Studies in Mass Spectrometry. Double Hydrogen Migration in Adducts of p-Benzoquinone with Bi-1-cycloalken-1-yls under Electron Impact[1a]

Joseph Deutsch[1b] and Asher Mandelbaum

Contribution from the Department of Chemistry, Israel Institute of Technology, Haifa, Israel. Received March 1, 1969
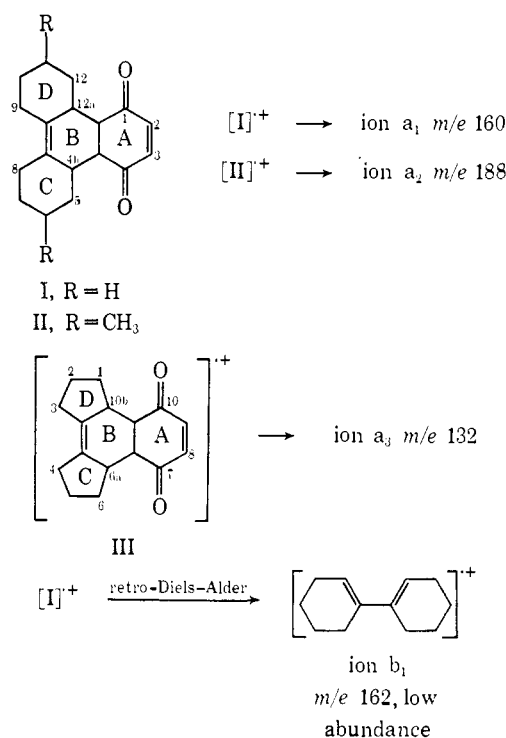
Abstract: The retro-Diels–Alder fragmentation of the adducts (I) of p-benzoquinone with bi-1-cyclohexen-1-yl and with related dienes under electron impact is accompanied by double hydrogen migration. Examination of the mass spectra of deuterium-labeled adducts revealed that the two migrating atoms are attached at positions 8 and 9. A possible mechanism is suggested.

The various factors that govern the McLafferty rearrangement of ketones under electron impact have been the subject of extensive investigation.[2] One of the most interesting points emerging is the rigorous proximity requirement between the carbonyl oxygen atom and the migrating γ-hydrogen atom.[2a] It has been shown[2a] that if this distance (estimated from models) exceeds 1.8 Å in rigid systems, the fragmentation takes a different course, and although fragments may be formed which are similar in their m/e values to those expected from McLafferty rearrangement, the hydrogen atoms migrate from positions other than those γ to the carbonyl carbon atom.

We describe herein a system in which hydrogen migrations took place by a mechanism different from the McLafferty rearrangement in which a six-membered cyclic transition state is involved, despite the availability of γ-hydrogens sufficiently close to the carbonyl oxygen atom ($\sim$1.5 Å).

In the mass spectrum (Figure 1) of the Diels–Alder adduct of p-benzoquinone with bi-1-cyclohexen-1-yl[3] (Ia) m/e 160 peak was the most intense ($\% \Sigma_{40}$ 17.7). The corresponding peak appeared at m/e 188 in the mass spectrum of the adduct of p-benzoquinone with bi-1-(4-methylcyclohexen)-1-yl[3] (II). The most intense peak in the mass spectrum of the adduct of p-benzoquinone with bi-1-cyclopenten-1-yl (III) was at m/e 132 ($\% \Sigma_{40}$ 25.6).

The relationship between the m/e values of the corresponding ions a in the three analogous compounds I, II, and III leads to the conclusion that these most abundant ions (m/e 160, 188, and 132, respectively) contain the two rings C and D, which were originally contributed by the dienes during the course of synthesis. A normal retro-Diels–Alder fragmentation would lead to m/e 162 ion in the case of I, to 190 for II, and to 134 for III. These ions (b₁, b₂, and b₃, respectively) are of very low intensity, relatively to ions a₁, a₂, and a₃ (see Figure 1). Ions of type a may be formed only by the migration of two hydrogen atoms from rings C and D to ring A

[I]·⁺ ⟶ ion a₁ m/e 160

[II]·⁺ ⟶ ion a₂ m/e 188

I, R = H
II, R = CH₃

ion a₃ m/e 132

III

[I]·⁺ $\xrightarrow{\text{retro-Diels–Alder}}$ ion b₁
m/e 162, low abundance

followed by the cleavage of bonds 12a–12b and 4a–4b in I and II, and of bonds 6a–6b and 10a–10b in III.

Since the Diels–Alder additions were carried out at room temperature it may be assumed on the basis of previously accepted rules in the literature[4] that the adducts I, II, and III have the *endo* configuration. This point has been proved by correlation with compounds of known stereochemistry.[5] Measurement (using Dreiding models)[2a] of the approximate distances for the unstrained conformations of the *endo* adducts (*e.g.*, I) shows that H-12 and H-5 may be very close ($\sim$1.5 Å) to the carbonyl oxygen atoms. Such a small distance permits the occurrence of a double McLafferty rearrangement (I → aa)[2a] giving rise to the m/e 160 ion. In order to examine this possibility 4b,8,8,9,9,12a-d_6-tetradecahydrotriphenylene-1,4-dione (IV) was prepared (from 2,2,6,6-d_4-cyclohexanone). The most intense peak in the mass spectrum of IV was at m/e 164. The suggested

(1) (a) Presented in part at the EUCHEM Symposium on Mass Spectrometry, Sarlat, France, Sept 1965. (b) Based in part on the D.Sc. and M.Sc. theses of J. Deutsch.

(2) (a) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, p 155; (b) F. W. McLafferty and T. Wachs, *J. Am. Chem. Soc.*, **89**, 5043 (1967); T. Wachs and F. W. McLafferty, *ibid.*, **89**, 5044 (1967); A. Mandelbaum and K. Biemann, *ibid.*, **90**, 1975 (1968).

(3) A. Mandelbaum and M. Cais, *J. Org. Chem.*, **26**, 2633 (1961).

(4) (a) J. G. Martin and R. K. Hill, *Chem. Rev.*, **61**, 537 (1961); (b) M. F. Ansell, J. W. Lown, D. W. Turner, and D. A. Wilson, *J. Chem. Soc.*, 3036 (1963); (c) A. S. Onishchenko, "Diene Synthesis," L. Mandel, Transl., Israel Program for Scientific Translations, Jerusalem, 1964, p 37.

(5) J. Deutsch and A. Mandelbaum, paper in preparation.

double McLafferty rearrangement (I → aa) would obviously lead to m/e 166 ion, as no deuterium atom resides at C_5 and C_{12}. Thus the shift of ion a to m/e 164 excludes this possibility. The two migrating hydrogen atoms must therefore originate at two of the other four labeled positions 4b, 8, 9, and 12a.

I

aa
m/e 160

→ ion a_4
m/e 164

IV
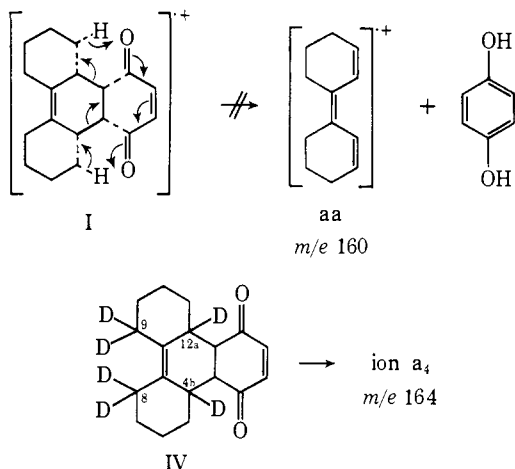
Inspection of models suggests that the two migrating hydrogen atoms may come only from positions 8 and 9, since the other two possible hydrogen atoms at positions 4b and 12a are very far from the carbonyl oxygen atoms in the *endo* adduct. Direct clarification of this point would require preparation of I, specifically deuterated only at positions 8 and 9 or only at 4b and 12a. However, bi-1-cyclohexen-1-yl (Va) is prepared by dehydration of the pinacol VI or of 1-cyclohexenyl-1-cyclohexanol (VII), and symmetry considerations in VI and in VII do not permit synthesis of the required specifically labeled dienes Vb or Vc. It was therefore necessary to

VI

Va

VII

Vb

Vc
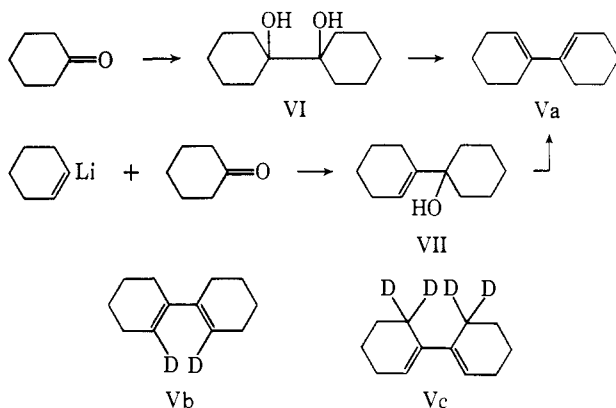
determine the origin of the two migrating hydrogen atoms by using a mixture of known composition of dienes, deuterated at different but known positions.

An equimolar mixture of $2\text{-}d_1\text{-}1,1'$-dicyclohexenyl (IX) and $6,6\text{-}d_2\text{-}1,1'$-dicyclohexenyl (X), obtained from the reaction of $2,2\text{-}d_2$-cyclohexanone (VIII)[6] and cyclohexenyllithium, should give an equimolar mixture of adducts XI and XII, labeled with deuterium at positions 8 (d_2) or 4b (d_1). If the migrating hydrogen atoms under electron impact originate from positions 8 and 9 (as expected), both XI and XII would give rise to monodeuterio ion a, which would thus be shifted to m/e 161. If, on the other hand, the hydrogen atoms would migrate

(6) J. Deutsch and A. Mandelbaum, *Tetrahedron Letters*, 1351 (1969)

VIII

VIIa

IX

X

IX + X →

XI

XII

XIII
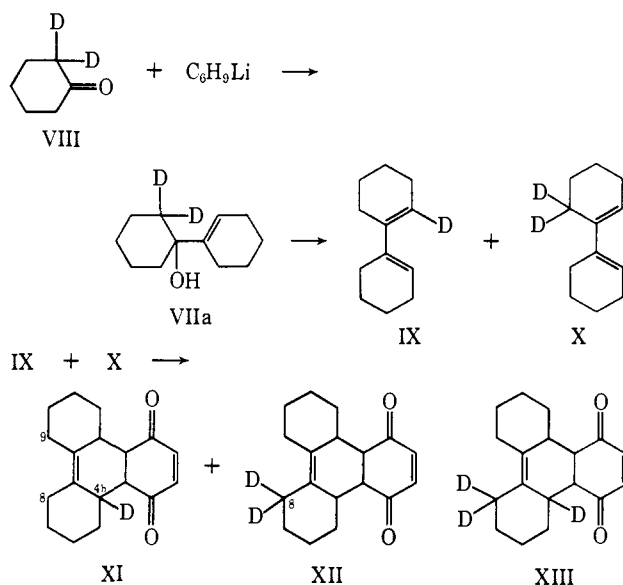
from positions 4b and 12a, XI would give rise to m/e 160 ion a while XII would yield m/e 162 dideuterio ion a. If one hydrogen atom were to migrate from position 8 and the other from 12a (or from 9 and 4b), three ions a would be expected of m/e 160 (from XI), 161 (from both XI and XII), and 162 (from XII), in the abundance ratio 1:2:1, if the isotope effect[7] is neglected.

The mixture obtained by synthesis contained also undeuterated material I and a small amount of trideutero analog XIII. The ratio of abundances of adducts containing $d_0:d_1{}^8:d_2:d_3$ was 65.5:80:100:8.9. The undeuterated material I was obtained in part from the reaction of unlabeled cyclohexanone which was a minor constituent of $2,2\text{-}d_2$-cyclohexanone (VIII),[6] used in the synthesis. An additional source of undeuterated adduct I is the reaction with $2\text{-}d_1$-cyclohexanone, followed by the elimination of DOH.[8] The major part of I, however, probably originates from a coupling reaction of cyclohexenyllithium, or from the reaction of cyclohexenyllithium with cyclohexanone, which might be present in

(7) D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem·
Soc.*, 86, 284 (1964); ref 2a, p 156; J. K. MacLeod and C. Djerassi, *J. Am. Chem. Soc.*, 89, 5182 (1967).

(8) The monodeuterio material is expected to contain small amount of XIV as a contaminant of XI. XIV is formed from $2\text{-}d_1$-cyclohexanone, which was present in the $2,2\text{-}d_2$-cyclohexanone[6] used in the synthesis (18.8%). The concentration of XIV was estimated as 4.7%, neglecting the isotope effect, which may operate in the dehydration.

IX

Va

XI

I

XIV
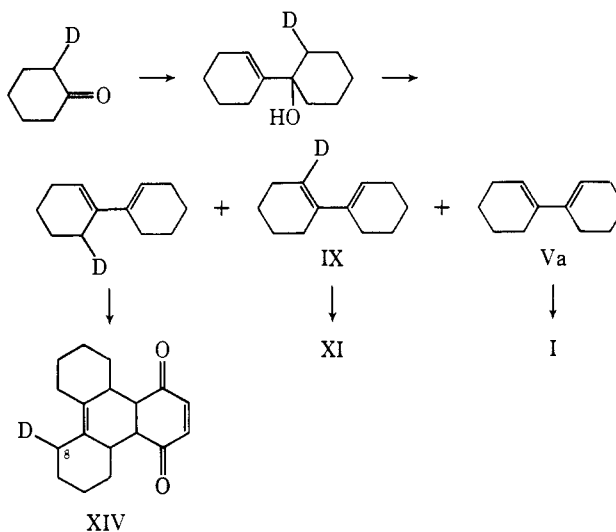
1-chlorocyclohexene used for the preparation of cyclo-hexenyllithium.

The d_3 analog XIII originates from the small amount of 2,2,6-d_3-cyclohexanone which was present in the starting material. The relatively high abundance of the d_2 material XII is ascribed to an isotope effect operating in the dehydration of VIIa.

The expected ratios of intensities of m/e 160, 161, and 162 peaks for the three possible mechanisms for the double hydrogen migration (I → a) are tabulated in Table I and compared to those found experimentally in the mass spectrum of the mixture. A correction was made in the calculation due to the presence of the relatively small amount of 8-d_1 adduct XIV.[8] The isotope effect[7] could not be estimated and was neglected in the calculation.

Table I. Comparison of Abundances of Ions a Calculated for the Three Possible Mechanisms with Those Found Experimentally in the Mass Spectrum of Mixture I + XI + XII

| | Calculated[a] abundances[b] of ions a, if hydrogens migrate from positions | | | |
m/e	8 and 9	4b and 12a	8 and 12a or 9 and 4b	Found
160	43	100	96	44
161	100	39.5	100	100
162	27.5	99	50	29.5

[a] See text. [b] In arbitrary units, the most intense peak taken as 100.

The comparison of the calculated and found abundances of ions a (Table I) shows unambigously that the two migrating hydrogens come from positions 8 and 9, as could be expected on the basis of the above discussion.

The same conclusion about the origin of the migrating two hydrogen atoms was reached in the similarly labeled mixture of adducts of 1-cyclopentenyl-1-cyclohexene and p-benzoquinone (XVa and XVb). This system,

XV   XVa   XVb
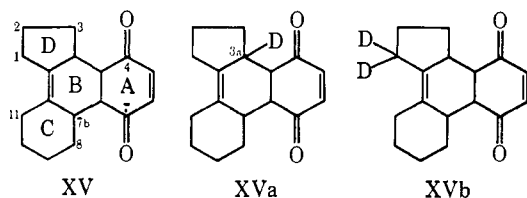
based on the asymmetric diene XVI, was prepared in order to lower the concentration of the unlabeled diene, which was relatively high in the case of bi-1-cyclohexen-1-yl due to coupling of the lithium reagent or due to its reaction with cyclohexanone present in cyclohexenyl chloride. These two possible reactions do not affect the synthesis of the mixture of deuterated 1-cyclopente-
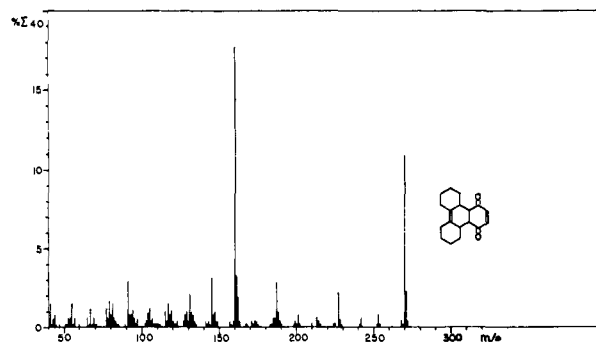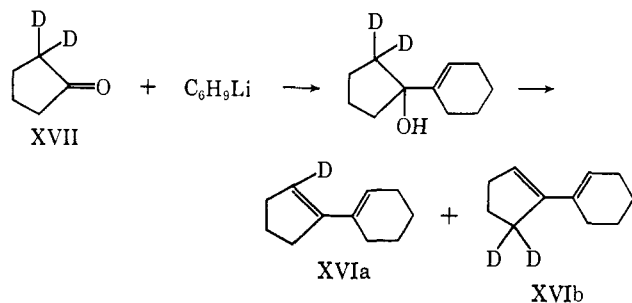

XVII

XVIa   XVIb

Figure 1. Mass spectrum of 1,4,4a,4b,5,6,7,8,9,10,11,12,12a,12b-tetradecahydrotriphenylene-1,4-dione (I).

nyl-1-cyclohexenes (XVIa and XVIb), since they lead to bi-1-cyclohexen-1-yl (Va), which leads to ions clearly distinguishable from the lower molecular weight analog. The comparison of calculated and found abundances of ions a_{15} (m/e 146, 147, and 148) is presented in Table II.

Table II. Comparison of Abundances of Ions a Calculated for Three Possible Mechanisms with Those Found in the Mass Spectrum of Mixture of XV + XVa + XVb

| | Calculated[a] abundances[b] of ions a_{15}, if hydrogens migrate from positions | | | |
m/e	1 and 11	3a and 7b	1 and 7b or 3a and 11	Found
146	14	68	55.5	17.5[c]
147	100	31.5	100	100
148	24	100	68.5	24.5

[a] See text. [b] In arbitrary units, the most intense peak taken as 100. [c] This value includes the abundance of $C_{11}H_{12}D$ (m/e 146) ion, which is formed from rings B, C, and part of D (compare J. Deutsch and A. Mandelbaum, Israel J. Chem., 3, 55 (1965)). The abundance of m/e 145 ($C_{11}H_{13}{}^+$) ion was 6% of m/e 146 ion a_{15} in the unlabeled compound.

This comparison again shows unambiguously that the two hydrogen atoms migrate from positions 1 and 11 in XV, which are equivalent to positions 8 and 9 in I.

It should be noted that the hydrogen migration from positions 8 and 9 to form ion a from the molecular ion of I (or from positions 1 and 11 in the case of XV, etc.) requires a seven-membered cyclic transition state, provided that there is no skeletal rearrangement in the molecular ion prior to fragmentation. The high specificity of this hydrogen migration seems to eliminate the possibility of such a drastic skeletal rearrangement of the molecular ion. The intermediacy of seven-membered-ring transition states has been reported for several hydrogen migrations under electron impact.[9] Apparently the allylic character of positions 8 and 9 is the reason that the hydrogen atoms migrate from these positions rather than those from 5 and 12, although the latter seem to be more suitable for migration if only steric factors (six-membered-ring transition state and relative proximity of the hydrogens to oxygen atoms, based on Dreiding models) are considered. Availability of al-

(9) W. Carpenter, A. M. Duffield, and C. Djerassi, Chem. Commun., 1022 (1967); N. C. Rol, Rec. Trav. Chim., 84, 413 (1966); S. D. Sample, D. A. Lightner, D. Buchardt, and C. Djerassi, J. Org. Chem., 32, 997 (1967); E. J. Moriconi, J. F. Kelly, and R. A. Salamone, ibid., 33, 3448 (1968); R. Brandt and C. Djerassi, Helv. Chim. Acta, 51, 1750 (1968); G. Eadon, and C. Djerassi, J. Am. Chem. Soc., 91, 2724 (1969).

lylic hydrogens has been reported[10] to enhance migration of hydrogens in systems which otherwise might be expected to undergo quite different fragmentation reactions under electron impact.

The presence of the 2,3 double bond is necessary for the rearrangement leading to the formation of ions a. In the reduction products of the adducts XVIII and XIX no analogs of ions a were detected under electron impact. Instead normal retro-Diels–Alder fragments (ions b) were of relatively high abundance. In the mass


ion b₁, R = H; m/e 162
ion b₂, R = CH₃; m/e 190

XVIIIa, R = H
b, R = CH₃

XIX

ion b₃
m/e 134
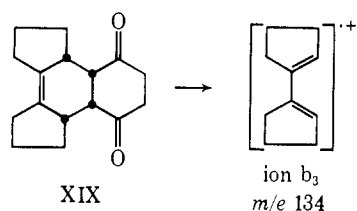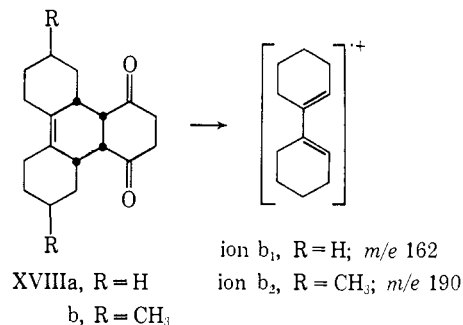
spectra of the adducts of naphthoquinone XX and XXI both ions a and b were detected. Other interesting

$\xrightarrow{-e}$ ion a₁ + ion b₁
m/e 160   m/e 162

XX

$\xrightarrow{-e}$ ion a₃ + ion b₃
m/e 132   m/e 134

XXI
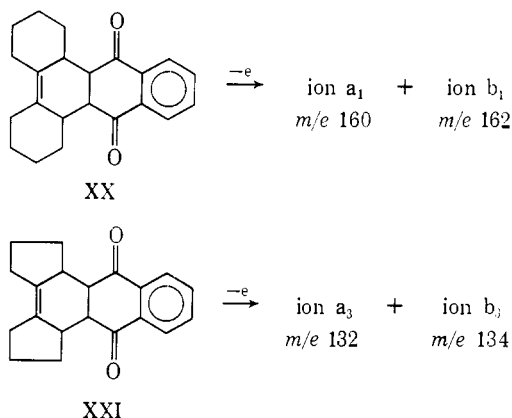
fragmentation processes of these compounds XVIII–XXI and their analogs will be dealt with elsewhere.

From the above results and assuming absence of skeletal rearrangement in the molecular ion prior to fragmentation, the following "arrows–fishhooks" mechanism can be suggested to visualize the formation of ion a.

or isomer thereof

I

ion a₁
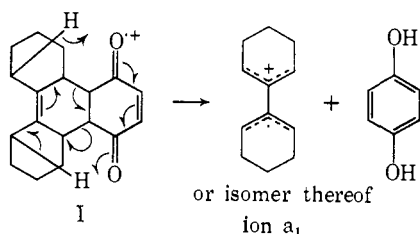
This formulation would explain the absence of ion a in XVIIIb and XIX, in which the 2,3 double bond between the two carbonyl groups has been reduced. Naphthoquinone adducts XX and XXI in which this double bond is a part of a benzo ring undergo this rearrangement much less readily, and the other possible decomposition of this system, namely the retro-Diels–Alder fragmentation, becomes more pronounced.

Experimental Section[11]

Compounds 1,[3] II,[3] III,[12] VIII,[6] XVII,[6] XVIII,[3] XIX,[12] XX,[13] and XXI[12] were prepared according to reported procedures. Bi-(2,6,6-d₃-1-cyclohexen-1-yl) was prepared from 2,2,6,6-d₄-cyclohexanone[14] in the usual way.[3] 1-(1-Cyclopentenyl)-1-cyclohexene (XVI) was prepared according to Skvarchenko,[15] but the dehydration was effected with pyridine and phosphoryl chloride[3,12] (see preparation of IX and X).

4b,8,8,9,9,12a-d₆-1,4,4a,4b,5,6,7,8,9,10,11,12,12a,12b-Tetradecahydrotriphenylene-1,4-dione (IV). The mixture of bi-1-(2,6,6-d₃-cyclohexen)-1-yl (150 mg, 0.9 mmol) and sublimed p-benzoquinone (100 mg, 0.92 mmol) was allowed to stand in the dark at room temperature for 3 days in a closed vial. Trituration with methanol (1 ml) and recrystallization yielded IV (60 mg), mp 113–115° (from methanol), molecular weight 276 (mass spectrum); calcd for $C_{18}H_{16}D_6O_2$, 276.

Mixture of 2-d₁-1-Cyclohexenyl-1-cyclohexene (IX) and 6,6-d₂-1-Cyclohexenyl-1-cyclohexene (X). A solution of 2,2-d₂-cyclohexanone (VIII)[6] (9 g) in dry ether (10 ml) was added dropwise to a stirred solution of 1-cyclohexenyllithium, prepared[16] from 1-cyclohexenyl chloride (20 g) and lithium (2.5 g) in dry ether (300 ml) at 0°. After 1 hr saturated NH₄Cl solution (300 ml) was carefully added; the organic layer was separated, washed with water, and dried (CaCl₂) and the ether removed by evaporation. 1-(1-Cyclohexenyl)-2,2-d₂-cyclohexanol (VIIa) (5.5 g) was distilled at 95–105° (0.2 torr). The solution of VIIa (5 g) in dry pyridine (30 ml) and phosphoryl chloride (8 ml) was heated on a steam bath for 1 hr, and cold water (100 ml) was added carefully after cooling. Extraction with pentane (two 50-ml portions), washing with 10% HCl and saturated Na₂CO₃, solvent evaporation, and distillation (60–65° (0.05 torr)) yielded the mixture of IX and X (2.3 g). The mixture contained also d₀- and d₃-bi-1-cyclohexen-1-yl (see text).

Mixture of 1-(2-d₁-1-Cyclopentenyl)-1-cyclohexene (XVIa) and 1-(5,5-d₂-1-Cyclopentenyl)-1-cyclohexene (XVIb). 2,2-d₂-Cyclopentanone (XVIII)[6] (5 g) was added to 1-cyclohexenyllithium prepared[16] from 1-cyclohexenyl chloride (20 g), lithium (2 g), and ether (250 ml) at 0°, and the mixture was stirred for 1 hr at 0°. Addition of saturated aqueous NH₄Cl solution (250 ml) followed by separation, water washing of the organic solution, drying, and evaporation yielded 1-(1-cyclohexenyl)-2,2-d₂-cyclopentanol (VIIb), which was dehydrated without further purification. The dehydration was affected by heating VIIb with pyridine (50 ml) and phosphoryl chloride (12 ml) for 1 hr followed by work-up similar to that described for IX and X. The mixture of XVIa and XVIb was obtained by distillation at 68–70° (0.3 torr) (3 g), and it contained 6.6% undeuterated 1-cyclopentyl-1-cyclohexene (see text) and bi-1-cyclohexen-1-yl (Va).

2,3,3a,4,7,7b,8,9,10,11-Decahydro-1H-cyclopenta[l]phenanthrene-4,7-dione (XV). Freshly prepared 1-cyclopentenyl-1-cyclohexene (180 mg), freshly sublimed p-benzoquinone (100 mg), and hydroquinone (100 mg) were gently warmed at 100° until a homogenous solution was formed. Pentane was added, and the yellow solution was separated from a black precipitate. Cooling of the pentane solution at −40° and recrystallization of the precipitate from methanol yielded XV (60 mg), mp 88–90°. Anal. Calcd for $C_{17}H_{20}O_2$:

(11) Melting points are uncorrected. Mass spectra were measured with an Atlas CH4 mass spectrometer fitted with a TO-4 ion source and direct inlet system, operated without heating. The samples were heated externally, if necessary, until the ion current was sufficient to provide usable mass spectra. The ionization energy was maintained at 70 eV.
(12) D. S. Greidinger and D. Ginsburg, J. Org. Chem., 22, 1406 (1957).
(13) F. Bergmann, H. E. Eschinazi, and M. Neeman, ibid., 8, 179 (1943).
(14) J. Seibl and T. Gäumann, Helv. Chim. Acta, 46, 2857 (1963).
(15) W. R. Skvarchenko, L. Vzen-Lan, and R. Ya. Levina, Zh. Obshch. Khim., 32, 1023 (1962).
(16) E. A. Braude and J. A. Coles, J. Chem. Soc., 2014 (1950).

(10) S. Meyerson and L. C. Leitch, J. Am. Chem. Soc., 88, 56 (1966).

C, 79.65; H, 7.86. Found: C, 79.52; H, 8.21; mol wt, 256 (mass spectrometry).

A mixture of XVa and XVb was prepared in a similar way from the mixture of dienes XVIa and XVIb.

Mixture of 4b-d_1- and 8,8-d_2-1,4,4a,4b,5,6,7,8,9,10,11,12,12a,12b-Tetradecahydrotriphenylene-1,4-dione (XI and XII). The mixture of dienes IX and X (300 mg) and freshly sublimed p-benzoquinone (200 mg) was allowed to stand at room temperature for 2 days. Trituration with methanol (2 ml) and recrystallization yielded the mixture of adducts XI and XII (200 mg), mp 110–112° (from methanol). The composition of the mixture was determined by mass spectrometry (see Discussion).

Micellar Effects upon Phosphorylation and Phosphate Ester Hydrolysis[1]

C. A. Bunton, L. Robinson, and L. Sepulveda[2]

Contribution from the Department of Chemistry, University of California at Santa Barbara, Santa Barbara, California 93106. Received March 14, 1969

Abstract: The reactions between hydroxide or fluoride ion and p-nitrophenyl diphenyl phosphate, catalyzed by micelles of cetyltrimethylammonium bromide, are inhibited by phenyl, diphenyl, and p-t-butylphenyl phosphate. With decreasing pH the reaction with hydroxide ion becomes unimportant, and micellar-catalyzed reactions between the substrate and inorganic phosphate ions and phenyl and p-t-butylphenyl phosphate dianions can be observed. Diphenyl phosphate monoanion is unreactive. For the micellar catalyzed reaction the reactivity sequence is t-BuC$_6$H$_4$OPO$_3{}^{2-}$ > C$_6$H$_5$OPO$_3{}^{2-}$ > HOP$_4{}^{2-}$ and depends upon the nonbonding interactions between the cationic micelle and the nucleophilic anion, rather than their inherent nucleophilicities. The second-order rate constants for the micellar-catalyzed reaction with hydroxide ion agree well with those calculated at low pH in borate buffer.

Cationic micelles are effective catalysts of reactions between uncharged substrates and nucleophilic anions, and the kinetic dependence upon detergent concentration can be explained in terms of reactions occurring in both the aqueous and micellar phases.[3–7] Both fluoride and hydroxide ions attack triaryl phosphates[8] and their reactions with p-nitrophenyl diphenyl phosphate are catalyzed by the cationic detergent cetyltrimethylammonium bromide (CTA), but retarded by the anionic detergent sodium lauryl sulfate (NaLS) and the uncharged polyether Igepal.[7] The catalysis by the cationic micelles is inhibited by added anions. We had earlier found that the catalyzed hydrolyses of the dianions of 2,4- and 2,6-dinitrophenyl phosphates were strongly inhibited by bulky anions, such as those of aryl phosphates,[9] and the present work had the twofold purpose of studying the inhibition of the micellar catalyzed reaction of hydroxide or fluoride ion with p-nitrophenyl diphenyl phosphate by aryl phosphate dianions and attempting to establish a micellar-catalyzed phosphorylation of an aryl phosphate dianion by p-nitrophenyl diphenyl phosphate (I). This system is very satisfactory for this purpose, because it is easy to make structural modifications of the aryl phosphate dianion, without affecting its nucleophilicity so far as reaction in water is concerned, by introducing bulky alkyl groups into the aryl group to increase the binding between the nucleophile and the micelle.

As well as examining the micellar-catalyzed reaction between p-nitrophenyl diphenyl phosphate and hydroxide ion of known concentration we also measured the reaction rate in buffers, so that we could compare the second-order rate constant calculated directly with that calculated from the hydroxide ion concentration estimated from the pH of the solution.

A number of workers have drawn analogies between micellar- and enzyme-catalyzed reactions.[3–7,9,10] The main similarities appear to be in the hydrophobic interactions between the substrate and catalyst; as in enzymic reactions chemically similar substrates can act either as a catalyst or an inhibitor, and the importance of phosphorylation in biological systems makes it useful to examine micellar-catalyzed phosphorylation. A few experiments were also carried out on the effects of detergents on the reactions between pyridine and p-nitrophenyl diphenyl or 2,4-dinitrophenyl phosphate,[11] but the rate enhancements were small and these reactions were not studied extensively.

Experimental Section

Materials. The preparation and purification of most of the reagents have been described.[6,7,9] Pyridine was redistilled before use.

Kinetics. The reactions were followed spectrophotometrically using a Gilford spectrophotometer with a water-jacketed cell compartment. Nucleophilic attack gives p-nitrophenoxide ion which can be detected spectrophotometrically.

(1) Support of this work by the National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service, is gratefully acknowledged.

(2) University of Chile–University of California Cooperative Program Fellow, on leave from the Faculty of Chemistry and Pharmacy, University of Chile, Santiago.

(3) F. M. Menger and C. E. Portnoy, *J. Amer. Chem. Soc.*, **89**, 4698 (1967).

(4) L. R. Romsted and E. H. Cordes, *ibid.*, **90**, 4404 (1968).

(5) (a) T. C. Bruice, J. Katzhendler, and L. R. Fedor, *ibid.*, **90**, 1333 (1968); (b) C. Gitler and A. Ochoa-Solano, *ibid.*, **90**, 5004 (1968).

(6) C. A. Bunton and L. Robinson, *ibid.*, **90**, 5972 (1968).

(7) (a) C. A. Bunton and L. Robinson, *J. Org. Chem.*, **34**, 773 (1969); (b) C. A. Bunton and L. Robinson, *ibid.*, **34**, 780 (1969).

(8) J. R. Cox and O. B. Ramsay, *Chem. Rev.*, **64**, 343 (1964).

(9) C. A. Bunton, E. J. Fendler, L. Sepulveda, and K-U. Yang, *J. Amer. Chem. Soc.*, **90**, 5512 (1968).

(10) D. G. Herries, W. Bishop, and F. M. Richards, *J. Phys. Chem.*, **68**, 1842 (1964).

(11) A. J. Kirby and A. G. Varvoglis, *J. Chem. Soc.*, B, 135 (1968).