[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY, HARVARD UNIVERSITY]

Bicyclic Structures Prohibiting the Walden Inversion. Further Studies on Triptycene and its Derivatives, Including 1-Bromotriptycene[1]

BY PAUL D. BARTLETT AND EDWARD S. LEWIS

In previous papers of this series[2-4] observations have been reported of the unreactivity of hydrogen, halogen and hydroxyl when situated at the bridgehead of a 2,2,1-bicycloheptane or 2,2,2-bicyclooctane ring system. Most conspicuous was the total failure of displacement reactions of the S_N1 or S_N2 type,[5] although reductive displacement of bromine by hydrogen[3] and replacement of the amino group by hydroxyl or halogen[2] under conditions suggesting an S_Ni[6] displacement were accomplished. The previous work on triptycene (9,10-*o*-benzenoanthracene, or 2,3,5,6,7,8-tribenzobicyclo-2,2,2-octatriene-2,5,7) (VI, X = H in the preceding paper[6a]) suggested a total absence of the resonance possibilities in the anion which impart to triphenylmethane its special acidic character. Work which was then under way to extend this study to the carbonium ion and the free radical was interrupted by World War II and is here reported.

All the compounds in question have two special properties which may be concerned in the nonoccurrence of displacement reactions. In the first place the rear face of the carbon atom holding the functional group is so effectively shielded as to prevent the approach, synchronized with the departure of the displaced group, of either an attacking nucleophilic reagent or a solvating molecule. In the second place, and particularly with triptycene and its derivatives, the molecule is forced to occupy a geometrical form as unfavorable as possible to the resonance structures which would be concerned in the stabilization of a carbonium ion, carbanion or free radical. Although in previous papers we have stressed the steric inhibition of resonance as being probably crucial in the unreactivity of such systems, the recently emphasized importance of solvation of a carbonium ion[7] leaves open the possibility that the hindrance to direct approach of a solvating molecule is an equally important factor. Exploratory experiments in this Laboratory to produce a bicyclic halogen compound which should have the shielding to prevent solvation without restricting the bond angles have not been successful. However, recent work by Brown and Fletcher on open-chain halides with high steric hindrance about the central carbon atom[8] and an extension of such systems to the very highly hindered halides obtainable from tri-*t*-butylcarbinol and its derivatives[9] have shown that such halides have strongly enhanced, rather than hindered, reactivity despite the fact that no very close approach of a solvent molecule to the central carbon atom is possible in concert with the departure of the halide ion.

The synthesis of bromotriptycene, involving contributions by a succession of workers over a period of about ten years, is reported in an accompanying paper.[6a] The structure of bromotriptycene, shown with fair certainty by its method of synthesis, is confirmed by the close similarity in ultraviolet absorption spectra between bromotriptycene and triptycene, by the reduction of bromotriptycene to triptycene by means of sodium, and by the oxidation of bromotriptycene to anthraquinone as the only obtainable product. The last observation shows that the bromine cannot be located in one of the aromatic rings for it would undoubtedly diminish the susceptibility of that ring to oxidative attack and a bromoanthraquinone would therefore be the product of oxidation.

Properties and Behavior of Bromotriptycene.—The conductivity of bromotriptycene in liquid sulfur dioxide at 0° was measured by Dr. Norman N. Lichtin. In sharp contrast to triphenylmethyl chloride and triphenylmethyl bromide, bromotriptycene yields a colorless solution in sulfur dioxide with a conductivity differing from that of the pure solvent by no more than the experimental error.

Bromotriptycene was boiled for five days with alcoholic sodium hydroxide without any detectable hydrolysis. During the reduction of bromotriptycenequinone dioxime to bromodiaminotriptycene by boiling with sodium sulfide there was no displacement of bromine by this rather strong nucleophilic reagent. Bromotriptycene was recovered nearly quantitatively after heating in toluene solution with stannic chloride under conditions which produced chloroanthracene from anthracene dibromide. These experiments demonstrate that the triptycyl positive ion, if it exists at all, cannot be formed by methods applicable to analogous triarylmethyl compounds.

Attempts were made to prepare the triptycyl free radical by the reaction of bromotriptycene

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[1] From a thesis presented by E. S. Lewis for the degree of Ph.D. at Harvard University, 1947. These results were presented in part before the Tenth National Organic Symposium at Boston in June, 1947.

[2] P. D. Bartlett and L. H. Knox, THIS JOURNAL, **61**, 3184 (1939).

[3] P. D. Bartlett and S. G. Cohen, *ibid.*, **62**, 1183 (1940).

[4] P. D. Bartlett, M. J. Ryan and S. G. Cohen, *ibid.*, **64**, 2649 (1942).

[5] E. D. Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

[6] W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman and A. D. Scott, *J. Chem. Soc.*, 1252 (1937).

[6a] P. D. Bartlett, S. G. Cohen, J. D. Cotman, Jr., N. Kornbliem, J. R. Landry, and E. S. Lewis, THIS JOURNAL, **72**, 1003 (1950).

[7] C. G. Swain, *ibid.*, **70**, 1118 (1948).

[8] H. C. Brown and R. S. Fletcher, *ibid.*, **71**, 1845 (1949).

[9] M. S. Swain, Thesis, Radcliffe College, 1948.

with copper powder, zinc dust and molecular silver, the last-named reagent being tried not only at ordinary temperatures but at 280° in carefully dried mineral oil as a solvent. In no case was any reaction observed.

Bromotriptycene reacts slowly with both sodium and magnesium but we did not succeed in halting this reaction at the stage of formation of an organometallic compound. Neither was it possible to obtain any evidence of the formation of such a compound by passing carbon dioxide through the solutions before hydrolysis. In the reaction with sodium using mineral oil as a solvent at 140°, the starting material was quantitatively reduced to unsubstituted triptycene and the mineral oil contained after carbonation a small amount of an unidentified acidic substance.

The failure of bromotriptycene to undergo nucleophilic displacement even under the most drastic conditions is scarcely surprising in view of previous results. However, the present example represents the most stringent test yet made of this point since triphenylmethyl bromide, to which triptycene is closely related structurally, would yield these reactions too rapidly for measurement. The successful reduction of bromotriptycene to triptycene was also foreshadowed by the sodium reduction of the addition product of maleic anhydride to 9-bromoanthracene.[3] Since this is a two-electron reduction the conditions under which it takes place should afford some information concerning the behavior of either the triptycyl free radical or the triptycyl carbanion, both fragments being presumably involved to at least a transitory degree. Since no carbonation of triptycylsodium was achieved it follows that either our carbon dioxide, despite drying, contained enough water to hydrolyze the organometallic compound, or else the triptycyl carbanion is not only more strongly basic than the carbanion derived from triphenylmethane, but it is actually more basic than the simple aliphatic carbanions related to the hydrocarbon solvents. It is only at the expense of these solvents or of stray water that hydrogen could be provided for such yields of triptycene as were obtained in these reductions. On the other hand, it would be possible to represent the debromination of bromotriptycene as proceeding through the triptycyl free radical which then takes a hydrogen atom from the hydrocarbon solvent. If this is the course of the reaction, then the triptycyl free radical must be more reactive toward hydrogen than ordinary aliphatic free radicals which, produced under similar circumstances, often undergo reaction with one another rather than exclusively with the solvent.[10] As to the relative ease of formation of the carbonium ion, free radical and carbanion, it has already been demonstrated[11] that the apocamphyl radical is formed in the decomposition of the related peroxide apparently as easily as acyclic free radicals under the same circumstances,[12] although the apocamphyl *positive ion* cannot be produced.

As another method of approach to the triptycyl free radical, an attempt was made to prepare 1,1-ditriptycyl starting with the addition of quinone to 9,9-dianthryl. Although a product was obtained from this reaction, its analysis was incompatible with a composition corresponding to more than one molecule of benzoquinone to two of dianthryl. Models show that the strain involved in the projected reaction would be very great.

Because of the demonstrated possibility[11] of forming bicyclic free radicals in the decomposition of an acyl peroxide, a few experiments were made toward the synthesis of triptycene-1-carboxylic acid. This approach was abandoned at the stage of oxidation of 1-formyl-2,5-dihydroxytriptycene to the corresponding quinone when it was observed that these vigorous oxidizing conditions did not oxidize the aldehyde group to a carboxyl group.

The Question of the Mills–Nixon Effect in Triptycene.—It was suggested previously[4] that because of the rigid bond angles in the interior of the bicyclo-2,2,2-octane ring system, triptycene should show as strong a Mills–Nixon effect as hydrindene. One approach to this question would be the measurement of the oxidation potential of triptycenequinone. Since the quinone must have a double bond in the unfavorable position within the bicycloöctane ring, whereas the hydroquinone has no more than slightly damped resonance, the oxidation potential of the quinone should be higher in proportion to the unfavorableness of the position of its double bond. Table I lists the oxidation potentials of a series of quinones including triptycenequinone and some analogs taken from the interesting thesis of H. B. Dunkle in 1937. Many of these compounds were measured in alcohol solutions containing somewhat less than 95% alcohol. From known effects of solvent on certain quinones a correction of not more than a few millivolts has been made to all these cases to make them comparable with our measurement in 95% ethanol. The standard oxidation potential determined in this solvent for triptycenequinone

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[10] See, for example, M. S. Kharasch and E. K. Fields, THIS JOURNAL, **63**, 2316 (1941).

[11] M. S. Kharasch, F. Englemann and W. H. Urry, *ibid.*, **65**, 2428 (1943).

[12] The reaction of Kharasch, Englemann and Urry is perhaps the most convincing example yet on record of the occurrence of a true hydrocarbon free radical in the course of the decomposition of an acyl peroxide. With most acyl peroxides the alternative possibility exists (F. G. Edwards and F. R. Mayo, THIS JOURNAL, **72**, March (1950)) that carboxylate radicals undergo reactions in which the carbon dioxide is directly displaced by collision with a solvent molecule such as carbon tetrachloride which donates a chlorine atom. In the formation of chloroapocamphane from the peroxide of apocamphane-1-carboxylic acid on decomposition in carbon tetrachloride it is impossible that the apocamphane carboxylate radical should be attacked by a carbon tetrachloride molecule and the carbon dioxide displaced with inversion. Neither does any analogy exist which would lead us to expect a possible attack of this kind on the front face of C_1 of the apocamphane ring system. This leaves it overwhelmingly probable that free apocamphyl radicals exist in the course of this reaction.

was −0.666 v. which is not far from the value of −0.641 v. for hydrindenequinone.[13] In general the ascending order of standard potentials in Table I coincides with the order of strain which might be assigned to the quinone double bond from an inspection of the structures of the disubstituted quinones. Since the oxidation potentials of the quinones register a difference in stability or strain between the quinone and its hydroquinone, no information is afforded about the degree of Mills–Nixon effect in triptycene itself. It seems likely, however, that where a demonstrable effect exists in the quinone it will not be wholly absent in the parent hydrocarbon and might possibly affect its behavior upon the attack of an oxidizing agent.

TABLE I

STANDARD OXIDATION POTENTIALS OF SOME 2,3-DISUBSTITUTED *p*-BENZOQUINONES

Quinone	E^0	Solvent	Ref.
o-Xyloquinone	−0.585	Water	*a*
5,6,7,8-Tetrahydro-1,4-naphthoquinone	− .588	Water	*a*
	− .597	95% EtOH	*b*
5,8-Dihydro-1,4-naphthoquinone	− .617	95% EtOH	*b*
5,8-Endoethylene-5,6,7,8-tetrahydro-1,4-naphthoquinone	− .639	95% EtOH	*b*
5,8-Endoethylene-5,8-dihydro-1,4-naphthoquinone	− .648	95% EtOH	*b*
Hydrindenequinone	− .641	Water	*a*
Triptycenequinone	− .666	95% EtOH	
5,8-Endomethylene-5,6,7,8-tetrahydro-1,4-naphthoquinone	− .682	95% EtOH	*b*
5,8-Endomethylene-5,8-dihydro-1,4-naphthoquinone	− .708	95% EtOH	*b*
(Benzoquinone	− .711)	95% EtOH	*c*

[a] Arnold and Zaugg, ref. 13. [b] H. B. Dunkle, Thesis, Harvard University, 1937. [c] J. B. Conant and L. F. Fieser, THIS JOURNAL, 45, 2208 (1923).

The Absorption Spectrum of Triptycene.—The absorption spectrum of triptycene does not show any recession from aromatic properties as might be looked for in the light of the susceptibility of triptycene to oxidation. Triphenylmethane[14] has absorption maxima at 249, 255, 262 and 271 mμ, with log E 2.83, 3.02, 3.04 and 2.84, respectively. Triptycene shows two maxima, at 271 and 278 mμ, with log E 3.66 and 3.56, respectively, and a shoulder at about 263 mμ with log E 3.25. If one of the maxima of triphenylmethane is to be attributed to hyperconjugation of the very reactive hydrogen atom, as has been done in the case of the alkylbenzenes,[15] then the absence of this band in triptycene, which is incapable of such hyperconjugation, would be expected. However, the difference in symmetry between the two compounds might also be responsible for differing complexities of their spectra.

The absorption at the maxima in triptycene is more intense than in triphenylmethane by factors of 3.3 and 5.5, and these maxima are at longer wave lengths than their apparent equivalents in triphenylmethane by 9 and 7 mμ, respectively. This is the type of change normally associated with intensified conjugation. Triptycene is unfavorably constituted for conjugation involving the bridgehead carbon atoms, but it is very favorably constituted for contributions of structures such as[16]

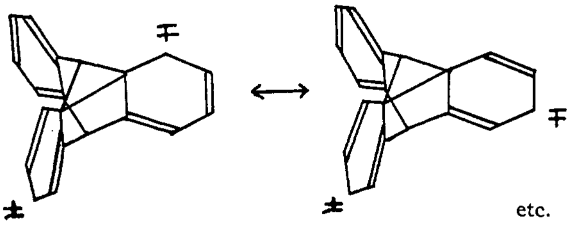

Fig. 1.

This is a type of conjugation recently considered for dihydroacetophenones[17] and rejected in favor of strong hydrogen hyperconjugation. Experimentally the present case differs from that of the dihydroacetophenones by involving higher intensities as well as longer wave lengths in the conjugated than in the unconjugated compound, and by being free from the difficulties inherent in work with readily isomerized compounds. Theoretically, hydrogen hyperconjugation is about as improbable in triptycene as it can be anywhere, while the cross-ring interaction is strengthened by the possibility of 108 nearly equivalent structures of the type shown. It is interesting in this connection that evidence is accumulating for the occurence, in favorable cases, of mesomeric ions involving contributing structures akin to those here postulated. Such favorable cases include the intermediate stages in the i-sterol rearrangement,[18] the solvolysis of 2,3-diphenyl-2-butyl toluenesulfonate[19] and of norbornyl toluenesulfonate.[20]

Experimental

Conductivity Measurement.—The conductivity of bromotriptycene was measured by Dr. N. N. Lichtin, using an apparatus similar to that of Ziegler.[21] At 0° the conductivity of the colorless solution of bromotriptycene in sulfur dioxide exceeded that of the pure solvent by no more than the experimental error.

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[13] R. T. Arnold and H. F. Zaugg, THIS JOURNAL, 63, 1317 (1941).

[14] L. C. Anderson, *ibid.*, 50, 208 (1928).

[15] F. A. Matsen, W. W. Robertson and L. L. Chuoke, *Chem. Revs.*, 41, 273 (1947).

[16] This was pointed out to us by Prof. R. B. Woodward, to whom we are indebted for helpful discussions.

[17] E. A. Braude, E. R. H. Jones, F. Sondheimer and J. B. Toogood, *J. Chem. Soc.*, 607 (1949); *cf.* K. Bowden and E. R. H. Jones, *ibid.*, 52 (1946).

[18] S. Winstein and R. Adams, THIS JOURNAL, 70, 838 (1948).

[19] D. J. Cram, *ibid.*, 71, 3863, 3875 (1949).

[20] S. Winstein and D. S. Trifan, *ibid.*, 71, 2953 (1950).

[21] K. Ziegler and H. Wolschitt, *Ann.*, 479, 90 (1930).

At a concentration of 155 l. per mole, the specific conductance of the solution was 1.8×10^{-7} mho. The specific conductance of the solvent taken at this time was 0.5×10^{-7} mho, although the usual value was between 1×10^{-7} and 2×10^{-7} mho. Triphenylmethyl chloride, under the same conditions, has a specific conductance of about 1×10^{-4} mho.[22]

Attempted Reaction of Bromotriptycene with Sodium Hydroxide.—A solution of 0.82 g. of bromotriptycene and 35 g. of sodium hydroxide in 300 cc. of ethanol was boiled for five days. The resulting dark brown solution was diluted with 1000 cc. of water and then extracted with 500 cc. of benzene. The benzene solution was washed with acid, then evaporated to dryness. The residue was dissolved in petroleum ether and put through an adsorption column containing alumina. Elution with more petroleum ether gave at first white crystals which were identified by mixed melting point as unaltered bromotriptycene. Later fractions were slightly yellow from the various oxidation products of the alcohol. The total recovery was 0.74 g. or 90%. The water solution was evaporated to a small volume, acidified and filtered to remove the precipitated resins. This clear solution gave no precipitate or cloudiness with silver nitrate solution.

Attempted Reaction of Bromotriptycene with Stannic Chloride.—A solution of 0.20 g. of bromotriptycene and about 2.4 g. of stannic chloride in 5 cc. of toluene was heated on the steam-bath for twelve hours. The solution was washed with concentrated hydrochloric acid, then with water, then with dilute sodium hydroxide and finally with water. The toluene was boiled away, leaving a white crystalline solid weighing 0.195 g., which corresponds to a recovery of 97.5%, m. p. (uncor.) 247–250°, mixed with bromotriptycene m. p. 247–250°.

Attempted Reaction of Bromotriptycene with Molecular Silver.—A solution of 0.26 g. of bromotriptycene in 30 cc. of benzene was shaken with molecular silver in an evacuated system at room temperature overnight. No color was produced. A different sample of the same batch of molecular silver gave a pronounced color in less than five minutes with triphenylmethyl chloride. After this treatment 0.24 g. (92%) of a white crystalline substance was recovered m. p. 240–246°, mixed m. p. with bromotriptycene 241–246°.

Four grams of molecular silver and 150 cc. of white mineral oil were stirred overnight in an atmosphere of nitrogen, from which oxygen had been removed with a solution of benzophenone ketyl in toluene. Then 1.00 g. of bromotriptycene was added, and the mixture was stirred for one-half hour more to remove any air added. The flask was then heated in a bath at 280° for ten hours. No color or cloudiness was produced at any temperature. The solute was separated from the mineral oil by adsorption on alumina and elution with petroleum ether. The separation was not complete, however, and all but the latest fractions were contaminated with mineral oil. One of the later fractions gave white crystals m. p. 237–241° (uncor.) both alone and mixed with bromotriptycene, m. p. 214° mixed with triptycene. The combined eluates were concentrated by the removal of petroleum ether and after standing in the ice-box for several days, large crystals of bromotriptycene formed from this solution. The recovered material weighed 0.72 g., or 72%, but there was more material not recovered from the mother liquor. The imperfect recovery may be partly due to the volatility of bromotriptycene, since it sublimes appreciably even at 100°.

No reaction was observed on ten hours of boiling of bromotriptycene with copper powder or zinc dust in benzene.

The Reaction of Bromotriptycene and Sodium.—Bromotriptycene and sodium did not react in boiling toluene in three hours without stirring.

Ten grams of sodium was heated with 200 cc. of white mineral oil with vigorous stirring to 140°. A good emulsion was produced; on settling the sodium was still bright. After thirty minutes 0.7 g. of bromotriptycene was added and stirring was continued for five hours. Dry carbon dioxide was then passed into the mixture for two hours while it was cooling. The mixture was then hydrolyzed by passing wet nitrogen into the cold mixture, and finally by adding water. The resulting emulsion was separated by centrifugation. The water layer was extracted with ether, then acidified and re-extracted. This last ether extract contained a small amount of a brown oily substance which was soluble in dilute potassium carbonate solution. The mineral-oil phase was dried and put through an adsorption column containing Brockmann alumina. Elution with petroleum ether gave first several fractions containing mineral oil, then a fraction containing nothing, followed by several fractions containing a white crystalline substance. The first fraction melted at 241–245°; later fractions melted variously from 247–250°, but no one of these fractions depressed the melting point of any other one. The melting point when mixed with bromotriptycene was 210–216°, but mixed with a sample of triptycene (m. p. 246–248°) there was no depression. The combined yields totalled 0.53 g., corresponding to a quantitative yield.

The above reaction was repeated using 2,2,4-trimethylpentane (isoöctane) as a solvent. One hour of boiling brought about only 10% reaction.

Test for Presence of Bromine.—The product of this reaction was originally identified by its failure to give silver bromide in a test devised by Dr. W. F. Sager. In this test a very small amount of the sample is decomposed with fuming nitric acid in a sealed melting-point tube at about 180°, as in the Carius procedure. The tube is then broken open in a small test-tube containing aqueous hydrazine hydrate to reduce any bromine formed, then silver nitrate is added. Bromotriptycene and other halogen compounds give a considerable precipitate, even though small amounts are used. This method uses very considerably smaller amounts than a sodium fusion, and appears to give superior results in this case. The Beilstein test for halogen gave inconclusive results with bromotriptycene.

The Reaction of Bromotriptycene with Magnesium.—Bromotriptycene was added to an ether solution of ethylmagnesium bromide containing excess magnesium. After stirring for three hours, carbon dioxide was added, but on hydrolysis no solid acid fraction was formed. The neutral ether-soluble product was identified as triptycene.

Oxidation Potential of Triptycenequinone.—Triptycenehydroquinone was titrated potentiometrically with ceric sulfate solution in 95% alcohol. The mid-point of the titration curves gives, to a first approximation, the oxidation potential which can be corrected to 1 molar hydrogen-ion concentration. This gave in the case of triptycenehydroquinone −0.666 v. Benzohydroquinone gave −0.706 v., compared to the accepted value under these conditions of −0.711 v. The difference can be attributed to contact potentials, etc. The error is probably not greater than 0.01 v.

Absorption Spectra.—The absorption spectra were measured using a Beckman quartz spectrophotometer. The solvent used was Rohm and Haas pure isoöctane, which had been treated once with activated alumina before use.

Oxidation of Bromotriptycene.—Two-tenths of a gram of bromotriptycene was dissolved in 50 cc. of glacial acetic acid, then 0.5 g. of chromic anhydride was added and the solution was heated on the steam-bath for two hours. At the end of this time the solution was clear green. It was diluted with water and the resulting yellow precipitate gave on recrystallization from benzene 0.04 g. (30%) of product of m. p. 282–284° and melting at 283.5–283.8° mixed with anthraquinone.

Summary

1-Bromotriptycene does not undergo displacement reactions under vigorous treatment with alcoholic alkali, sodium sulfide, stannic chloride, copper powder, zinc dust or molecular silver. Oxida-

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[22] N. N. Lichtin, Thesis, Harvard University, 1948, p. 67.

tion yields only anthraquinone. In boiling isooctane or in carefully dried mineral oil at 140°, 1-bromotriptycene is reduced to triptycene, no ditriptycyl being produced. Ditriptycyldiquinone is not formed by the addition of benzoquinone to 9,9-dianthryl. 1-Aldehydotriptycenequinone was made and its aldehyde group found to be very resistant to oxidation.

The oxidation potential of triptycenequinone is −0.666 v., close to that of hydrindenequinone, suggesting similar strain in the location of a double bond in the two compounds.

The absorption spectra of triptycene and of 1-bromotriptycene are closely similar. They show fewer maxima than triphenylmethane, and the maxima appear at longer wave lengths and with markedly higher intensities. A kind of cyclopropanic conjugation is proposed for which triptycene is especially favorably constituted.

CAMBRIDGE, MASSACHUSETTS RECEIVED JULY 29, 1949

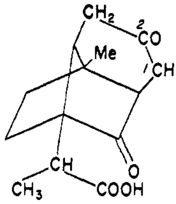
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Structure of the Santonides

BY R. B. WOODWARD AND E. G. KOVACH

Santonide and parasantonide are isomeric neutral substances of the formula $C_{15}H_{18}O_3$ which were first prepared more than seventy years ago by acetic acid treatment and pyrolysis of santonic acid.[1] The compounds are of more than ordinary interest in view of the complexity of the structural problem which they present and, further, because of their remarkable optical properties (*vide infra*). With the elucidation of the structure of santonic acid (I) recently in this Laboratory,[2] it became possible for the first time to make a rational approach to the formulation of the santonides.

Since the santonides differ in empirical composition from santonic acid by the elements of a water molecule, it has been assumed generally in the past that they were simple enol-lactones of that acid. It is now readily apparent, however, that this trivial solution of the structural problem is invalid, since (II), and all other enol-lactone structures derived directly from (I), *possess a carbon–carbon double bond in an impossibly strained position.*[3] This view receives decisive support from the fact that on hydrolysis, the santonides are converted not into santonic acid, but into two new isomeric acids, isosantonic acid (from santonide) and parasantonic acid (from parasantonide). Further, in sharp contrast to santonic acid, which requires very vigorous treatment for transformation to the santonides, the isomeric acids are very smoothly reconvertible to the respective santonides under very mild conditions. One of two assumptions must therefore be made: (i) the loss of water does not lead to a lactone *or* (ii) the reaction is attended by rearrangement of the skeleton of the molecule.



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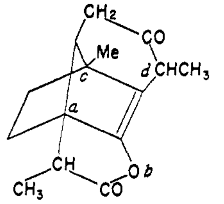
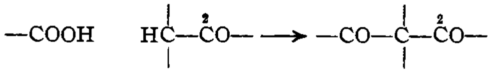


II

We consider first, and reject, the first of these possibilities. In detail, the only alternative to lactone formation is a loss of water involving the carboxyl group and a hydrogen atom alpha to the C.2 carbonyl group of santonic acid



$$-\mathrm{COOH}\quad \mathrm{H}\overset{|}{\underset{|}{\mathrm{C}}}-\overset{2}{\mathrm{C}}\mathrm{O}- \longrightarrow -\mathrm{CO}-\overset{|}{\underset{|}{\mathrm{C}}}-\overset{2}{\mathrm{C}}\mathrm{O}-$$

The reaction is not without analogy,[4] and in the case in point would lead to the somewhat, but not greatly, strained structure (III).[5] The necessity for the use of very vigorous conditions in effecting the transformation of santonic acid to the santonides is reminiscent of the circumstances obtaining in the analogous cases. On the other hand, the very facile reconstitution of the santonides from

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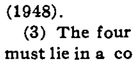
(1) Cannizzaro and Valente, *Rend. accad. Lincei*, III, **2**, 134, (1878); *Gazz. chim. ital.*, **8**, 309 (1878); Francesconi, *ibid.*, **25**ii, 471 (1895); *Rend. accad. Lincei*, V, **12**,ii, 204, 267, 304 (1903).

(2) Woodward, Brutschy and Baer, THIS JOURNAL, **70**, 4216 (1948).

(3) The four groups *a*, *b*, *c* and *d* attached to a double bond (A) must lie in a common plane if the system is to be strainless. [*Bredt's rule* (Bredt, *Ann.*, **437**, 1 (1924)) follows as a simple corollary from this principle as applied to small bicyclic systems]. It is clear that in (II) (above) the geometry of the molecule necessitates marked deviation from this condition, and that (II) consequently represents a very highly strained molecule. The same conclusion may be reached by noting that (II) contains a *trans*-substituted double bond *within a seven-membered ring*. Finally reference may be made to the recent elegant experimental demonstrations [Prelog, Ruzicka, Barman and Frenkiel, *Helv. Chim. Acta*, **31**, 92 (1948); Prelog, Barman and Zimmerman, *ibid.*, **32**, 1284 (1949)] that an unstrained double bond at the bridgehead of a [1,3,*n*] bicyclic system is only possible when $n \geqslant 5$; (II) contains a bridgehead double bond in a [1,3,3] bicyclic system. Similar considerations apply to enol-lactone formulas which may be derived from (I) by utilizing the C.2 carbonyl group.



A

(4) α-Campholonic acid → 2,6-diketocamphane [Miyake and Watanabe, *Proc. Imp. Acad.* (*Tokyo*), **11**, 322 (1935); (*cf. C. A.*, **30**, 2949 (1936); Komppa and Beckmann, *Ber.*, **69**, 2783 (1936)]; cyclohexanone-3-acetic acid → bicyclo[2,2,2]octane-2,6-dione [Bartlett and Woods, THIS JOURNAL, **62**, 2933 (1940)].

(5) A new *trans* bicyclo[0,3,3]octane system [strain about 7 kc./mole; *cf.* Barrett and Linstead, *J. Chem. Soc.*, 436 (1935)] would be created in the change. In this respect the reaction would resemble the formation of the keto-anhydride $C_{15}H_{14}O_4$ from santonic acid (*cf.* ref. 2).