium reagent to the more reactive carbonyl group. These then gave the respective regioisomeric quinone **9b** (92%) and **9c** (75%) upon thermolysis (*p*-xylene,138 °C). In a similar fashion **26** (R_1 = OMe, R = Ph) gave **9d** (92%) and **27** gave **17** (95%). Treatment of **17** with HBr in THF followed by oxidation (Ag_2O) of the resulting hydroquinone gave **14** (50%). Quinone **21** (70%) was obtained from **9a** upon treatment with mercaptoethanol followed by an oxidative work up. Quinone **19** (53%) was obtained analogously using thiophenol.

The facility of *o*-quinone methide formation from (trimethylsilyl)methyl-1,4-benzoquinones under mild and



Reagents: a) 1-lithio-3-(trimethylsilyl) propyne, THF, -78°C, then H_2O of TMSCl;
b) 2-lithio-3-(trimethylsilyl)propene, THF, -78°C; c) *p*-xylene, reflux; d) Ag_2O, *p*-xylene



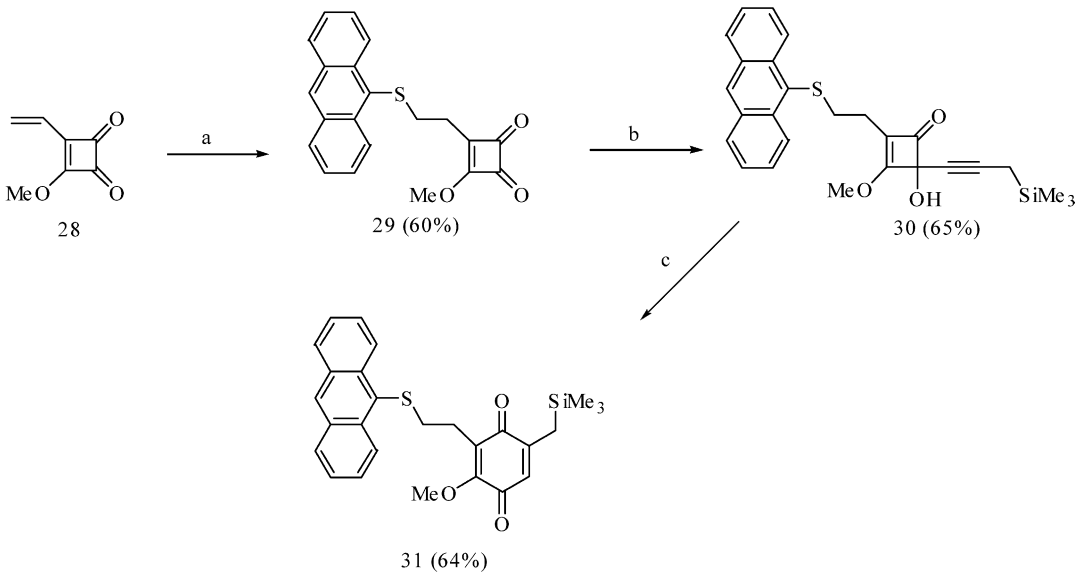
Scheme 5.

neutral conditions can be used as a paradigm to guide the design of potentially bioactive compounds. For example, quinones bearing an intercalating group as well as the (trimethylsilyl)methyl group might effectively cleave DNA. To this end, quinone **31** was prepared as outlined in Scheme 6. Addition of 9-thioanthracene to 3-methoxy-4-alkenylcyclobutene-1,2-dione gives **29** in 60% yield.[14] This was converted to **30** upon addition of 1-lithio-3-trimethylsilylpropyne, thermolysis of which (acetonitrile, reflux) gave the desired quinone **31** in 64% yield.

When quinone **31** was incubated with supercoiled DNA at 51 °C for 21 h cleavage to the relaxed circular form was observed as evidenced by agarose gel electrophoresis with ethidium bromide stain. Moreover, it was observed that added ethidium bromide inhibits cleavage of the supercoiled DNA by effectively competing for the intercalation sites.

3. Conclusions

In conclusion, the most significant aspects of this work include the following: (1) trialkylsilyl (or triarylsilyl)-methyl-1,4-benzoquinones **4** function as excellent precursors to *o*-quinone methide intermediates **6**; (2) the quinone methides can be generated under mild and neutral conditions; (3) the mechanism involves nucleophilic attack at the silyl group with displacement of the corresponding vinylogous enolate anion; (4) anion stabilizing groups on the quinone nucleus at those positions that enhance anion stabilization facilitate the rate of the reaction; (5) a general method for the synthesis of trialkylsilyl (or triarylsilyl)-methyl-1,4-benzoquinones from substituted cyclobuten-1,2-diones is presented; (6) quinone **31**, bearing an intercalating group as well as well as a (trimethylsilyl)-methyl substituent, was prepared and observed to cleave supercoiled DNA.



Reagents: a) 9-thioanthracene; b) 1-lithio-3-trimethylsilylpropyne; c) acetonitrile, reflux

Scheme 6.

4. Experimental

4.1. General

All air or water sensitive reactions were carried out under a slight pressure of nitrogen or argon. Dry solvents were distilled from calcium hydride. THF and ethyl ether were further distilled from sodium (benzophenone indicator). Unless specified as dry, solvents were unpurified reagent grade. Glassware was flame-dried under a stream of nitrogen or argon, where appropriate. In cases where products were isolated by 'aqueous work-up', the procedure was to quench the reaction by addition of 5% NH_4Cl to the reaction mixture followed by dilution with ethyl ether. The combined organic layers were washed with brine and dried with $MgSO_4$ before concentration in vacuo to yield the crude products. Flash column chromatography was performed using E.Merck silica gel (230–400 mesh) or Fisher Scientific florisil (100–200 mesh). Radial chromatography was performed on a model 7924T chromatotron from Harrison Research, Palo Alto, CA. Melting points were taken on a Buchi 50 melting point apparatus and are not corrected. NMR spectra were recorded on a Bruker 250 or 300 MHz or General Electric QE 300, QE 500 or Omega 500 MHz NMR spectrometers. IR spectra were obtained on a Perkin Elmer 1620 spectrophotometer (single beam). Low resolution mass spectra were obtained from a Finnigan 400 spectrometer; high resolution mass spectra were obtained on a VG Analytic 7070E spectrometer. Elemental analyses were performed by Robertson Laboratories, Inc., Madison, NJ.

4.1.1. 2,3-Dimethoxy-4-hydroxy-4-(3-trimethylsilylpropyn-1-yl)cyclobut-2-en-1-one 25, $R_1=OCH_3$—representative procedure for alkynyllithium addition. *n*-Butyllithium (1.8 mL of a 1.6 M solution in hexane, 2.88 mmol) was added to a solution of 3-trimethylsilylpropyne (331 mg, 2.96 mmol) in 50 mL of dry THF at −78 °C. After 10 min, a pre-cooled solution of dimethyl squarate (350 mg, 2.46 mmol) in 25 mL of THF was added via cannula over 5 min. The mixture was stirred for 10 min and then quenched with 5% NH_4Cl (20 mL) and allowed to warm to room temperature. Ether (100 mL) was added and the aqueous layer was extracted twice with ether (2× 20 mL). The combined organic layers were washed with brine and dried over anhyd. $MgSO_4$. Evaporation of the solvent followed by flash chromatography on silica gel (hexanes/ethyl acetate, 3:1) afforded 469 mg (75%) of the title compound as a cream colored solid: mp 75–76 °C; IR ($CDCl_3$) 3580, 1785 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.18 (s, 3H), 3.96 (s, 3H), 2.79 (br s, 1H), 1.56 (s, 2H), 0.11 (s, 9H); ^{13}C NMR (500 MHz, CDCl3) δ 181.6, 165.2, 135.2, 89.1, 78.8, 73.2, 59.8, 58.5, 7.4, −2.0; LRMS *m/e* (rel. intens.) EI 239 (4), 73 (100); CI 255 (100), 237 (19), 223 (18); HRMS CI *m/e* calcd for $C_{12}H_{18}O_4Si$: (MH^+) 255.1052, found: 255.1040.

4.1.2. 2,3-Dimethoxy-4-hydroxy-3-(trimethylsilylpropen-2-yl)cyclobut-2-en-1-one, 26, $R_1=OCH_3$, R= CH_3—representative procedure for alkenyllithium addition. A solution of 2-bromoallyltrimethylsilane (1.20 g, 6.21 mmol) in 10 mL of dry THF was introduced dropwise to a solution of *t*-butyllithium (8.0 mL of a 1.5 M solution in hexanes, 12.0 mmol) in 100 mL of THF at −78 °C. After stirring for 30 min, a solution of dimethyl squarate (0.80 g, 5.63 mmol) in 50 mL of THF at −78 °C was added via cannula over 5 min. The resulting solution was stirred for 10 min and then quenched with 5% NH_4Cl and allowed to warm to ambient temperature. Ether (100 mL) was added and the aqueous layer was separated and back-extracted with ether (2×20 mL). The combined organic layers were washed with brine and dried with anhy. $MgSO_4$. Evaporation of the solvent followed by flash column chromatography (hexanes/ethyl acetate, 3:1) afforded 1.03 g (72%) of the title compound as a light yellow oil. IR ($CDCl_3$) 3580, 1775 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.20 (s, 1H), 4.91 (s, 1H), 4.10 (s, 3H), 3.96 (s, 3H), 2.71 (s, 1H), 1.64 (d, J=0.6 Hz, 2H), 0.05 (s, 9H); LRMS *m/e*

(EI, rel. intens.) 256 (M^+, 25), 241 (22), 225 (32), 73 (100). Anal. Calcd for $C_{14}H_{20}O_4Si$: 56.22% C; 7.86% H, found: 55.97% C, 7.94% H.

4.1.3. 2,3-Dimethoxy-4-(3-trimethylsilyl-1-propynyl)-4-trimethylsiloxycyclobenone, 27. 1-Lithio-3-trimethylsilylpropyne was generated and added to dimethyl squarate (150 mg, 1 mmol) as described for **25**. The resulting solution was stirred for ten min at −78 °C and then quenched by addition of trimethylsilylchloride (0.18 mL, 1.4 mmol). The solution was stirred at −78 °C for an additional ten min and then concentrated in vacuo. The residue was diluted with ether and quickly filtered through a plug of fluorisil. Concentration in vacuo gave 324 mg (95%) of the title compound as a clear oil. IR ($CDCl_3$) 1780 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.15 (s, 3H), 3.94 (s, 3H), 1.56 (s, 2H), 0.22 (s, 9H), 0.11 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 181.7, 166.2, 134.5, 88.5, 79.5, 74.3, 59.6, 58.4, 7.4, 1.2, −1.9; HRMS *m/e* (CI) calcd for $C_{15}H_{27}O_4Si_2$: 327.1428, found: 327.1427.

4.1.4. 2-*n*-Butyl-4-hydroxy-3-methoxy-4-(3-trimethylsilyl-1-propynyl)cyclobutenone, 25 R_1=*n*-butyl. The representative procedure for **25** was followed using 3-*n*-butyl-4-methoxycyclobut-3-ene-1,2-dione, **24**, R_1=*n*-butyl, as the starting material. Purification by flash column chromatography (hexanes/ethyl acetate, 3:1) gave 534 mg (54%) of the product as a yellow solid: mp 42–43 °C; IR ($CDCl_3$) 3580, 2230, 1765 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.21 (s, 3H), 3.55 (bs, 1H), 2.04 (t, J=7.0 Hz, 2H), 1.55 (s, 2H), 1.49 (pentet, J=7.1 Hz, 2H), 1.30 (sextet, J=7.1 Hz, 2H), 0.87 (t, J=7.1 Hz, 3H), 0.09 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 187.9, 180.7, 129.3, 89.9, 82.9, 73.5, 59.4, 28.9, 22.4, 21.5, 13.7, 7.5, −2.0 (3C); LRMS *m/e* (EI, rel. intens.) 280 (M^+, 1), 265 (17), 73 (100). CI 281 (MH^+, 100); HRMS (CI) *m/e* calcd for $C_{15}H_{24}O_3Si$: (MH^+) 281.1573, found: 281.1553.

4.1.5. 2-*n*-Butyl-4-hydroxy-3-methoxy-4-(3-trimethylsilylpropenyl)-cyclobutenone, 26 R_1=*n*-butyl. The representative procedure for **26** was followed using 4-*n*-butyl-3-methoxycyclobutenedione **24** (R=*n*-butyl) and 3-trimethylsilylpropyne as starting materials. Flash chromatography (hexanes/ethyl acetate, 4:1) gave 550 mg (53%) as a light yellow oil. IR ($CDCl_3$) 3580, 3460, 1760; ^1H NMR ($CDCl_3$) δ 5.15 (d, J=0.5 Hz, 1H), 4.89 (s, 1H), 4.04 (s, 3H), 2.07 (m, 2H), 1.60 (s, 2H), 1.47 (pentet, J=7.4 Hz, 2H), 1.30 (sextet, J=7.4 Hz, 2H), 0.87 (t, J=7.4 Hz, 3H), 0.02 (s, 9H); ^{13}C NMR (CDCl3) δ 191.6, 182.3, 143.6, 129.0, 111.2, 94.0, 59.3, 29.3, 22.5, 21.6, 21.5, 13.6, −1.0 (3C); LRMS *m/e* (EI, rel. intens.) 282 (M^+, 0.6), 208 (1.5), 73 (100); HRMS (EI) *m/e* calcd for $C_{15}H_{26}O_3Si$: (M^+) 282.1651, found: 282.1640.

Also isolated in 10% yield (101 mg) was the regioisomer as a yellow oil. IR ($CDCl_3$) 3590, 2960, 1765; ^1H NMR ($CDCl_3$) δ 5.07 (s, 1H), 4.88 (d, J=0.9 Hz, 1H), 4.00 (s, 3H), 2.32–2.45 (m, 3H overlapping methylene and hydroxy protons), 1.64 (quintet, J=7.1 Hz, 2H), 1.60 (d, J=1.0 Hz, 2H), 1.38 (sextet, J=7.4 Hz, 2H), 0.92 (t, J=7.3 Hz, 3H), 0.04 (s, 9H); ^{13}C (CDCl3) δ 188.7, 157.5, 154.8, 144.8, 111.1, 91.5, 58.1, 28.8, 25.1, 23.0, 22.1, 13.7, −1.0 (3C); LRMS *m/e* (EI, rel. intens.) 282 (M^+, 0.05), 239 (0.5), 73 (100); HRMS (EI) *m/e* calcd for $C_{15}H_{26}O_3Si$: (M^+) 282.1651, found: 282.1641.

4.1.6. 2-Bromo-3-triphenylsilyl-1-propene. Triphenylsilyllithium was prepared by mixing triphenylsilyl chloride (4.72 g, 16 mmol) with thinly sliced lithium metal wire (0.54 g, 80 mmol) in 20 mL of dry THF for 22 h at ambient temperature. The resulting green solution was cooled to 0 °C and then added to freshly dried CuI (1.52 g, 8 mmol). The mixture was stirred at 0 °C for 30 min and then cooled to −78 °C. A pre-cooled solution of 2,3-dibromopropene (6.6 mmol) in 5 mL of THF was added to the mixture. The resulting mixture was stirred at −78 °C for 30 min and then allowed to warm to ambient temperature. The reaction mixture was poured into a mixture of 1:1 pentane/5% NH_4Cl (60 mL) and stirred vigorously. The mixture was filtered through glass wool and the layers were separated. The aqueous layer was back-extracted with ether. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The resulting tan solid was purified by flash column chromatography (silica gel, hexanes/ethyl acetate, 12:1) followed by crystallization from boiling hexanes to afford 1.98 g (79%) of the title compound as white crystals: mp 91.5–92.5 °C; IR ($CDCl_3$) 3052, 3014, 1618, 1487, 1428, 1193, 1111, 872, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70–7.50 (m, 6H), 7.50–7.26 (m, 9H), 5.34 (d, J=1.6 Hz, 1H), 5.30 (d, J=1.8 Hz, 1H), 2.98 (d, J=0.8 Hz, 2H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 135.9, 133.5, 129.8, 129.2, 127.8, 117.4, 30.0; HRMS *m/e* (CI) calcd for $C_{21}H_{19}Si$: 299.1256, found: 299.1230; 341 (4), 340 (15), 339 (4), 338 (10), 302 (2), 301 (7), 263 (20), 261 (20), 260 (24), 259 (100).

4.1.7. 4-Hydroxy-2,3-dimethoxy-4-(1-((triphenylsilylmethyl)ethenyl)-2-cyclobutenone, 26, R_1=OMe, R=Ph. To a cooled (−78 °C) solution of *t*-butyllithium (3.7 mmol) in 50 mL of dry THF was added a pre-cooled (−78 °C) solution of 2-bromo-3-triphenylsilylprop-1-ene (644 mg, 1.7 mmol) in 40 mL of dry THF via cannula. The resulting solution was stirred for 15 min at −78 °C. A pre-cooled solution (−78 °C) of dimethyl squarate (200 mg, 1.4 mmol) in 50 mL of dry THF was added via cannula. The reaction mixture was stirred for 30 min at −78 °C and then worked up. Purification by flash column chromatography (silica gel, hexanes/ethyl acetate, 1:1) provided the title compound as a white solid (365 mg, 59%): mp 112–113 °C; IR ($CDCl_3$) 3580, 1773 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.3 (s, 1H), 2.51 (d, J=15 Hz, 1H), 2.6 (d, J=15 Hz 1H), 3.86 (s, 3H), 3.91 (s, 3H), 4.9 (s, 1H), 5.2 (s, 1H), 7.36–7.43 (m, 9H), 7.57–7.58 (m, 6H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 17.7, 58.5, 60.1, 89.1, 114.9, 127.95, 129.7, 134.4, 134.5, 136.0, 141.8, 165.8, 184.3; HRMS *m/e* (EI, rel. intens.) calcd for $C_{27}H_{26}O_4Si$: 442.1600, found: 442.1633; 442 (1.4), 410 (4.4), 411 (1.3), 364 (40.6), 365 (8.8), 349 (19), 350 (4.3), 259 (100), 260 (20.7), 261 (5.1), 180 (12.9), 181 (33.5), 182 (6.5), 105 (30.8).

4.1.8. 2,3-Dimethoxy-5-((trimethylsilylmethyl)-1,4-benzoquinone, 9a. Representative procedure for the rearrangement of 4-alkenyl substituted cyclobutenones to trimethylsilylmethyl-substituted benzoquinones. *Method A*. A solution of **26** (R_1=OMe, R=CH_3), (1.01 g, 3.94 mmol), in 100 mL of *p*-xylene was heated at reflux for

15 min. After cooling to ambient temperature, Ag_2O (2.0 g, 7.94 mmol) was added and the mixture was stirred for 15 min. Filtration and evaporation of the solvent gave the crude product. Purification by flash column chromatography (hexanes/ethyl acetate, 5:1) yielded 0.90 g (89%) of the title compound as a deep red oil. IR ($CDCl_3$) 2690, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.23 (t, $J=0.8$ Hz, 1H), 4.04 (s, 3H), 3.94 (s, 3H), 1.97 (d, $J=0.8$ Hz, 2H), 0.02 (s, 9H); LRMS *m/e* (EI, rel. intens.) 254 (M^+, 12), 239 (16), 226 (33), 211 (19), 195 (10), 73 (100). Anal. Calcd for $C_{12}H_{18}O_4Si$: C, 56.67; H, 7.13, found: C, 56.44; H, 6.99.

Method B. Heating a solution of 4-alkynyl substituted cyclobutenone, **25** ($R_1=OMe$), in *p*-xylene at reflux for 15 min followed by evaporation of the solvent and purification by flash column chromatography provided the title compound directly without the need for Ag_2O oxidation. The spectral properties were identical to the product derived from **26**.

4.1.9. 2,3-Dimethoxy-5-trimethylsilyl-6-((trimethylsilyl)-methyl)-1,4-benzoquinone, 17. A solution of cyclobutenone **27** (297 mg, 0.91 mmol) and 60 mL of dry *p*-xylene was heated at reflux for 1 h. Concentration in vacuo followed by flash column chromatography on silica gel (hexanes/ethyl acetate, 10:1) provided 190 mg (65%) of the product as an orange oil. IR ($CDCl_3$) 1641, 1564 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 9H), 0.28 (s, 9H), 2.27 (s, 2H), 3.90 (s, 3H), 4.02 (s, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) Δ 188.15, 184.38, 156.17, 145.24, 143.19, 138.73, 60.95, 60.87, 21.19, 1.95, −0.23; HRMS (EI, rel. intens.) *m/e* calcd for $C_{15}H_{27}O_4Si_2$; 327.1475, found: 327.1421; 326 (0.8), 311 (7.8), 298 (22), 281 (4), 268 (3), 253 (11), 147 (8), 135 (11), 133 (12), 89 (12), 73 (100), 59 (13).

4.1.10. 2,3-Dimethoxy-6-((triphenylsilyl)methyl)-1,4-benzoquinone, 9d. A solution of cyclobutenone **6** ($R_1=$ OMe, R=Ph; 25 mg, 0.05 mmol)) in 1 mL of *p*-xylene was heated at reflux for 30 min. The solution was cooled to room temperature and treated with Ag_2O (350 mg, 1.5 mmol). After 15 min, the solution was filtered. Concentration followed by flash column chromatography (hexanes/ethyl acetate, 4:1) yielded 20.3 mg (92%) of the product as a yellow solid: mp 122.5–123 °C; IR ($CDCl_3$) 1655 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.8 (s, 2H), 3.6 (s, 3H), 3.96 (s, 3H), 6.15 (s, 1H), 7.37–7.43 (m, 9H), 7.53–7.55 (m, 6H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 183.5, 183.3, 146.9, 144.8, 144.2, 135.8, 132.9, 129.9, 128.5, 128.0, 60.9, 60.9, 16.7; LRMS (EI, rel. intens.) *m/e* 440 (4.98), 425 (9.9), 363 (7.1), 347 (3.9), 259 (100), 260 (22.4), 213 (18.1), 181 (36.9), 180 (13.3), 155 (14); Analysis calcd for $C_{27}H_{24}O_4Si$: C, 73.61; H, 5.49, found: C, 73.53; H, 5.42.

4.1.11. 3-*n*-Butyl-2-methoxy-5-((trimethylsilyl)methyl)-1,4-benzoquinone, 9c. This quinone was prepared by thermolysis of **25** ($R_1=n$-butyl) according to method B. Purification by flash column chromatography (hexanes/ethyl acetate, 95:5) gave 390 mg (75%) of the product as a golden yellow oil. IR ($CDCl_3$) 1650, 1595 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.22 (t, $J=0.9$ Hz, 1H), 4.01 (s, 1H), 2.43 (t, $J=$ 7.1 Hz, 2H), 1.98 (d, $J=0.9$ Hz, 2H), 1.35–1.32 (m, 4H), 0.91 (t, $J=7.0$ Hz), 0.01 (s, 9H); LRMS *m/e* (EI, rel. intens.) 280 (9), 265 (22), 209 (25), 73 (100); Anal. Calcd for $C_{15}H_{24}O_3Si$: C, 64.24; H, 8.63, found: C, 64.24; H, 8.74.

4.1.12. 3-*n*-Butyl-2-methoxy-6-((trimethylsilyl)methyl)-1,4-benzoquinone, 9b. This quinone was prepared by thermolysis of **26** ($R_1=n$-butyl, $R=CH_3$) according to method A. Purification by flash column chromatography (hexanes/ethyl acetate, 95:5) provided 366 mg (92%) of the title compound as a golden yellow oil. IR ($CDCl_3$) 2980, 1670, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.30 (t, $J=1.0$ Hz, 2H), 3.92 (s, 3H), 2.40 (t, $J=7.1$ Hz, 2H), 1.95 (d, $J=$ 1.0 Hz, 2H), 1.34–1.38 (m, 4H), 0.90 (t, $J=7.1$ Hz, 3H), 0.02 (s, 9H); LRMS *m/e* (CI, rel. intens.) 281 (MH^+, 100), 267 (4). Anal. Calcd for $C_{15}H_{24}O_3Si$: C, 64.24; H, 8.63, found: C, 64.24; H, 8.96.

4.1.13. 5,6-Dimethoxy-2-thiophenyl-3-((trimethylsilyl)-methyl)-1,4-benzoquinone, 19. A mixture of quinone **9a** (100 mg, 0.39 mmol), thiophenol (83.0 mg, 0.79 mmol) in 5 mL of THF was stirred at room temperature for 16 h. Evaporation of the solvent and flash column chromatography (hexanes/ethyl acetate, 3:1) gave the intermediate hydroquinone, which was oxidized with Ag_2O (218 mg, 0.867 mmol) in 10 mL of benzene. Filtration of the silver salts, evaporation of the solvent and purification by flash column chromatography (hexanes/ethyl acetate, 3:1) gave 75.0 mg (53%) of the product as a red solid: mp 61–62 °C; IR ($CDCl_3$) 1665, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.27–7.20 (m, 5H), 3.99 (s, 3H), 3.94 (s, 3H), 2.52 (s, 2H), 0.08 (s, 9H); LRMS *m/e* (CI, rel. intens.) 363 (MH^+, 100); Anal. Calcd for $C_{18}H_{20}O_4SSi$: C, 59.64; H, 6.12, found: C, 59.77; H, 5.94.

4.1.14. 5,6-Dimethoxy-2-(2-hydroxyethyl-1-thio)-3-trimethylsilylmethyl-1,4-benzoquinone, 21. A mixture of **9a** (100 mg, 0.39 mmol), mercaptoethanol (34.0 mg, 0.44 mmol) and 5 mL of absolute ethanol was stirred at room temperature for 15 min. Evaporation of the solvent followed by flash column chromatography (hexanes/ethyl acetate, 3:1) gave 110 mg of the intermediate hydroquinone, which was oxidized with Ag_2O (175 mg) in 10 mL of benzene at ambient temperature for 15 min. Purification of the quinone by flash column chromatography (hexanes/ethyl acetate, 3:2) furnished 92 mg (70%) of the product as a deep red oil in >96% purity (^1H NMR). IR ($CDCl_3$) 3500, 2960, 1670–1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.02 (s, 3H), 3.96 (s, 3H), 3.74 (q, $J=5.9$ Hz, 2H), 3.13 (t, $J=6.0$ Hz, 2H), 2.45 (s, 2H), 2.28 (t, $J=6.1$ Hz, 1H), 0.05 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 181.7, 180.2, 150.3, 145.2, 144.0, 135.3, 61.6, 61.2, 61.0, 37.3, 22.3, −0.6 (3C); HRMS (EI, rel. intens.) *m/e* calcd for $C_{14}H_{22}O_5SSi$: 330.0957, found: 330.0960; 330 (1), 149 (40), 73 (100); LRMS (CI, rel. intens.) 331 (MH^+, 100), 287 (22).

4.1.15. Heterocyclic quinone 23 and symmetrical dimer 22. Quinone **21** (80 mg, 0.24 mmol) was heated at reflux in 200 mL of acetonitrile/water (197:3) for 3 h. The solvent was removed and the residue oxidized with Ag_2O (183 mg, 0.73 mmol) in 10 mL of benzene/acetonitrile (9:1) at ambient temperature for 30 min. After filtration and removal of the solvent, purification by flash chromatography (chloroform/methanol, 97:3) gave 24.7 mg (40%) of **23** as a red solid: mp 108–109 °C; IR ($CDCl_3$) 2950, 2860,

1650 (br), 1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.70 (s, 2H), 4.03 (t, $J=5.5$ Hz, 2H), 4.02 (s, 3H), 3.94 (s, 3H), 3.18 (t, $J=5.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 181.1, 181.0, 148.1, 145.2, 143.6, 135.8, 71.2, 64.2, 61.4, 61.2, 33.5; MS (EI, rel. intens.) *m/e* 256 (M^+, 18), 213 (30), 185 (27), 129 (37), 85 (66), 69 (100), 57 (87); Anal. Calcd for $C_{11}H_{12}O_5S$: C, 51.55; H, 4.72, found: C, 51.41; H, 4.83. Further elution gave dimer **22** which was re-purified by flash column chromatography (chloroform/methanol, 20:1) to give 18.8 mg (30%) of **22** as an orange solid: mp 114–116 °C; IR ($CDCl_3$) 3540, 1660, 1575 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.99 (s, 6H), 3.98 (s, 6H), 3.78 (m, 4H), 3.22 (t, $J=5.4$ Hz, 4H), 2.96 (s, 4H), 2.60 (br s, 2H); HRMS (EI, rel. intens.) *m/e* calcd for $C_{22}H_{26}O_{10}S_2$: 514.0967, found: 514.0947; 514 (M^+, 5), 257 (7), 227 (18), 215 (21), 60 (100).

4.1.16. Reaction of quinone 9a with *n*-butylvinyl ether. Chromanol, 13. A mixture of quinone **9a** (100 mg, 0.39 mmol), *n*-butylvinyl ether (800 mg, 8.0 mmol) and 10 mL of acetonitrile/water (9:1) was heated at reflux for 2.5 h. The mixture was concentrated in vacuo and 25 mL of ether was added. The layers were separated and the aqueous layer extracted twice with ether (2×10 mL). The combined organic layers were washed twice with brine (2×5 mL) and dried over $MgSO_4$. Evaporation of the solvent and purification by flash column chromatography (hexanes/ethyl acetate, 3:1) gave 80 mg (72%) of **13** as a yellow oil. IR ($CDCl_3$) 3550, 2985, 1620–1580 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.46 (s, 1H), 5.26 (t, $J=2.7$ Hz, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.84 (dt, $J=9.5$, 6.7 Hz, 1H), 3.59 (dt, $J=9.6$, 6.6 Hz, 1H), 2.91–2.84 (m, 1H), 2.54–2.49 (m, 1H), 2.02–1.97 (m, 1H); 1.92–1.85 (m, 1H), 1.54 (quintet, $J=7.0$ Hz, 2H), 1.30 (sextet, $J=7.3$ Hz, 3H), 0.87 (t, $J=7.3$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 142.2, 141.2, 138.7, 138.5, 118.6, 108.9, 96.7, 68.0, 61.2, 60.8, 31.6, 26.4, 20.3, 19.2, 13.7; LRMS (EI, rel. intens.) *m/e* 282 (M^+, 21), 182 (100); Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85, found: C, 63.85; H, 7.80.

4.1.17. 5-Bromo-2,3-dimethoxy-6-((trimethylsilyl)-methyl)-1,4-benzoquinone, 14. Hydrogen bromide was bubbled through a methylene chloride solution (100 mL) of quinone **17**, (548 mg, 1.7 mmol) for five min. Nitrogen was then bubbled through the solution to purge any residual HBr. The solution was poured into 10% $NaHCO_3$, the layers were separated and the aqueous layer extracted with methylene chloride (3×15 mL). The solvent was evaporated in vacuo and the residue re-dissolved in benzene and treated with Ag_2O (1.2 g, 5.1 mmol) and K_2CO_3 (700 mg, 5.1 mmol) and stirred for 1.5 h. The mixture was filtered and concentrated in vacuo. The product was purified by flash column chromatography (florisil, hexanes/ethyl acetate, 10:1) to give 285 mg (50%) of the product as an orange solid: mp 54–55 °C; IR ($CDCl_3$) 1660, 1636, 1585 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.01 (s, 3H), 3.97 (s, 3H), 2.31 (s, 2H), 0.08 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 180.9, 176.5, 148.7, 144.4, 144.3, 128.4, 61.5, 61.2, 23.7, −0.4; HRMS (EI, rel. intens.) *m/e* calcd for $C_{12}H_{18}O_4SiBr$: 333.0158, found: 333.0143; 334 (0.6), 332 (0.5), 317 (0.6), 319 (0.6), 304 (1.4), 306 (1.1), 253 (2.5), 223 (1.2), 195 (0.7), 139 (3), 137 (3), 73 (100).

4.2. General procedure for the reaction of ((trimethylsilyl)methyl)-1,4-benzoquinones with alcohols

A solution of the benzoquinone in 10 mL of the alcohol was heated at reflux for the appropriate time. The alcohol was removed in vacuo and the intermediate hydroquinone was re-dissolved in benzene and oxidized by the addition of 20 equiv of Ag_2O at room temperature for 15 min. Filtration of the solution and evaporation of the solvent gave the crude product which was purified by flash column chromatography.

4.2.1. 2,3-Dimethoxy-5-(ethoxymethyl)-1,4-benzoquinone, 10a. Quinone **9a** was heated at reflux in absolute ethanol for 45 min. After oxidation and purification by flash column chromatography (silica gel, hexanes/ethyl acetate, 3:1), the title compound was isolated in 82% yield as an orange oil which solidified upon cooling: mp 38–39 °C; IR ($CDCl_3$) 1660, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.63 (t, $J=2.2$ Hz, 1H), 4.32 (d, $J=2.2$ Hz, 2H), 4.02 (s, 3H), 3.98 (s, 3H), 3.58 (q, $J=7.0$ Hz, 2H), 1.23 (t, $J=7.0$ Hz, 3H); LRMS (EI, rel. intens.) *m/e* 226 (95), 197 (69), 180 (100), 164 (49), 150 (41), 67 (60); Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24, found: C, 58.49; H, 6.32.

Further elution with hexanes/ethyl acetate, 2:1 gave 5% of the symmetrical dimer **11a** as an orange solid: mp 133–134 °C; IR ($CDCl_3$) 1660, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.39 (t, $J=0.8$ Hz, 1H), 4.06 (s, 3H), 4.00 (s, 3H), 2.63 (d, $J=0.8$ Hz, 2H); LRMS (EI, rel. intens.) *m/e* 362 (M^+, 8), 347 (13), 181 (14), 67 (100); Anal. Calcd for $C_{18}H_{18}O_8$: C, 59.67; H, 5.01: found: C, 59.38; H, 4.89.

4.2.2. 3-*n*-Butyl-6-(ethoxymethyl)-2-methoxy-1,4-benzoquinone, 10b. Quinone **9a** was heated in refluxing ethanol for 6 h according to the general procedure. Oxidation and purification by column chromatography (hexanes/ethyl acetate, 9:1) furnished 63% of the product as a yellow oil along with 11% of recovered starting material. IR ($CDCl_3$) 1660, 1655, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.70 (t, $J=2.1$ Hz, 1H), 4.32 (d, $J=2.1$ Hz, 2H), 3.98 (s, 3H), 3.59 (q, $J=7.0$ Hz, 2H), 2.42 (t, $J=7.0$ Hz, 2H), 1.28–1.41 (m, 4H), 1.25 (t, $J=7.0$ Hz, 3H), 0.91 (t, $J=7.1$ Hz, 3H); MS (CI, rel. intens.) *m/e* 253 (MH^+, 100), 239 (16), 209 (13); Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99, found: C, 66.58; H, 8.30.

Further elution using hexanes/ethyl acetate, 2:1 gave 5% of the symmetrical dimer **11b** as a yellow oil. IR ($CDCl_3$) 1670, 1655, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.44 (s, 2H), 3.98 (s, 2H), 2.63 (s, 4H), 2.40 (t, $J=7.2$ Hz, 4H), 1.32–1.37 (m, 8H), 0.90 (t, $J=7.0$ Hz, 6H); HRMS (EI, rel. intens.) *m/e* calcd for $C_{24}H_{30}O_6$: 414.2042, found: 414.2044; 205 (26), 177 (14), 91 (31), 55 (100).

4.2.3. 3-*n*-Butyl-5-(ethoxymethyl)-2-methoxy-1,4-benzoquinone, 10c. According to the general procedure, **9c** was heated at reflux in absolute ethanol for 45 min. Oxidation and purification by flash column chromatography (hexanes/ethyl acetate, 9:1) furnished 67% of the title compound as a yellow oil that solidified upon cooling: mp 39–40 °C; IR ($CDCl_3$) 1660, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.62 (t, $J=$

2.1 Hz, 1H), 4.33 (d, J=2.1 Hz, 2H), 4.02 (s, 3H), 3.59 (q, J=7.0 Hz, 2H), 2.41 (br. triplet, J=7.1 Hz, 2H), 1.38–1.32 (m, 4H), 1.25 (t, J=7.0 Hz, 3H), 0.91 (t, J=7.0 Hz, 3H); LRMS (CI, rel. intens.) *m/e* 253 (MH^+, 100), 209 (53), 137 (36); Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99, found: C, 66.51; H, 7.94.

Further elution with hexanes/ethyl acetate, 2:1) gave 7% of the symmetrical dimer **11c** as a yellow oil. IR ($CDCl_3$) 1670, 1650, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.36 (s, 2H), 4.01 (s, 6H), 2.62 (s, 4H), 2.43 (t, J=7.0 Hz, 4H), 1.30–1.43 (m, 8H), 0.92 (t, J=7.0 Hz, 6H); HRMS (EI, rel. intens.) *m/e* calcd for $C_{24}H_{30}O_6$ 414.2042, found: 414.2066; 209 (38), 207 (59), 165 (41), 55 (100).

4.2.4. 2,3-Dimethoxy-5-(*iso*-propoxymethyl)-1,4-benzoquinone, 10d. Quinone **9a** was heated in refluxing *iso* propanol for 10 h according to the general procedure. Oxidation and purification by column chromatography (hexanes/ethyl acetate, 3:1) gave 65% of the product as a red oil. IR ($CDCl_3$) 1660, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.66 (t, J=2.3 Hz, 1H), 4.32 (d, J=2.3 Hz, 2H), 4.02 (s, 3H), 3.98 (s, 3H), 3.67 (heptet, J=6.1 Hz, 1H), 1.19 (d, J=6.1 Hz, 6H); LRMS (EI, rel. intens.) *m/e* 240 (M^+, 6), 198 (38), 180 (23), 155 (25), 153 (39), 67 (100); Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71: found: C, 59.63; H, 6.83.

4.2.5. 5-(*tert*-Butoxymethyl)-2,3-dimethoxy-1,4-benzoquinone, 10e. Quinone **9a** was heated in *tert*-butanol at reflux for 44 h according to the general procedure. Oxidation and purification by flash column chromatography (hexanes/ethyl acetate, 3:1) gave 45% of the title compound as a red oil. IR ($CDCl_3$) 1660, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.66 (t, J=2.3 Hz, 1H), 4.27 (d, J=2.3 Hz, 2H), 4.02 (s, 3H), 3.98 (s, 3H), 1.23 (s, 9H); LRMS (EI, rel. intens.) *m/e* 254 (M^+, 1), 198 (21), 153 (24), 57 (100); Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.14: found: C, 61.81; H, 7.39.

4.2.6. Reaction of benzoquinone 9a with water. 2,3-Dimethoxy-5-hydroxymethyl-1,4-benzoquinone, 10f. Quinone **9a** was heated in 10 mL of acetonitrile/water (9:1) at reflux for 1.5 h. Following oxidation with Ag_2O according to the general procedure and flash column chromatography (chloroform/methanol, 97:3) 18% of the title compound was isolated as an orange solid: mp 72–73 °C; IR ($CDCl_3$) 3610, 3520, 2960, 1660, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.61 (s, 1H), 4.53 (s, 2H), 4.03 (s, 3H), 3.99 (s, 3H), 2.10 (br s, 1H); LRMS (EI, rel. intens.) *m/e* 198 (M^+, 12), 180 (11), 150 (17), 84 (47), 67 (67), 55 (100); Anal. Calcd for $C_9H_9O_5$: C, 54.55; H, 5.09, found: C, 54.28; H, 5.00. In addition to **10f**, 67% of the symmetrical dimer **11 a** was isolated.

Reaction of quinone **9a** in 95:5 acetonitrile/water for 8 h gave 22% of xanthen **12** after flash column chromatography (hexanes/ethyl acetate, 5:2) as a yellow solid: mp 144–145 °C; ^1H NMR ($CDCl_3$) δ 6.31 (s, 1H), 5.39 (s, 1H), 3.98 (s, 6H), 3.96 (s, 3H), 3.93 (s, 3H), 3.22 (dd, J=9.8, 6.6 Hz, 1H), 2.90 (dd, J=16.8, 6.7 Hz, 1H), 2.85 (dd, J=16.7, 10.0 Hz, 1H), 1.41 (d, J=14.9 Hz, 1H), 1.33 (d, J=14.8 Hz, 1H), 0.12 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 193.9, 193.0, 147.2, 146.4, 142.9, 141.2, 139.4, 113.5, 108.1, 81.9, 61.3, 60.9, 60.7, 60.5, 51.8, 27.9, 26.9, 0.0 (3C); IR ($CDCl_3$) 3545, 1695, 1600 cm^{-1}; MS (CI, rel. intens.) *m/e* 437 (MH^+, 100), 183 (35); Anal. Calcd for $C_{21}H_{28}O_8Si$: C, 57.78; H, 6.47, found: C, 57.40; H, 6.15.

Further with chloroform/methanol (1:1) followed by oxidation of the resulting product and purification by flash chromatography (chloroform/methanol, 97:3) gave 46% of the symmetrical dimer **11a** and 12% of the quinone **10f**.

4.2.7. 5-(Acetoxymethyl)-2,3-dimethoxy-1,4-benzoquinone, 10g. Sodium acetate (5 equiv) and quinone **9a** were dissolved in 10 mL of acetic acid and heated at reflux for 30 min. The acetic acid was evaporated with the aid of toluene and the residue was filtered through a short pad of silica gel, eluted with ethyl acetate. The crude hydroquinone was oxidized with Ag_2O and purified by flash column chromatography (hexanes/ethyl acetate, 3:1) to provide 79% of **10g** as an orange solid: mp 51–52 °C; IR ($CDCl_3$) 1755, 1660, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.50 (t, J=1.9 Hz, 1H), 4.97 (d, J=2.0 Hz, 1H), 4.03 (s, 3H), 4.00 (s, 3H), 2.14 (s, 3H); LRMS (CI, rel. intens.) *m/e* 241 (MH^+, 100), 183 (63); Anal. Calcd for $C_{11}H_{12}O_6$: C, 55.00; H, 5.04, found: C, 55.10; H, 4.96. In pure acetic acid the reaction gave 54% of **10g** after 4 h at reflux.

4.2.8. 2,3-Dimethoxy-6-ethoxymethyl-5-trimethylsilyl-1,4-benzoquinone, 18. The quinone **17** (67 mg, 0.21 mmol) was dissolved in 8 mL of absolute ethanol and then heated to reflux for 2 h according to the general procedure. Oxidation of the mixture followed by column chromatography (silica gel, hexanes/ethyl acetate, 4:1) gave 17 mg (27%) of the title compound as an orange oil. IR ($CDCl_3$) 1650, 1587 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.30 (s, 2H), 3.98 (s, 3H), 3.96 (s, 3H), 3.52 (q, J=7.1 Hz, 2H), 1.19 (t, J=7.1 Hz, 3H), 0.30 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 188.6, 183.3, 149.3, 148.6, 145.4, 143.8, 66.5, 63.3, 61.0, 60.9, 15.1, 0.8; HRMS CI (rel. intens.) *m/e* calcd for $C_{14}H_{23}O_5Si$: 299.1315, found: 299.1311, 300 (20), 299 (100), 284 (15), 283 (83), 255 (40), 183 (8).

4.2.9. Bis(5-bromo-2,3-dimethoxy-6-methylene-1,4-benzoquinone), 16 and 2-bromo-3-ethoxymethyl-5,6-dimethoxy-1,4-benzoquinone, 15. According to the general procedure, a solution of quinone **14** (53 mg, 0.16 mmol) in 10 mL of absolute ethanol was heated to reflux for 20 min. Oxidation with Ag_2O followed by flash column chromatography (silica gel, hexanes/ethyl acetate, 3:1) gave 4 mg (10%) of the symmetrical dimer, **16**, as an orange solid along with 27 mg (55%) of the ethanol addition product **15** as an orange oil.

Dimer **16**: mp 172–175 °C (decomp.); IR ($CDCl_3$) 1664, 1637 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.02 (s, 6H), 4.00 (s, 6H), 2.97 (s, 4H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 180.7, 176.4, 145.1, 144.2, 134.5, 61.6, 61.4, 28.7; HRMS (CI, rel. intens.) *m/e* calcd for $C_{18}H_{16}O_8{}^{81}Br^{79}Br$: 519.9191, found: 519.9224; 523 (47), 521 (62), 519 (26), 446 (14), 445 (71), 444 (25), 442 (21), 441 (40), 365 (53), 364 (23) 363 (100), 361 (21), 263 (55), 261 (54), 183 (44), 175 (47), 173 (52).

Quinone **15**. IR ($CDCl_3$) 1667, 1638, 1600 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.49 (s, 2H), 4.05 (s, 3H), 3.98 (s, 3H), 3.59 (q, $J=7.1$ Hz, 2H), 1.21 (t, $J=7.1$ Hz, 3H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 180.3, 176.8, 145.3, 144.1, 141.3, 137.4, 67.2, 65.6, 61.5, 61.3, 15.1; HRMS (EI, rel. intens.) *m/e* calcd for $C_{11}H_{13}O_5Br$: 303.9947, found: 303.9968; 306 (4), 304 (4), 288 (3), 286 (3), 277 (13), 275 (14), 260 (28), 258 (22), 247 (10), 245 (9), 233 (13), 219 (6), 217 (7), 197 (10), 179 (6), 119 (32), 117 (34), 66 (80), 53 (100).

4.2.10. ((2-Anthracenethio)ethyl)-4-hydroxy-3-methoxy-4-((3-trimethylsilyl)-1-propynyl)-2-cyclobuten-1-one, 30. To a cooled (−78 °C) solution of propargyltrimethylsilane (0.15 mL, 0.9 mmol) in 10 mL of dry THF was added *n*-BuLi (0.83 mmol) via syringe. The resulting solution was stirred for 5 min at −78 °C and then added via cannula to a cold solution of cyclobutenedione[15] **29** (200 mg, 0.58 mmol) in 40 mL of dry THF. Aqueous work-up after five min gave the crude product as a yellow oil. Purification by radial chromatography (silica gel, hexanes/ethyl acetate, 8:2) afforded 157 mg (63%) of the title product as an orange oil. IR (neat) 3308, 1758, 1622 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.93 (d, $J=8.9$ Hz, 2H), 8.44 (s, 1H), 7.98 (d, $J=8.4$ Hz, 2H), 7.60–7.57 (m, 2H), 7.50–7.47 (m, 2H), 4.4 (br s, 1H), 4.02 (s, 3H), 3.09 (m, 2H), 2.18 (m, 2H), 1.58 (s, 2H), 0.08 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 187.9, 181.6, 134.6, 131.6, 128.9, 128.8, 128.2, 126.9, 126.6, 126.0, 125.2, 89.7, 82.7, 73.1, 59.3, 33.2, 22.9, 7.4, −2.1; HRMS (EI, rel. intens.) *m/e* calcd for $C_{27}H_{28}O_3SSi$: 460.1528, found: 460.1546; 462 (12), 461 (10), 460 (54), 325 (13), 252 (31), 251 (100), 210 (12), 179 (19), 178 (19), 165 (17), 161 (16), 73 (57).

4.2.11. 2-Methoxy-3-(2-anthracenethio)ethyl)-5-((trimethylsilyl)methyl)-1,4-benzoquinone, 31. A solution of **30** (129 mg, 0.28 mmol) in 10 mL of acetonitrile was heated to reflux for 1 h. The solution was cooled to room temperature and the solvent was removed in vacuo. Purification by radial chromatography (silica gel, hexanes/ethyl acetate, 10:1) yielded 82 mg (64%) of the title compound as a bright red oil. IR (neat) 1644, 1598, 1516 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.91 (d, $J=8.8$ Hz, 2H), 8.46 (s, 1H), 8.00 (d, $J=8.5$ Hz, 2H), 7.6–7.46 (m, 4H), 6.12 (s, 1H), 3.66 (s, 3H), 2.96 (m, 2H), 2.64 (m, 2H), 1.89 (s, 2H), −0.04 (s, 9H); ^{13}C NMR (500 MHz, $CDCl_3$) δ 186.9, 183.1, 155.4, 149.6, 134.4, 131.7, 129.2, 128.92, 128.89, 128.79, 127.6, 126.9, 126.5, 125.2, 60.6, 35.2, 24.0, 21.1, −1.6; HRMS (CI, rel. intens.) *m/e* calcd for $C_{27}H_{31}O_3SiS$: 463.1763, found: 463.1695; 464 (15), 163 (100), 461 (28), 255 (15), 253 (35), 211 (39), 179 (79), 112 (21), 97 (25), 95 (19), 91 (28), 85 (50), 83 (34), 81 (47).

4.3. General procedure for the measurement of reaction rates of (trialkylsilyl)methyl)-1-4-benzoquinones in EtOD-d_6

The quinone (10. mg) was dissolved in 0.50 mL of EtOD-d_6 in an NMR tube. To this solution was added 5 μL of dry *p*-xylene to serve as an internal standard. Proton NMR spectra of the solution were taken every 5–7 min on a 300 MHz instrument at a constant temperature of 70 °C. The integral of the reactant (cm) was divided by the integral of the methyl peak of *p*-xylene (cm) to standardize the measurements. The relative concentration of the reactant was taken to be the fraction of the initial standardized measurement (time 0=1.00). The natural log of the relative concentration was plotted against time. The k_{obs} was found from the slope of the line and the half life for the reaction was found by dividing the natural log of 2 by k_{obs}. An alternate procedure was required for the measurement of the reaction rate of the triphenylsilyl-substituted quinone **9d** due to the low solubility in ethanol. In this case, a solution of 40 mg of quinone **9d** was dissolved in 50 mL of absolute ethanol and heated to 70 °C in a jacketed flask equipped with a circulating bath. 20 μL of toluene was added to the solution to act as an internal standard. Samples of the solution were taken approximately every 3 h and diluted with acetonitrile for analysis by HPLC. A Hewlett–Packard HP 1050 equipped with a YMC ODS-AQ column was used for the analysis. The mobile phase consisted of acetonitrile/water containing 0.1% phosphoric acid. As with the ^1H NMR experiments, the peak area of the starting material was divided by the peak area of the toluene peak to standardize the measurement. The relative concentration of quinone **9d** was calculated in the same manner as the other quinones studied by NMR.

4.4. Procedure for the study of quinone 31 with supercoiled DNA

Ten microliters of a solution of 2 mg of quinone **31** in 1 μL of $CHCl_3$ was put into a microfuge tube. The solution was then concentrated to dryness in vacuo. To the residue was added 1.1 mL of ΦX174 supercoiled DNA and 18.9 μL of TE buffer (10 mM tris·HCl, 1mM EDTA, pH 7.2). The mixture was incubated at 51 °C for 21 h. The samples which contained ethidium bromide were composed of 10 μL of an ethidium bromide solution (1.4 μL of ethidium bromide in 28.6 μL of TE buffer), 1.1 μL of DNA and 8.9 μL of TE buffer. After the incubation, the mixtures were cooled to 0 °C and 2 μL of a loading buffer (0.25% bromophenol blue, 40% (w/v) sucrose in water) was added. A 7 μL portion of this mixture was loaded onto a 1% agarose gel and developed for 1 h at 101 V.

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