

Organic and Biological Chemistry

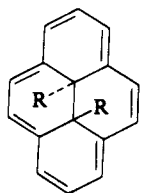
8,16-Oxido[2.2]metacyclophane-1,9-diene. A Valence Tautomer of Pyrene *cis*-15,16-Epoxyde¹

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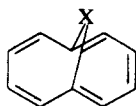
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Abstract: A synthesis of 8,16-oxido[2.2]metacyclophane-1,9-diene (**10**) is described. Although 8,16-oxido[2.2]metacyclophane is a valence tautomer of pyrene *cis*-15,16-epoxyde (**7**), there is no indication from spectral evidence that equilibration to pyrene *cis*-15,16-epoxyde occurs at room temperature. However, the ease with which the bridging oxygen atom in **10** undergoes expulsion or rearrangement either on treatment with strong acid or heating in neutral solvent strongly suggests that pyrene *cis*-15,16-epoxyde is present in these reactions as a transient intermediate species.

The syntheses of *trans*-15,16-dimethyldihydropyrene^{4,5} and *trans*-15,16-diethyldihydropyrene⁶ (**2**) first demonstrated the possibility of preparing aromatic molecules having substituents placed within the cavity of the aromatic π -electron cloud. The choice of the *trans*-15,16-dihydropyrene molecule as a framework was made as a result of an examination of molecular models which indicated the perimeter carbon skeleton of *trans*-15,16-dihydropyrene to be very nearly planar. This has since been confirmed by Hanson who made an X-ray crystallographic examination of 2,7-diacetoxy-*trans*-15,16-dimethyldihydropyrene and showed that the maximum deviation of a perimeter atom from a mean plane was no more than 0.027 Å.⁷



1, R = CH₃
2, R = C₂H₅



3a, X = CH₂
b, X = O
c, X = NR

At the time of initiation of these studies it was thought that the perimeter of *cis*-15,16-dihydropyrenes would probably deviate sufficiently from planarity to reduce the aromatic delocalization energy. However, since our first publication, Professor Vogel has described a brilliant

series of studies demonstrating the aromatic character of *cis*-1,6-bridged cyclodecapentaenes (**3a-c**).⁸ Even though these cyclodecapentaene derivatives are clearly aromatic by all of the usual criteria, the X-ray crystallographic examination of 1,6-methanocyclodecapentaene-2-carboxylic acid by Dobler and Dunitz clearly shows that the perimeter carbon skeleton deviates appreciably from planarity.⁹ Since examination of molecular models suggested that the deviation from planarity of the perimeter of *cis*-15,16-dihydropyrene was less than that for the 1,6-methanocyclodecapentaenes, we were encouraged to undertake experimental work directed toward a synthesis of a *cis*-15,16-dihydropyrene derivative.

The initial approach to our syntheses of *trans*-15,16-dialkyldihydropyrenes was based on preparing an appropriate *trans*-8,16-dialkyl[2.2]metacyclophane-1,9-diene in the expectation that it would undergo valence tautomerization to give the desired dihydropyrene.¹⁰ Similarly, Vogel's syntheses of bridged cyclodecapentaenes have utilized approaches through the corresponding valence tautomers.⁸ It was natural, therefore, that in considering how to prepare a *cis*-15,16-dihydropyrene derivative our attention turned again to the corresponding valence tautomer, a *cis*-[2.2]metacyclophane-1,9-diene.

Unfortunately, however, all of the known methods of preparing [2.2]metacyclophanes yield only the *trans* isomer. In this instance *trans* refers to the stepwise geometry of the benzene rings as illustrated by **4**. This geometry has been confirmed by several X-ray studies.^{11,12} Although Gault, Price, and Sutherland have shown that the nmr spectrum of [2.2](2,5)pyridophane¹³ is temperature dependent, indicating a rapid equilibration between

(1) Aided in part by a grant from the National Science Foundation.

(2) National Institutes of Health Postdoctoral Fellow, 1966-1968.

(3) Visiting Professor, on sabbatical leave from Oxford University, 1966-1967.

(4) V. Boekelheide and J. B. Phillips, *Proc. Natl. Acad. Sci. U. S.*, **51**, 550 (1964); cf. V. Boekelheide and J. B. Phillips, *J. Am. Chem. Soc.*, **85**, 1545 (1963).

(5) V. Boekelheide and J. B. Phillips, *ibid.*, **89**, 1695 (1967).

(6) V. Boekelheide and T. Miyasaka, *ibid.*, **89**, 1709 (1967).

(7) A. W. Hanson, *Acta Cryst.*, **18**, 599 (1965).

(8) E. Vogel and H. D. Roth, *Angew. Chem.*, **76**, 145 (1964); for a summary, see E. Vogel, Special Publication No. 21, The Chemical Society, London, 1967, p 113.

(9) M. Dobler and J. D. Dunitz, *Helv. Chim. Acta*, **48**, 1429 (1965).

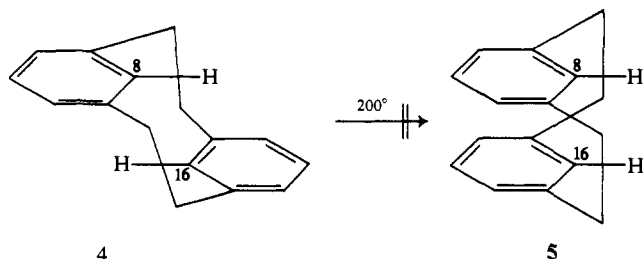
(10) W. S. Lindsay, P. Stokes, L. G. Humber, and V. Boekelheide, *J. Am. Chem. Soc.*, **83**, 943 (1961).

(11) C. J. Brown, *J. Chem. Soc.*, 3278 (1953).

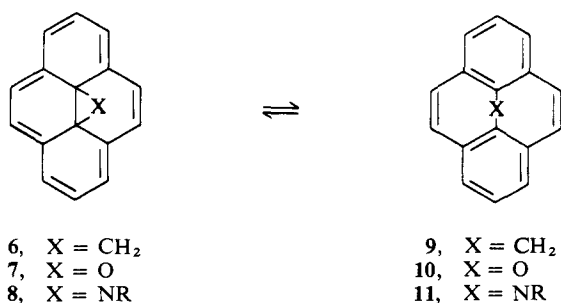
(12) A. W. Hanson, *Acta Cryst.*, **15**, 956 (1962).

(13) The nomenclature used is that recommended by B. H. Smith, "Bridged Aromatic Compounds," Academic Press, New York, N. Y., 1964, p 10.

the *trans* and *cis* conformations above 13.5°,¹⁴ comparable studies of the temperature dependence of the nmr spectrum of [2.2]metacyclophane as well as studies on the optical stability of optically active 4-methyl[2.2]metacyclophane clearly demonstrate that there is no conversion of *trans* conformer (**4**) to *cis* conformer (**5**) up to 190°, the highest temperatures employed.¹⁵ This effectively eliminates the possibility of preparing *cis*-8,16-dialkyl[2.2]-metacyclophanes by any of the established procedures.



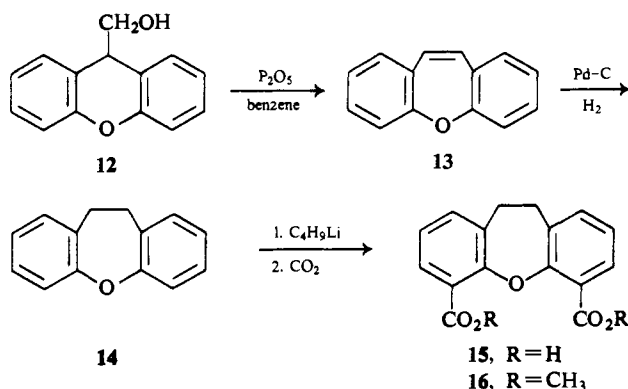
An alternative approach which appeared to offer a solution to this difficulty was to prepare a *cis*-15,16-dihydropyrene having an additional ring bridging the 15 and 16 positions. In this case the presence of the bridging atoms requires the metacyclophane valence tautomer to assume *cis* geometry. Examination of molecular models suggested that the most favorable small ring with regard to steric considerations would be a three-membered ring. Thus, the most likely candidates for study were the cyclopropane derivative (**6**), the epoxide (**7**), and the aziridine (**8**). The corresponding valence tautomers are shown by formulas **9**, **10**, and **11**. In a preliminary communication we have described the synthesis of the oxygen analog **10**,¹⁶ and the present report presents the details of this work. In an accompanying paper, the synthesis of the imino analog **11** is described in detail,¹⁷ and in a recent related publication a preliminary description of the synthesis of a derivative of the methylene analog **9** is presented.¹⁸



Of the three *cis*-[2.2]metacyclophane-1,9-dienes illustrated by formulas **9**, **10**, and **11**, a synthesis of the oxygen analog has inherent advantages. In his many studies on metalation reactions, Gilman has shown that diphenyl ether readily undergoes metalation with *n*-butyllithium and on carbonation gives the 2,2'-dicarboxylic acid.^{19a} Thus, it could be expected that dibenz[*b,f*]oxepine (**13**)

would undergo substitution in a similar manner to introduce carboxylic acid groups at the two free positions *ortho* to the ether bridge. This metalation procedure is much more difficult to apply with aromatic amines,¹⁷ and, of course, could not be used at all for the methylene analog **9**.

Anet has described the preparation of dibenz[*b,f*]oxepine (**13**) by an acid-catalyzed rearrangement of xanthene-9-carbinol (**12**), although no yield was given for the reaction.^{19b} We have found that treatment of xanthene-9-carbinol (**12**) with phosphorus pentoxide in boiling benzene readily gives dibenz[*b,f*]oxepine (**13**) in 85% yield. Since xanthene-9-carbinol is easily accessible by lithium aluminum hydride reduction of the commercially available xanthene-9-carboxylic acid, dibenz[*b,f*]oxepine can be made conveniently in quantity.



Attempted metalation of dibenz[*b,f*]oxepine (**13**) with *n*-butyllithium followed by carbonation gave an oily mixture of acids whose nmr spectrum indicated the presence of a butyl group, presumably the result of addition of *n*-butyllithium to the stilbene double bond. To avoid this, **13** was reduced over a 5% palladium-on-charcoal catalyst to give the corresponding 10,11-dihydrodibenz[*b,f*]oxepine (**14**) in 89% yield.²⁰ Metalation of **14** with *n*-butyllithium then occurred as expected giving, after carbonation, the desired dicarboxylic acid **15**. Because **15** proved to be rather insoluble and difficult to purify, it was converted directly to the corresponding dimethyl ester **16**, which could be readily handled and was isolated pure in 30% yield. Actually, an analytically pure sample of **15** was prepared by hydrolysis of the ester. Reduction then of the diester **16** with lithium aluminum hydride proceeded smoothly in high yield to give the dicarbinol **17**. In later studies it was found that the conversion of **14** to **17** could be improved markedly both in over-all yield and in ease of operation by treating the metalation product of **14** with paraformaldehyde. This one-step procedure gives the pure dicarbinol **17** in 55% yield.

Treatment of the dicarbinol **17** with phosphorus tribromide in benzene gave the corresponding dibromide **18** in 90% yield. Several reagents were investigated for effecting the ring closure of **18** by a Wurtz reaction. By far the most satisfactory was phenyllithium which brought about the conversion of **18** to **19** in 76% yield. The

(14) I. Gault, B. J. Price, and I. O. Sutherland, *Chem. Commun.*, 540 (1967).

(15) T. Sato, S. Akabori, M. Kainosho, and K. Hata, *Bull. Chem. Soc. Japan*, **39**, 856 (1966); **41**, 218 (1968).

(16) B. A. Hess, Jr., A. S. Bailey, and V. Boekelheide, *J. Am. Chem. Soc.*, **89**, 2746 (1967).

(17) B. A. Hess, Jr., and V. Boekelheide, *ibid.*, **91**, 1672 (1969).

(18) H. B. Renfro, *ibid.*, **90**, 2194 (1968).

(19) (a) K. Oita and H. Gilman, *J. Am. Chem. Soc.*, **79**, 337 (1957);

(b) F. Anet, *Can. J. Chem.*, **35**, 1084 (1957).

(20) Recently, E. D. Bergmann, I. Shahak, and Z. Aizenshtat (*Tetrahedron Letters*, 3469 (1968)) have assigned the 10,11-dihydrodibenz[*b,f*]oxepine structure to a substance having rather different properties than those we claimed.¹⁶ Through correspondence and an exchange of samples with Professor Bergmann we have learned that the substance described in their report is actually a dimer and not **14**.

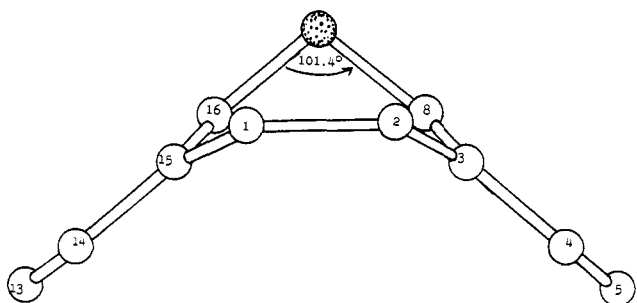
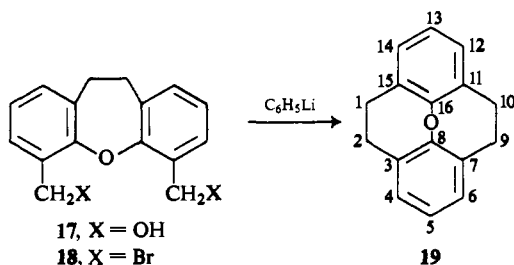


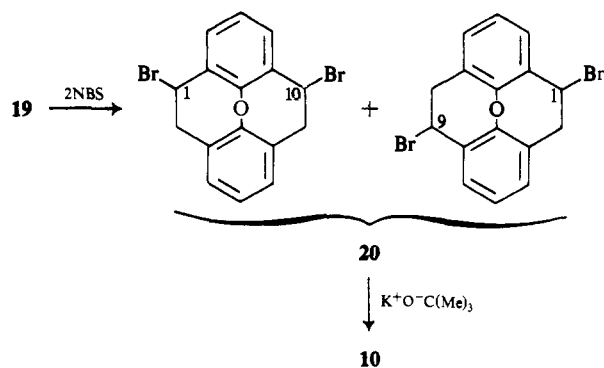
Figure 1. A representation of the geometry of 8,16-oxido[2.2]-metacyclophane as deduced from X-ray studies.²¹



assignment of structure to **19** is well supported by spectral evidence. The mass spectrum shows the expected parent molecular ion (m/e 222) and the nmr spectrum shows the six aromatic protons as a singlet at τ 3.22 with the bridging methylenes as an AA'BB' multiplet at τ 6.12–7.62. A complete theoretical analysis of the AA'BB' pattern gave values of τ 6.36 and 7.31 for the two chemical shifts (see Experimental Section).

Because of its unusual *cis* geometry it was of interest to examine 8,16-oxido[2.2]metacyclophane by X-ray crystallographic analysis and we are indebted to Dr. Hanson for this study.²¹ The molecular geometry is illustrated by Figure 1 which shows a cutaway portion of the carbon skeleton. The bond angle subtended by the ether oxygen is 101.4°. The aromatic rings are at an angle of 99.6° and each is slightly distorted to a boat shape. The important point about the geometry, though, is that it leads to rather different predictions about the chemistry of *cis*-[2.2]metacyclophanes than for the corresponding *trans* isomers. For example, in the case of *trans*-[2.2]metacyclophane (**4**) substitution at the benzylic position fails because the resulting ion or radical does not have the proper geometry for stabilization by the aromatic ring.¹⁰ On the other hand such substitution reactions would appear to be feasible in the case of the *cis* geometry shown in Figure 1.

When *cis*-8,16-oxido[2.2]metacyclophane (**19**) was treated with 2 molar equiv of N-bromosuccinimide and a trace of azobisisobutyronitrile for initiation, substitution occurred smoothly to give a mixture of dibromides (**20**). Examination of the mixture by tlc showed the presence of two compounds in about equal amount. The nmr spectrum of the mixture is in accord with that to be expected for a 50:50 mixture of the 1,9- and 1,10-dibromides, with all of the bromine atoms being *cis* to the ether bridge. Fractional crystallization of this mixture from cyclohexane



gave a pure sample of one of the isomers, presumably the 1,9-dibromide, although the spectral evidence is not conclusive.

In practice the mixture of dibromides (**20**) was subjected directly to dehydrobromination using either 1,5-diazabicyclo[4.3.0]nonene or potassium *t*-butoxide in *t*-butyl alcohol. The conversion to *cis*-8,16-oxido[2.2]metacyclophane-1,9-diene proceeded in high yield.

All of the spectral properties of the white crystals, mp 119–120°, which were isolated are in accord with structure **10** rather than its valence tautomer, pyrene *cis*-15,16-epoxide (**7**). The mass spectrum shows the expected parent molecular ion at m/e 218 with a strong signal at 202 corresponding to loss of oxygen and formation of the pyrene ion.²² The ultraviolet spectrum shows absorption bands at 239 (15,750) and 302 $m\mu$ (ϵ 16,300) with no absorption in the visible as would be expected for **7**. The ultraviolet absorption of **10** is similar to that of *cis*-stilbenes such as dibenzcycloheptene²³ and clearly shows the bridging double bonds to be in conjugation with the aromatic rings. Probably, it is this conjugation effect, which is completely lacking in the *trans*-[2.2]metacyclophane-1,9-dienes,²⁴ that makes the *cis*-[2.2]metacyclophane-1,9-diene (**10**) energetically more favorable than the pyrene *cis*-15,16-epoxide valence tautomer (**7**), a reversal of the energy relationships that prevail in the *trans* series.

Finally, the nmr spectrum of **10** has signals only in the aromatic region. The aromatic ring protons appear as an A₂B pattern in the range of τ 2.66–3.30, whereas the four protons of the bridging ethylenes give a sharp singlet at τ 2.92. The fact that these protons exhibit a chemical shift at such low field is in keeping with the conjugation effect observed in the ultraviolet spectrum and suggests an appreciable ring current through the peripheral carbon skeleton. This is also borne out by magnetic susceptibility measurements.²⁵ The exaltation of the diamagnetic susceptibility for **10** is 39.8 (± 3) $\times 10^{-6}$ ml/mol or an exaltation of 2.9 (± 0.2) benzene equivalents. If the two aromatic rings of **10** were isolated, the exaltation should have been no greater than 2.0 benzene equivalents and so there is obviously an appreciable peripheral ring

(22) We are indebted to Dr. R. Aplin, Oxford University, for investigating the mass spectra of derivatives of this series in some detail and in confirming our conclusion regarding the ejection of oxygen.

(23) E. Müller and H. Kessler, *Ann.*, **692**, 58 (1966).

(24) H.-R. Blattmann, D. Meuche, E. Heilbronner, R. J. Molyneux, and V. Boekelheide, *J. Am. Chem. Soc.*, **87**, 130 (1965); cf. H.-R. Blattmann, doctoral dissertation, Eidg. Tech. Hochschule, Zurich, 1967.

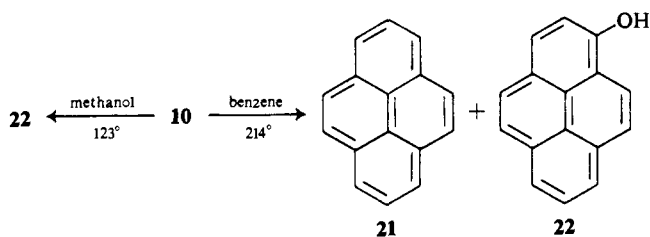
(25) We are indebted to John L. Laity and the late Professor Hyp Dauben for these measurements. The details of these experiments will be reported elsewhere.

(21) M. Mathew and A. W. Hanson, *Acta Cryst.*, in press.

current. On the other hand, the exaltation is far smaller than that to be expected for a dihydropyrene, where *trans*-15,16-dimethyldihydropyrene (**1**), for example, shows an exaltation of 6.6 benzene equivalents.²⁵

In view of the spectral evidence it is clear that of the two valence tautomers, **7** and **10**, the *cis*-8,16-oxido[2.2]metacyclophane-1,9-diene (**10**) predominates at room temperature and the pyrene *cis*-15,16-epoxide (**7**), if present, is at too low a concentration to be detected. This, of course, is the exact reverse of what is found in the *trans*-15,16-dihydropyrene series.^{5,6} In the *trans*-15,16-dihydropyrene examples, though, isomerization to give appreciable amounts of the corresponding metacyclophane valence tautomer could be accomplished by either light or heat.²⁴ It was of interest, therefore, to see whether light or heat might effect the isomerization of **10** to **7**. Although **10** was transformed by ultraviolet light, there was no evidence for the formation of **7** and the structures of the transformation products are still under investigation.

On the other hand, when **10** was heated in a benzene solution in a sealed tube at 214° for 20 hr, there was a complete disappearance of **10** and the formation of two new compounds, pyrene (**21**) and 1-pyrenol (**22**), isolated in yields of 36 and 47%, respectively. The pyrene was readily identified by comparison with authentic material, particularly through their nmr spectra and R_f values on tlc. To prove the identity of the 1-pyrenol all three possible pyrenols were synthesized independently,²⁶ and it was shown that they could be distinguished readily from each other by their nmr spectra in acetonitrile. The spectrum of 1-pyrenol shows a doublet at τ 1.57 ($J = 9$ cps), a multiplet at 1.74–2.27, and a doublet at 2.41 ($J = 9$ cps), whereas 2-pyrenol has a multiplet at τ 1.67–2.13 and a singlet at 2.29, and 4-pyrenol has a doublet of doublets at τ 1.38 ($J = 7$ cps, $J' = 2$ cps), a multiplet at 1.60–2.09, and a singlet at 2.51. Thus, it was easy to distinguish 1-pyrenol by its nmr spectrum, and there was no evidence for the formation of either of the other two pyrenols. In contrast to these results with benzene as solvent, thermolysis of **10** in dry methanol occurred at 123° and gave only 1-pyrenol (**22**) in essentially quantitative yield.



The pyrene *cis*-15,16-epoxide valence tautomer (**7**) would be expected to be a deep emerald green, comparable to the *trans*-15,16-dihydropyrenes in its visible and ultraviolet absorption spectrum. Although **7**, if formed in these thermal reactions, was not present in high enough concentrations to be detected visually, the products are best explained by assuming **7** as an intermediate. In this event expulsion of oxygen could give pyrene or migration of oxygen by either a 1,3 shift or two 1,2 shifts would yield 1-pyrenol. At first sight the absence of 4-pyrenol in the

(26) H. Vollman, H. Becker, M. Corell, and H. Streck, *Ann.*, **531**, 1 (1937).

Table I. Visible Absorption Spectrum of a Solution of *cis*-8,16-Oxido[2.2]metacyclophane-1,9-diene (**10**) in Trifluoroacetic Acid^a

Maxima, $\mu\mu$	Rel intens	Maxima, $\mu\mu$	Rel intens
421	0.18	485 (sh)	0.19
444	0.47	592	0.02
454	0.75	647	0.06
469	1.00	675 (sh)	0.04

^a Relative intensities are given rather than extinction coefficients since the concentration of the colored intermediate is not known.

product is puzzling. However, if one examines the structures of the probable intermediates, it is seen that the reaction path to 1-pyrenol would be predicted to be more favorable than that to 4-pyrenol. Thus, the rearrangement of **7** to **23** and on to **22** involves **24** as an intermediate, which still retains a naphthalene ring, whereas the rearrangement of **23** to 4-pyrenol (**26**) involves **25** as an intermediate which has no aromatic ring. A similar argument can be applied to explain the preferential path for rearrangement if a concerted 1,3 shift describes the mechanism. Also, it is possible that this thermal rearrangement may be related to rearrangements observed in the similar norcaradiene-cycloheptatriene system.²⁷ Finally, the fact that the rearrangement occurs at much lower temperature in methanol than in benzene and in this case gives only 1-pyrenol is in agreement with the proposed reaction path inasmuch as one would expect a somewhat polar transition state in the production of the intermediates involving oxygen migration.

Recently, Vogel has shown that 11,11-dihalogen-1,6-methano[10]annulenes undergo thermal decomposition in benzene in the gas phase to give naphthalene and what is apparently the corresponding dihalocarbene, since in the presence of cyclohexene the dihalonorcaranes are formed.²⁸ If the thermal decomposition of **10** in benzene to give pyrene were following an analogous course, the expulsion of oxygen would be as an oxygen atom which should add readily to cyclohexene giving cyclohexene epoxide. When the thermal decomposition of **10** was carried out in cyclohexene, a very complex mixture of products resulted, including polymeric substances. It appears unlikely that the thermal decomposition of **10** to give pyrene is a single-step expulsion of an oxygen atom but rather is a multistep process involving intermediate radical species.

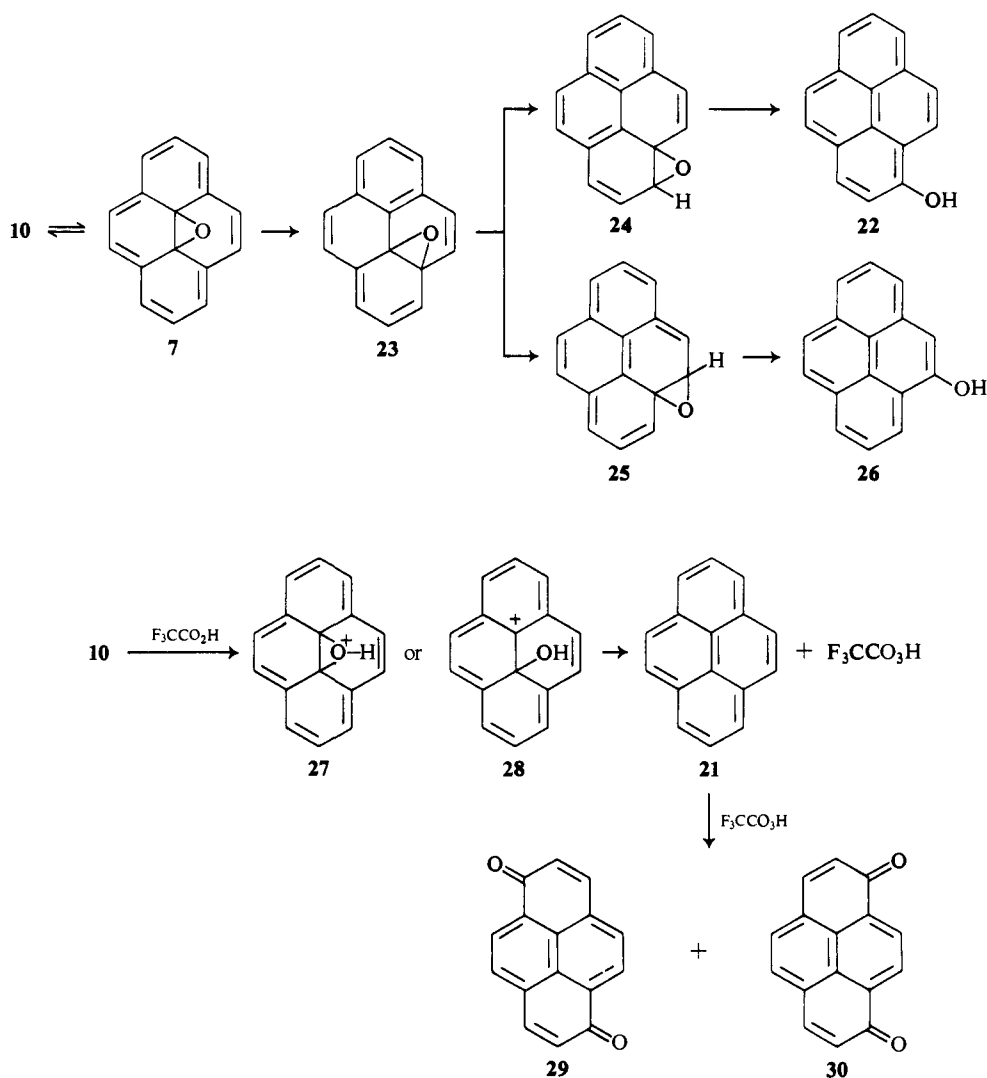
In the case of *trans*-[2.2]metacyclophanes oxidation and electrophilic substitution reactions readily establish a carbon-carbon bond between the 8 and 16 positions of the metacyclophane.^{5,6,29,30} It was of interest to explore similar conditions as means of isomerizing **10** to **7**. Solution of **10** in strong acid—trifluoroacetic acid or concentrated sulfuric acid—gave an immediate deep green color with the intensity of the color increasing to a maximum and then slowly fading. The visible spectrum of the solution in trifluoroacetic acid at maximum intensity of color is summarized in Table I and is clearly very similar

(27) J. A. Berson, *Accounts Chem. Res.*, **1**, 152 (1968).

(28) V. Rautenstrauch, H.-J. Scholl, and E. Vogel, *Angew. Chem.*, **80**, 278 (1968).

(29) V. Boekelheide, C. Ramey, E. Sturm, T. Miyasaka, and B. A. Hess, Jr., *J. Org. Chem.*, in press.

(30) N. L. Allinger, M. A. Da Rooge, and R. B. Hermann, *J. Am. Chem. Soc.*, **83**, 1974 (1961); N. L. Allinger, B. J. Gordon, S.-E. Hu, and R. A. Ford, *J. Org. Chem.*, **32**, 2272 (1967).



to that of the *trans*-15,16-dialkyldihydropyrenes.^{5,6} The behavior of **10** in trifluoroacetic acid at 30° was followed by observing the intensity of absorption at 469 m μ . This absorption reached a maximum 22 min after solution, and its decay was then followed for a 12-hr period at 30°. A plot of the log of the absorption intensities against time for the period of 1 hr after maximum absorption until 12 hr later gave a straight line, suggesting that the colored intermediate decomposes in a first-order or pseudo-first-order fashion.

Product analyses of solutions of **10** in trifluoroacetic acid were made after various periods of time and with various concentrations of **10**. Quenching with water of the reaction mixture after attainment of maximum intensity of the colored intermediate never led to recovery of any **10**, indicating that the formation of the colored intermediate is an irreversible process. Instead, the major products isolated after the solution had stood at room temperature for 1 hr were pyrene (24%) and two pyrene quinones (9%), **29** and **30**. Thin layer chromatograms indicated the presence of other products but these occurred in too minute quantities for isolation and identification. The presence of the quinones requires the formation of an oxidizing agent during the reaction and the fact that the yield of pyrene decreases with longer reaction times indicates that it is undergoing further reaction.

The reaction sequence outlined above appears to us to be the most reasonable one for coordinating and explaining these observations. We would propose that the colored intermediate is either the protonated pyrene *cis*-15,16-epoxide (**27**) or its carbonium ion isomer **28**. There is no obvious basis for choosing between these two structures at present. Reaction of the colored intermediate (**27** or **28**) with trifluoroacetic acid gives pyrene plus trifluoroacetic acid. Subsequent reaction of pyrene with trifluoroacetic acid yields the two quinones, **29** and **30**, plus small amounts of other unidentified products. In fact, we have shown independently that pyrene does react with trifluoroacetic acid to give quinones **29** and **30** plus small amounts of other products whose behavior in tlc chromatograms corresponds to that of the minor products from the reactions with **10**. Also, we have shown that under the same reaction conditions pyrene does not react to any appreciable extent with air and trifluoroacetic acid.

In view of the thermal rearrangement of **10** in methanol to give 1-pyrenol, it is possible of course that **10** may in part undergo an acid-catalyzed rearrangement to 1-pyrenol. Oxidation of 1-pyrenol would occur very readily with trifluoroacetic acid to give the same quinones, **29** and **30**. Although 1-pyrenol could not be detected among the products from the reaction of **10** with trifluoroacetic acid, there is insufficient evidence to eliminate it as one of

the intermediates contributing to quinone formation.

In view of the ease of expulsion of the bridging oxygen from **10** it might have been expected that triphenylphosphine or triethyl phosphite would be extremely effective for the conversion of **10** to pyrene. In fact, **10** was recovered unchanged after heating in the presence of either triphenylphosphine or triethyl phosphite even in solutions of boiling xylene. This rather puzzling result emphasizes the need for a deeper understanding of the mechanism of these reactions.

In summary, *cis*-8,16-oxido[2.2]metacyclophane (**10**) is a reactive molecule which thermally or by acid catalysis undergoes expulsion or rearrangement of the bridging oxygen atom. Although the direct evidence for the valence tautomerization of **10** to pyrene *cis*-15,16-epoxide (**7**) is limited, these rearrangement and expulsion reactions are most readily explained by postulating that such a valence tautomerization does occur. This behavior and this interpretation are common also to the methylene¹⁸ and nitrogen analogs.¹⁷

Experimental Section³¹

Dibenz[*b,f*]joxepine (13). To a solution of 20.9 g of xanthene-9-carbinol in 1.5 l. of benzene there was added 180 g of phosphorus pentoxide and the mixture was boiled under reflux for 15 min. After the mixture had been cooled to room temperature, the benzene solution was removed by decantation and the residual solid was washed twice with benzene by decantation. The combined benzene extracts were cooled to 0°, 200 ml of a saturated aqueous solution of sodium chloride was added, and after the mixture had been shaken the benzene layer was separated. The benzene extract was washed successively with water, an aqueous saturated sodium chloride solution, and water. It was then dried and concentrated to give 15.8 g (85%) of a white solid, mp 103–107° (lit.¹⁹ mp 109–110°). This was used without further purification.

10,11-Dihydrodibenz[*b,f*]joxepine (14). A mixture of 16.6 g of dibenz[*b,f*]joxepine (**13**) and 2.0 g of a 5% palladium-on-charcoal catalyst in 200 ml of ethyl acetate was subjected to hydrogenation at room temperature and atmospheric pressure. When the hydrogen uptake was complete, the catalyst and solvent were removed, leaving a colorless oil. Distillation of this residual oil gave 14.9 g (89%) of a colorless oil, bp 100–103° (0.2 mm); nmr (CDCl₃), multiplet at τ 2.70–3.08 (8 H) and a singlet at 6.95 (4 H).

Anal. Calcd for C₁₄H₁₂O: C, 85.68; H, 6.16. Found: C, 85.86, 85.78; H, 6.40, 6.28.

4,6-Dicarbomethoxy-10,11-dihydrodibenz[*b,f*]joxepine (16). To a solution of 10.2 g of 10,11-dihydrodibenz[*b,f*]joxepine (**14**) in 250 ml of ether there was added 130 ml of a 1.6 *N* solution of *n*-butyllithium in hexane and the resulting mixture was boiled under reflux in a nitrogen atmosphere for 68 hr. It was then cooled and added to a slurry of Dry Ice in 1.0 l. of ether. After addition of 800 ml of water and stirring of the mixture, the ether layer was separated and washed again with 200 ml of water. The combined aqueous solutions were acidified and extracted with three 500-ml portions of ether. The ether extracts were combined, dried, and treated with an excess of diazomethane at 0°. Concentration of the ether solution gave a dark red oil which was taken up in benzene and chromatographed over silica gel. The main eluate fraction gave 6.4 g of a yellow solid, mp 78–90°. Recrystallization of this from methanol yielded 4.8 g (30%) of pale yellow crystals, mp 91–95°. Further crystallization from methanol gave colorless crystals, mp 94.5–95.5°; $\lambda_{\text{max}}^{\text{EtOH}}$ 282 m μ (ϵ 3620); $\lambda_{\text{max}}^{\text{CHCl}_3}$ 5.78 μ ; nmr (CDCl₃), doublet of doublets at τ 2.47 (2 H, $J = 7$, $J' = 2.5$ cps), doublet of doublets at 2.78 (2 H, $J = 7$, $J' = 2.5$ cps), triplet at 3.00 (2 H, $J = 7$, $J' = 7$ cps), singlet at 6.10 (6 H), and a singlet at 6.88 (4 H).

(31) Analyses by Microtech Laboratories and A. Bernhardt Micro-analytical Laboratories. Ultraviolet and visible spectra were measured with a Cary Model 15, infrared spectra with a Beckman IR-5A, and nmr spectra with a Varian A-60. Mass spectra were determined by the Morgan and Schaffer Corp. We are indebted to the National Science Foundation for the funds for the purchase of the Varian A-60.

Anal. Calcd for C₁₈H₁₆O₅: C, 69.22; H, 5.16. Found: C, 69.07; H, 5.27.

4,6-Dicarboxy-10,11-dihydrodibenz[*b,f*]joxepine (15). A solution of 1.0 g of 4,6-dicarbomethoxy-10,11-dihydrodibenz[*b,f*]joxepine (**16**) in 15 ml of methanol containing 0.75 g of potassium hydroxide was boiled under reflux for 2 hr. After concentration, the residue was taken up in 10 ml of water, acidified, and extracted with chloroform. Concentration of the chloroform extract under reduced pressure gave a yellow oil which crystallized on scratching. After recrystallization from acetic acid it yielded 792 mg (87%) of white rhombic crystals, mp 234–235°.

Anal. Calcd for C₁₆H₁₂O₅: C, 67.60; H, 4.26. Found: C, 67.73; H, 4.34.

4,6-Bis(hydroxymethyl)-10,11-dihydrodibenz[*b,f*]joxepine (17). **A. From LiAlH₄ Reduction of 16.** A solution of 500 mg of 4,6-dicarbomethoxy-10,11-dihydrodibenz[*b,f*]joxepine (**16**) in 25 ml of ether was added dropwise with stirring to a slurry of 150 mg of lithium aluminum hydride in 25 ml of ether. The mixture was boiled under reflux for 0.5 hr, cooled to 0°, and decomposed by careful addition of water. The ether solution was decanted and concentrated to give 375 mg (91%) of a white solid, mp 122–124°. Recrystallization from benzene gave white crystals, mp 123–124°; uv $\lambda_{\text{max}}^{\text{EtOH}}$, 236 (ϵ 6920), 268 m μ (sh, 1680); ir. $\lambda_{\text{max}}^{\text{CHCl}_3}$ 2.90 μ ; nmr (CDCl₃), multiplet at τ 2.76–3.12 (6 H), singlet at 5.27 (4 H), singlet at 6.42 (2 H), and singlet at 6.92 (4 H).

Anal. Calcd for C₁₆H₁₆O₃: C, 74.98; H, 6.29. Found: C, 75.06; H, 6.26.

B. From Metalation of 14 Plus Formaldehyde. To a solution of 16.2 g of 10,11-dihydrodibenz[*b,f*]joxepine (**14**) in 400 ml of ether there was added 210 ml of a 1.6 *N* solution of *n*-butyllithium in hexane, and the resulting mixture was boiled under reflux in a nitrogen atmosphere for 60 hr. Then a suspension of 11.2 g of paraformaldehyde in 50 ml of ether was added gradually over a period of 0.5 hr. The mixture was then boiled under reflux for a short time and cooled. After acidification with 25% sulfuric acid, the ether layer was separated and the aqueous phase was extracted with chloroform. The combined ether and chloroform extracts were washed successively with water, aqueous bicarbonate, and water. Concentration of the solution gave a dark oil which was taken up in chloroform and chromatographed over silica gel. This gave 12.1 g (55%) of a cream colored solid, mp 121–123°. Recrystallization from benzene gave white crystals, mp 123–124°, identical in all respects with the sample obtained in A.

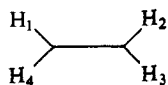
4,6-Bis(bromomethyl)-10,11-dihydrodibenz[*b,f*]joxepine (18). To a mixture of 1.0 g of 4,6-bis(hydroxymethyl)-10,11-dihydrodibenz[*b,f*]joxepine (**17**) in 30 ml of benzene there was added 1.5 ml of phosphorus tribromide, and the resulting solution was boiled under reflux for 45 min. It was then cooled to 0° and 50 ml of water was added. The benzene layer was separated and the aqueous layer was extracted with benzene. The combined benzene extracts were washed with an aqueous solution of sodium chloride and concentrated to give 1.5 g of a white solid. This was taken up in benzene and chromatographed over silica gel, yielding 1.40 g (93%) of white crystals, mp 121–123°. Recrystallization from hexane gave white crystals, mp 124–125°; nmr (CDCl₃), multiplet at τ 2.61–3.12 (6 H), singlet at 5.15 (4 H), and singlet at 6.92 (4 H).

Anal. Calcd for C₁₆H₁₄Br₂O: C, 50.28; H, 3.28. Found: C, 50.99; H, 3.95.

8,16-Oxido[2.2]metacyclophane (19). To a boiling solution of 913 mg of 4,6-bis(bromomethyl)-10,11-dihydrodibenz[*b,f*]joxepine (**18**) in 800 ml of ether there was added 4.0 ml of a 1.2 *N* solution of phenyllithium in ether over a 5-min period. The reaction mixture was boiled under reflux an additional 5 min and cooled to 0°, and 200 ml of water was added. The ether layer was separated, washed with water, dried, and concentrated to give a yellow oil. This was taken up in hexane and chromatographed over silica gel. The main eluate fraction gave a white solid which, after sublimation, yielded 395 mg (76%) of white crystals, mp 81–89°. A small portion recrystallized from methanol gave white crystals, mp 94–95°; uv, $\lambda_{\text{max}}^{\text{cyclohexane}}$ 236 (4590) and 263 m μ (sh, ϵ 585); nmr (CCl₄), singlet at τ 3.22 (6 H), and an AA'BB' multiplet at 6.12–7.62; mass spectrum, *m/e* 222 (see Table II).

Anal. Calcd for C₁₆H₁₄O: C, 86.45; H, 6.35. Found: C, 86.25; H, 6.24.

Chemical shift for 1 and 2 = –30.8; and chemical shift for 3 and 4 = +30.8; probable coupling constants: 1,2 = 8.4; 1,3 = 5.6; 1,4 = –14.9; 2,3 = –14.9; 2,4 = 5.6; and 3,4 = 9.8. From the calculation one cannot assign the chemical shifts to the two types of protons. However, several coupling constant assignments can

Table II. The Calculated Spectrum of the AA'BB' Pattern of the Bridging Methylene Protons in 8,16-Oxido[2.2]metacyclophane (19)

Line	Exptl freq ^a	Calcd freq	Calcd intens
8	53.1	53.1	0.190
13	43.4	43.4	0.624
36	42.1	42.1	0.744
29	36.8	36.9	1.630
53	35.8	35.8	1.701
47	35.8	35.8	1.395
22	28.5	28.5	2.035
9	26.5	26.5	1.882
3	26.5	26.5	2.299
12	22.9	22.8	1.376
40	21.5	21.5	1.256
43	9.2	9.2	0.869
20	-9.2	-9.2	0.869
34	-21.5	-21.5	1.256
25	-22.9	-22.8	1.376
55	-26.5	-26.5	2.299
45	-26.5	-26.5	1.882
51	-28.5	-28.5	2.035
21	-35.8	-35.8	1.395
1	-35.8	-35.8	1.701
5	-36.8	-36.9	1.630
38	-42.1	-42.1	0.744
24	-43.4	-43.4	0.624
41	-53.1	-53.1	0.190

^a All frequency values are given in hertz above (+) and below (-) the central point of the pattern. Although this assignment is not certain, H₁ and H₂ as drawn are *cis* to the oxygen bridge.

be made. The large negative coupling constant (-14.9) is most likely the *gem*-coupling constant between 1 and 4 and 2 and 3. The smallest coupling constant (5.6) is most likely that between 1 and 3 and 2 and 4 due to the geometry of the molecule. The two larger coupling constants (8.4 and 9.8) are thus those between adjacent hydrogens 1 and 2 and 3 and 4 and are of the magnitude expected from geometrical considerations.

1,9(10)-Dibromo-8,16-oxido [2.2]metacyclophane (20). A mixture of 1.0 g of 8,16-oxido[2.2]metacyclophane (19), 1.6 g of N-bromosuccinimide, and a few crystals of azobisisobutyronitrile in 500 ml of carbon tetrachloride was boiled under reflux for 1 hr. After the reaction mixture had cooled, it was filtered and the filtrate concentrated to give 1.8 g of a solid. The nmr spectrum of this solid was in accord with its being a mixture of two stereoisomers (20), and tlc over silica gel showed two closely moving spots. For the next reaction this mixture was used as such. However, seven fractional crystallizations from cyclohexane gave one isomer in a pure state as white crystals, mp 149.5–150.5°; nmr (CDCl₃), singlet at τ 2.95 (6 H), doublet of doublets at 4.87 (2 H, $J = 7.5$ and 9.5 cps), doublet of doublets at 5.51 (2 H, $J = 9.5$ and 14 cps), and doublet of doublets at 6.62 (2 H, $J = 7.5$ and 9.5 cps). It is not possible from these data to decide which of the two possible structures corresponds to this isomer.

Anal. Calcd for C₁₆H₁₂Br₂O: C, 50.56; H, 3.18; Br, 42.05. Found: C, 50.27; H, 3.49; Br, 41.93.

8,16-Oxido [2.2]metacyclophane-1,9-diene (10). To a solution of 30 ml of *t*-butyl alcohol in which 400 mg of potassium had been dissolved there was added 444 mg of the crude mixture of dibromides (20) from the experiment above. The mixture was boiled under reflux for 30 min and cooled, and 100 ml of water was added. This was then extracted with three 75-ml portions of ether. The combined ether extracts were washed with water, dried, and concentrated to give 223 mg of an oil. This was taken up in cyclohexane and chromatographed over silica gel. The main eluate yielded a white solid which was sublimed to give 191 mg (91%) of white crystals, mp 102–112°. Recrystallization of a sample from cyclohexane yielded white crystals, mp 119–120°; uv, $\lambda_{\text{cyclohexane}}^{\text{max}}$ 239 (15,750) and 302 m μ (ϵ 16,300); nmr (CCl₄), A₂B

multiplet at τ 2.66–3.30 (6 H), and a singlet at 2.92 (4 H); mass spectrum, *m/e* 218 with a strong signal at 202.

A similar experiment in which the crude dibromide 20 was dissolved in benzene containing 2 equiv of 1,5-diazabicyclo[4.3.0]nonene and boiled under reflux for 2 hr followed by a similar work-up gave 10 in 64% yield.

Anal. Calcd for C₁₆H₁₀O: C, 88.05; H, 4.62. Found: C, 87.84; H, 4.65.

Thermolysis of 8,16-Oxido [2.2]metacyclophane-1,9-diene (10) in Methanol. A solution of 40 mg of 8,16-oxido[2.2]metacyclophane-1,9-diene (10) in 10 ml of dry methanol was heated in a sealed tube at 123° for 16 hr. The solution was then concentrated and the residue taken up in chloroform. The chloroform solution was then extracted with an aqueous 10% potassium hydroxide solution. Acidification of the aqueous solution gave 14 mg of a white solid which was identified as 1-pyrenol by its nmr spectrum and its behavior on tlc. Concentration of the chloroform solution gave 25 mg of a white solid whose nmr spectrum was superimposable with that of the starting material, 10. There was no spectral indication of pyrene, which can readily be detected in minute quantity.

Thermolysis of 8,16-Oxido [2.2]metacyclophane-1,9-diene (10) in Benzene. A solution of 60 mg of 8,16-oxido[2.2]metacyclophane-1,9-diene (10) in 5 ml of benzene was heated in a sealed tube at 214° for 20 hr. A thin layer chromatogram of the solution at this point indicated the presence of two components plus a trace of starting material. The benzene solution was diluted with 50 ml of chloroform and extracted with three 25-ml portions of an aqueous 10% potassium hydroxide solution. The combined aqueous extracts were acidified and extracted with ether. After the ether extract had been washed with water and dried, it was concentrated to give 28 mg of a light tan solid, mp 172–176°. The identity of this substance with authentic 1-pyrenol was established by a mixture melting point determination,²⁶ a comparison of nmr spectra (acetonitrile), and a comparison of behavior on tlc.

The chloroform solution, after the extraction with the potassium hydroxide solution described above, was washed with water, dried, and concentrated to give 28 mg of a dark solid. This was treated with boiling cyclohexane, and then the cyclohexane solution was filtered. Concentration of the filtrate gave 20 mg of pale yellow crystals, mp 153–155°. This was shown to be identical in all respects with an authentic sample of pyrene.

When the thermolysis of 10 was carried out in the presence of cyclohexene at 248°, pyrene was isolated in 50% yield but the remaining material was a complex mixture of products whose retention times on vpc ranged from about that of cyclohexanone to considerably longer. There was evidence of appreciable polymer formation.

Reaction of 8,16-Oxido [2.2]metacyclophane-1,9-diene (10) with Trifluoroacetic Acid. A. A solution of 100 mg of the diene in 100 ml of trifluoroacetic acid was allowed to stand at room temperature for 7 hr. It was then heated at 80° in a sealed tube for 9 hr. The reaction mixture was diluted with 500 ml of water and extracted with two portions of ether (350 ml). The combined ether phases were washed successively with 500 ml of water, 800 ml of a 5% sodium bicarbonate solution, and 500 ml of water. After the ether was dried, concentration gave 80 mg of a black residue. Tlc showed two major spots, one of which was of the same *R_f* value as pyrene. A small portion of the residue was subjected to preparative tlc, using silica gel with a hexane-ethyl acetate mixture. The highest band was recovered and was shown to be pyrene by comparison of its ultraviolet spectrum with that of authentic material. From the remainder of the product residue were separated two other bands of very close *R_f* value, one of which was red and the other, yellow. It required three preparative separations by thin layer chromatography to separate the two materials completely. The yellow band was identified as 1,6-pyrenequinone (29) by comparison of its *R_f* value and its ultraviolet, visible, and infrared spectra with those of an authentic sample. The red material was identified as 1,8-pyrenequinone (30) in a similar fashion. The above spectra were compared also with those which were reported and were in good agreement.³² The preparative tlc of the total product residue indicated that there were several additional bands present directly above the two bands for the quinones. None of these was isolated or identified.

B. Several control experiments were also run. When pyrene

(32) A. J. Fatiadi, *J. Chromatog.*, 20, 319 (1965).

was dissolved in trifluoroacetic acid and treated under the same reaction conditions as in A, only pyrene was recovered. Pyrene was also allowed to react under the same conditions as in A with a solution of trifluoroacetic acid containing trifluoroacetic acid. In this case the same two quinones, **29** and **30**, were isolated and identified as in A. The thin layer chromatogram of the oxidation product mixture indicated that there were numerous other products present of both lower and higher R_f values than those of the two quinones.

C. A small amount of the diene was dissolved in trifluoroacetic acid. It was observed that the solution rapidly became green reaching a maximum intensity after 30 to 40 min. The color faded very slowly requiring several days to become a light yellow and remain that color. The visible spectrum showed an intense band at 469 m μ with considerably weaker bands between 550 and 700 m μ . The appearance and disappearance of the band at 469 m μ was followed with time holding the reaction mixture at 30°. The band reached a maximum intensity at 22 min and then slowly faded in intensity. A plot of the log of absorption vs. time gave a good straight line for those values of absorption recorded for decay of the 469-m μ band from about 1 hr after maximum intensity until about 11 hr after the maximum intensity had been reached.

D. A solution of 4.228 mg of the diene in 100 g of trifluoroacetic

acid was allowed to stand for 1 hr. To it was then added 100 ml of water. This was extracted with three portions of chloroform (a total of 250 ml) and the combined chloroform extracts were washed successively with two 100-ml portions of water, 100 ml of a 10% aqueous sodium bisulfite solution, and 100 ml of a saturated sodium bicarbonate solution. After the chloroform solution was dried, it was concentrated. From the residue pyrene was isolated by preparative tlc using the silica gel with a 5% solution of ethyl acetate in hexane as the eluent. The pyrene was dissolved in 500 ml of cyclohexane and a quantitative ultraviolet spectrum indicated that 0.931 mg (24%) of pyrene was present. There were two fluorescent bands directly below the pyrene band which were in the area where starting material would be present. Examination of the ultraviolet spectrum of these two bands indicated that essentially no starting material was present.

The two quinones were isolated by preparative tlc, using silica gel with ethyl acetate as eluent. The two quinones (together) were dissolved in 50 ml of methanol. Their ultraviolet spectrum indicated that 4.8% of 1,6-pyrenequinone (**29**) and 4.4% of 1,8-pyrenequinone (**30**) were present. The amount of each in the mixture was determined by measuring the absorption of the solution of the mixture at two different wavelengths for which the extinction coefficients were known for both compounds.^{3,2}

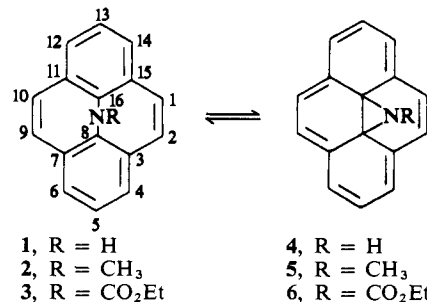
8,16-Imino[2.2]metacyclophane-1,9-diene. A Valence Tautomer of Pyren-*cis*-15,16-imine¹

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Abstract: A synthesis of 8,16-imino[2.2]metacyclophane-1,9-diene (**1**) and certain simple N-substituted derivatives is described. Although **1** is a valence tautomer of pyren-*cis*-15,16-imine (**4**), spectral examination of the compound at room temperature is in complete accord with structure **1** and provides no evidence for the presence of pyren-*cis*-15,16-imine. On the other hand, **1** and its N-substituted derivatives undergo rearrangement and expulsion reactions of the imine bridge which are best explained by invoking pyren-*cis*-15,16-imine as an intermediate. These rearrangement and expulsion reactions occur thermally in neutral solvents or may be initiated by solution in strong acid. The nature of the substituent on the imino nitrogen plays an important role in determining the ease with which these expulsion and rearrangement reactions occur.

In an accompanying paper,³ the background and reasons for interest in *cis*-15,16-dihydropyrenes are discussed. Since *cis*-bridged [2.2]metacyclophane-1,9-dienes are valence tautomers of the corresponding *cis*-15,16-dihydropyrenes, a natural synthetic approach has been to prepare suitable *cis*-bridged [2.2]metacyclophane-1,9-dienes. In the previous paper a synthesis of 8,16-oxido[2.2]metacyclophane-1,9-diene is described,³ and in this report the synthesis of 8,16-imino[2.2]metacyclophane-1,9-diene (**1**), a valence tautomer of pyren-*cis*-15,16-imine (**4**), is presented as well as certain aspects of its chemistry.⁴



In undertaking a synthesis of 8,16-imino[2.2]metacyclophane-1,9-diene (**1**) we were hopeful that we could follow a reaction sequence similar to the successful route worked out for 8,16-oxido[2.2]metacyclophane-1,9-diene.³ Therefore, the commercially available 10,11-dihydro-5H-dibenz[*b,f*]azepine (**7**) was methylated and the N-methyl derivative (**8**) was subjected to metalation with *n*-butyllithium followed by carbonation. Un-

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(2) National Institutes of Health Postdoctoral Fellow, 1966-1968.

(3) B. A. Hess, Jr., A. S. Bailey, B. Bartusek, and V. Boekelheide, *J. Am. Chem. Soc.*, **91**, 1665 (1969).

(4) The numbering system used for the [2.2]metacyclophanes is that recommended by B. H. Smith, "Bridged Aromatic Compounds," Academic Press, New York, N. Y., 1964, p 8.