Free-Radical Alkylations of 2-Hydroxy-1,4-naphthoquinone[1]

EARL S. HUYSER AND BIJAN AMINI

Department of Chemistry, University of Kansas, Lawrence, Kansas 66044

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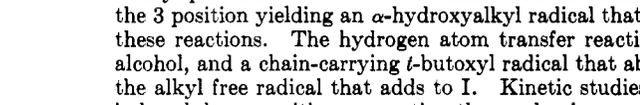
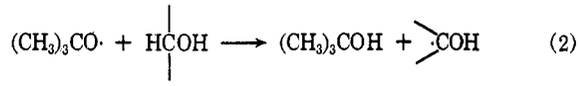
2-Hydroxy-1,4-naphthoquinone (I) can be alkylated in the 3 position by reaction of I with a hydrocarbon and *t*-butyl peroxide. A free-radical chain reaction consisting of the addition of an alkyl radical to the quinone at the 3 position yielding an α-hydroxyalkyl radical that transfers a hydrogen atom to the peroxide is proposed for these reactions. The hydrogen atom transfer reaction yields the keto form of the alklation product, *t*-butyl alcohol, and a chain-carrying *t*-butoxyl radical that abstracts a hydrogen atom from the hydrocarbon producing the alkyl free radical that adds to I. Kinetic studies of the reaction indicate that the peroxide undergoes an induced decomposition supporting the mechanism proposed for these reactions.

In an earlier investigation, it was shown that *t*-butyl peroxide is reduced by α-hydroxyalkyl radicals.[2] The transfer of a hydrogen atom from the α-hydroxyalkyl radical to the peroxide linkage, reducing the peroxide to a molecule of *t*-butyl alcohol and a *t*-butoxyl radical, results in oxidation of the α-hydroxyalkyl radical to an aldehyde or ketone. In the reactions investigated, namely, the oxidation of primary and secondary alcohols (eq 1 and 2), the α-hydroxyalkyl radical was formed by abstraction of an α-hydrogen from the alcohol by the *t*-butoxyl radical produced in the hydrogen atom transfer reaction. The chain sequence (eq 1 and 2) involves the peroxide as a reactant and accounts for both the oxidation of the alcohol and the observation that the peroxide is consumed in these reactions at a rate faster than that of its unimolecular decomposition at the same temperature. The present investigation is concerned with the reaction of *t*-butyl peroxide with an α-hydroxyalkyl radical produced by the addition of an alkyl radical to a suitable enol. The enolic compound used in this work was 2-hydroxy-1,4-naphthoquinone (I).

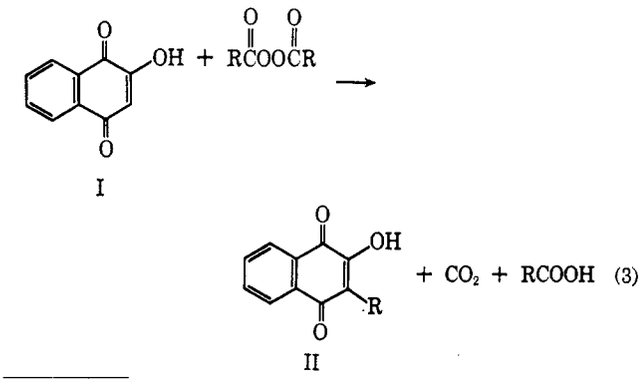


(1)



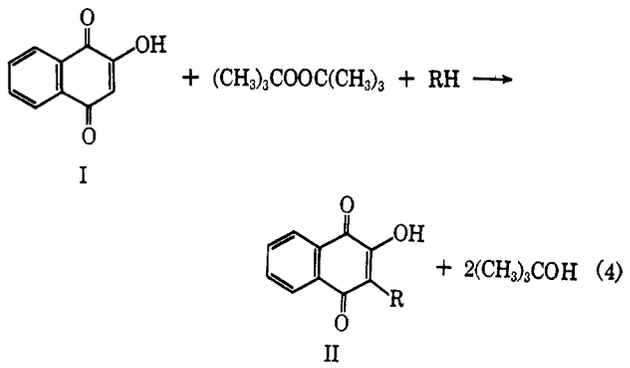
(2)

Fieser and his coworkers reported the synthesis of a number of 2-hydroxy-3-alkyl-1,4-naphthoquinones in yields ranging from 30 to 60% for straight-chain alkyl groups and from 1 to 30% for α-substituted groups by the reaction of I with acyl peroxides (reaction 3).[3]



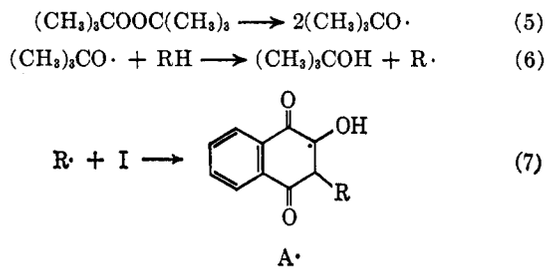
(3)

Carbon dioxide and a carboxylic acid were also produced in these reactions. We have found that similarly substituted 2-hydroxy-1,4-napthhoquinones can be prepared in higher yields by reaction of I, *t*-butyl peroxide, and a suitable hydrocarbon (reaction 4). An advantage of this procedure over that used previously, aside from the higher yields (Table I), is that synthesis of an acyl peroxide as one of the reactants is not necessary.



(4)

The reaction sequence given in eq 5–14 is a possible mechanism for these alkylation reactions. Reactions 6, 7, and 8 comprise a chain sequence of radical-



(5)–(14)

(1) This work was supported by a grant (AM 08517) from the National Institutes of Health.

(2) E. S. Huyser and C. J. Bredeweg, *J. Am. Chem. Soc.*, **86**, 240 (1964).

(3) L. F. Fieser and A. E. Oxford, *ibid.*, **64**, 2060 (1942); L. F. Fieser, E. Berliner, F. J. Bondhus, F. C. Chang, W. G. Dauben, M. G. Ettlinger, G. Fawaz, M. Fields, C. Heidelberger, H. Heymann, W. R. Vaughan, A. G. Wilson, E. Wilson, M. Wu, M. T. Leffler, K. E. Hamlin, E. J. Matson, E. E. Moore, M. B. Moore, and H. E. Zaugg, *ibid.*, **70**, 3174 (1948).

TABLE I

ALKYLATIONS OF 2-HYDROXY-1,4-NAPHTHOQUINONE

Hydrocarbon (mole)	I, mole	Peroxide, mole	Product (mole)	Conversion,[a] %
Toluene (0.26)	0.0075	0.024	2-Hydroxy-3-benzyl-1,4-naphthoquinone (0.0049)[b]	66
Ethylbenzene (0.25)	0.0127	0.038	2-Hydroxy-3-(1′-phenylethyl)-1,4-naphthoquinone (0.0081)[c]	64
Cumene (0.26)	0.0132	0.037	2-Hydroxy-3-(1′-methyl-1′-phenylethyl)-1,4-naphthoquinone (0.0091)[d]	69
Diphenylmethane (0.25)	0.013	0.038	2-Hydroxy-3-diphenylmethyl-1,4-naphthoquinone (0.0104)[e]	80
Cyclohexane (0.56)	0.0075	0.024	2-Hydroxy-3-cyclohexyl-1,4-naphthoquinone (0.0040)[f]	53

[a] Based on amount of I initially present. [b] Registry no.: 15451-49-9 [c] 15451-42-0. [d] 15451-43-1. [e] 15451-44-2. [f] 4042-30-2.

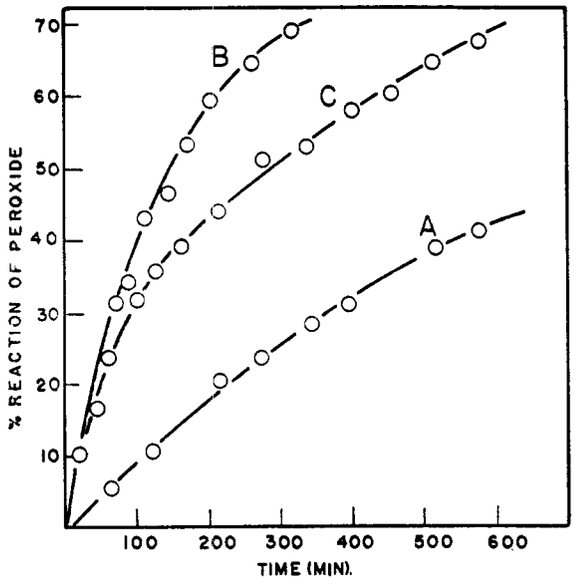


Figure 1.—Decomposition rates of *t*-butyl peroxide at 125°: reaction A, ethylbenzene (0.190 mole), *t*-butyl peroxide (0.011 mole); reaction B, ethylbenzene (0.203 mole), *t*-butyl peroxide (0.0043 mole), I (0.011 mole); reaction C, ethylbenzene (0.373 mole), *t*-butyl peroxide (0.023 mole), I (0.0078 mole).

propagating reactions that accounts for the stoichiometry of the alkylation reaction 4. A key step in this chain sequence is reaction 8, a hydrogen atom transfer reaction in which A· is oxidized to the keto tautomer of II and the peroxide is reduced to a molecule of *t*-butyl alcohol and a *t*-butoxyl radical. The *t*-butoxyl radical propagates the chain by abstraction of a hydrogen atom from the hydrocarbon giving another molecule of *t*-butyl alcohol and an alkyl radical that can add to I producing A·. The limiting feature of this synthetic route to 2-hydroxy-3-alkyl-1,4-naphthoquinones is the hydrogen atom abstraction reaction. If more than one type of alkyl radical can be produced by the abstraction of different hydrogens by the *t*-butoxyl radical, a mixture of products will result. In our reactions, we used only hydrocarbons having benzylic hydrogens, which are far more reactive toward hydrogen atom abstraction by *t*-butoxyl radicals than any other hydrogens of the hydrocarbon, or, as is the case with cyclohexane, a hydrocarbon that can yield only a single alkyl radical in the hydrogen atom abstraction reaction.

Support for a mechanism involving reaction of the peroxide in a chain-propagating reaction was obtained from the rates of decomposition of *t*-butyl peroxide in ethylbenzene found both in the presence and the absence of I. If the chain sequence 6, 7, and 8 is operative, the peroxide would be consumed not only in reaction 5, the unimolecular decomposition, but also in the chain-propagating reaction 8. The rate at which the peroxide reacts in such a case would be given by eq 15.

$$\frac{-d[\mathrm{Per}]}{dt} = k_5[\mathrm{Per}] + k_8[\mathrm{A}\cdot][\mathrm{Per}] \qquad (15)$$

The observed rate of decomposition of *t*-butyl peroxide in ethylbenzene in the presence of a greater than a stoichiometric amount of I relative to the peroxide (reaction B in Figure 1) is markedly faster than the rate of the unimolecular decomposition of the peroxide in ethylbenzene alone (reaction A). Furthermore, the rate of reaction of the peroxide is enhanced only as long as I is present to participate in the chain reaction. This is evidenced by the observed rate of reaction of the peroxide when less than a stoichiometric amount of I relative to the peroxide is present (reaction C). In this case, the initial ratio of quinone to peroxide is about 1:3 and rate enhancement is observed during the reaction of the first 35–40% of the peroxide, a period during which the quinone is still present in appreciable concentration.

Decomposition of *t*-butyl peroxide in a solvent such as ethylbenzene is, as would be expected, a reaction that is first order in peroxide since the rate is adequately described by the first term of the rate equation (eq 15). We observed that the induced decomposition of the peroxide in the presence of a stoichiometric excess of I relative to the peroxide (reaction B) was also first order in peroxide (Figure 2). The rate law for the in-

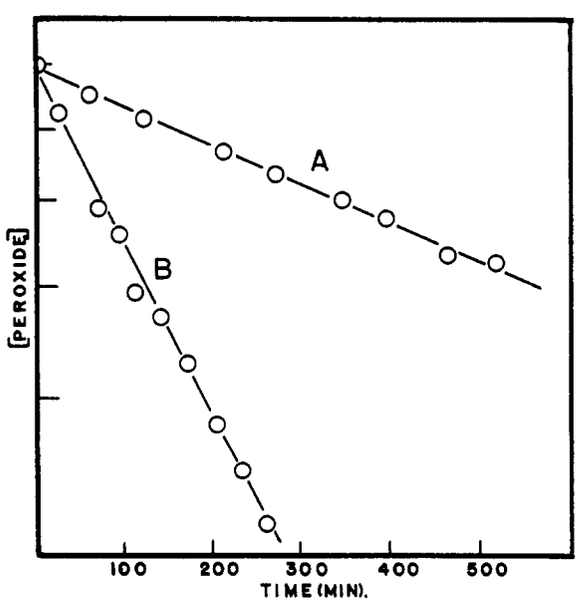


Figure 2.—First-order plots for *t*-butyl peroxide decomposition in ethylbenzene (A) and in ethylbenzene and a stoichiometric excess of I relative to the peroxide (B).

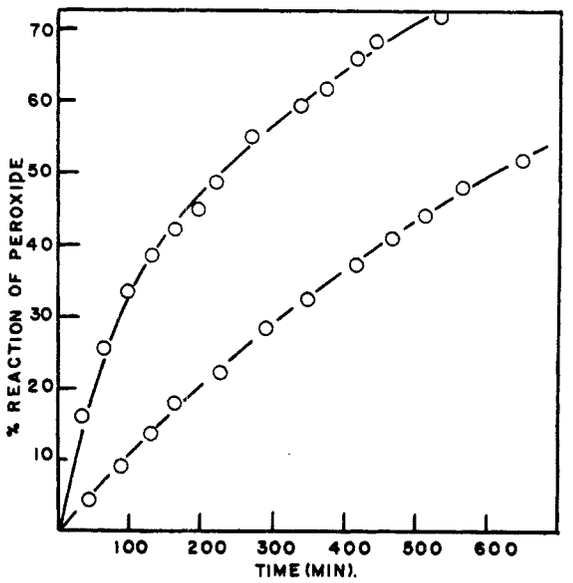


Figure 3.—Decomposition rates of acetyl peroxide at 70°: reaction D (top curve), acetic acid (1.048 moles), acetyl peroxide (0.058 mole), I (0.018 mole); reaction E (bottom curve), acetic acid (1.048 moles), acetyl peroxide (0.062 mole).

duced decomposition of the peroxide derived on the basis of steady-state concentrations for all radicals depends on the termination reaction (or reactions). In this case, there are three chain-carrying radicals and, hence, the six possible termination reactions shown in eq 9–14. Only the derived rate laws involving the cross-termination reactions 9 and 10 predict the reaction rate in the presence of I to be a first-order reaction in peroxide. Our attempts to distinguish be-

$$\frac{-d[Per]}{dt} = \left[k_5 + \left(\frac{-k_5k_9 \pm (k_5^2k_9^2 + 8k_5k_6k_8k_9[RH])^{1/2}}{4k_9}\right)\right][Per] \quad (16)$$

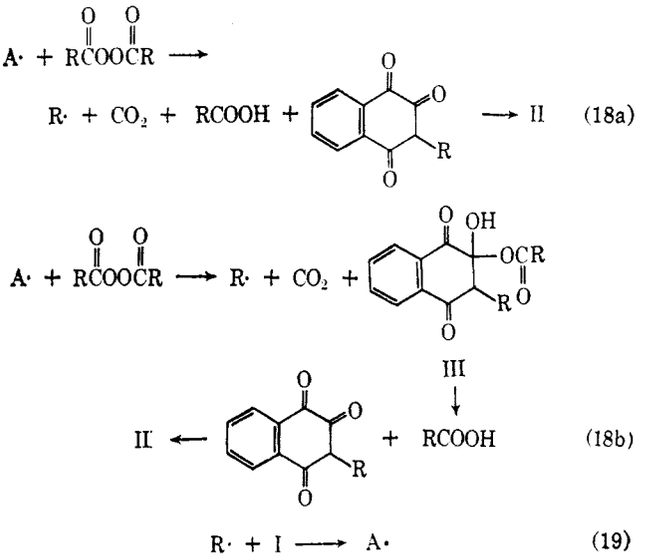
(termination reaction 9)

$$\frac{-d[Per]}{dt} = \left[k_5 + \left(\frac{-k_5k_{10} \pm (k_5^2k_{10}^2 + 8k_5k_7k_8k_{10}[I])^{1/2}}{4k_{10}}\right)\right][Per] \quad (17)$$

(termination reaction 10)

tween these two termination reactions by varying the concentration of I were not successful, owing to the very low solubility of I in ethylbenzene. The rate found for reaction B involved a very nearly saturated solution of I in ethylbenzene. At lower concentrations of I, the amount of peroxide necessary to maintain a sufficiently high ratio of I to peroxide for determination of the induced decomposition rate was too low to allow for reliable analyses of the peroxide.

The decomposition rate of acetyl peroxide in acetic acid is also markedly enhanced by the presence of I (Figure 3). Rate enhancement is observed only until the quinone is consumed (reaction D) after which time the rate of decomposition of the peroxide is essentially the same as that found in acetic acid alone (reaction E). The alkylations of I with acyl peroxides very likely proceed by a chain mechanism (reactions 18 and 19) quite similar to that proposed for the *t*-butyl peroxide induced reactions. The induced decomposition of acyl peroxides may proceed by a hydrogen atom transfer process similar to that proposed for the *t*-



butyl peroxide reaction as shown in eq 18a. However, the reaction of A· with the acyl peroxide may involve the alternate path 18b in which the hemiacylal III is formed as a reaction intermediate. The keto tautomer of II and the carboxylic acid would result from the decomposition of the hemiacylal. The formation of hemiacylals in the reactions of α-hydroxyalkyl radicals with acetyl peroxide was suggested by Kharasch and coworkers[4] to account for the enhanced rates of decomposition of the peroxide and formation of a ketone and acetic acid as reaction products. Support for hemiacylal formation comes from the fact that α-alkoxyalkyl radicals, which do not react with *t*-butyl peroxide,[2] do react with acyl peroxides, yielding isolable acylals.[5]

Experimental Section

Materials.—The hydrocarbons were commercial materials and distilled twice before using. 2-Hydroxy-1,4-naphthoquinone (Aldrich Chemical Co.) was recrystallized from chloroform, mp 195–196°. *t*-Butyl peroxide and 25% solution of acetyl peroxide in dimethyl phthalate were obtained from Lucidol Corp. and used without further purification.

Alkylations of 2-Hydroxy-1,4-naphthoquinone.—Mixtures consisting of the hydrocarbon, *t*-butyl peroxide, and 2-hydroxy-1,4-naphthoquinone in the amounts shown in Table I were sealed in a 100-ml round-bottom flask and heated for 4–7 hr at 125°. Owing to the insolubility of I in the hydrocarbons, the mixtures were not homogeneous but became so after about 2 hr at 125°. The excess hydrocarbon was removed from the reaction mixtures on a rotary evaporator and the resulting residue mixed with hot benzene, a solvent in which the 2-hydroxy-1,4-naphthoquinone was not soluble but which did dissolve the alkylation product. The unreacted 2-hydroxy-1,4-naphthoquinone was removed by filtration and the benzene solution concentrated, leaving the crude crystalline alkylation product which was recrystallized from a suitable solvent. The following 2-hydroxy-3-alkyl-1,4-naphthoquinones were prepared in the yields listed in Table I in the manner described.

2-Hydroxy-3-benzyl-1,4-naphthoquinone was recrystallized from petroleum ether (60–80°)–benzene: mp 175–176.5° (lit.[6] mp 175–176°); infrared absorptions (KBr) at 3358, 1652, 1581, 1490, and 698 cm^{-1}; nmr signals ($DCCl_3$) at δ 7.94 (four protons), 7.32 (five protons), and 3.90 ppm (singlet, two protons).

2-Hydroxy-3-(1′-phenylethyl)-1,4-naphthoquinone was recrystallized from cyclohexane as pale yellow needles: mp 110.5–111.5°; infrared absorptions (KBr) at 3358, 1640, 1587, 724, and

(4) M. S. Kharasch, H. N. Friedlander, and W. H. Urry, *J. Org. Chem.*, **14**, 91 (1949).
(5) W. E. Cass, *J. Am. Chem. Soc.*, **68**, 976 (1946); **69**, 500 (1947).
(6) L. F. Fieser, *ibid.*, **48**, 3201 (1926).

684 cm^{-1}; nmr signals ($DCCl_3$) at δ 7.15–8.16 (nine protons), 4.73 (quartet, one proton), and 1.76 ppm (doublet, three protons).

Anal. Calcd for $C_{18}H_{14}O_3$: C, 77.67; H, 5.07. Found: C, 77.48; H, 4.88.

2-Hydroxy-3-(1′-methyl-1′-phenylethyl)-1,4-naphthoquinone was recrystallized from cyclohexane as pale, yellow needles: mp 137–137.5°; infrared absorptions (KBr) at 3308, 1648, 1590, 772, 732, and 704 cm^{-1}; nmr signals ($DCCl_3$) at δ 7.39–8.04 (four protons), 7.23 (five protons), and 1.82 ppm (singlet six protons).

Anal. Calcd for $C_{19}H_{16}O_3$: C, 78.06; H, 5.51; Found C, 78.13; H, 5.62.

2-Hydroxy-3-(diphenylmethyl)-1,4-naphthoquinone was recrystallized from cyclohexane: mp 188–188.5° (lit.[6] mp 186.5°); infrared absorptions (KBr) at 3355, 1652, 1589, 1492, 744, 724, and 698 cm^{-1}; nmr signals (DMSO) at δ 7.92 (four protons), 7.27 (ten protons), and 5.95 ppm (singlet, one proton).

2-Hydroxy-3-cyclohexyl-1,4-naphthoquinone was recrystallized from cyclohexane: mp 136–137.5° (lit.[3] mp 136.5–137.5°; infrared absorptions at 3355, 1661, 1589, 726, and 675 cm^{-1}; nmr signals ($DCCl_3$) at δ 7.60–8.04 (*ca.* four protons), 3.08 (multiplet, *ca.* one proton), 1.15–2.12 ppm (multiplet, *ca.* ten protons).

Kinetic Measurements. *t*-Butyl Peroxide Determinations.—Solutions containing *t*-butyl peroxide and I in ethylbenzene (molar ratio of I to ethylbenzene about 1:50, the limit of solubility of the quinone at 125°) were placed in a 100-ml round-bottom flask with an 8-in. neck. The flask was sealed with a rubber septum and suspended in a constant-temperature oil bath set at 125°. Samples (1.0–1.5 ml) were withdrawn at various time intervals with a syringe equipped with a 10-in. needle. The peroxide content of the withdrawn sample was determined by gas chromatographic analysis of a mixture consisting of an accurately weighed quantity of the sample and benzene which served as an internal standard. A correction factor relating the mole ratios of *t*-butyl peroxide and benzene to the ratios of their chromatographic peak areas was determined from mixtures containing known amounts of each. The gas chromatographic analysis were performed with an F & M Model 5750 instrument equipped with a hydrogen flame detector using a 6 ft × $^1/_8$ in. column packed with 2% DEGS and 8% SF-96 on 60/80 mesh Chromosorb W. The chromatograms were traced with a Mosely recorder equipped with a disk intergrator.

Acetyl Peroxide Determinations.—Solutions consisting of acetyl peroxide (dissolved in dimethyl phthalate) and I in acetic acid were placed in a 100-ml round-bottom flask equipped with an 8-in. neck. The flask was sealed with a rubber septum and placed in a constant-temperature bath set at 70°. Samples were withdrawn at various time intervals and their peroxide content was determined by the iodometric method outlined by Silbert and Swern.[7]

Registry No.—I, 83-72-7.

(7) L. S. Silbert and D. Swern, *Anal. Chem.*, **30**, 385 (1958).

1,4-Diphosphoniacyclooctene and Diene Salts. Their Formation, Hydrolysis, and Attempted Conversion to 1,4-Diphosphacyclooctatetraenes

A. M. AGUIAR AND M. G. RAGHANAN NAIR

Chemistry Department, Tulane University, New Orleans, Louisiana

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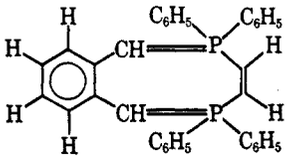
Our interest in the 1,4-diphosphorus cyclohexanes[1-3] led us to prepare 1,4-diphosphorus derivatives of benzocyclooctene and diene in order to obtain the diylide tetraene (A).



A

Reaction of *o*-bis(bromomethyl)benzene (I) with ethylenebis(diphenylphosphine) (II)[4] or *cis*-vinylenebis(diphenylphosphine) (III)[5] (in refluxing benzene) gave 1,1,4,4-tetraphenyl-1,4-diphosphonia-6,7-benzocyclooctene-6 dibromide (IV) and 1,1,4,4-tetraphenyl-1,4-diphosphonia-6,7-benzocyclooctadiene-2,6 dibromide (V), respectively, in quantitative yields (Scheme I).

Infrared spectral analysis of both IV and V showed bands at 1430–1440 and 1105–1110 cm^{-1}, expected of a phenylphosphonium salt. Solubilities and titration with aqueous silver nitrate confirmed this conclusion. Elemental analysis showed IV to be a 1:1 adduct of I and II and V to be a 1:1 adduct of I and III. Preparation of picrates of both IV and V by treatment with aqueous sodium picrate followed by elemental analysis of these materials showed that all of the halogen in IV and V was ionic. Both IV and V are, therefore, cyclic. The solubilities and melting points also make it unlikely that IV or V are very long polymeric phosphonium salts.

Molecular weight data obtained for methanolic solutions of V employing an osmometer show it to be associated and effectively a 1:1 electrolyte at concentrations above 0.01 *M* (with an effective mol wt = $^1/_2$ mol wt) but to dissociate at decreasing concentrations (Table I). Extrapolation to infinite dilution proved to be impossible owing to lack of reliability of the instrument at very low concentrations. Conductance mea-

TABLE I

MOLECULAR WEIGHT DETERMINATIONS OF V IN METHANOL SOLUTION BY OSMOMETRIC METHOD

Concn, moles/l.	Mol wt
0.0137	323
0.0272	332
0.0530	337

(1) A. M. Aguiar, H. J. Aguiar, and D. J. Daigle, *J. Am. Chem. Soc.*, **87**, 671 (1965).

(2) A. M. Aguiar and H. J. Aguiar, *ibid.*, **88**, 4090 (1966).

(3) A. M. Aguiar, K. C. Hansen, and G. S. Reddy, *ibid.*, **89**, 3067 (1967). The rhodium catalyst was suggested by Professor A. I. Meyers of Louisiana State University in New Orleans.

(4) A. M. Aguiar and J. Beisler, *J. Org. Chem.*, **29**, 1660 (1964).

(5) A. M. Aguiar and D. J. Daigle, *J. Am. Chem. Soc.*, **86**, 2299 (1964).