((Trimethylsilyl)methyl)-1,4-benzoquinones. Generation and Trapping of *o*-Quinone Methides

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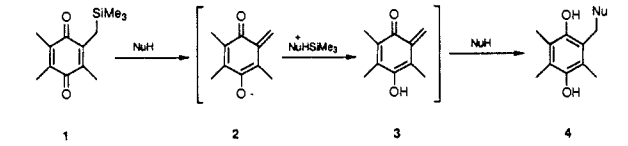
In this communication we report the conversion of ((trimethylsilyl)methyl)-1,4-benzoquinones **1** to reactive electrophilic *o*-quinone methides **3**, a transformation that takes place when **1** is treated with various nucleophilic species under neutral conditions (Scheme I). This unusual reaction is envisaged to involve nucleophilic attack on the trimethylsilyl group of **1** to give the corresponding vinylogous enolate anion **2** which leads to *o*-quinone methide **3** upon *O*-protonation. These reactive intermediates then proceed to hydroquinones **4** or related products via Michael additions or cycloadditions to the enone moiety. To our knowledge, no direct precedent for the conversion of **1** to **3** has previously been reported.[1] This is of particular interest since the chemistry of *o*-quinone methides of structural type **3**, i.e., those having a hydroxyl or alkoxy group in conjugation with the methylene group, have not received extensive attention.[2]

Besides synthetic applications, the electrophilic character of *o*-quinone methides of structural type **3** has important biological implications. Specifically, such intermediates have been suggested as alkylating agents generated in vivo from appropriately substituted quinones in a bioreductive activation process.[3] *The results presented here compliment evidence that such intermediates are electrophilic alkylating agents.*[4]

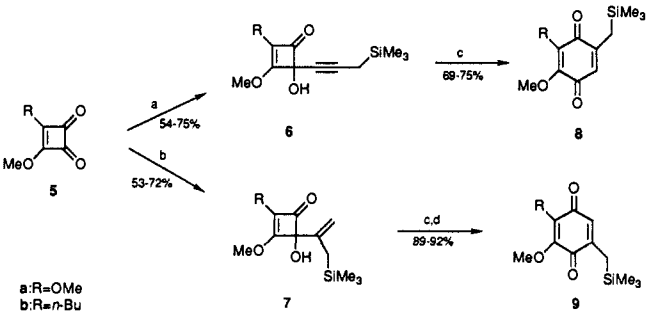
Synthesis of the ((trimethylsilyl)methyl)quinones **8** and **9** rests upon the previously reported ring expansion of cyclobutenones to quinones and related aromatic compounds (Scheme II).[5-7] These specific examples were prepared starting with the cyclobutenediones **5a,b**, which were converted to **6a,b** and **7a,b**, respectively, upon treatment with 1-lithio-3-(trimethylsilyl)propyne and 2-lithio-3-(trimethylsilyl)propene in THF at −78 °C.[8] Thermolysis of **6a** and **6b** in *p*-xylene at reflux gave the respective quinones **8a** and **8b** in good yields. Analogously, thermolysis of **7a** and **7b** gave the corresponding hydroquinones which were converted directly to the quinones **9a** and **9b** upon oxidative workup (Ag_2O/*p*-xylene).[9]

A set of reactions illustrating the intermediacy of the *o*-quinone methides and their ease of formation is outlined in Scheme III. When ethanolic solutions of the quinones **10** were heated at reflux for 0.5–6 h and the reaction worked up under oxidative conditions,

Scheme I

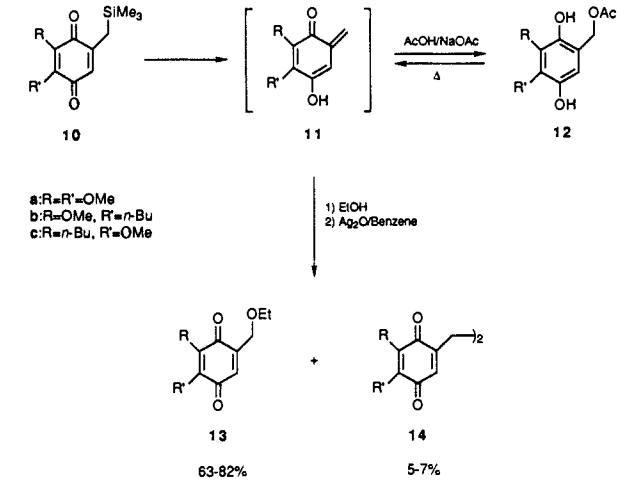


Scheme II

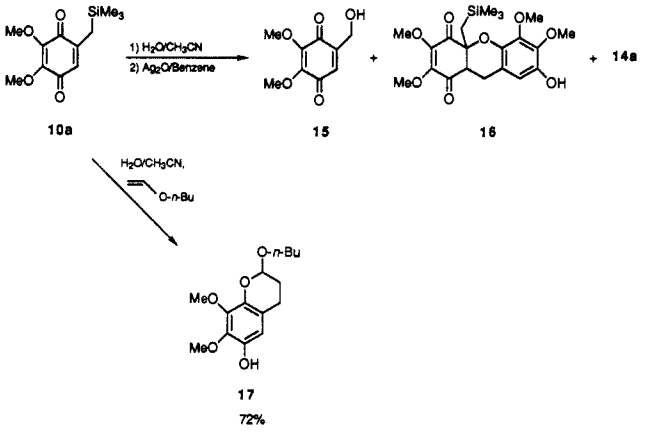


Reagents: (a) 1-Lithio-3-(trimethylsilyl)propyne,THF, -78 °C; (b) 2-Lithio-3-(trimethylsilyl)-propen, THF, -78 °C; (c) *p*-Xylene, reflux; (d) Ag_2O, *p*-Xylene, rt.

Scheme III



Scheme IV



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(4) For examples of both nucleophilic and electrophilic trapping of an *o*-quinone methide generated reductively from anthracyclines, see: (a) Egholm, M.; Koch, T. H. *J. Am. Chem. Soc.* **1989**, *111*, 8291–8293. (b) Kleyer, D. L.; Koch, T. H. *J. Am. Chem. Soc.* **1983**, *105*, 5154–5155.

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(9) The microanalytical and/or spectral (IR, LRMS, HRMS, ^1H and ^{13}C NMR) data for all new compounds reported here are in agreement with their assigned structures.

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the corresponding ethoxymethyl derivatives **13** were isolated (63–82%) along with minor amounts (5–7%) of the symmetrical dimer **14**. Interestingly, these reactions also proceed at ambient temperatures but at a slower rate. For example, a solution of **10a** in absolute ethanol stirred at room temperature for 24 h resulted in **13a** and **14a** in 45% and 22% yields, respectively.

These data agree with the proposed *o*-quinone methides **11** as intermediates. In this regard, the alkoxyquinones are envisaged to arise via Michael addition of ethanol to the enone followed by oxidation of the resulting hydroquinone.[10] The dimer **14** could result from a number of possible pathways, but an attractive possibility involves Diels–Alder dimerization of the *o*-quinone methides **11** to the corresponding spiropyrans.[11] The symmetrical dimer, in its half-reduced oxidation state, would then result directly from an intramolecular elimination. Subsequent oxidation of this would then give the symmetrical diquinone dimer **14**.

Further evidence for the *o*-quinone methide intermediate comes from the observations that **10a** gave the hydroquinone **12a** (85%) in refluxing glacial acetic acid/sodium acetate and that this hydroquinone gave a similar product distribution as observed for **10a** when subjected to refluxing ethanol. Thus, the conversion of **10a** and **12a** to **13a** and **14a** strongly suggests the *o*-quinone methide **11a** as a common transient intermediate.

Additional studies illustrating the synthetic utility of the ((trimethylsilyl)methyl)quinone/*o*-quinone methide conversion are given in Scheme IV. Thermolysis of **10a** in 5% aqueous acetonitrile followed by oxidative workup afforded three products: the alcohol **15** (12%), the xanthen derivative **16** (22%), and the ethylene dimer **14a** (46%). The xanthen derivative is viewed as arising from the Diels–Alder cycloaddition of the quinone **10a** with the *o*-quinone methide **11a**.[12] Interestingly, the amount of water had a dramatic effect on the product distribution. For example, when 10% rather than 5% aqueous acetonitrile was employed, a 67% yield of **14a** and 18% of **15** were isolated. Only traces of **16** were detected. These results are consistent with a mechanism in which water functions as the reagent to induce *o*-quinone methide formation (Scheme I, NuH = H_2O).[13] At low water concentration (5%), the concentration of the *o*-quinone methide is also low, and thus it is easily intercepted by an unreacted quinone in a Diels–Alder cycloaddition to give **16**. As the water concentration is increased (10%) so follows the *o*-quinone methide concentration, and dimerization as described previously takes place to give **14a**.

Finally, an example of Diels–Alder trapping of the *o*-quinone methide is illustrated by the synthesis of **17**. That is, generation of the *o*-quinone methide in 10% aqueous acetonitrile in the presence of excess *n*-butyl vinyl ether gave the chromanol **17** in 72% yield.[14,15]

In conclusion, the most significant aspects of this study include the following: (a) ((trimethylsilyl)methyl)-1,4-benzoquinones **1** function as excellent precursors to *o*-quinone methide intermediates **3**; (b) the *o*-quinone methides **3** do not undergo tautomerization, which suggests that ketonization is slower than nucleophilic addition; (c) the position of the trimethylsilyl group in **1** dictates the specific quinone methide formed; and (d) the conversion of **1** to **3** can be accomplished under mild and neutral conditions and thus allows the synthetic utilization of these reactive electrophilic intermediates.

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Supplementary Material Available: A table of spectroscopic data (IR, MS, ^1H and ^{13}C NMR) for compounds **6–17** (2 pages). Ordering information is given on any current masthead page.

(10) Subjecting **10a** to isopropyl alcohol (10 h, reflux) furnished the corresponding isopropoxymethylquinone and **14a** in 67% and 10% yields, respectively (oxidative workup). Analogously, the reaction of **10a** in *tert*-butyl alcohol (44 h) gave 45% of the *tert*-butoxymethylquinone and 22% of **14a**.

(11) For examples of the formation of unsymmetrical *o*-quinone methide dimers see: (a) Chauhan, M. S.; Dean, F. M.; Matkin, D.; Robinson, M. L. *J. Chem. Soc., Perkin Trans. 1* **1973**, 120–125. (b) Chauhan, M. S.; Dean, F. M.; McDonald, S.; Robinson, M. S. *J. Chem. Soc., Perkin Trans. 1* **1973**, 359–363.

(12) For examples of similar dimerizations see: (a) Smith, L. I.; Tess, R. W. H.; Ullyot, G. E. *J. Am. Chem. Soc.* **1944**, *66*, 1320–1323. (b) Chandrasenan, K.; Thomson, R. H. *J. Chem. Soc. C* **1966**, 123–124. (c) References 2d and 2e.

(13) Heating **10a** in dry benzene at reflux for 90 h gave >98% of recovered starting material.

(14) A 74% yield of **17** was obtained when **12a** was heated in refluxing acetonitrile in the presence of excess *n*-butyl vinyl ether.

(15) For trapping of *o*-quinone methides in Diels–Alder reactions, see: (a) Bolon, D. A. *J. Org. Chem.* **1970**, *35*, 3666–3670. (b) References 1 and 11a.

Synthesis and Structure of Azo Dyes with Short, Intramolecular Selenium–Nitrogen Contacts

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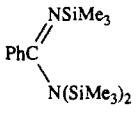
Recently there has been considerable interest in the synthesis and structures of both organic and inorganic selenium–nitrogen (Se–N) compounds. Some important milestones include the structural characterization of (a) dimers of the cyclic seven-π-electron radicals 1,2,4,6-selenatriazinyl, $(Ph_2C_2N_3Se)_2$,[1] 1,2,3,5-diselenadiazolyl, $(PhCN_2Se_2)_2$,[2] and 1,2,4-triselena-3,5-diazolylium, $(Se_3N_2^{\bullet+})_2$,[3] and (b) metal complexes of the acyclic, binary Se–N anions, Se_3N^- and $Se_2N_2^{-\bullet}$.[4,5] We have prepared eight-membered 1,5-$P_2^VN_4Se_2$ rings by the cyclocondensation reaction of $Ph_2P(NSiMe_3)[N(SiMe_3)_2]$ with organoselenium trichlorides.[6] In an attempt to obtain the unknown 1,5-$C_2N_4Se_2$ ring, we have found that the reaction of $PhC(NSiMe_3)[N(SiMe_3)_2]$ (**1**) with $RSeCl_3$ (R = Me, Ph) unexpectedly produces the *intensely colored* diazenes **2a** and **2b** rather than the expected eight-membered ring. The X-ray structure of **2a** reveals a nearly planar structure in which the hypervalent selenium atoms are connected by short, intramolecular contacts (ca. 2.65 Å) to one nitrogen of the azo group. A better synthesis of **2b** (and its sulfur analogue) involves the reaction of **1** with 3 mol of PhECl (E = S, Se).



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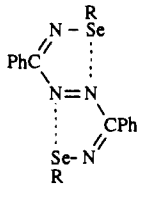

2a (R = Me), **2b** (R = Ph)

The dark red azo compound **2a** was obtained in 44% yield by the slow addition of **1** to an equimolar amount of $MeSeCl_3$ in acetonitrile at 23 °C.[7,8] An X-ray structural analysis confirmed

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