A Mechanistic Study of the Thermal Disproportionation Reaction of Quinone Monoketals

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Received June 1, 1987

Thermolysis of quinone monoketals **1a–d** at 180 °C leads to disproportionation to the *p*-alkoxyphenols **2a–d** and the carbonyl compounds derived from the alcohol moiety of the ketal. The thermolysis of 4,4-dimethoxy-2,5-cyclohexadienone (**1a**) followed first-order kinetics, and the rate of reaction decreased by a factor of 3.6 when the methoxy groups were replaced with methoxy-d_3 groups. The suggested mechanism for the reaction involves reversible dissociation of **1a** into a *p*-methoxyphenoxy–methoxy radical pair, followed by rate-controlling hydrogen atom transfer to give *p*-methoxyphenol and formaldehyde. Although **1a** has a half-life of about 4 h at 180 °C, the monoethylene glycol ketal of benzoquinone was recovered in >90% yield after heating for 24 h at the same temperature. Finally, acid-catalyzed exchange reactions of 3,3,6,6-tetramethoxy-1,4-cyclohexadiene with alcohols furnished a convenient route to quinone bisketals not obtainable in good yield via anodic oxidation.

Introduction

In recent years, the methods of preparation, chemical reactivity, and synthetic utility of *p*-quinone monoketals have been extensively studied.[1] One limitation associated with the use of quinone monoketals in organic synthesis is their facile reduction to the hydroquinone oxidation state. Electron-transfer reductions by organocopper, alkyllithium, and Grignard reagents[2–4] are well-known processes. Less familiar are the thermal and acid-catalyzed reductions of quinone monoketals, which occur incidental to the desired cycloaddition reactions[5–7] (Scheme I) and detract from their synthetic utility. The mechanism of the thermal disproportionation reaction of quinone monoketals to their respective *p*-alkoxyphenols was of major interest to us. We report herein the delineation of major mechanistic points of the thermal disproportionation reactions of 4,4-dimethoxy–2,5-cyclohexadienone (**1a**) and related quinone monoketals.

Preparative Thermolyses

The major product isolated from thermolysis of **1a** at 180 °C was the phenol **2a** (80%). Formaldehyde was not established as the oxidation product from thermolysis of **1a**; however, benzaldehyde was isolated as its (2,4-dinitrophenyl)hydrazone derivative from thermolysis of **1b**. In a degassed solvent, the thermolyses are clean; however, more complex product mixtures result from reactions conducted in the presence of oxygen. Thermolysis of the mixed monoketals **1b–d** gave mixtures of phenols (**2b**/**2a** = 30:70; **2c**/**2a** = 45:55; **2d**/**2a** = 35:65). The low selectivity of phenols obtained from thermolysis of the above monoketals indicates that the relative strength of the carbonyl group formed in these disproportionation reactions is not an important consideration.

Scheme I. Illustrative Acid-Catalyzed and Thermal Disproportionation Reactions of Quinone Monoketal

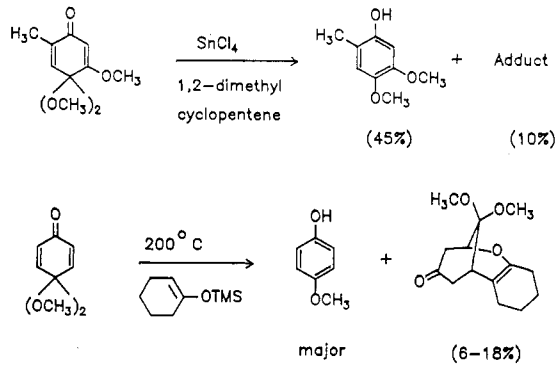
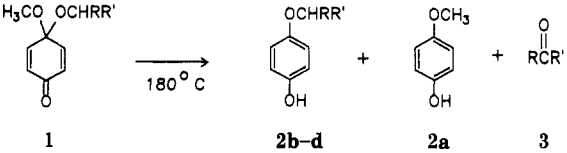


Table I. Kinetics of Thermolysis of 1a and 1a-d_6

entry[a]	compd	solv	temp, °C	conc, M	10^5 k, s^{-1}
1	**1a**	THF	180	0.034	6.8_1
2	**1a**	THF	180	0.167	6.7_8
3	**1a**[b]	THF	180	0.33	6.6_4
4	**1a**[b]	THF	180	0.16	6.8_5
5	**1a**[c]	THF	180	0.16	6.6_5
6	**1a**	CH_3CN	180	0.16	5.1_3
7	**1a**-d_6	THF	180	0.034	1.8_6
8	**1a**	THF	190	0.16	$18._1$
9	**1a**	THF	165	0.16	2.8

[a] The rate constants reported are averages of two or three runs. [b] Concentration of added *p*-methoxyphenol = 0.016 M. [c] Concentration of added *p*-methoxyphenol = 0.033 M.



a, R = R′ = H; **b**, R = H, R′ = Ph; **c**, R = H, R′ = CH_3; **d**, R = R′ = CH_3

Mechanistic Studies

The kinetics of thermolysis of **1a** were studied first since the order of the reaction would exclude several mechanistic

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(2) Such reductions have been well-studied in the case of *p*-quinol derivatives. For examples, see: (a) Wessely, F.; Holzer, L.; Vilcsek, H. *Monatsh. Chem.* **1952**, *83*, 1252. (b) Wessely, F.; Holzer, L.; Vilcsek, H. *Monatsh. Chem.* **1953**, *84*, 655. (c) Polansky, O.; Schinzel, E.; Wessely, F. *Monatsh. Chem.* **1956**, *87*, 24. (d) For recent mechanistic studies, see: Miller, B.; Haggerty, J. G. *J. Chem. Soc., Chem. Commun.* **1984**, 1617.

(3) (a) Nilsson, A.; Ronlân, A. *Tetrahedron Lett.* **1975**, 1107. (b) Henton, D. R.; Anderson, D. K.; Manning, M. J.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 3422. (c) Pelter, A.; Ward, R. S.; Rao, R. R. *Tetrahedron Lett.* **1983**, *24*, 621. (d) Pelter, A.; Ward, R. S.; Rao, R. R. *Tetrahedron* **1985**, *41*, 2933. (e) Semmelhack, M. F.; Keller, L.; Sato, T.; Speiss, E. J. *J. Org. Chem.* **1982**, *47*, 4382. (f) Semmelhack, M. F.; Keller, L.; Sato, T.; Speiss, E. J.; Wulff, W. *J. Org. Chem.* **1985**, *50*, 5566.

(4) For a mechanistic study of additions of organolithium reagents to *p*-quinone monoketals, see: (a) Liotta, D.; Saindane, M. Waykole, L. *J. Am. Chem. Soc.* **1983**, *105*, 2922. (b) Hunig, S.; Wehner, G. *Chem. Ber.* **1980**, *113*, 324.

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(6) Duthaler R.; Wegmann, U. H.-U. *Helv. Chim. Acta* **1984**, *67*, 1760.

(7) See also: DeSchepper, R.; Swenton, J. S. *Tetrahedron. Lett.* **1985**, 4831.

0022-3263/87/1952-5360$01.50/0

possibilities. These determinations were conducted by heating degassed solutions of **1a** in sealed ampules and monitoring the formation of *p*-methoxyphenol by UV spectroscopy. The data obtained from thermolysis of **1a** are summarized in Table I. A plot of ln $[\mathbf{1a}]_0/[\mathbf{1a}]_t$ versus time showed good linearity (correlation coefficient 0.995) up to ca. 65% conversion of **1a** to **2a**, but curvature was observed after this point. Analysis of the kinetic data as a second-order reaction also gave reasonably linear plots; however, the calculated rate constant varied by a factor of about 2.5 for three different initial concentrations of **1a** (0.034, 0.17, 0.33 M).

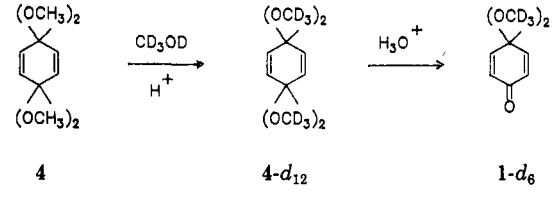
$$[\mathbf{1a}]_t = [\mathbf{1a}]_0 e^{-kt} \quad (1)$$

(where k is the first-order rate constant)

A second reaction pathway competing with the unimolecular thermolysis of **1a** during the latter stages of the reaction would account for the nonlinearity of the kinetic plots in the second half-life. One possibility is that the *p*-methoxyphenol formed in the reaction serves as an acid catalyst for the conversion **1a** → **2a**. However, addition of up to 20% of *p*-methoxyphenol relative to the starting concentration of **1a** (entries 3–5) did not alter the initial rate or the observed rate constant for the reaction. A second possibility was that the formaldehyde formed in the reaction was causing deviation from first-order behavior. The results from addition of paraformaldehyde to the kinetic run at zero time were not reproducible but did result in an apparent increase in the reaction rate.

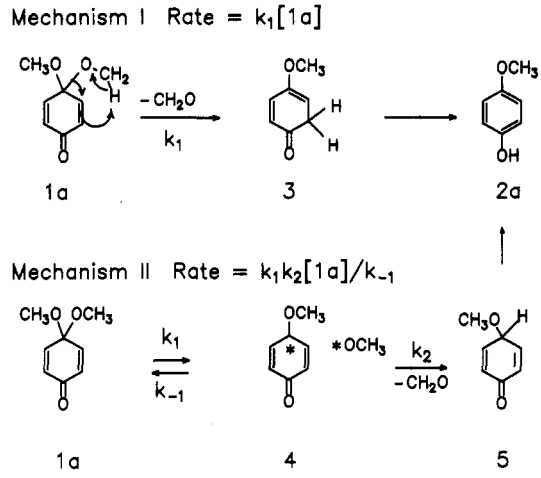
The data above indicate that the thermal reaction of **1a** to produce *p*-methoxyphenol is not autocatalyzed by the phenol. Although the thermolysis of **1a** is complicated by formaldehyde formation, the kinetic results do exclude a second-order mechanism for the decomposition. In addition, the nearly identical rate constants obtained for the thermolysis of **1a** conducted in tetrahydrofuran (Z = 61.1)[8,9] and acetonitrile (Z = 71.3)[8,9] suggest a nonpolar transition state for the reaction. The apparent activation parameters for the reaction calculated[11] from the data of Table I were $\Delta H^{\ddagger} = 28 \pm 2$ kcal/mol and $\Delta S^{\ddagger} = -16 \pm 5$ eu.

Since several mechanistic possibilities for the disproportionation could involve the hydrogen of the methoxy group in the rate-determining step, the kinetic isotope effect for the thermolysis was measured. Although **1a**-d_6 could be prepared by anodic oxidation of 1,4-dimethoxybenzene-d_6 in methanol-d_4 followed by acid hydrolysis, a less expensive alternative was investigated. When **4** in methanol-d_4 was treated with a trace of acetic acid, ketal exchange occurred, affording **4**-d_{12} (>96% d_{12} by ^{1}H NMR analysis after three exchanges). The tetramethoxy compound **4** also underwent exchange reactions with ethanol, 1-butanol, benzyl alcohol, and ethylene glycol to afford the respective bisketal in yields of 93%, 90%, 96%, and 50% (see Experimental Section for details).



4 **4**-d_{12} **1**-d_6

Scheme II. Two Mechanisms for the Thermal Disproportionation of 1a[a]



[a] An asterisk (*) indicates either a radical, cation, or anion.

The thermolysis of **1a**-d_6 was appreciably slower than that of **1a**, exhibiting an isotope effect of ≃3.6 (run 7). Therefore, it was clear that substantial breakage of the carbon–hydrogen bond of the methoxy group was occurring in the rate-determining step.

Discussion

A number of mechanistic pathways can be envisioned for the conversion of 4,4-dimethoxy-2,5-cyclohexadienone (**1a**) to *p*-methoxyphenol and formaldehyde. Two mechanisms consistent with the present data are outlined in Scheme II. One of these could be viewed as an intramolecular retrohetero-ene[12] reaction (mechanism I), producing **5**, which would then tautomerize to **2a**. Mechanism I would be first order in **1a**, show a primary isotope effect, and possess a nonpolar transition state.

The second mechanism is a stepwise process involving a dissociation and a hydrogen-transfer process (mechanism II). The initial cleavage would produce **6** as a charged or neutral species (as indicated by the asterisk). Disproportionation of this caged pair would result in transfer of a hydrogen from the methoxy moiety to the oxygen, the ortho carbon, or the para carbon of the ring (only the latter possibility is shown) with formation of **7** and formaldehyde. Tautomerization of **7** to **2a** would complete the reaction scheme. Mechanism II would also follow a first-order rate law and show a substantial isotope effect if the dissociation step were a preequilibrium and hydrogen transfer were rate determining. If the initial dissociation occurred to produce a radical pair, a minimal solvent effect on the equilibrium constant would be expected.

Evidence for the intermediacy of the dienone **5**, and thus support for mechanism 1, could be obtained from the thermolysis of **1a**-d_6. The retrohetero-ene reaction of **1a**-d_6, as outlined in Scheme II for **1a**, would involve deuterium transfer to the 6-position of the 2,4-cyclohexadienone **5**. Even if there were no isotope effect for the conversion of **5** to **2a**, there should still be 33% deuterium present in the 2-position of **2a**. The 500-MHz ^{1}H NMR spectra of both *p*-methoxyphenol and its acetate obtained from thermolysis of **1a**-d_6 (96% d_6 by ^{1}H NMR analysis) indicated no deuterium present at the ortho positions (10% deu-

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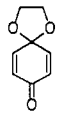
(10) Groebel, B. T.; Konz, E.; Millauer, H.; Pistorius, R. *Synthesis* **1979**, 605.
(11) Wiberg, K. *Physical Organic Chemistry*; Wiley: New York; 1964; pp 374–379.
(12) Oppolzer, W.; Snieckus V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476.

terium could have been easily detected). To ensure that the absence of deuterium did not result from inadvertent exchange with protons during manipulation of the sample, the ^2H NMR spectrum of the crude thermolysis reaction mixture was measured in CCl_4. The ^2H NMR spectrum showed only a broad singlet at δ 3.72 for the CD_3O group of the product, *p*-methoxyphenol; no absorption for a deuterium bonded to the aromatic ring was detected.

Although mechanism I was initially favored, this pathway was not supported by the experimental data. Thus, mechanism II, or some variation of it, best describes the sequence of reactions leading to the formation of *p*-methoxyphenol and formaldehyde from thermolysis of **1a**.

Mechanism II suggests that structural features which decrease either the equilibrium constant for the dissociation step or the rate constant for intermolecular hydrogen transfer should slow the rate of disproportionation of quinone monoketals. Indeed, thermolysis of the ethylene glycol ketal **8** at 180 °C for 24 h led to nearly quantitative recovery of starting material. It is not known if a decrease



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in the equilibrium constant for the dissociation step or the rate constant for the hydrogen-transfer step is responsible for the increased thermal stability of **8** relative to **1a**. Regardless, it appears advisable to use the mono(ethylene ketal) of quinones for high-temperature thermal reactions of quinone monoketals (e.g., Diels–Alder reactions). Of course, the use of Lewis acid catalysis to accelerate the Diels–Alder reactions of these compounds would be complicated by the acid-catalyzed disproportionation reaction.

The facile acid-catalyzed ketal exchange chemistry of **4** to produce the respective quinone bisketals merits comment since it is known that reaction of **1a** in a mixture of methanol, trimethyl orthoformate, and hydrochloric acid at room temperature gives 1,2,4-trimethoxybenzene in >80% yield.[10] The high yield exchange chemistry noted herein suggests that the cation formed from acid-catalyzed loss of methanol from the bisketal **4** undergoes kinetic addition of alcohol at the carbon bearing the alkoxy function. The formation of 1,2,4-trimethoxybenzene presumably arises via the less favored reaction of this cation at the alternate allylic position which then undergoes irreversible aromatization to form 1,2,4-trimethylbenzene. Thus, under careful kinetic conditions the ketal exchange products can be isolated in high yield. Since anodic oxidation of 1,4-dimethoxy aromatics in alcohols other than methanol gives lower yields and more complicated reaction mixtures,[1a] this exchange chemistry offers a route to bisketals not readily available from direct anodic oxidation.

Summary. The favored mechanism for disproportionation of **1a** into *p*-methoxyphenol and formaldehyde involves dissociation of the quinone monoketal into a *p*-methoxyphenoxy–methoxy radical pair followed by rate-determining hydrogen transfer. A homolytic rather than a heterolytic dissociation of **1a** is proposed since there is no solvent effect on the rate of the reaction. In addition, performing the thermolysis of **1a**-d_6 in methanol to effect 20% conversion of **1a**-d_6 gave only unchanged **1a**-d_6 and *p*-methoxyphenol-d_3. The absence of any products incorporating methanol from solvent in the above experiment disfavors dissociation into a *p*-methoxyphenoxy cation and a methoxide anion. If mechanism II is followed, the values calculated for the activation parameters incorporate both the equilibrium constant for the dissociation step and the rate constant for the hydrogen-transfer step; thus, numbers reported for $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ are only apparent values. Reactions of the dimethoxy monoketal **1a** at temperatures greater than 150 °C will be complicated by the disproportionation reaction studied herein; however, the ethylene glycol ketal **8** is stable at 180 °C for 24 h and would be a better substrate for conducting high-temperature reactions of quinone monoketals. Finally, the ketal exchange chemistry noted herein serves as a complementary route to quinone bisketals not conveniently available from direct anodic oxidation of the 1,4-dimethoxy aromatic compound.

Experimental Section[13]

General. All melting points were determined in capillaries in a Thomas-Hoover "Unimelt" apparatus and are uncorrected. Reported boiling points are also uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 283B spectrometer on KBr disks unless otherwise noted, reported in cm^{-1}, and calibrated by using the polystyrene band at 1601.4 cm^{-1}. ^1H NMR spectra were determined at 80 MHz on an IBM NR-80 spectrometer using deuteriochloroform as solvent and residual chloroform as standard. The ^1H 500-MHz NMR and ^2H NMR (acetone-d_6 as external standard) spectra were recorded by Dr. Charles Cottrell. Ultraviolet spectral data were recorded on both a Beckman DU-1 quartz spectrophotometer (with a Model B hydrogen lamp power supply) and a Beckman DU-7 instrument. The maxima are reported in nanometers with the extinction coefficients in parentheses. Mass spectral and exact mass measurements were obtained by Richard Weisenberger on a Kratos MS-30 mass spectrometer connected to a DS-55 data system. Alumina and silica gel were obtained from E. Merck Co. Tetrahydrofuran (THF) was purified by distillation from benzophenone ketyl directly into the reaction flask. Petroleum ether, bp 35–60 °C (PE), diethyl ether (Et_2O), ethyl acetate (EtOAc), benzene (C_6H_6), chloroform ($CHCl_3$), methylene chloride (CH_2Cl_2), and all other solvents used in the UV kinetics or chromatography were dried and distilled before use. Compounds not explicitly referenced are commercially available.

Thermolysis of Quinone Monoketals 1a–d. The procedure described for the thermolysis at 180 °C of **1a** is representative of the thermolysis of the other monoketals. For these compounds, only the following information is given: grams (moles), thermolysis media (mL), duration, and relevant spectroscopic data. The byproducts **3a,c,d** were not isolated in the thermolyses of **1a,c,d**, respectively.

4,4-Dimethoxy-2,5-cyclohexadien-1-one (1a).[13] A clear homogeneous solution of **1a** (0.2 g, 1.25 mmol) in THF (0.5 mL) in a glass tube (13 cm × 8 mm) was degassed (four freeze-thaw cycles, 0.1 mmHg) and sealed under vacuum. The tube was heated at 180 °C for 12 h and cooled to room temperature, and the contents were concentrated in vacuo; TLC analysis (CH_2Cl_2 as eluant) showed one spot. The residue was partitioned between CH_2Cl_2 (20 mL) and a 10% KOH solution (25 mL), and the aqueous phase was separated, acidified with concentrated HCl (5 mL), and extracted with Et_2O (2 × 25 mL). The organic phases were combined, washed with brine solution (10 mL), dried over $CaSO_4$, and concentrated in vacuo to afford a dark solid. The solid was recrystallized from CH_3OH to yield **2a** (0.163 g, 80%) as white crystalline needles: mp 53–55 °C (lit.[14] mp 55–57 °C).

4-(Benzyloxy)-4-methoxy-2,5-cyclohexadien-1-one (1b):[15] 0.3 g (1.3 mmol); THF (0.5 mL); 4.5 h. A sample of the crude product mixture (10 mg) was analyzed by ^1H NMR spectroscopy in order to determine the **2b**[16]/**2a** ratio, by using the integration

(13) 4,4-Dimethoxy-2,5-cyclohexadien-1-one (**1a**) is commercially available but can readily be prepared via the anodic oxidation/hydrolysis route discussed in ref 3b and: Henton, D. R.; McCreery, R. L.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 369.

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(16) *Beilstein*; Springer Verlag: Berlin; Vol. 6, p 845.

areas given: ^{1}H NMR δ 9.98 (s, 1 H, 4.5), 7.75 (unstr. m, 5 H, 35), 7.29 (s, 4 H, 24), 6.77 (s, 4 H, 39), 5.0 (br, s, disappears upon D_2O wash, 1 H, 6.1), 4.94 (s, 2 H, 5.4), 3.76 (s, 3 H, 36), 2.91 (br s, disappears upon D_2O wash, 1 H, 5.8). Benzaldehyde (**3b**) was isolated as its (2,4-dinitrophenyl)hydrazone derivative (orange needles): mp 235 °C (lit.[17] mp 237 °C).

4-Ethoxy-4-methoxy-2,5-cyclohexadien-1-one (1c):[15] 0.2 g (1.2 mmol); THF (0.5 mL); 4.5 h. A sample of the crude product mixture (10 mg) was analyzed by ^{1}H NMR spectroscopy in order to determine the **2c**[18]/**2a** ratio, by using the integration areas given: ^{1}H NMR δ 6.77 (s, 8 H, 71), 5.19 (br s, 1 H, 8.5), 5.1 (br s, 1 H, 7.1), 3.89 (q, 2 H, 17), 3.76 (s, 3 H, 21), 1.29 (t, 3 H, 25).

4-Isopropoxy-4-methoxy-2,5-cyclohexadien-1-one (1d):[15] 0.2 g (1.1 mmol); THF (0.5 mL) 4.5 h. A sample of the crude product mixture (10 mg) was analyzed by ^{1}H NMR spectroscopy in order to determine the **2d**/**2a** ratio, by using the integration areas given: ^{1}H NMR δ 6.77 (s, 8 H, 85), 4.32 (septet, 1 H, 11), 3.76 (s, 3 H, 39), 1.22 (d, 6 H, 42).

Mono(ethylene ketal) of Benzoquinone, 8.[19] The thermolysis of the title compound was performed as described for **1a**: 0.1 g (0.658 mmol); THF (0.5 mL); 24 h. The starting monoketal was isolated in >90% yield, and the spectral properties (^{1}H NMR, IR) of the sample were in good agreement with those reported in the literature.

Transketalization Reactions of 1,1,4,4-Tetramethoxy-2,5-cyclohexadiene and Their Hydrolyses to the Respective Quinone Monoketals. The procedure described for the synthesis of 4,4-di(methoxy-d_3)-2,5-cyclohexadien-1-one (**1a**-d_6) is representative of the room-temperature transketalization reactions of 1,1,4,4-tetramethoxy-2,5-cyclohexadiene (**4**)[20] and hydrolyses of the corresponding quinone bisketals. For the other compounds, only one exchange was performed. The following information is given for these transketalization reactions: grams (moles); transketalization media (mL); duration; purification procedure; product yield; and relevant spectroscopic data. For the hydrolyses of the respective quinone bisketals, the following information is supplied: grams (moles); hydrolysis media (mL, ratio), time and temperature; purification procedure; product yield; and spectroscopic data.

4,4-Di(methoxy-d_3)-2,5-cyclohexadien-1-one (1a-d_6). A clear homogeneous solution of **4** (0.2 g, 1.0 mmol), CD_3OD (0.5 mL), and a drop of glacial HOAc was allowed to react at room temperature. The reaction was monitored by ^{1}H NMR spectroscopy, and its progress was evaluated as a function of the disappearance of the methoxy resonance of the starting material and the appearance of the methoxy resonance corresponding to the methanol (4 mol) produced in the exchange reaction. After 3 h, the initial exchange gave an estimated ratio of 55% deuteriated material to 45% protonated material. The reaction mixture was concentrated in vacuo, and a fresh aliquot of CD_3OD (0.5 mL) was then added. After another 3-h period, the second exchange reaction had increased the amount of deuterium incorporation to approximately 85%. A third exchange reaction performed on the original mixture afforded 1,1,4,4-tetra(methoxy-d_3)-2,5-cyclohexadiene (**4**-d_{12}) (0.2 g, 95%) with an isotopic label incorporation of >96% as indicated by ^{1}H NMR integration: ^{1}H NMR δ 6.07 (s, 4 H), 3.35 (s, attributed to the small amount of nondeuteriated bisketal, 12 H). The deuteriated bisketal was then directly hydrolyzed to the corresponding monoketal.

A clear homogeneous solution of **4**-d_{12} (0.2 g, 0.001 mol) in $(CH_3)_2CO$ (5 mL) was cooled to 0 °C. An aliquot of a chilled 2% acetic acid solution (1 mL) was added dropwise with vigorous stirring. The hydrolysis was maintained at 0 °C for 30 min, slowly warmed to room temperature, and then stirred for an additional 1.5 h, after which time the reaction was judged to be complete by TLC (2:1 Et_2O/PE as eluant). After 2 h, the hydrolysis was quenched by the addition of a saturated solution of $NaHCO_3$ (5 mL), followed by a small portion of solid $NaHCO_3$ (1 g). This heterogeneous mixture was then concentrated in vacuo at 40 °C. The aqueous residue was taken up in PE (15 mL) and extracted to remove any water-soluble quinone produced. The organic layer was concentrated in vacuo to give a yellow liquid, which was taken up in CH_2Cl_2 (20 mL) and washed with brine solution (5 mL). The organic layer was dried ($CaSO_4$) and concentrated in vacuo to give a light yellow oil (0.13 g, 85%). The yellow oil was molecularly distilled (bath temperature 80–90 °C (0.5 Torr)) to afford the title compound (0.12 g, 80%) as a light yellow oil: IR (neat) 3040 (m), 2930 (s), 2830 (m), 2120 (m), 2070 (s), 1690 (s, br), 1640 (s), 1620 (s), 1600 (w), 1510 (s), 1390 (s), 1315 (s), 1270 (m), 1240 (s), 1180 (s, br), 1140–1050 (s, br), 960 (s), 850 (s), 800–750 (s, br), 670 (s); ^{1}H NMR δ 6.34 (AB q, J_{AB} = 9 Hz, $\Delta\nu$ = 23 Hz, 4 H), 3.22 (s, corresponding to nondeuteriated monoketal, 6 H).

4,4-Diethoxy-2,5-cyclohexadienone. The title compound was prepared by transketalization as described for **4**-d_{12}: 0.2 g (1 mmol); EtOH (0.5 mL); 24 h; triturated three times at low temperature with PE (5–10 mL). The PE extracts were concentrated in vacuo to afford 1,1,4,4-tetraethoxy-2,5-cyclohexadiene (0.23 g, 91%) as a light yellow oil, which crystallized in the freezer: mp 39–41 °C (lit.[13] mp 40–42 °C). Hydrolysis was performed as described for **1a**-d_6: 0.2 g (0.78 mmol); $(CH_3)_2CO$/2% HOAc (5:1); 0.5 h at 0 °C and then an additional 3.5 h at 25 °C; molecular distillation (bath temperature 80–90 °C (0.1 Torr)) afforded the title compound (0.13 g, 93%) as a yellow oil: IR (neat) 2980 (s), 1683 (s), 1640 (s), 1440 (m), 1420 (m), 1360 (s), 1261 (m), 1220 (s), 1180 (s), 1110 (s), 800–750 (s, br); ^{1}H NMR δ 6.52 (AB q, J_{AB} = 10 Hz, $\Delta\nu$ = 47 Hz, 4 H), 3.61 (t, J = 7 Hz, 4 H), 1.21 (t, J = 7 Hz, 3 H); mass spectrum, exact mass calcd for $C_{10}H_{14}O_3$ m/e 182.0943, obsd m/e 182.0947.

4,4-Dibutoxy-2,5-cyclohexadien-1-one. The title compound was prepared by transketalization as described for **4**-d^{12}: 0.2 g (1 mmol); *n*-BuOH (0.5 mL); 24 h; molecular distillation (bath temperature 94–96 °C (0.4 Torr)) afforded 1,1,4,4-tetrabutoxy-2,5-cyclohexadiene (0.33 g, 90%) as a water-white oil: IR (neat) 2960 (s), 2939 (s), 2878 (s), 1465 (m), 1110 (s), 1070 (s), 1040 (s), 955 (s), 842 (m); ^{1}H NMR δ 6.05 (s, 4 H), 3.59 (t, J = 6 Hz, 8 H), 1.91 (unstr. m, 8 H), 1.41 (unstr. m, 8 H), 0.89 (t, J = 6 Hz, 12 H).

Hydrolysis was performed as described for **1a**-d_6: 0.30 g (1.5 mmol); $(CH_3)_2CO$/2% HOAc (5:1); 0.5 h at 0 °C and then an additional 4.5 h at 25 °C; molecular distillation (bath temperature 116–120 °C (0.1 Torr)) afforded the title compound (0.32 g, 90%) as a light yellow oil: IR (neat) 2960 (s), 2940 (s), 2870 (s), 2830 (s), 1691 (s), 1675 (s), 1641 (s), 1462 (s), 1387 (s), 1318 (m), 1305 (m), 1205 (m), 1110 (s), 1082 (s), 1065 (s), 1038 (s), 960 (s), 910 (m), 851 (s); ^{1}H NMR δ 6.51 (AB q, J_{AB} = 10 Hz, $\Delta\nu$ = 48 Hz, 4 H), 3.47 (t, J = 7 Hz, 4 H), 1.3 (unstr. m, 8 H), 0.72 (t, J = 7 Hz, 6 H); mass spectrum, exact mass calcd for $C_{14}H_{22}O_3$ m/e 238.6126, obsd m/e 238.6130.

1,1,4,4-Tetrakis(benzyloxy)-2,5-cyclohexadiene. The title compound was prepared by transketalization as described for **4**-d_{12}: 0.2 g (1 mmol); $PhCH_2OH$ (0.5 mL); 48 h. The solid was collected by vacuum filtration, washed with several small portions of cold water, and dried in vacuo for 24 h to afford the title compound (0.50 g, 96%) as a white crystalline solid: mp 130–132 °C; IR (KBr) 3020 (s), 2940 (s), 2880 (s), 1955 (m), 1878 (m), 1810 (m), 1610 (m), 1497 (s), 1458 (s), 1210 (s), 1110 (s), 1080 (s), 1038 (s), 1020 (s), 960 (s), 810 (m), 732 (s), 695 (s); ^{1}H NMR δ 7.23 (s, 20 H), 6.17 (s, 4 H), 4.59 (s, 8 H); ^{13}C NMR δ 138.4, 134.8, 130.7, 128.3, 127.5, 126.6, 123.6, 64.7; mass spectrum, exact mass calcd for $C_{34}H_{32}O_4$ m/e parent ion not observed. Hydrolysis to the monoketal was not performed.

Bis(ethylene ketal) of Benzoquinone.[19] The title compound was prepared by transketalization as described for **1a**-d_6: 0.2 g (1 mmol); $HO(CH_2)_2OH$ (0.5 mL); 72 h. The solid was collected by vacuum filtration, washed with several small portions of cold water, and dried in vacuo for 24 h to afford the title compound (0.1 g, 50%) as white needles: mp 232 °C (lit.[19] mp 233–235 °C). Hydrolysis to the corresponding mono(ethylene ketal) of benzoquinone, 8,[19] was accomplished by a known procedure.

Attempted Trapping Experiments. Thermolysis of 1a-d_6 in Methanol. The thermolysis of the title compound was performed as described for **1a**: 0.2 g (1.25 mmol); CH_3OH (0.5 mL); 2 h. A ^{1}H NMR spectrum of the crude thermolysis mixture indicated that **1a**-d_6 and **2a**-d_3 were the major products; **1a** and

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2a were also present in trace amounts, consistent with the isotopic purity of the starting material.

Thermolysis of 4,4-Diethoxy-2,5-cyclohexadien-1-one in Methanol. The thermolysis of the title compound was performed as described for **1a**: 0.2 g (1.1 mmol); CH_3OH (0.5 mL); 4 h. A ^1H NMR spectrum of the reaction mixture indicated that the starting monoketal and **2c** were present; **1a** was not detected.

Thermolysis of 1a in Ethanol. The thermolysis of the title compound was performed as described for **1a**: 0.2 g (1.25 mmol); EtOH (0.5 mL); 4 h. A ^1H NMR spectrum of the reaction mixture indicated that **1a** and **2a** were present; 4,4-diethoxy-2,5-cyclohexadien-1-one was not detected.

Kinetic Procedure. Standardized solutions of **1a** and **1a**-d_6 were prepared at room temperature, and aliquots (0.5 mL) were placed in glass tubes (13 cm × 8 mm). Once filled, the kinetic samples were degassed by a series of four freeze–thaw cycles (0.1 mmHg), and the tubes were then sealed under vacuum. At zero time, all the tubes for a particular kinetic run were placed in a silicon oil kinetic bath maintained at a constant temperature of 180 ± 0.5 °C (except for activation parameter runs). The kinetic samples were retrieved from the bath every 30 min. A typical kinetic run included data points for the first 5 h of reaction with the infinity absorbance sample being pulled from the bath 24 h from zero time (100% conversion to the product phenol). The kinetic samples were analyzed by UV spectroscopy at 293 nm and the rate constants are felt to be reliable to ±5%.

Acknowledgment. We thank the National Science Foundation for partial support of this work.

Registry No. **1a**, 935-50-2; **1a**-d_6, 110614-47-6; **1b**, 73010-55-6; **1c**, 73010-52-3; **1d**, 73010-54-5; **4**, 15791-03-4; **4**-d_{12}, 110614-50-1; **8**, 35357-34-7; 4,4-diethoxy-2,5-cyclohexadien-1-one, 81453-27-2; 4,4-dibutoxy-2,5-cyclohexadien-1-one, 110614-48-7; 1,1,4,4-tetrakis(benzyloxy)-2,5-cyclohexadiene, 110614-49-8; 1,4-benzoquinone bis(ethylene ketal), 35357-33-6; 1,1,4,4-tetraethoxy-2,5-cyclohexadiene, 72205-84-6; 1,1,4,4-tetrabutoxy-2,5-cyclohexadiene, 110614-51-2.

Synthesis of Hydrocarbon-Strapped Porphyrins Containing Quinone and Phenolic Groups

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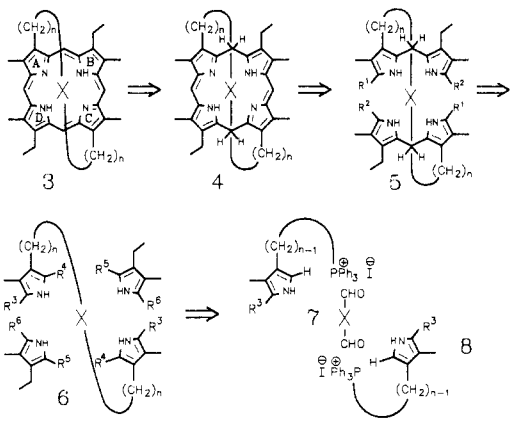
Received January 26, 1987

A general synthesis of strapped porphyrins is described and is illustrated for porphyrins bearing quinone and phenol groups in the bridging strap, which is exclusively a polymethylene chain. The NMR and optical spectra of the strapped porphyrins are discussed.

Synthetic metalloporphyrins enjoy continuing popularity as models for metalloenzymes, oxygen transport and storage proteins, and biological electron-transport systems.[1] Covalent attachment of potential ligands, bulky blocking groups, and other interactive species to a porphyrin macrocycle has been a frequently used strategy in the synthesis of heme protein models. This strategy can control coordination of the metalloporphyrin by a steric or neighboring group effect. This allows access to well-defined 5-coordinate iron(II) or 6-coordinate mixed-ligand systems. It can also allow the design of models where the relative orientation and separation of two reaction centers have been predetermined. Iron porphyrins bearing covalently bound imidazole,[2] thioether,[3] and thiolate[4] groups

Scheme I



have been prepared as models for the active centers of hemoglobin, myoglobin, cytochrome *c*, and cytochrome P_{450}. Binucleating porphyrins,[5] which contain a second metal binding site attached to a porphyrin ring, have been

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