[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF MICHIGAN]

Reactions of Hindered α- and β-Substituted Acids. VI. Monocarboxylic Bromoacids[1,2]

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In order to determine the extent to which the occurrence of the Wagner–Meerwein rearrangement is influenced by the participation of a carboxyl group either α or β to the carbon carrying a replaceable bromine the reactions of 2-bromodibenzo-[2.2.2]bicycloöctadiene-2-carboxylic acid and 3-bromodibenzo[2.2.2]bicycloöctadiene-*cis*- and *trans*-2-carboxylic acids with hydroxide, bicarbonate and silver ion have been examined. The highly hindered nature of the bridge carbons in this bicyclic system is further demonstrated by the absence of intermolecular substitutions, and dehalogenative decarboxylation and β-lactone formation are found to be inhibited for the 3-bromo-*trans*-isomer owing to the peculiar geometry of the system which results in a non-coplanar conformation for the reacting centers. The preference for *trans*-dehydrohalogenation appears to be more complex than in simple systems due to steric interaction between bromine and the carboxyl group which produces a conformation less unfavorable for *trans*- than for *cis*-dehydrohalogenation. A further example of *cis*-dehalogenative decarboxylation is described, and hindrance to other modes of decomposition permits more extensive occurrence of the Wagner–Meerwein rearrangement.

The nature of the Wagner–Meerwein rearrangement in which a dibenzo[2.2.2]bicycloöctadiene system is transformed into a 3,4,7,8-dibenzo[3.2.1]-bicycloöctadiene system has been elucidated in previous papers[2,4,5,6] in this series, and in a number of instances it was necessary to assume participation of the carboxyl groups attached either to the carbon carrying the replaceable group (α-lactonization)[5,7] or to the carbon adjacent to it (β-lactonization)[5–7] in order to account for the anomalous *cis*-dehalogenative decarboxylations and the smooth Walden inversions encountered.

In order to determine to what extent such participation is actually necessary to the occurrence of these reactions, which compete with the rearrangements, we have investigated the behavior of the analogous monobasic bromoacids under similar conditions.

The preparations of 3-bromodibenzo[2.2.2]bicycloöctadiene-*cis*-2-carboxylic acid (I) and 3-bromodibenzo[2.2.2]bicycloöctadiene-*trans*-2-carboxylic acid (II) have been described in a previous paper,[2] and the preparation of 2-bromodibenzo-[2.2.2]bicycloöctadiene-2-carboxylic acid (III) is described herewith. In initial attempts to add α-bromoacrylic acid[8] to anthracene both refluxing xylene and toluene were used as reaction media, but no III was ever obtained. However, its presence was inferred from the isolation of its hydrolysis products, the nature of which is discussed in the sequel. There was extensive decomposition which rendered isolation difficult, and consequently recourse was had to the lower boiling benzene. Under these conditions III was obtained in good yield.

As has been amply demonstrated for this system[4–7] there are four reaction paths open: (A) substitution, (B) dehalogenative decarboxylation, (C) dehydrohalogenation and (D) rearrangement. The structure of the system is such as to inhibit any direct displacement of the bromine in any of the compounds[7] and consequently requires internal displacement through a β-lactone intermediate, even though the conformation is such that the bromine, β-carbon and carboxylate ion oxygen cannot conveniently become coplanar, and the same may be said of dehalogenative decarboxylation when the bromine and carboxyl groups are *trans*. Thus in neither case is the ideal geometry for minimal activation energy realized. Similarly *trans*-dehydrohalogenation is inhibited, and bimolecular *cis*-dehydrohalogenation, as encountered by Cristol and Hause[9] in a closely related system, is observed, since the competing reactions are for the most part independent of the base strength and so to all intents are unimolecular.

The three isomeric bromoacids (I, II and III) were subjected to treatment with three reagents: 10% aqueous potassium hydroxide, acetone–sodium bicarbonate[10,11] and silver nitrate. The original compounds, the reaction products and related substances are pictured in Fig. 1, and reaction data are recorded in Table I. As for reactions studied previously[2,4–7] no simple substitution products were isolated, but more significant was the failure to detect evidence of any but rearranged substitution products.

As will be observed from Table I and Fig. 1 three isomeric hydroxyacids were obtained by rearrangement: one each from the respective bromoacids, and each was oxidizable to a characteristic keto-acid (indicated by the same numeral followed by a) which in turn was oxidizable to 3,3′-spirobiphthalide. Arguments in support of the designated gross skeletal structure based upon this series of oxidations have been presented in an earlier paper,[4] and by analogy with the related dibasic acids (VIII and IX) the same arguments may be applied to VI, VII and XI. Thus only the configurations of the hydroxyls in VI and VII are open to question, XI being the product of lactone (XII) hydrolysis.

The stereospecificity of the rearrangement of II by acetone–bicarbonate is also of interest and helps to give insight as to its mechanism. Since a single

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(1) Abstracted from a portion of the Ph.D. dissertation of A. C. Schoenthaler, University of Michigan, 1955.

(2) Preceding paper in this series, W. R. Vaughan and A. C. Schoenthaler, THIS JOURNAL, **79**, 5777 (1957).

(3) Allied Chemical and Dye Corporation Fellow, 1954–1955.

(4) W. R. Vaughan, M. V. Andersen, Jr., and R. Q. Little, Jr., THIS JOURNAL, **76**, 1748 (1954).

(5) W. R. Vaughan and R. Q. Little, Jr., *ibid.*, **76**, 2952 (1954).

(6) W. R. Vaughan and R. Q. Little, Jr., *ibid.*, **76**, 4130 (1954).

(7) W. R. Vaughan and K. M. Milton, *ibid.*, **74**, 5623 (1952).

(8) C. S. Marvel, J. Dec, H. G. Cooke, Jr., and J. C. Cowan, *ibid.*, **62**, 3495 (1940).

(9) S. J. Cristol and N. L. Hause, *ibid.*, **74**, 2139 (1952).

(10) S. J. Cristol and W. P. Norris, *ibid.*, **75**, 2645 (1953).

(11) W. R. Vaughan and R. L. Craven, *ibid.*, **77**, 4629 (1955).

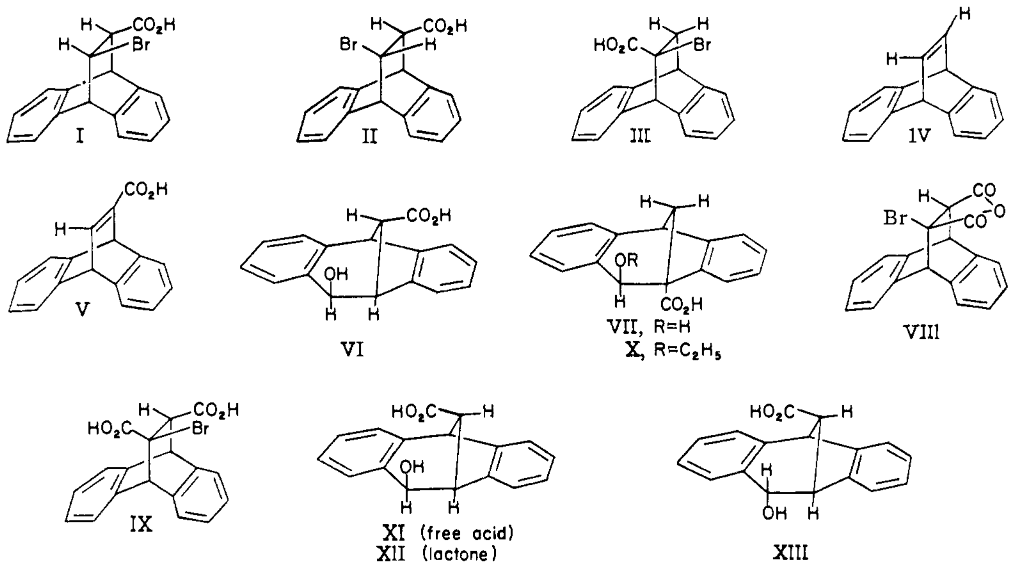

FIG. 1

pure product is obtained, it is obvious that a free carbonium ion never is formed, for this would involve a structure which could be attacked by hydroxide ion to give a *syn*- or *anti*-hydroxy acid with nearly equal probability. A mechanism of the type suggested by Cram,[12] where the departure of the bromide and migration of the phenyl group take place simultaneously, seems more probable. While a completely concerted mechanism in which the hydroxyl enters as the phenyl group migrates and the bromide leaves is attractive and would account for the observed stereospecificity, there are several examples in the literature where this sort of mechanism has been considered for the Wagner–Meerwein rearrangement and rejected because experimental support was totally lacking.[12-15]

TABLE I

SUMMARY OF REACTION DATA

Reagent	Bromo-acid	Observed reaction[a]	Yield,[b] %	Product
10% aq. KOH	I	A	5	IV
		B	95	V
	II	B	45	V
		C	55	VI
	III	C	100	VII
Acetone–$NaHCO_3$	I	A	24	IV
		B	76	V
	II	A	4	IV
		B	32	VI
		C	64	VII
$AgNO_3$	I	A	19	IV
		C	81	XII[c]
	II	C	100	VI[d]
	III	C	100	VII[e]

[a] A = dehalogenative decarboxylation, B = dehydrohalogenation, C = Wagner–Meerwein rearrangement. [b] Figures refer to percentage of total product. [c] Hydrolysis affords XI. [d] Mixture of epimeric hydroxyacids from which VI was isolated (see text). [e] Mixture of epimeric hydroxy acids (see text).

Alternatively, one may consider it to pass through an ion-pair intermediate which must collapse preferentially in one direction to give the rearranged carbon skeleton. Usually such an ion-pair is considered able to collapse in either direction,[14] but earlier papers in this series[2,4-7] and work in other laboratories[16,17] have shown that there is a distinct preference for the [3.2.1] system when the carbonium ion derived from a [2.2.2] system is formed. The apparent general prevalence of such a rearrangement suggests that the former system may be thermodynamically more stable than the latter, for in each instance there is ample opportunity for equilibration to occur, but only the rearranged skeleton is produced. While the cited experimental observations of preference for the [3.2.1] structure do not prove that it is the thermodynamically more stable one, the facts are undeniable, and under conditions favoring carbonium ion reactions it is not unreasonable to adopt an ion-pair mechanism as a working hypothesis. If this is done, the assignment of the *syn* configuration for the hydroxyl in VI follows. That II produces the same hydroxy acid in acetone–bicarbonate must be attributed to the necessarily curtailed longevity of a carbonium ion in this medium and the consequent more rapid association with water *before* the completely rearranged carbonium ion can be formed.

The sole product obtained when the α-bromoacid III is treated with base is the rearranged acid VII; just as with II, a single pure isomer was obtained.

The same compound VII, apparently in a different crystalline modification, also was isolated in an attempted synthesis of III. The two had identical empirical formulas and both gave the same keto-acid (VIIa) on oxidation, yet they could be recrystallized from the same solvent to constant melting points seven degrees apart. Seeding a solution of one form with the second or dissolving the two separately in base and acidifying failed to convert either form into the other. This suggested that one was the *syn*-hydroxy acid and the other the

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[12] D. J. Cram, THIS JOURNAL, **71**, 3863 (1949).

[13] P. D. Bartlett and I. Pockel, *ibid.*, **59**, 820 (1937); **60**, 1585 (1938).

[14] D. J. Cram, *ibid.*, **74**, 2129 (1952).

[15] S. Winstein and K. C. Schreiber, *ibid.*, **74**, 2165 (1952).

[16] W. von E. Doering, *ibid.*, **71**, 1514 (1949).

[17] M. S. Newman and Y. T. Yu, *ibid.*, **74**, 507 (1952).

anti-hydroxy acid. However, both gave the same methyl and *p*-phenyl phenacyl esters (identity established by melting point, mixed melting point and infrared spectra) so there is little doubt the compounds are the same substance which exists in two different non-interconvertible crystalline forms.

From the same attempted preparation of III there was isolated a second substance whose properties suggest that it is 2-ethoxy-3,4,7,8-dibenzo-[3.2.1]bicyclooöctadiene-1-carboxylic acid (X). The elemental analysis of X, as well as that of its methyl ester, corresponds to this structure. No anthraquinone was produced when X was allowed to stand several hours in contact with hot alkaline potassium permanganate. Beyond this, the substance was not further characterized.

The *syn*-hydroxy configuration is assigned to VII (and X) for the same reason that it was given to VI; the rearrangement is believed to be of the same stereospecific nature with both II and III.

The rearranged material obtained from II and III and silver ion appeared to be a mixture of *syn*- and *anti*-hydroxy acids. The forms could not be separated by fractional crystallization into the pure isomers; however, in the case of II, a small amount of VI was isolated. Although the mixtures melted over a wide range, both gave acceptable elemental analyses for a rearranged hydroxy acid. Oxidation of the mixtures resulted in excellent yields of the keto acids VIa and VIIa, respectively. The fact that high yields of a single pure product were obtained from each proves that the gross structures of the isomers within each mixture are the same. The identity of the product with the keto acid resulting from oxidation of the pure *syn* isomer VI shows that the rearrangement has taken the same course here as with base, and that the existence of isomers is due entirely to the configuration of the hydroxyl group.

The formation of epimeric hydroxyacids means that the *rearranged* carbonium ion must be capable of comparatively free existence,[18] but that the initial loss of bromide is indeed concerted with phenyl migration. Otherwise, Compound I would give the same *unrearranged* carbonium ion as II, and hence at least some of the same products from both I and II. The strong pull exerted by silver ion apparently is sufficient to remove the bromide from the "phenonium-bromide" ion pair, which then as a "free" carbonium ion rearranges to the expanded ring system before reacting with the solvent as for II or III, or with its own carboxyl as for I. With aqueous base II affords but one member of the epimeric pair, and this may be attributed to the relatively high concentration of hydroxide which can replace bromide in the ion pair; and the new ion pair then suffers a rapid and stereospecific collapse. And thus the configuration of the hydroxyacids produced by aqueous base is best pictured as *syn*.

The major product from the *cis*-β-bromo adduct (I) is 2-*syn*-hydroxy-3,4,7,8-dibenzo[3.2.1]bicyclooctadiene-*cis*-6-carboxylic acid-2,6-lactone (XII). The lactonic character of XII was determined by its insolubility in cold dilute base, elemental analysis and infrared spectrum (carbonyl absorption at 1770 cm.$^{-1}$). In addition to XII, about 11% more rearranged material was isolated in the form of a mixture of *syn*- and *anti*-2-hydroxy-3,4,7,8-dibenzo[3.2.1]bicyclooöctadiene-*cis*-6-carboxylic acids, (XI) and (XIII), respectively. Subsequently, XII was transformed to XI by dissolution in hot sodium hydroxide and acidification. The actual ratio of XI to XII produced directly in the reaction is uncertain, since isolation of the two was accomplished by dissolving second crops (from evaporation of the crude reaction mixture) in sodium hydroxide and precipitation of the compounds with acid. Since the material went into solution completely only after warming, some XII was certainly present, and it may be that no XI was produced directly in the reaction at all. Both XII and the hydroxyacid mixture (XI and XIII) gave only 2-keto-3,4,7,8-dibenzo[3,2.1]bicyclooöctadiene-*cis*-6-carboxylic acid (XIa) smoothly with permanganate. There only remains the question of carboxyl orientation in VI: *syn* or *anti* to the carbinol carbon? This is answered readily since the ketoacid VIa produced on oxidation is different from the isomeric ketoacid XIa produced by oxidation of the hydroxyacid XI obtained by hydrolysis of the *lactone* XII produced by silver ion induced rearrangement of I, which necessarily possessed the *cis* configuration. Thus VI, VII and X are presumed to have the *syn* configuration with the carboxyl *trans* in VI.

It now is appropriate to examine the differences among the present reactions and those of the related dibasic acids VIII and IX. It will be noted that the weaker base (acetone–bicarbonate, which was selected for its demonstrated effectiveness in promoting dehalogenative decarboxylation[10,11]) is less effective in promoting dehydrohalogenation than hydroxide. This is to be expected, but in its reaction with II it is rearrangement rather than dehalogenative decarboxylation which is the chief beneficiary of the medium change. This is unexpected. Thus the most striking characteristics of the reaction of II with bases are the complete absence of a product from β-lactone formation and the all but negligible occurrence of dehalogenative decarboxylation. This is particularly surprising when one recalls that these two reactions account for the entire product when the stereochemically similar 2-bromodibenzo[2.2.2]bicyclooöctadiene-*cis*-2,3-dicarboxylic anhydride (VIII) is treated with bases, no dehydrohalogenation being observed. Since these two reactions require approximately the same transition state geometry, as pointed out above, any structural features tending to favor or inhibit an approximately coplanar conformation of bromine, C^3, C^2 and carboxyl will promote or inhibit both reactions. At the same time any structural features tending to favor or inhibit an approximately coplanar arrangement of bromine, C^3, C^2 and hydrogen will promote or inhibit *cis*-dehydrohalogenation, as described by Cristol and Hause for this bicyclic system.[9] It may be presumed that there is no departure from normal bond angles in II, or in VIII. Consequently, as in the anomalous *cis*- addition of bromine to male-

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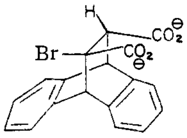
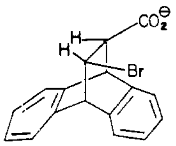
[18] W. A. Bonner and C. J. Collins, THIS JOURNAL, **77**, 99 (1955), and preceding papers.

ate ion,[19] the mutual repulsions of the two carboxylate ions formed by opening the anhydride ring of VIII provide a structural situation resulting in a conformation more nearly approximating that required for β-lactonization and dehalogenative decarboxylation and less favorable for *cis*-dehydrohalogenation (which is also inhibited by the double negative charge on the ion), *e.g.*

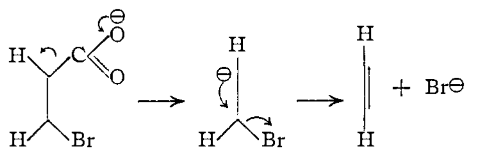


While this argument may be satisfactory to account for the difference in behavior between II and VIII, it only serves to emphasize the apparently anomalous character of the reaction of I with bases as compared with II: *trans*-dehydrohalogenation, contrary to the observations of Cristol and Hause,[9] is preferred and *cis*-dehalogenative decarboxylation is preferred, contrary to previous experience with a cyclic system.[11] To be sure very little of the latter reaction occurs in the presence of hydroxide, which can effect dehydrohalogenation, but a substantial fraction of I undergoes dehalogenative decarboxylation in acetone–bicarbonate. And at the same time it is surprising to find no rearrangement but quite effective dehydrohalogenation under these conditions.

In view of these facts we suggest that in the absence of a carboxyl group on C^3 as in the *trans*-diacid epimeric with VIII (IX) bromine is forced out of the normal position by the neighboring carboxyl, which in turn is also displaced, with the result that the α-hydrogen, C^2, C^3 and bromine are nearly enough coplanar to permit normal *trans*-dehydrohalogenation and inhibit rearrangement, *e.g.*

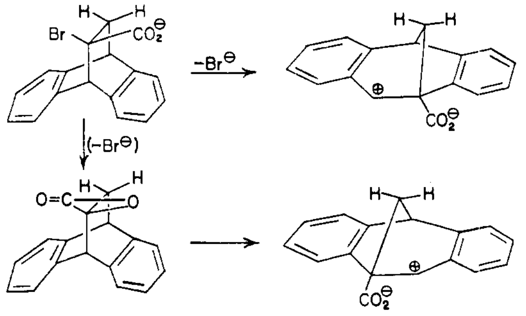


Since the dipolar mechanism for dehalogenative decarboxylation is supposed to be inoperative in acetone solution[10] it may be argued that this reaction occurs by a two-step mechanism reminiscent of Cristol's *cis*-dehydrohalogenation,[9] *e.g.*



Ordinarily this mechanism may be considered to require too much energy to compete successfully with the various other reactions which are to be expected of a β-haloacid,[11] but in this instance the geometry of the system would seem to exclude everything but dehydrohalogenation. While a similar mechanism is possible for II, *cis*-dehydrohalogenation and rearrangement are able to compete more successfully, owing to undisturbed geometry therein.

The complete absence of dehydrohalogenation in the reaction between III and hydroxide reflects both the greater resistance of an α-haloacid to this reaction as compared to a β-haloacid[20] and the system's inertness to simple displacement. Displacement *via* an α-lactone is feasible, and indeed such an intermediate has been proposed to account for other phenomena in this system.[5–7] However, we have no evidence to date to indicate actual displacement of halogen by hydroxyl *via* an α-lactone. It has been assumed in the reactions of simple α-haloacids[21] that an α-lactone normally is opened by attack on the alkyl carbon, and thus the absence of such evidence is not surprising. However, this assumption has been based on the behavior of β-lactones and is applied to nearly neutral solution. If the analogy to β-lactones is extended further, one might expect a true α-lactone to be opened by attack on the carbonyl carbon at high *p*H values, but in the present case, as in previous examples, there is available an essentially unimolecular mode of decomposition. Whether an α-lactone really is involved cannot be established without knowing the absolute configurations of optically active starting materials and product, *e.g.*



The lack of substitution products with silver nitrate is not surprising, nor is the absence of dehydrohalogenation, since attack under these conditions is electrophilic and therefore unlikely to promote the latter as long as a comparatively facile competing rearrangement is possible, while the β-lactonization (of II) necessary for substitution is not a particularly easy reaction in neutral to acidic solution.[11] The dehalogenative decarboxylation of I proceeds more extensively than with hydroxide though somewhat less extensively than with bicarbonate-acetone. Thus it may be reasonably argued that the dipolar mechanism[10] operates more effectively under these conditions, until the acidity of the system reaches so high a level as to inhibit ionization of the carboxyl altogether.[11] The lack of dehalogenative decarboxylation of II, as before, may be attributed to a conformation which operates to favor rearrangement.

In the base-induced reactions there is nothing significant beyond ordinary solvation, in the way of assistance in the removal of bromine, so that where rearrangement is encountered it is a result of displacement of bromine by the migrating phenyl. Thus where the geometry of the system per-

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(19) I. Roberts and G. E. Kimball, THIS JOURNAL, 59, 947 (1937).

(20) *E.g.*, only the α-bromoacid is formed from α,β-dibromopropionate (ref. 8).

(21) For discussion and leading references see L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 175–178.

mits it, other reactions can compete quite successfully—even to the exclusion of rearrangement (I). But where development of a carbonium ion center is assisted by electrophilic attack on bromine, rearrangement becomes the dominant reaction. For, as suggested above, the available evidence would seem to indicate a preference for the [3.2.1]bicyclooctane system; and thus the reaction proceeds with the rearrangement of the [2.2.2]bicycloöctane system.

The following significant conclusions emerge from this study: (1) The dehalogenative decarboxylation reaction is at least as sensitive to conformation as dehydrohalogenation; (2) *trans*-dehydrohalogenation may be preferred to *cis*-dehydrohalogenation even in the bicyclo[2.2.2]octadiene system due to steric interaction between bromine and the carboxyl group which produces a conformation less unfavorable for *trans* than for *cis* elimination; (3) *cis*-dehalogenative decarboxylation can occur without participation of a *β*-carboxyl group; (4) the Wagner–Meerwein rearrangement assumes a major role in reactions of the present system whereas the presence of a second carboxyl group inhibits it through distortion of the ring resulting in lack of coplanarity of the reacting centers; (5) such rearrangement is stereospecific insofar as the position and/or configuration of the carboxyl groups is concerned, but the configuration of the new hydroxyl may be a function of the reagent and/or reaction medium.

Experimental[22]

2-Bromodibenzo[2.2.2]bicyclooctadiene-2-carboxylic Acid (III). (A) In Benzene.—A mixture of 2.92 g. (0.0193 mole) of *α*-bromoacrylic acid[8] and 3.42 g. (0.0193 mole) of anthracene was refluxed in 60 ml. of sodium-dried benzene for three weeks. After this period the solution was treated with Norit, filtered, and evaporated to dryness in an air stream. The resulting solid was pulverized and placed in a vacuum sublimation apparatus held at 100° (0.5 mm.) for 12 hours. The 5.68 g. of residue (89%), m.p. 177.5–180.0°, was recrystallized once from xylene to give 4.01 g. (63%), m.p. 185–186°. Recrystallization from xylene for analysis gave fine white prisms, m.p. 187–188°.

Anal. Calcd. for $C_{17}H_{13}BrO_2$: C, 62.02; H, 3.98; Br, 24.28. Found(S): C, 62.22; H, 4.14; Br, 24.10.

The methyl ester was prepared (diazomethane) and recrystallized from methanol–water as a white microcrystalline solid, m.p. 100.0–101.5°.

Anal. Calcd. for $C_{18}H_{15}BrO_2$: C, 62.99; H, 4.41; Br, 23.29. Found(S): C, 63.15; H, 4.60; Br, 23.15.

(B) In Xylene.—In this case, 3.25 g. (0.0215 mole) of *α*-bromoacrylic acid was refluxed with 3.83 g. (0.0215 mole) of anthracene in 25 ml. of xylene for seven days. The black, gummy material which separated when the solution was cooled and concentrated could not be induced to crystallize. It was then taken up in *ca.* 500 ml. of ethanol, and water (*ca.* 600 ml.) was added to the point of incipient turbidity while maintaining the solution at the steam-bath temperature. After two hours digestion in this manner, the solution was filtered from a caramel-like material which had deposited. The filtrate was digested overnight on the steam-bath. The now concentrated solution had deposited 0.62 g. of cream colored solid, m.p. 204.5–208.5°. This material gave a faint Beilstein test and fluoresced when exposed to ultraviolet light. Three recrystallizations from acetic acid–water followed by vacuum sublimation at 100° (0.1 mm.) to remove anthracene and a fourth recrystallization gave 0.114 g. (1.8%) of 2-*syn*-ethoxy-3,4,7,8-dibenzo-[3.2.1]bicyclooctadiene-1-carboxylic acid (X) as halogen-free, non-fluorescent white prisms, m.p. 211.5–212.2°. A mixed melting point with anthracene gave 195–209°; with VII, 188–192°.

Anal. Calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found (G): C, 77.34; H, 6.33.

A small amount of the above acid was dissolved in dilute sodium hydroxide and a few milliliters of 1% potassium permanganate was added. The mixture was allowed to stand overnight on the steam-bath which resulted in nearly complete decolorization of the permanganate. A vat test for anthraquinone on the reaction mixture was negative.[23]

In the usual manner, the methyl ester was prepared by treatment with diazomethane. Recrystallization from methanol–water afforded a white microcrystalline solid, m.p. 144.0–145.5°.

Anal. Calcd. for $C_{20}H_{20}O_3$: C, 77.90; H, 6.54. Found (S): C, 77.72; H, 6.63.

The filtrate afforded 0.72 g. (12.6%) of VII in two crops, m.p. 204.0–205.5°. Four recrystallizations from acetic acid–water resulted in a constant melting point of 205.0–205.5°. The infrared spectra of this acid and VII were identical. A mixed melting point with VII was 209–210°.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found (G): C, 76.70; H, 5.48.

Treatment of this acid with diazomethane followed by recrystallization from methanol–water gave the methyl ester which proved to be identical with that of VII (fine cottony needles, m.p. 174.0–174.5°, no depression on admixture with an authentic sample [see below], superimposable infrared spectra).

The *p*-phenylphenacyl ester was prepared by the directions of Cheronis[24] and was recrystallized once from ethanol–water and twice from ethanol to give fine white prisms, m.p. 204–205°. The substance did not depress the melting point of an authentic sample (see below).

Anal. Calcd. for $C_{31}H_{24}O_4$: C, 80.85; H, 5.25. Found (S): C, 80.82; H, 5.36.

(C) In Toluene.—In this case toluene was used as a solvent and a mixture of 7.55 g. (0.050 mole) of *α*-bromoacrylic acid and 8.91 g. (0.050 mole) of anthracene was refluxed for seven days. The reaction mixture was concentrated to a black gum in an air stream, triturated with hot ethanol (large mechanical loss), treated with Norit, and filtered. Evaporation of the ethanol gave a gummy brown solid which became crystalline on standing in a desiccator over calcium chloride for two weeks. This was pulverized prior to vacuum sublimation (85° (0.2 mm.), 10 hr.) which removed part of the anthracene. The residue showed fluorescence and gave a positive Beilstein test; treatment with 200 ml. of cold 5% sodium bicarbonate partially dissolved it, leaving behind 1.11 g. (12%) of VII in two crops, m.p. 211–212°, showing no mixed melting point depression and an infrared spectrum identical with the VII obtained from the treatment of III with base as described below.

3-Bromodibenzo[2.2.2]bicyclooctadiene-*cis*-2-carboxylic Acid (I) Plus 10% Potassium Hydroxide.—The bromo acid I[2] (0.217 g., 0.000660 mole) was warmed on the steam-bath for one hour in 10 ml. of 10% potassium hydroxide. Precipitation of a white gelatinous material began after the first few moments of heating, the reaction flask was shaken intermittently throughout the remainder of the run. The solid was then filtered, dried, and proved to be 0.005 g. (3.7%) of IV, m.p. 119–120°, previously reported[9] 118.5–119.0°. The substance was soluble in acetone, benzene and petroleum ether (60–75°) and gave a negative Beilstein and positive Bayer test. The presence of anthraquinone in the solution in which a permanganate oxidation had been conducted was indicated by a positive vat test.[23] The infrared spectrum of the material was consistent with the structure assigned. This material was identical in all respects to an analytical sample obtained from the treatment of I with sodium bicarbonate in acetone as described below.

The filtrate was clarified with Norit, filtered, and acidi-

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[22] Melting points are uncorrected. Analyses by Mrs. Anna Griffen, University of Michigan (G) and Spang Microanalytical Laboratory, Ann Arbor, Mich. (S). Infrared spectra were obtained on a Perkin-Elmer model 21 double beam recording spectrophotometer.

[23] L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, Mass., 1955, p. 163.

[24] N. D. Cheronis, "Micro and Semimicro Techniques," Vol. VI of "Technique of Organic Chemistry," A. Weissberger, ed., Interscience Publishers, Inc., New York, N. Y., 1954, p. 540.

fied while hot to precipitate 0.134 g. (82%) of V, m.p. 245.0–246.5° dec., showing no depression with authentic material.[5]

3-Bromodibenzo[2.2.2]bicycloöctadiene-*trans*-2-carboxylic Acid (II) Plus 10% Potassium Hydroxide.—To 70 ml. of 10% potassium hydroxide, 1.517 g. (0.00462 mole) of II[2] was added and the resulting mixture was heated on the steam-bath for one hour. Acidification with concentrated hydrochloric acid was conducted while the solution was still hot, and the mixture of white solids which precipitated was digested briefly, cooled, and filtered. Concentration of the filtrate to *ca.* 20 ml. afforded additional product which was filtered and washed free of the accompanying inorganic salts with water. The combined organic residues were then subjected to a 3.5-hour Soxhlet extraction with water, leaving 0.479 g. (42%) of V, m.p. 242.5–243.5° dec., identical with an authentic sample[5] (no depression of mixed melting point, infrared spectra superimposable).

The aqueous extract gave 0.622 g. (51%) of VI in two crops, m.p. 199–201° dec. One recrystallization from benzene–petroleum ether (60–75°) gave a white microcrystalline solid, m.p. 200.5–201.5°.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found (G): C, 76.55; H, 5.19.

It was discovered that this acid could exist in two crystalline modifications. The second form was obtained when the sodium salt was acidified in the cold, it decomposed with gas evolution when placed in the bath at 150°, quickly resolidified, and remelted at 197–199°. A hydrate was suspected, but the behavior on heating was unaffected after drying the second form over phosphorus pentoxide for 48 hours at 56° (0.1 mm.). The lower melting form could be converted to the higher by acidification of its sodium salt at steam bath temperatures or by recrystallization from benzene–petroleum ether (60–75°).

The methyl ester was prepared (diazomethane) and was recrystallized from methanol–water as fine white plates, m.p. 122.0–124.5°.

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found (S): C, 77.31; H, 5.77.

2-Bromodibenzo[2.2.2]bicycloöctadiene-2-carboxylic Acid (III) Plus 10% Potassium Hydroxide.—To 30 ml. of 10% potassium hydroxide solution, 1.062 g. (0.00322 mole) of III was added, and the mixture was maintained at the steam-bath temperature for one hour. A slight cloudiness initially present disappeared after the addition of 10 ml. of water. The reaction mixture was acidified while hot with concentrated hydrochloric acid, cooled, and 0.811 g. (95%) of VII, m.p. 211–212°, was filtered. Recrystallization of a small sample for analysis gave fine white prisms, m.p. 211.5–212.0°.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found (S): C, 76.72; H, 5.44.

This acid described above could not be transformed into VII′ when dissolved in acetic acid and recrystallized in the presence of seeds of VII′. The reverse process, where VII was used as the seeding agent, also failed to interconvert the two. When each was separately dissolved in base it was precipitated with its melting point unaltered upon acidification. However, the two forms gave the same methyl and *p*-phenylphenacyl esters, possessed identical infrared spectra.

The methyl ester (diazomethane) was recrystallized from methanol–water to give fine cottony needles, m.p. 174.0–174.5°. No depression on admixture with the methyl ester of VII′ was observed. Likewise, the infrared spectra of the two samples were found to be identical.

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found (S): C, 77.43; H, 5.93.

The *p*-phenylphenacyl ester prepared according to the directions of Cheronis,[24] was recrystallized once from ethanol–water and twice from ethanol to give fine white prisms, m.p. 204–205°. The melting point remained the same when mixed with the corresponding derivative of VII′ and the two esters had superimposable infrared spectra.

Anal. Calcd. for $C_{31}H_{24}O_4$: C, 80.85; H, 5.25. Found (S): C, 80.82; H, 5.29.

Oxidation of VI with Alkaline Potassium Permanganate.—A mixture of VI (0.373 g., 0.00140 mole) and potassium permanganate (0.180 g., 0.00114 mole, 1.22 equivalents) was heated in 40 ml. of 5% sodium hydroxide for an hour on the steam-bath. The excess permanganate was then discharged with sodium bisulfite prior to filtration of the manganese dioxide. The resulting clear solution was acidified with concentrated hydrochloric acid while still hot. A few minutes digestion resulted in the crystallization of VIa. After cooling in the ice-bath, 0.315 g. (85%) of VIa, m.p. 266.5–267.5°, was filtered off. A small sample was recrystallized twice from acetic acid–water to give fine white needles, m.p. 268.5–269.5°. The substance dissolved in concentrated sulfuric acid to produce a yellow solution which was discharged, with reprecipitation of the material, when diluted with water. This behavior was exhibited by the analogous rearranged keto acids previously studied.[4]

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found (S): C, 77.34; H, 4.68.

The methyl ester was prepared (diazomethane) and recrystallized from methanol–water as fine white prisms, m.p. 143–144°.

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found (S): C, 77.77; H, 5.10.

Oxidation of VIa with Manganese Dioxide in Sulfuric Acid.[4]—The keto acid VIa (0.020 g., 0.000075 mole) was dissolved in 0.8 ml. of concentrated sulfuric acid. Next, 0.6 ml. of water was added, followed by 0.065 g. (0.000074 mole) of manganese dioxide (in portions) while the solution was still hot. The resulting mixture was placed in an oil-bath held at 140–145°. Frothing began at once and continued with gradual diminution for a half-hour; the heating was maintained for another 15 minutes. The solution was stirred occasionally throughout, and by the end of the 45 minutes, solution was complete. The dark brown solution was poured into *ca.* an equal volume of water and digested on the steam-bath until the solids had crystallized. They were then filtered, washed with 5 ml. of water, 2 ml. of 5% sodium bicarbonate and 2 ml. of water, in that order. The residue was triturated with 10 ml. of hot absolute ethanol, filtered, the filtrate clarified with Norit, and evaporated in a current of air. There was recovered 0.003 g. (16%) of 3,3′-spirobiphthalide, m.p. 202.0–206.5°. This melting point was unchanged on admixture with an authentic sample.[4]

Oxidation of VII with Alkaline Potassium Permanganate.—In the manner previously described, 0.197 g. (0.000741 mole) of VII and 0.086 g. (0.000544 mole, 1.1 equivalents) of potassium permanganate in 35 ml. of dilute sodium hydroxide gave 0.150 g. (77%) of VIIa, m.p. 208.5–209.5°. One recrystallization from acetic acid–water gave fine cottony needles, m.p. 210.5–211.5°.

The keto acid gave the characteristic yellow color with concentrated sulfuric acid which was discharged with reformation of the solid upon dilution.[4]

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found (S): C, 77.28; H, 4.67.

Treatment with diazomethane followed by methanol–water recrystallization provided the methyl ester as small irregular rods, m.p. 150–151°.

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found (S): C, 77.70; H, 5.18.

Oxidation of VIIa with Manganese Dioxide in Sulfuric Acid.—In the method previously described, 0.100 g. (0.000379 mole) of VIIa was oxidized to 0.027 g. (28%) of 3,3′-spirobiphthalide, m.p. 204.5–206.0°; no depression of the melting point of an authentic sample.[4]

Reaction of I with Sodium Bicarbonate in Acetone.—With continuous stirring, 1.005 g. (0.00306 mole) of I[2] and 0.500 g. (0.00595 mole) of sodium bicarbonate was refluxed in 50 ml. of acetone for 24 hours. The solvent was removed in a current of air, and the resulting solids were dried, powdered, and extracted continuously with 60–75° petroleum ether for 15 hours.

The residue from the extraction was dissolved in 10 ml. of warm 5% sodium bicarbonate, decolorized with Norit, and acidified with hydrochloric acid, whereupon 0.419 g. (55%) of V separated, m.p. 244–245°, no depression with authentic[5] V.

The hydrocarbon fraction yielded 0.107 g. (17%) of IV, m.p. 117–121°. The melting point was raised to 119–120° after one recrystallization from ethanol–water and vacuum sublimation at 90° (0.5 mm.).

Anal. Calcd. for $C_{16}H_{12}$: C, 94.08; H, 5.92. Found(S): C, 94.19; H, 6.02.

Reaction of II with Sodium Bicarbonate in Acetone.—A mixture of 0.802 g. (0.00244 mole) of II[2] and 0.420 g. (0.00500 mole) of sodium bicarbonate was refluxed, with stirring, for 48 hours. The acetone was then evaporated in an air stream and the residue was triturated with 20 ml. of 5% sodium hydroxide. A small part remained undissolved. After filtration, this was taken up in ether. The filtrate was then extracted with ether, the ether extract combined with the first ether fraction, shaken with a few milliliters of water, dried, and evaporated to give 0.028 g. of crude IV, m.p. 102–115°. One vacuum sublimation gave 0.017 g. (3.4%) of IV, m.p. 113–117°. A mixed melting point with an analytical sample of IV (from I plus sodium bicarbonate in acetone as described above) was 116.0–118.5°. The infrared spectra of the two samples were identical.

Acidification of the aqueous layer gave a gum which formed 0.533 g. of tan crystals after standing ten days in the refrigerator. A 5.5-hour Soxhlet extraction removed all of the material from the thimble, but V crystallized out in the pot (200 ml. water) and was filtered while the solution was still hot. In this manner, 0.117 g. (20%) of V, m.p. 244–246° (no depression with authentic[5] V) was recovered.

Evaporation of the filtrate gave 0.365 g. (56%) of crude VI, m.p. 175–196°. One recrystallization from benzene–petroleum ether gave 0.260 g. (40%), m.p. 200.5–201.5°, showing no depression when mixed with a small portion of the analytical sample of VI described previously.

Reaction of I with Silver Nitrate in Aqueous Acetone.—To a solution of 1.016 g. (0.00309 mole) of I[2] in 30 ml. of acetone was added 33 ml. of 0.1 *M* silver nitrate solution. A white opalescence was first observed but this soon gave way to the yellow silver bromide. After standing 12 hours a mixture of silver bromide (0.571 g., 98%) and white needles had deposited. The organic material was dissolved away from the silver bromide with acetone after the reaction mixture had been filtered. However, it separated again in the filtrate and was removed before the addition of three milliliters of potassium bromide which caused precipitation of a slight additional amount of silver bromide. This was then filtered to give a clear solution.

The white solid which first separated (m.p. 199.5–210.0°) was subjected to vacuum sublimation (10 hours, 80° (1 mm.)) and the residue from this treatment was nearly pure XII, 0.472 g. (62%), m.p. 215–217°. One recrystallization of a small amount of this material from acetic acid–water gave fine white needles, m.p. 217.0–217.5°.

Anal. Calcd. for $C_{17}H_{12}O_2$: C, 82.23; H, 4.95. Found (S): C, 82.13; H, 4.86.

The material was insoluble in cold dilute sodium hydroxide but went into solution slowly upon warming. The infrared spectrum of the material showed a carbonyl absorption at 1770 cm.$^{-1}$.

Dissolution of 0.055 g. (0.00022 mole) of the material in hot base and then acidification with hydrochloric acid caused the precipitation of 0.051 g. (86%) of XI, m.p. 200.0–201.5°. This was recrystallized from acetic acid–water as small plates, m.p. 201.0–201.5°.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found (S): C, 76.98; H, 5.53.

The solution from which the second crop of silver bromide had been filtered was concentrated in an air stream until all the acetone had evaporated and a further amount of solid was collected. This was subjected to vacuum sublimation as before (24 hours, 100° (1 mm.)). The combined sublimates totaled 0.110 g. (17%) of IV, m.p. 103–109°, and were recrystallized once from ethanol–water (Norit) and resublimed. This raised the melting point to 116–118°. This substance did not depress the melting point of previously characterized IV.

The residue from the second sublimation nearly all dissolved in dilute sodium hydroxide when heated on the steam-bath. Filtration from the small amount of dark colored residue and then acidification gave 0.091 g. (11%, XIII + an isomer, m.p. 170–193°). This was subjected to a third vacuum sublimation (which yielded no more IV) and recrystallized from acetic acid–water to give 0.061 g. (8%), m.p. 185–203°.

Oxidation of XII with Alkaline Potassium Permanganate.—By heating on the steam-bath in 15 ml. of 5% sodium hydroxide, 0.205 g. (0.000830 mole) of XII was dissolved after a few minutes. Potassium permanganate (0.131 g., 0.000830 mole, 1.5 equivalents) was then added and the oxidation carried out as was described for the case of VI. The yield of XIa was 0.163 g. (75%), m.p. 245.0–247.5°. One recrystallization from acetic acid–water gave small white plates, m.p. 247–248°. As with the other keto acids in this series, a yellow color was produced when XIa dissolved in concentrated sulfuric acid. This could be discharged by reprecipitating XIa with water.

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.26; H, 4.58. Found (S): C, 77.28; H, 4.69.

The methyl ester (diazomethane) was recrystallized from methanol–water as fine white prisms, m.p. 126–128°.

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.68; H, 5.07. Found (S): C, 77.74; H, 5.34.

Oxidation of XIa with Manganese Dioxide in Sulfuric Acid.—In the manner described for the similar oxidation of VIa, 0.052 g. (0.000197 mole) of XIa gave 0.008 g. (16%) of 3,3′-spirobiphthalide, m.p. 200–203°. A mixed melting point of this material with an authentic sample[4] depressed the latter but two degrees. The product was then redissolved in ethanol, treated with Norit, filtered, and evaporated to a residue whose melting point was 203.0–204.5°. The mixed melting point with an authentic sample[4] using this material was undepressed.

Oxidation of the Hydroxyacid Mixture with Alkaline Permanganate.—In the manner described for the oxidation of VIIa, the present (XIII + isomer) mixture (0.012 g., 0.000047 mole) gave, with 0.008 g. (0.0005 mole, 1.5 equivalents) of potassium permanganate, 0.007 g. (56%) of XIa, m.p. 243.5–244.5°. This material did not depress the melting point of previously characterized XIa.

Reaction of II with Silver Nitrate in Acetone.—Thirty-three milliliters of 0.1 *M* silver nitrate was added to a solution of 1.015 g. (0.00308 mole) of II[2] in 35 ml. of acetone. A small amount of white precipitate formed at once but was soon replaced by the yellow silver bromide. At the end of eight hours standing, 0.558 g. (97%) of the latter was filtered; 3 ml. of 5% potassium bromide solution was added to the filtrate, and a slight additional amount of silver bromide was removed. The solution was then evaporated to *ca.* 10 ml. in an air stream, thereby inducing the separation of an oil which became partially crystalline upon standing in the refrigerator for four days. The mixture of gum and crystals was filtered, dissolved in 5% sodium hydroxide, and precipitated in completely crystalline form by the addition of concentrated hydrochloric acid. A total of 0.758 g. (92%) of white solid was obtained, m.p. 161.0–183.5°, after melting with gas evolution and resolidifying when plunged in the bath at 150°. Three recrystallizations from benzene–petroleum ether (60–75°) gave a m.p. of 164–185° (after initial decomposition when placed in the bath at 100°).

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found (S): C, 76.84; H, 5.38.

Soxhlet extraction of a portion of this material with water for four hours left as a residue 0.030 g. of VI, m.p. 197.5–199.5°, showing no depression with the previously characterized material.

The water-soluble fraction consisted of 0.156 g. of white solid, m.p. 188–200° after melting with gas evolution, and resolidification upon placement in the bath at 100°. Further separation of this mixture was not attempted.

Oxidation of the Hydroxyacid Mixture with Alkaline Potassium Permanganate.—In the manner described for the oxidation of VI, 0.147 g. (0.000647 mole) of the mixture of hydroxy acids just described and 0.068 g. (0.00054 mole, 1.25 equivalents) of potassium permanganate gave 0.156 g. (91%) of VIa, m.p. 267.0–268.5°, showing no depression of the melting point of previously characterized VIa.

Reaction of III with Silver Nitrate in Aqueous Acetone.—Thirty-two milliliters of 0.1 *M* silver nitrate was added to a solution of 0.956 g. (0.00291 mole) of III in 30 ml. of acetone. A yellow precipitate of silver bromide began forming at once and, after eight hours standing, 0.531 g. (97%) was filtered. Excess silver ion was precipitated by adding 3 ml. of 5% potassium bromide. The resulting filtrate was evaporated in an air stream to *ca.* 5 ml. which caused a mixture of fine silky needles and an oil to separate. After 22 hours refrigeration the oil had solidified and the combined solids, 0.746 g. (96%, VII + epimer), m.p. 169–185° dec., were removed by filtration. A partial purification was accomplished by dissolving the solid in dilute bicarbonate (a minute amount of insoluble material was removed) followed by acidification with hydrochloric acid which gave a white solid, m.p. 173.5–185.5°.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.67; H, 5.30. Found (S): C, 76.77; H, 5.41.

Oxidation of the Hydroxyacid Mixture with Alkaline Potassium Permanganate.—A portion of the mixture (0.315 g., 0.00118 mole), was treated with 0.187 g. (0.00118 mole, 1.5 equivalents) of potassium permanganate by the method used in the oxidation of VI. This resulted in 0.289 g. (92%) of VIIa, m.p. 209.0–210.5°, showing no depression with the previously characterized VIIa.

ANN ARBOR, MICH.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Rearrangement of Bromofenchone by Base. The Structure of γ-Fencholenic Acid and the Synthesis of Dihydro-α-fencholenic Acid

BY D. S. TARBELL AND F. C. LOVELESS[1]

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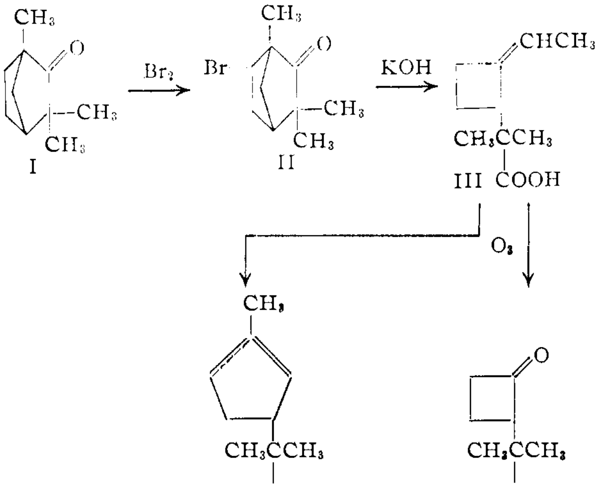
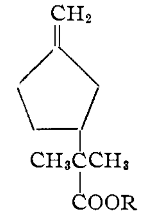
Bromination of *dl*-fenchone yields the hitherto undescribed crystalline *dl*-bromofenchone. Treatment of this with alcoholic alkali yields a mixture of *dl*-γ-fencholenic acid and the corresponding ester. Catalytic reduction of both γ- and α-*dl*-fencholenic acids yields the same acid, *dl*-α-(3-methylcyclopentyl)-isobutyric acid, the structure of which has been established by synthesis from 3-methylcyclopentanone by the Reformatsky reaction. γ-Fencholenic acid has been shown not to possess an ethylidenecyclobutane structure III as postulated by Semmler and Bartelt, but to be a methylenecyclopentane derivative VI; it yields formaldehyde and the expected cyclopentanone derivative on ozonization. The bromofenchone rearrangement is analogous to other base-catalyzed rearrangements and, although the position of the bromine has not been established rigorously, it is probably on the 10-carbon.

In connection with work on another problem in the fenchone field, we became interested in the report[2] that bromination of fenchone (I) yielded 6-bromofenchone (II), which was converted by base to γ-fencholenic acid; to this acid was assigned[2] structure III. The assignment of structure III was based on ozonization to a keto acid, regarded as IV, which was characterized as the crystalline semicarbazone. The γ-fencholenic acid was reported to isomerize very readily on standing to α-fencholenic acid. The structure of the latter compound does not seem to have been established; the nitrile corresponding to it is formed by the action of sulfuric acid on fenchone oxime, and the α-fencholenic acid is obtained by hydrolysis of the nitrile.[3] The postulated[2] structure V (or a double bond isomer) is a reasonable one for α-fencholenic acid; we have provided synthetic evidence for its correctness below.

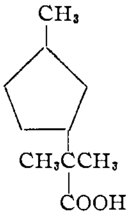


The bromination of fenchone and some transformation products of bromofenchone recently have been studied,[4] without establishing any of the structures involved.

If structures II-V are correct, the reactions involved are unusual; furthermore, the sequence might be useful for the preparation of cyclobutanone derivatives of an interesting type. We have, therefore, reinvestigated these compounds, have found that γ-fencholenic acid has the structure VI, rather than III, and have established the structures of γ- and α-fencholenic acids (VI and V) by the synthesis of the dihydrofencholenic acid VII. The position of the double bond in α-fencholenic acid is not, of course, established by this synthesis.



VIa, R = H
VIb, R = C_2H_5
VIc, R = CH_3



VII

The bromination of fenchone has been carried out[2,5] with bromine in sealed tubes. This method proved unsatisfactory, and we tried several other brominating agents without much success. However, the treatment of *dl*-fenchone with bromine and copper powder[4] on the steam-bath for many hours yielded, in addition to much unchanged fenchone, a crystalline monobromofenchone, m.p. 44.5°, and oily material with the composition of a monobromofenchone. Previous workers[2,4,5] have not reported a crystalline bromofenchone. Bromination of *d*-fenchone by the same procedure yielded an oily monobromo compound, $[\alpha]_D$ +14.3°,

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