was repeated until hydrocarbons of the desired isotopic purity had been reached.

The course of the exchange reaction could be examined continuously by monitoring either the parent peaks of the partially exchanged hydrocarbons or the formation of HD in the mass spectrometer. Since the exchange process was proportional to the distance from equilibrium, the rate became extremely slow as equilibrium was approached. For this reason, the hydrogen mixture was usually removed before complete equilibration in order to minimize the amount of olefin hydrogenation.

Acknowledgment.—This work was sponsored by the Gulf Research and Development Company as part of the research program of the Multiple Fellowship on Petroleum.

Macro Rings. XXXI. Quinone Derived from [2.2]Paracyclophane, an Intramolecular–Molecular Complex[1]

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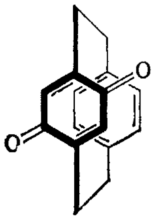
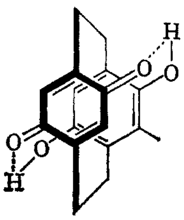
The quinone derived from [2.2]paracyclophane has been synthesized. Its ultraviolet absorption spectrum exhibits a band at 340 mμ (ϵ 597) not present in model compounds which is probably due to a charge-transfer transition. An aryn was demonstrated to intervene as an intermediate in the conversion of 4-bromo[2.2]paracyclophane to 4-hydroxy[2.2]paracyclophane with potassium *t*-butoxide in dimethyl sulfoxide. In a new reaction, the paracyclophanyl aryn reacted with dimethyl sulfoxide to give 4-hydroxy-5-thiomethoxy[2.2]paracyclophane.

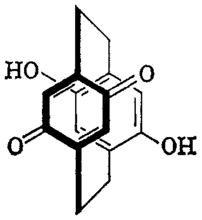
The fixed geometry of [2.2]paracyclophane, known from X-ray diffraction studies,[2] suggests that, with proper structural modification, intramolecular–molecular complexes based on this ring system might be composed. Accordingly, synthetic experiments designed to produce quinones I–III were initiated. The latter two compounds are exotic quinhydrones, which differ from each other in a very interesting way. In II, the proximity of the interannular oxygens would allow maximum interannular hydrogen bonding, a feature absent in III. The synthesis of I has been realized, and progress has been made toward the syntheses of II and III.



I

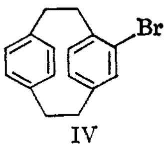


II

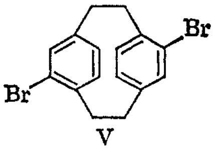


III

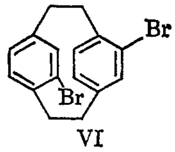
Production and Reaction of Aryns in the [2.2]-Paracyclophane System.—Bromination of [2.2]paracyclophane with 1 equiv of bromine and a trace of ferric bromide gave high yields of the monobromo derivative IV, whereas 2 moles of bromine gave a mixture of at least two dibromo derivatives (V and VI),[3] the structures of which are based on nmr spectra.[3b] The fact that only traces of the dibromides were produced when only 1 equiv of bromine was used provides further evidence that an electron-withdrawing substituent in one ring deactivates both rings toward further electrophilic attack.[4] Treatment of 4-bromo[2.2]paracyclophane (IV) with potassium *t*-butoxide in dimethyl sulfoxide[5] produced a mixture of ether VII, phenol VIII, and the unexpected thioether phenol IX (Scheme I).



IV

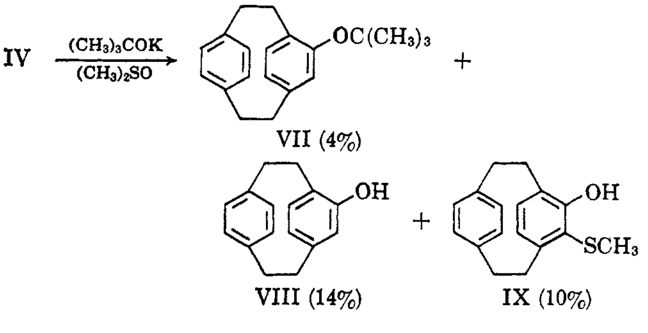


V



VI

Scheme I



The last compound probably arose by addition of the elements of dimethyl sulfoxide to an intermediate aryn, followed by demethylation of the sulfonium salt. An attractive mechanism for the direct production of phenol VIII from IV involves addition of *t*-butoxide anion to the aryn intermediate, followed by an intramolecular elimination reaction to give the phenol and isobutylene (Scheme II). Much high molecular weight material also seemed to be produced in this reaction.

The structure assigned to IX was based on the following evidence. The infrared spectrum in carbon tetrachloride of IX gave a band at 3373 cm^{-1} whose extinction coefficient was unaffected by dilution and which appeared to be associated with the presence of an intramolecular hydrogen bond. In contrast, phenol VIII showed hydroxylic absorption at 3571 cm^{-1}.

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[1] The authors wish to thank the National Research Foundation for a grant used in support of this research.

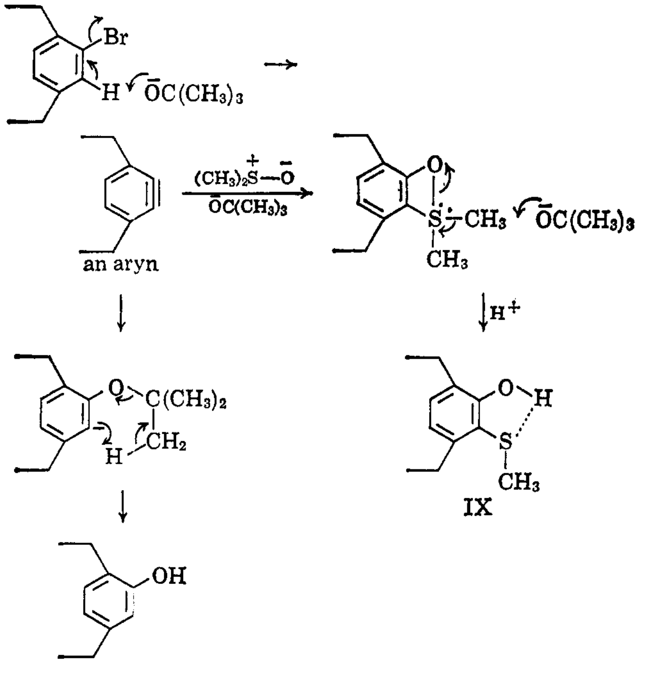
[2] D. A. Bekoe and K. N. Trueblood, private communication.

[3] (a) W. F. Gorham, Canadian Patent 638,335 (1962). (b) The data will be published (D. J. Cram and H. J. Reich) in connection with an extensive correlation of structures of disubstituted [2.2]paracyclophanes.

[4] (a) D. J. Cram and N. L. Allinger, *J. Am. Chem. Soc.*, **77**, 6289 (1955); (b) D. J. Cram, W. J. Wechter, and R. W. Kierstead, *ibid.*, **80**, 3126 (1958).

[5] D. J. Cram, B. Rickborn, and G. R. Knox, *ibid.*, **82**, 6412 (1960).

SCHEME II

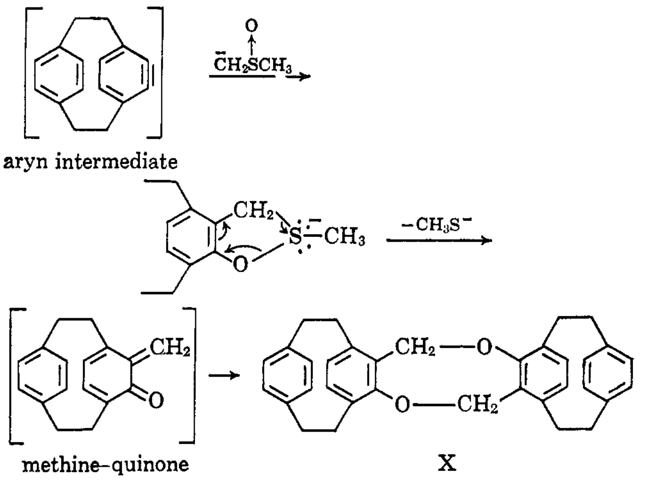


VIII

The ultraviolet spectrum of IX in 95% ethanol, with or without added hydrochloric acid, contained a peak at λ_{max} 323 mμ (log ε 3.08), which was shifted by addition of base by 28 mμ to λ_{max} 351 mμ (log ε 3.45). The model compound, *o*-methylthiophenol, gave λ_{max} 289 mμ (log ε 3.51), which was shifted by base to 308 mμ (lot ε 3.66).[6] The nmr spectrum of IX in carbon tetrachloride contained a singlet corresponding to three protons at τ 8.04 (CH_3–S). Methyl protons in dimethyl sulfide absorb at τ 7.92. A band at τ 3.41 (one proton) in the spectrum of IX was assigned as a hydroxyl proton since it disappeared when IX was treated with deuterium oxide. This low τ value for the hydroxyl proton should be compared with the value of τ 4.4 exhibited by *o*-chlorophenol at infinite dilution. By contrast, *p*-chlorophenol, in which no intramolecular hydrogen bonding is possible, gave τ 5.3 at infinite dilution.[7] Integration of the remaining complex series of peaks indicated the presence of eight methylenic and six aromatic protons. Finally, phenol thioether IX was desulfurized with Raney nickel to give phenol VIII in 63% yield; 17% of the starting material was recovered.

Phenol VIII was characterized as its acetate and methyl ether. Ether VII (low-melting solid) was not fully characterized. Its structural assignment was based on the presence of infrared bands at 1387 and 1364 cm^{-1} characteristic of the *t*-butyl group and on its smooth conversion to phenol VIII when treated with acid.

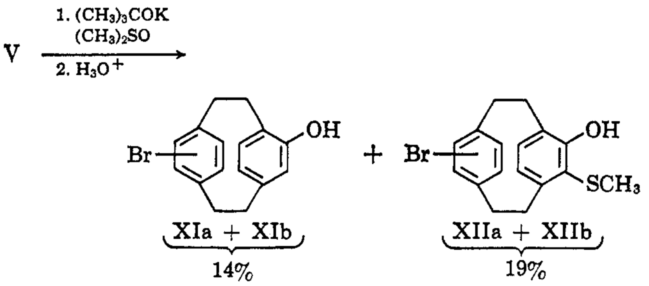
SCHEME III



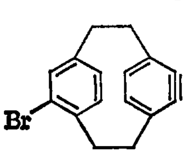
X

A fourth compound of higher molecular weight was isolated in trace amounts from the reaction of bromo compound IV with potassium *t*-butoxide–dimethyl sulfoxide. This substance possibly possesses structure X, produced by the complex series of reactions indicated in Scheme III.

The higher melting dibromide (probably of structure V, which possesses a center of symmetry), when treated with potassium *t*-butoxide in dimethyl sulfoxide, gave products which were treated with acid to convert any *t*-butyl ethers present to phenols. Chromatographic separation of the products produced four compounds in a pure state, XIa, XIb, XIIa, and XIIb. The structures of the individual isomers in each set were not assigned. A trace (1%) of what was probably a mixture of isomeric diphenolic compounds was also obtained (bands at 3550 and 3333 cm^{-1} in the infrared spectrum), but the pure components were not isolated. The spectral properties of XIa, XIb, XIIa, and XIIb are recorded in the Experimental Section.



The fact that a pure dibromide produces isomeric bromophenols and isomeric bromomethylthiophenols provides very strong evidence that an aryn (A) intervenes as an intermediate in these reactions. Apparently conditions were not forcing enough to produce more than small amounts of diphenols.



A
(aryn intermediate)

Synthesis of [2.2]Paracyclophanequinone (I).—Attempts to oxidize phenol VIII directly to quinone I with potassium nitrosodisulfonate[8] were unsuccessful. A water-soluble intermediate was formed, which slowly

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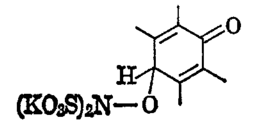
[6] E. A. Fehnel and M. Carmack, *J. Am. Chem. Soc.*, **71**, 2889 (1949).

[7] (a) C. M. Huggins, G. C. Pimentel, and J. M. Shoolery, *J. Phys. Chem.*, **60**, 1311 (1956); (b) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, p 69.

[8] H. J. Teuber and G. Thaler, *Ber.*, **92**, 667 (1959).

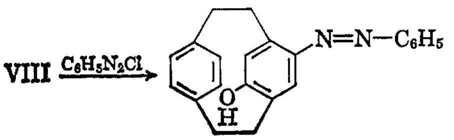
decomposed in acid solution to give starting material and only traces of carbonyl-containing product. In at least one case, Teuber[8] observed an intermediate of the part structure B to be unusually stable, but its



B

decomposition did not produce starting material as was observed in the present work. The unusual behavior of phenol VIII in this reaction is probably associated with the strain inherent in the highly confined ring system of the paracyclophane.

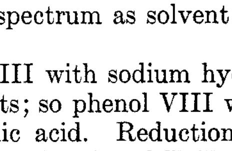
The successful conversion of phenol VIII to quinone I employed the diazonium coupling procedure.[9] Initially, VIII was coupled with benzenediazonium chloride to give XIII. This material gave a free hydroxyl



XIII (98%)

band at 3580 cm^{-1} in its infrared spectrum (dichloromethane), as well as a broad, weak band at 3254 cm^{-1} which disappeared on dilution, and thus must be associated with an intermolecular hydrogen-bonded hydroxyl. In this behavior, XIII resembles *p*-benzeneazophenol, but differs markedly from 1-benzeneazo-2-naphthol, which gives no detectable hydroxylic absorption at any concentration. Azo compound XIII also resembles *p*-benzeneazophenol in its change in ultraviolet absorption spectrum as solvent is changed from acid to base.

Reduction of XIII with sodium hydrosulfite gave a mixture of products; so phenol VIII was coupled with diazotized sulfanilic acid. Reduction of the product gave the unstable aminophenol XIV, which was characterized as is diacetyl derivative. Oxidation of XIV



XIV

with ferric sulfate in sulfuric acid solution[10] gave quinone I in 68% over-all yield from phenol. The compound gave a pink coloration in Craven's quinone test.[11]

Spectral Properties of [2.2]Paracyclophanequinone (I).—Figure 1 records the ultraviolet absorption spectrum of [2.2]paracyclophanequinone, [4.4]paracyclophanequinone,[12] an equal molar mixture of 2,5-dimethylbenzoquinone and *p*-xylene, and an equal molar mixture of 2,5-dimethylbenzoquinone and [8]paracyclophane.[13] The difference in the four curves attests to the presence of transannular effects in the paracyclophanequinones, particularly in the lower homolog in which the benzene and benzoquinone groups are held very close to one another. Particularly striking is the band at λ_{max} 340 mμ (ε 597) present in [2.2]paracyclophanequinone but absent in any of the model compounds. This absorption cannot be associated with deformation of the benzene ring from planarity since this band is absent in the spectrum of [8]paracyclophane–2,5-dimethylbenzoquinone. It seems probable that this absorption is due to a charge-transfer transition in this intramolecular–molecular complex. This band is absent in [4.4]paracyclophanequinone. This fact correlates with the observation that the charge-transfer complex of tetracyanoethylene with the [4.4] homolog possessed a spectrum more comparable with open-chain model complexes than the [2.2] or even the [6.6] complex.[14] In the [4.4]paracyclophane system, the lack of flexibility of the methylene bridges (as compared with the [6.6] homolog) actually seems to hold the rings apart and not provide the distance between the rings that is best for charge transfer. As with the tetracyanoethylene–paracyclophane complexes, possibly the [3.3] ring system will provide the best geometry for charge transfer between the benzene and quinone moieties. However, Weissman[15] observed that the rate of electron exchange between the aromatic rings of the radical anions of the [*m.n*]paracyclophanes varied with the values of *m* and *n* in the order [2.2] > [3.4] > [4.4] or [6.6].

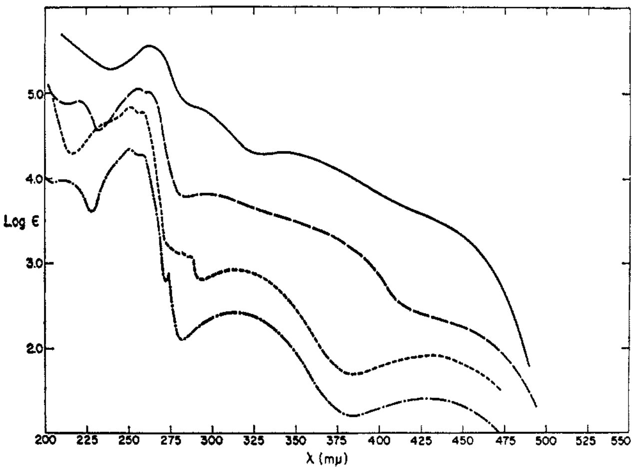


Figure 1.—Ultraviolet absorption spectra in acetonitrile taken on a Cary (Model 11PMS) spectrophotometer: · — · —, equal molar mixture of 2,5-dimethylbenzoquinone and *p*-xylene; - - - - (displaced upward by 0.5 log ε unit), equal molar mixture of 2,5-dimethylbenzoquinone and [8]paracyclophane; — — (displaced upward by 1.0 log ε unit), [4.4]paracyclophanequinone; ——— (displaced upward by 1.5 log ε units), [2.2]paracyclophanequinone (see ref 13b).

The presence of a charge-transfer band in quinone I recalls the observation of Cookson and Lewin[16] of a strong charge-transfer band in the ultraviolet spectrum of XV at λ_{max} 252 (ε 46,000).

The nmr spectrum of quinone I in deuterated chloroform exhibited four different kinds of proton absorptions. A multiplet of four protons (centered at

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(9) (a) F. Fieser, *Org. Syn.*, **17**, 9, 68 (1937); (b) J. Cason, *Org. Reactions*, **4**, 305 (1948).

(10) (a) L. I. Smith and W. B. Irwin, *J. Am. Chem. Soc.*, **63**, 1036 (1941); (b) L. I. Smith and J. A. King, *ibid.*, **63**, 1887 (1941).

(11) R. Craven, *J. Chem. Soc.*, 1605 (1931).

(12) D. J. Cram and R. A. Reeves, *J. Am. Chem. Soc.*, **80**, 3094 (1958).

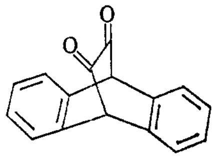
(13) (a) D. J. Cram and G. R. Knox, *ibid.*, **83**, 2204 (1961). (b) The authors wish to thank F. L. Harris for taking these spectra.

(14) (a) D. J. Cram and R. H. Bauer, *J. Am. Chem. Soc.*, **81**, 5971 (1959); (b) L. A. Singer and D. J. Cram, *ibid.*, **85**, 1080 (1963).

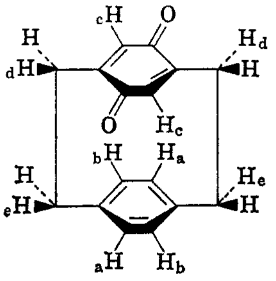
(15) S. Weissman, *ibid.*, **80**, 6462 (1958).

(16) R. C. Cookson and N. Lewin, *Chem. Ind.* (London), 984 (1956).

τ 3.23) appeared as an A_2B_2 pattern which is characteristic of *para*-substituted benzene rings in which the two substituents differed enough in their effects on their *o*-hydrogens to make them split one another.[17] In XV the hydrogens of the aromatic ring contain two kinds of hydrogens (a and b), two of which face the carbonyl groups of the quinone ring and two of which do not. Possibly the two hydrogens facing the carbonyl groups are moved upfield (protons a) and are those that possess τ values of about 3.27, and the other two hydrogens (protons b) are those that possess τ values of about 3.16. These two kinds of protons have a splitting constant of about $J_{AB} \sim 7$ cps.



XV



I

The protons attached to the quinone ring appear as a singlet at τ 4.22, which compares with τ 3.53 for 2,5-di-*t*-butylbenzoquinone.[18] This movement upfield is characteristic of the [2.2]paracyclophane system. The methylene protons are found as two multiplets, one of six protons centered at $\tau \sim 6.9$ and the second of two protons centered at $\tau \sim 7.7$. The latter probably are associated with either the d or e protons, but a choice between them cannot be made. It is surprising that these two protons are moved so far upfield from the other six protons, which are close in their absorption to those of [2.2]paracyclophane (τ 6.95).

Experimental Section

Spectra.—All ultraviolet spectra were recorded at 25° in a 1-cm cell with a Cary Model 14 spectrophotometer. Nmr spectra were run on a Varian Associates A-60 instrument with carbon tetrachloride as solvent and tetramethylsilane as internal standard. Infrared spectra were run on a Beckman spectrophotometer, Model IR-5.

4-Bromo[2.2]paracyclophane (IV).—The procedure is reported in somewhat more detail here than is found in the literature.[4] Iron powder (0.3 g) was stirred with dichloromethane (200 ml) and 30 ml of a solution of bromine (17.5 g or 6 ml) in carbon tetrachloride (400 ml) for 2 hr at 25°. After addition of 1800 ml more of dichloromethane, 20 g of [2.2]paracyclophane was added to the boiling solution. An additional 370 ml of bromine–carbon tetrachloride solution was then added dropwise to the boiling, stirred solution over a period of 6 hr. The resulting mixture was stirred at reflux for 14 hr. The solution was then washed twice with dilute sodium bisulfite solution, with water, and finally with saturated sodium chloride solution. The solution was dried and evaporated, and the product (IV) was obtained as an oil which rapidly solidified. Vapor phase chromatography of this material demonstrated the absence of starting material, and the presence of only a trace of dibrominated compound. The compound was used directly without further purification.

Reaction of 4-Bromo[2.2]paracyclophane with Potassium *t*-Butoxide in Dimethyl Sulfoxide.—Finely powdered 4-bromo[2.2]-cyclophane (18.5 g) was added rapidly to a stirred solution of potassium *t*-butoxide (40.7 g) and *t*-butyl alcohol (25 ml) in dimethyl sulfoxide (450 ml) at 120°. After 2 min, the reaction was quenched by pouring the black solution into water (1.5 l.). After acidification with 0.1 *M* hydrochloric acid, the mixture was extracted with dichloromethane; the organic solution was washed with saturated sodium chloride solution, dried, and evaporated. The residual dark gum in 200 ml of 1:1 benzene–ether was filtered through 200 g of silica gel, the column eluate was evaporated, and the residue was dissolved in 25 ml of benzene. Cyclohexane (225 ml) was added. The precipitated solid that separated failed to sublime at 200° (0.85 mm) and was rejected. The soluble material (12.6 g) was chromatographed on silica gel (600 g). Elution of the column with 9:1 pentane–benzene (4 l.) gave a 0.65-g (4%) recovery of starting material; 4:1 pentane–benzene (4 l.) eluted 1.50 g of mixtures of 4-*t*-butoxy-[2.2]paracyclophane (VII), whose infrared spectrum in methylene dichloride gave bands at 1387 (m) and 1364 cm^{-1} (s), and 4-methylmercapto-5-hydroxy[2.2]paracyclophane (IX). The same solvent mixture (6:1) eluted 1.47 g (9%) of IX (solid). Elution of the column with 1:1 pentane–benzene (1 l.) gave a semisolid material (0.38 g) which, when triturated with ether, decolorized with charcoal, and recrystallized from 3:1 ether–chloroform gave 0.033 g of what is probably ether X, mp 265–268° dec. Further elution of the column with 6 l. of the same solvent gave gums (1.13 g) which could not be molecularly distilled. Elution with benzene (5 l.) gave 2.70 g of crude 4-hydroxy[2.2]paracyclophane (VIII), which when rechromatographed gave 2.01 g (14%) of VIII. Continued elution of the column with benzene–ether mixtures gave dark gums.

The fraction containing a mixture of VII and IX was dissolved in 75 ml of acetic acid and swirled with 50 ml of concentrated hydrochloric acid (0.1 *M* hydrochloric acid had no effect on the ether). After 10 min at 25°, the mixture was poured into water and the organic material (1.36 g) was extracted with dichloromethane. Chromatographic treatment of this material gave 0.15 g (1%) of thioether phenol IX and 0.53 g (4%) of phenol VIII. In one experiment, a small amount of the *t*-butyl ether VII was isolated as a low-melting solid freely soluble in pentane, but the substance was not characterized.

Thioether phenol IX was recrystallized twice from pentane (charcoal), mp 91.5–92.3°. The infrared spectrum in carbon tetrachloride had a band at 3375 cm^{-1}, unaffected by dilution (intramolecularly bonded hydroxyl), and no band in free hydroxyl region. In dichloromethane the band appeared at 3344 cm^{-1} and was unaffected by dilution. The ultraviolet absorption spectrum (95% ethanol), with or without added hydrochloric acid, had λ_{max} 248 mμ (ϵ 4550), 254 (3760), 260 (2820), 292.5 (694), and 323 (1200), with a shoulder at 223 mμ (ϵ 13,040). In 95% ethanol containing a trace of base, the spectrum had λ_{max} 254 (ϵ 6600), 260 ((5550), and 351 (2840) with a shoulder at 248 mμ (ϵ 7300). The nmr spectrum (carbon tetrachloride) had τ 8.04 (three protons of a methylthio group as a singlet) and 3.41 (one proton of a hydroxyl group) which disappeared on addition of deuterium oxide. The aromatic (six protons) and methylenic (eight protons) patterns were too complex for in-interpretations. *Anal.* Calcd for $C_{17}H_{18}OS$: C, 75.51; H, 6.71; S, 11.86. Found: C, 75.59; H, 6.92; S, 11.56.

Phenolic compound VIII was recrystallized from slightly aqueous methanol, sublimed at 150° (0.35 mm), and recrystallized again from methanol–water (charcoal treatment) to give material, mp 229–232° (lit.[14a] mp 225–229°), undepressed by admixture with an authentic sample.[14a] In methylene dichloride, the infrared spectrum exhibited a free hydroxyl band at 3571 cm^{-1}. In neutral or slightly acidic 95% ethanol, the ultraviolet spectrum had λ_{max} 226 mμ (ϵ 29,600), 291 (1490), and 311 (1310). In 0.1 *M* ethanolic sodium hydroxide, the spectrum had λ_{max} 282 mμ (ϵ 4040) and shoulders at 222 mμ (ϵ 34,500), 288 (3990), and 325 (2110). This spectral data is comparable with that obtained with the same compound prepared by a different route.[19]

Compound X was again recrystallized from 3:1 ether–chloroform: mp 267–268° dec. The infrared spectrum of this compound (KBr disk) showed no bands associated with ordinary functional groups. The compound's extreme insolubility precluded the usual spectral and molecular weight measurements. *Anal.* Calcd for $(C_{17}H_{16}O)_x$: C, 86.40; H, 6.81. Found: C, 86.51; H, 6.82.

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[17] An example of a similar A_2B_2 pattern is that exhibited by *p*-chlorobenzaldehyde: N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "NMR Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962, Spectrum No. 146.

[18] Reference 17, Spectrum No. 314.

[19] K. C. Dewhirst and D. J. Cram, *J. Am. Chem. Soc.*, **80**, 3115 (1958).

4-Methoxy[2.2]paracyclophane.—Phenol VIII (0.350 g), methyl iodide (1 ml), anhydrous potassium carbonate (1.0 g), and acetone (25 ml) were stirred at reflux for 22 hr. Fresh additions of 1-ml portions of methyl iodide were made periodically during this time. After addition of water, the mixture was extracted with methylene dichloride and filtered through silica gel in 3:1 pentane–methylene dichloride to give 4-methoxy[2.2]-paracyclophane, mp 113–117°. Recrystallization of this material (charcoal treatment) from hexane gave mp 116–117°. The ultraviolet absorption spectrum in 95% ethanol had λ_{max} 225 mμ (ε 18,610), 281 (673), 289.5 (778), and 309 (635), with an inflection at 248 mμ (ε 3470). The infrared spectrum in methylene chloride had bands at 3466 (methyl), 1245 (aryl–oxygen), and 1042 cm^{-1} (methyl–oxygen). *Anal.* Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.48; H, 7.78.

4-Acetoxy[2.2]paracyclophane.—A solution of phenol VIII (0.200 g) in dry pyridine (5 ml) and acetic anhydride (5 ml) was heated at 100° for 2 hr and allowed to stand at room temperature for 14 hr. The mixture was diluted with dilute hydrochloric acid and extracted with dichloromethane, and the extract was washed with dilute acid, dilute base, and water, dried, and evaporated. The resulting solid (0.243 g) was filtered through a small pad of silica gel in 3:1 benzene–pentane to give 4-acetoxy-[2.2]paracyclophane (0.193 g). The material was recrystallized twice from cyclohexane (charcoal treatment): mp 132.5–133.5°. The infrared spectrum of the substance in carbon tetrachloride had a carbonyl ester band at 1774 cm^{-1}, a methyl band at 1370 cm^{-1}, and an aryl-oxygen band at 1205 cm^{-1}. *Anal.* Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.18; H, 6.90.

Reduction of this acetoxy compound with lithium aluminum hydride by the usual method gave phenol VIII of the same broad melting point as was obtained directly.

Desulfurization of 4-Methylmercapto-5-hydroxy[2.2]paracyclophane (IX) to 4-Hydroxy[2.2]paracyclophane (VIII).—A solution of IX (0.500 g) in purified dioxane (50 ml, distilled from lithium aluminum hydride) was heated under reflux with Raney nickel (about 5 g) which had been deactivated by treatment with boiling acetone (50 ml) for 2 hr.[20] The catalyst was collected and washed with hot acetone (1 l.) in small portions. The combined filtrates were evaporated, and the solid residue (0.425 g) was chromatographed on silica gel (25 g). Elution of the column with 1:1 pentane–benzene (200 ml) gave starting material (0.084 g, 17%). Elution with 99:1 benzene–ether (200 ml) gave phenol IX, 0.263 g (63%), which after sublimation at 140° (0.35 mm) and recrystallization from slightly aqueous ethanol gave mp 232–237°, undepressed by admixture with an authentic sample. The infrared spectrum of this compound was identical with that of authentic material.

4-Hydroxy-7-benzeneazo[2.2]paracyclophane (XIII).—A stirred solution of phenol IX (0.13 g) in methanol (10 ml) and 10% aqueous potassium hydroxide (2 ml) was treated with an excess of benzenediazonium chloride solution at 0° and was then kept at 0° for 10 min. The mixture was diluted with water and acidified, and the deep red precipitate was isolated with dichloromethane and chromatographed on silica gel (20 g). Elution of the column with benzene–ether mixtures gave azo compound XIII, 0.186 g (98%), which crystallized when triturated with cyclohexane. The material was recrystallized once from cyclohexane and twice from 3:1 cyclohexane–benzene to give a bright red compound, mp 167.5–168.5°. The infrared spectrum in methylene dichloride at 5 wt % gave bands at 3580 (sharp, free hydroxyl), 3341 (sharp, possibly free nitrogen-hydrogen bond), and 3254 cm^{-1} (broad, intermolecularly hydrogen-bonded hydroxyl and diazo groups). At 1% concentration, the first two bands remained, and the last one disappeared. The ultraviolet spectrum in 95% ethanol (neutral or slightly acidic) had λ_{max} 278 mμ (ε 5570), 295 (5670), and 393 (16,350) with shoulders at 215 mμ (ε 21,180) and 234 (13,820). In 0.05 *M* ethanolic sodium hydroxide the spectrum gave λ_{max} 310 mμ (ε 5670) and 493 (32,560) with a shoulder at 253 mμ (ε 8450). *Anal.* Calcd for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14; N, 8.53. Found: C, 80.38; H, 6.21; N, 7.78.

Spectral Data for Model Azo Compounds.—The compounds, *p*-benzeneazophenol and 1-benzeneazo-2-naphthol, were prepared for spectral comparisons. In the infrared spectrum in methylene dichloride (2% solution), the former gave bands at 3580 (sharp) and 3330 cm^{-1} (broad and weak). These bands were also present in very dilute solution. The infrared spectrum of the latter compound gave no hydroxyl bands in this region at any concentration. In 95% ethanol, *p*-benzeneazophenol in acidic or neutral solution gave an ultraviolet absorption spectrum with λ_{max} 235 mμ (ε 12,380), 349 (24,750), and an inflection at 420 mμ (ε 1240). In slightly basic solution, the spectrum exhibited λ_{max} 258 mμ (ε 9640) and 406 mμ (ε 25,370).

4-Acetoxy-7-acetylamino[2.2]paracyclophane.—A solution of sulfanilic acid (1.12 g) and anhydrous sodium carbonate (0.342 g) in 30 ml of water was treated at 15° with sodium nitrite (0.490 g) and poured onto an ice–water mixture (30 g) containing 0.71 ml of concentrated hydrochloric acid. The diazonium solution was kept at 0° for 30 min and then added portionwise to a stirred solution of phenol VIII (0.962 g) and sodium hydroxide (0.945 g) in methanol (130 ml) and water (20 ml) at 5°. The resulting red mixture was stirred at 25° for 5 hr and diluted with 200 ml of water. The mixture was stirred at 45–50° while a large excess of sodium hydrosulfite was added in 0.10-g portions until the red color disappeared. The precipitated yellow aminophenol was isolated by repeated extraction with ethyl acetate. This compound (XIV) was unstable, and was not characterized. When sublimed at 160–210° at 0.3 mm, the substance was obtained as a light pink solid with an indefinite melting point decomposition range at 200–235°. When exposed to light, the compound became dark brown in a few days.

A solution of crude aminophenol XIV (0.069 g) in dry pyridine (5 ml) and acetic anhydride (5 ml) was kept under nitrogen at 80° for 4 hr and poured into an excess of dilute hydrochloric acid. Extraction of the solution with chloroform gave a semicrystalline material which was chromatographed on silica gel (5.0 g). Elution of the column with 19:2 dichloromethane–methanol (30 ml) gave 4-acetoxy-7-acetylamino[2.2]paracyclophane (0.078 g, 84%) as a glass that solidified when triturated with dichloromethane. Two recrystallizations of this material from ether–chloroform (3:1) gave pale fawn leaflets, mp 211.5–213.5°. The infrared spectrum in chloroform of this material had bands at 3433 (w) and 3364 (w) (nitrogen–hydrogen bond), 1759 (s) (ester carbonyl), 1687 (s) (amide carbonyl), 1517 (m) (amide group), 1372 (ms) (acetyl methyl), and 1230 cm^{-1} (s) (aryl–oxygen–acetyl group). *Anal.* Calcd for $C_{20}H_{21}NO_3$: C, 74.29; H, 6.55; N, 4.33. Found: C, 73.72; H, 6.95; N, 3.93.

[2.2]Paracyclophanequinone (I).—The crude aminophenol XIV obtained from 0.962 g of phenol was heated with 2 *N* sulfuric acid (200 ml) and a few drops of ethanol until all had dissolved with the exception of a little dark gum. The solution was extracted with dichloromethane, and the organic solution was washed with 2 *N* sulfuric acid solution. The acid washes were combined with the original aqueous solution and heated at 100° with hydrated ferric sulfate (equivalent of 20 g of anhydrous material). After 2.5 hr, the solution was cooled, and the quinone was extracted with chloroform. The aqueous layer was heated an additional 5.5 hr and again extracted with chloroform. The combined chloroform layers were washed with water, dried, and evaporated to give 0.693 g (68%) of crude quinone. The compound was recrystallized from benzene and obtained as brownish yellow hard crystals which were sublimed at 110° at 0.1 mm to give the pure yellow solid of indefinite melting point. When heated from 150°, the compound darkened and sublimed slightly, but did not really melt, even at 300°. The same behavior was observed when the substance was heated from 225 to 300°. However, when placed in a bath preheated to 235°, the quinone melted immediately. The infrared spectrum in methylene dichloride had a very intense carbonyl peak at 1656 cm^{-1} and a medium peak at 1600 cm^{-1} (carbon–carbon double bond). *Anal.* Calcd for $C_{16}H_{14}O_2$: C, 80.57; H, 5.88. Found C, 80.64; H, 5.92.

Dibromination of [2.2]Paracyclophane.—The hydrocarbon (20 g) was treated with bromine (33.6 g, 11.5 ml) in the presence of iron powder (0.3 g) under conditions described for the preparation of 4-bromo[2.2]paracyclophane. The semisolid product was dissolved in the minimum quantity of boiling chloroform (400 ml), the solution was evaporated until crystallization began, and then enough ether was added to restore the original volume. The fawn, crystalline dibromo compound weighed 6.24 g, mp 242–246°; the second crop amounted to 5.28 g, mp 236–245°. Evaporation of the mother liquors gave gummy material that slowly solidified. Sublimation of the recrystallized first and second crops at 190–210° at 0.6 mm gave 10.19 g (29%) of

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[20] (a) G. B. Spero, A. V. McIntosh, and R. H. Levin, *J. Am. Chem. Soc.*, **70**, 1907 (1948); (b) S. Teich and D. Y. Curtin, *ibid.*, **72**, 2481 (1950).

dibromo compound as white hexagonal plates, mp 243–247°. Recrystallization of this material from 3:1 ether–chloroform gave pure isomer, mp 250–251°, probably of structure V. This structure, which has a center of symmetry, is probably the higher melting and more insoluble isomer.

Reaction of 4,15-Dibromo[2.2]paracyclophane (V) with Potassium *t*-Butoxide in Dimethyl Sulfoxide.—Pure dibromo compound V (mp 250–251°, 18.7 g) was added rapidly to a well-stirred solution of potassium *t*-butoxide (45.6 g) and *t*-butyl alcohol (29.5 ml) in purified dimethyl sulfoxide (500 ml) at 120°. During the vigorous reaction, the temperature rose to 140°. After 2 min, the mixture (black) was poured into 1.5 l. of water. The mixture was acidified and extracted with first dichloromethane and then chloroform, and the combined organic layers were washed with saturated sodium chloride solution, dried, and evaporated. The residue (gum) was filtered through 200 g of silica gel in 3:1 benzene–ether. The filtrate was evaporated, the residue was dissolved in acetic acid (500 ml), and 350 ml of concentrated hydrochloric acid was added, followed by 1.5 l. of water. The black glass that separated (13.45 g) was dissolved in a mixture of dichloromethane and chloroform, and the solution was washed with saturated sodium bicarbonate solution. The solution was dried, evaporated, and submitted to molecular distillation at temperatures up to 260° (0.4 mm). The distillate (6.61 g) was chromatographed on 400 g of silica gel, and elution with 4:1 pentane–benzene (4.8 l.) gave mixtures of two isomeric bromohydroxymethylthioparacyclophanes, XIIa and XIIb, 3.37 g (19%). Further elution with solvents containing increasing proportions of benzene gave only traces of material until 1:2 pentane–benzene (4.2 l.) eluted 2.09 g (13.5%) of a solid mixture of isomeric bromophenols XIa and XIb. Later fractions gave gums, which could not be crystallized.

Early fractions of the bromohydroxymethylthio[2.2]paracyclophane (XII) crystallized slowly, and, after three recrystallizations from hexane, a single pure isomer was isolated as white needles, mp 118.5–119.5°. The infrared spectrum of this compound in methylene dichloride exhibited an intramolecularly bonded hydroxyl group absorbing at 3358 cm^{-1}. The nmr spectrum in carbon tetrachloride had τ 7.99 (three protons of methylthio group as a singlet), 3.43 (one proton of the hydroxyl group as a singlet which disappeared on addition of deuterium oxide), and complex aromatic and methylene protons. *Anal.* Calcd for $C_{17}H_{17}BrOS$: C, 58.45; H, 3.91; Br, 22.88; S, 9.18. Found: C, 58.44; H, 4.92; Br, 22.76; S, 9.52.

Later noncrystalline fractions of XII were combined and divided into 16 fractions by careful rechromatography on silica gel, and the last nine fractions (0.33 of material involved) were again chromatographed. The last 50% of the material collected from this chromatograph was distilled at 165° (bath) at 0.9 mm to give a second isomer of XII as an oil. The infrared spectrum of this material closely resembled that of the solid isomer, but was sufficiently different in the fingerprint region to show that it contained none of the latter. The nmr spectrum in carbon tetrachloride of the compound had τ 7.99 (three protons of the methylthio group, singlet) and 3.38 (hydroxyl proton as singlet that disappeared on addition of deuterium oxide). The aromatic region (five protons) and methylenic region (eight protons) were very complex. *Anal.* Calcd for $C_{17}H_{17}BrOS$: C, 58.45; H, 4.91; S, 9.18. Found: C, 58.53; H, 4.94; S, 9.37.

The isomeric bromophenols, XIa and XIb, were obtained distributed among seven chromatographic fractions. Recrystallized separately from cyclohexane–benzene mixtures, all of these gave material melting between 170 and 180°. Second crops all gave solids melting about 150°.

Three recrystallizations of the lower melting crops (collected) from 1:2 cyclohexane–benzene gave large hard crystals, mp 154–157°. The infrared spectrum in methylene dichloride exhibited a free hydroxyl band at 3580 cm^{-1}. *Anal.* Calcd for $C_{16}H_{15}BrO$: C, 63.38; H, 4.99; Br, 26.36. Found: C, 63.55; H, 5.02; Br, 26.17.

Four recrystallizations of the higher melting crops (collected) from benzene gave either rods or needles, mp 181.5–184.5°, whose infrared spectrum in methylene dichloride gave a free hydroxyl band at 3584 cm^{-1}. The difference in the infrared spectra of the two isomers was slight, except in the 800–1000-cm^{-1} region, where differences were prominent.

A New General Approach to the Synthesis of Oxygen-Containing Heterocycles by Virtue of Hydroxyl Neighboring Group Participation. The Condensation of Enamines with Salicylaldehydes[1]

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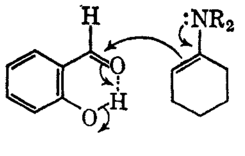
The reaction of cyclic and acyclic enamines with variously substituted salicylaldehydes has been shown to give quantitative yields of cyclic O,N-ketals having a pyran nucleus. Chromium trioxide–pyridine oxidation of such alcohols has provided an efficient, rather general, two-step synthetic route to tetrahydroxanthones, chromones, flavones, and isoflavones. Several other transformations of these products are described.

The present research was undertaken to test the possible utilization of a neighboring hydroxyl group, well known for its ability to function as a catalyst of amide and ester hydrolysis,[4,5] as a building block in the construction of oxygen heterocycles. Specifically, the conception was founded on the rationalization that intermediates of type **1**, believed to result in the reaction of enamines with aldehydes,[6] might be expected to respond to the well-established relative basicity order of alkoxide and phenoxide ions. In other words, despite the fact that **1** represents an unusual alkoxide ion (unusual in that it is zwitterionic and that its existence must, of necessity, be transitory), it appeared likely that **3** would quite possibly result if the R group bore a neighboring *phenolic* hydroxyl function as in **2**.[7] Neutralization of **3** could be readily accomplished by cyclization to a six-membered heterocyclic ring.



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(1) Unsaturated Heterocyclic Systems. XXII. For paper XXI of this series, see L. A. Paquette, *J. Am. Chem. Soc.*, **87**, 5186 (1965).

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(4) M. L. Bender, *Chem. Rev.*, **60**, 53, (1960); M. L. Bender, F. J. Kézdy, and B. Zerner, *J. Am. Chem. Soc.*, **85**, 3017 (1963).

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(7) Although the mechanistic detail has been pictured in a stepwise fashion, it is, of course, possible that the entire process may be concerted and not mediated by species **3**.