are not identical, but *cis*- and *trans*-decalyl ions, the latter being 1.4 kcal mol^{-1} more stable.[18] Because we obtained the same pmr spectrum from both *cis* and *trans* precursors, separate ionic species were not apparent even at temperatures as low as −130°. Quenching of the ion solutions prepared from either *cis*- or *trans*-9-decalol yielded mixtures in which the isomer distributions were the same; that is *cis*–*trans*, 2:1. This could reflect the faster rate of quenching of the *cis* isomer under our conditions, or the higher stability of the *cis*-decalyl ion. If the *trans*-decalyl ion were more stable under our conditions and the rates of quenching were identical for both isomers, then this ratio would be reversed.

Cycloundecanol **1** (n = 11) when dissolved in FSO_3H–SbF_5–SO_2ClF at −78° yields the 1-*n*-pentylcyclohexyl tertiary cation **2** (n = 11); pmr absorptions at δ 4.28 (6 H, α-CH_2), 1.5–3.0 (12 H, CH_2), and 1.3 (3 H, CH_3). The same spectrum was also obtained from 1-*n*-pentylcyclohexanol and 1-*n*-hexylcyclopentanol.

Similarly, cyclododecanol **1** (n = 12) when dissolved in FSO_3H–SbF_5–SO_2 at −78° yields the 1-*n*-hexylcyclohexyl tertiary cation **2** (n = 12); pmr absorptions at δ 4.29 (6 H, α-CH_2), 1.4–2.9 (14 H, CH_2), and 1.2 (3 H, CH_3). An identical spectrum was also obtained from 1-*n*-hexylcyclohexanol.

Quench products from the 1-*n*-pentyl- and 1-*n*-hexylcyclohexyl cations were complex mixtures, indicating further rearrangement of the initially formed ions. The spectra of the ions, however, are identical with those of the 1-ethyl- and 1-*n*-propylcyclohexyl cation, with the exception of one peak in the β-, γ-CH_2 region.

It should be noted that the 1-alkylcyclohexyl ions reported in this communication are those formed at low temperature, generally at −78°. Subsequent rearrangements take place at higher temperatures predominantly to alkylcyclopentyl cations which are under investigation.

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(18) A. F. Boschung, M. Geisel, and C. A. Grob, *Tetrahedron Lett.*, 5169 (1968); see also R. Fort and R. E. Hornisch, *Chem. Commun.*, 11 (1969).

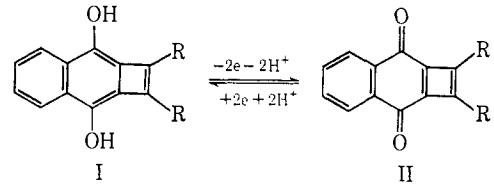
George A. Olah, David P. Kelly, Robert G. Johanson
Department of Chemistry, Case Western Reserve University
Cleveland, Ohio 44106
Received February 26, 1970

Electrochemical Evidence for the Antiaromaticity of Cyclobutadiene[1]

Sir:

The early simple conclusion that such 4π-electron systems as cyclobutadiene[2] are not aromatic has given way recently to indications that they are in fact antiaromatic,[3] *i.e.*, destabilized by conjugation. The type of evidence available involves rates or (preferably) equilibrium constants for the conversion of a saturated carbon into a trigonal atom, with consequent completion of the cyclic 4π-electron conjugated system. However, such a change generally involves an increase in strain as well as in electronic interactions; while a change in strain has been excluded[3a,b] as a major component in the apparent antiaromaticity of the cyclopropenyl anion, it was not ruled out as a factor in the antiaromaticity we have recently reported[3d] for a cyclobutadiene derivative. We now wish to describe evidence for the antiaromaticity of cyclobutadiene in which the antiaromatic interaction is brought in by an electron redistribution accompanied by only negligible changes in strain energy.

The system examined involves reversible oxidation of the hydroquinone Ia to the quinone IIa. Because of the low β–β' bond order in a naphthalene such as I, and the essentially full double bond in II, there

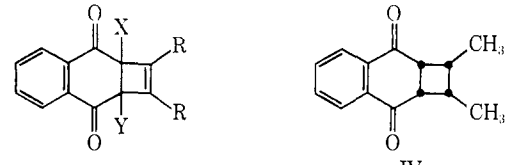


I II

a, R = C_6H_5
b, R = CH_3

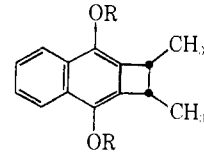
is a considerable increase in the cyclobutadiene character of the system in converting I to II, but only a slight geometric change. We have examined and corrected for any geometric effects by using a cyclobutenonaphthohydroquinone Vb as a model for the cyclobutadieno derivative Ia.

Irradiation of 2-butyne with naphthoquinone affords a 6% yield of the adduct IIIa,[4] which has recently been reported elsewhere.[5] This compound was con-



IIIa, X = Y = H; R = CH_3
b, X = Y = H; R = C_6H_5
c, X = Y = CH_3; R = C_6H_5
d, X = H; Y = Cl; R = C_6H_5

IV



Va, R = $COCH_3$
b, R = H

verted with ethylene glycol to the bisketal[4] of IIIa, mp 178–180°, and the cyclobutene double bond was hydrogenated over Pt to afford the bisketal[4] of IV,

(1) Taken in part from the Ph.D. Thesis of Robert Grubbs, Columbia University, 1968. Much of this material was described at the National Organic Chemistry Symposium, Salt Lake City, Utah, 1969. Support of this work by the National Institutes of Health, and technical help by Dr. K. Balasubramanian and Mr. William Chu, are gratefully acknowledged.

(2) M. P. Cava and M. J. Mitchell, "Cyclobutadiene and Related Compounds," Academic Press, New York, N. Y., 1967.

(3) (a) R. Breslow, J. Brown, and J. Gajewski, *J. Amer. Chem. Soc.*, **89**, 4383 (1967); (b) R. Breslow and M. Douek, *ibid.*, **90**, 2698 (1968); (c) R. Breslow and K. Balasubramanian, *ibid.*, **91**, 5182 (1969); R. Breslow and W. Chu, *ibid.*, **92**, 2165 (1970); (d) R. Breslow and W. Washburn, *ibid.*, **92**, 427 (1970).

(4) New compounds were characterized by satisfactory spectra, mass spectra, and in most cases C and H analyses.

(5) S. Farid, W. Kothe, and G. Pfundt, *Tetrahedron Lett.*, 4147 (1968).

mp 134–136°, which was hydrolyzed to the all-*cis*-diketone IV,[4] mp 78–80°. With acetic anhydride and sodium acetate, IV afforded the diacetate Va,[4] mp 114–115°, while with NaH, followed by acetic acid, IV was converted to the hydroquinone Vb, mp 163–166°. Compound Vb could be oxidized with N_2O_4 to the corresponding quinone, 2,3-(*cis*-3,4-dimethylcyclobuteno)-1,4-naphthoquinone,[4] mp 99–100°.

With NaH in tetrahydrofuran, IIIa was converted to the dienolate, but on quenching in H_2O this produced a hydroquinone Ib which rapidly formed a dimer.[4] Accordingly, the photoadduct IIIb[4,5] from naphthoquinone and diphenylacetylene was prepared, and converted to the dark green dienolate ion with NaH in tetrahydrofuran (or KO-*t*-Bu in dimethyl sulfoxide). With acetic anhydride this solution afforded a 95% yield of the diacetate[4] of Ia, mp 237–238°, while with methyl iodide it yielded chiefly the C-methylation product IIIc.[4,5] On quenching with aqueous NH_4Cl the dianion afforded the hydroquinone Ia,[4] which slowly went to three dimers,[4] mp 217–218°, mp 239–241°, and mp 229–231°, in 78% overall yield, together with *ca.* 20% recovered IIIb.

The hydroquinone Ia (1 mg) was quickly dissolved in 10 ml of ethanol and 10 ml of aqueous 0.2 *N* acetate buffer, pH 5.6. Dc polarography with a dropping mercury electrode shows a two-electron oxidation wave at $E_{1/2}$ 0.163 V (sce). By contrast, under the same conditions naphthohydroquinone has $E_{1/2}$ −0.113 V, while Vb has $E_{1/2}$ −0.153 V. The diffusion current for Ia decreased *ca.* 20% in 30 min presumably because of dimerization; however, initially the diffusion current corresponded to 75% of that expected for Ia, and the dimers and diketone IIIb were shown not to be responsible for the electrochemistry at 0.163 V.

The product IIa is even more unstable than Ia. IIa can be generated independently by treatment of IIId,[4] mp 173–175°, the photoadduct of diphenylacetylene and 2-chloronaphthoquinone, with NaH in tetrahydrofuran, but it yields only a dimer,[4] or a 1:1 adduct,[4] mp 289–291°, if the elimination is performed in the presence of diphenylisobenzofuran. The rapid dimerization of IIa makes the oxidation of Ia slightly irreversible electrochemically.

In order to confirm our assignment of potentials, we have also prepared the dianion of Ia from IIIb and NaH as described above, and examined its electrochemistry in purified anhydrous dimethylformamide with 0.1 *M* n-$Bu_4N^+ClO_4^-$ as electrolyte. A three-electrode-controlled potential instrument was used, with a platinum spiral anode, a dropping mercury cathode, and a calomel reference electrode isolated by a fine-porosity sintered disk. Under these conditions the dianion of Ia showed two one-electron oxidation waves, at −0.86 and −0.40 V (max). Naphthohydroquinone dianion had oxidation waves at −1.32 and −0.63 V (max), and naphthoquinone showed reduction waves at −0.65 and −1.42 V. The diffusion current due to the dianion of Ia diminished with time by irreversible destruction of the compound.

Thus both Ia and its dianion are more difficult to oxidize than is naphthohydroquinone or its dianion. By contrast, the cyclobutene analog Vb is more easily oxidized than naphthohydroquinone, since the slight strain effect[6] does not quite cancel the small substituent effect on the oxidation potential. The 0.27-V difference in oxidation potential between Ia and naphthohydroquinone corresponds to 12.4 kcal/mol, while the 0.31-V difference between I and Vb corresponds to 14.2 kcal/mol. The data on the dianions correspond to a 16 kcal/mol difference in the $\Delta G°$ for oxidation of Ia and of naphthohydroquinone dianions.

Obviously the irreversible dimerization of IIa affects these data, although the direction is such as to underestimate the antiaromaticity effect in IIa. Furthermore, small strain[6] and substituent effects must also be playing some role in the comparison of Ia with Vb. However, it seems clear that the bulk of the increased difficulty in oxidizing Ia is due to the antiaromaticity of the cyclobutadiene ring in IIa. Such antiaromaticity should raise the energy of Ia as well as IIa, although to a lesser extent, so our measurement reflects only a portion of the destabilization in a cyclobutadiene ring (as did our previous case,[3d] in which a 15 kcal/mol antiaromatic effect was seen from partial cyclobutadiene character). Thus the full antiaromatic destabilization of cyclobutadiene probably involves considerably more than the 12–16 kcal/mol of our present measurement.

(6) *Cf.* the small Mills–Nixon effect in the quinone redox potentials studied by R. T. Arnold and H. E. Zaugg, *J. Amer. Chem. Soc.*, **63**, 1317 (1941).

Ronald Breslow, Robert Grubbs, Shun-Ichi Murahashi
Department of Chemistry, Columbia University
New York, New York 10027
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Photooxidation of α-Chymotrypsin Sensitized by the Inhibitor N-Acetyl-3-nitrotyrosine

Sir:

Dye-sensitized photooxidation of proteins has been shown to be a valuable tool either for probing the degree of exposure of the photooxidizable amino acid residues[1,2] or for mapping the location of specific residues in predetermined regions of protein molecules.[3–5] The latter procedure involves the irradiation of proteins containing a linked sensitizer, so that only the amino acid side chains adjacent to the sensitizer can be modified. In this paper we describe a modification of this procedure which should enlarge the scope of the method and specifically direct the photooxidative attack toward the active site of enzymes.

This goal is achieved by using a reversible inhibitor of the given enzyme as the sensitizer. Although the complexed inhibitor is in equilibrium with unbound molecules, the concentration of the sensitizer in the catalytic region is comparatively very high; consequently, the photooxidation rate of the susceptible residues located in this region should be by far greater than that of the other susceptible residues which have a smaller probability of interacting with the free in-

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(3) M. Rippa and S. Pontremoli, *Arch. Biochem. Biophys.*, **133**, 112 (1969).
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