B, m.p. 69–140° dec., C, m.p. 163–180°, D, m.p. 142–168°, and E, m.p. 70–80°. The fractions were combined: A, C, and D gave first combined product, fractions B and E the second combined product. The first combined product (*p*-toluic acid) was recrystallized repeatedly from methanol; yield 0.78 g. (19%), m.p. and mixture m.p. 179–181.5° (lit.,[24] m.p. 181°). The second combined product (*p*-toluic anhydride) was recrystallized repeatedly from methanol–petroleum ether (b.p. 60–69°); yield 1.12 g. (12.3%), m.p. and mixture m.p. 95–96.5° (lit.,[25] m.p. 95°).

Hydrolysis of Benzoyl Bromide in 75% Methyl Diazoacetate.—EK benzoyl bromide (15.8 g., 0.087 mole) was added dropwise over 25 min. to a stirred mixture consisting of 75% methyl diazoacetate (17.58 g., 0.176 mole), previously dried azeotropically, and 25% water (5.9 g., 0.33 mole) at −4°. The temperature of the heterogeneous reaction mixture, initially cooled in ice, rose to 18° by the end of the acid bromide addition. Nitrogen was evolved rapidly from the initial addition of acid bromide. After nitrogen evolution ceased, crystals of product began to form in the mixture. Cooling in ice for several hours caused further separation of crystalline material (fraction A), m.p. 111–120°. The filtrate consisted of an upper organic layer, fraction B, and a lower aqueous layer that was separated and distilled. After collecting 2–3 ml. of distillate, b.p. 124°, the residual liquid was cooled to room temperature. A substance, m.p. 70–121°, separated (fraction C). Fractions A and C were combined and recrystallized repeatedly from water to give benzoic acid, m.p. and mixture m.p. 121–122°; yield 6.21 g. (60.1%). Bromine in acetic acid test was negative. Fraction B was a colorless liquid with an ester-like odor; yield 7.68 g., b.p. 215°. Bromine in acetic acid test was negative. This fraction was not identified.

Formation of Methyl Benzoate from Benzoyl Chloride and Methanol in Methyl Diazoacetate.—Benzoyl chloride (4.64 g., 0.033 mole) was added dropwise over 30 min. to a solution of methanol (3.96 g., 0.124 mole) in methyl diazoacetate (10.0 g., 0.100 mole), previously dried azeotropically. Nitrogen was evolved rapidly from the initial addition of acid chloride. After standing for 134 days, the reaction mixture was pale yellow and completely homogeneous. Distillation of the entire reaction mixture gave three fractions: (1) yield 4.44 g., b.p. 127.5–135°; (2) yield 1.51 g., b.p. 93–187°; (3) yield 2.13 g., b.p. 189.5–191°. Redistillation of fraction 1 gave a colorless distillate with an ester-like odor, product A; yield 2.25 g., b.p. 130–132°. Fraction 2 was added to residue from redistillation of fraction 1 and distilled to give more of product A; yield 0.84 g., b.p. 131–135°. Fraction 3 was added to residue from redistillation of fraction 2 and distilled to give a colorless distillate with an ester-like odor, product B; yield 2.84 g., b.p. 190–195°.

Product A was identified as methyl chloroacetate; total yield 3.09 g. (86.4%), n^{25}_{D} 1.4126 and d^{20}_{4} 1.184; lit. b.p. 130°,[26] n^{20}_{D} 1.42207[27] and d^{15} 1.22.[28] Product B was identified as methyl benzoate; yield 2.84 g. (63.3%), n^{25}_{D} 1.5118 and d^{20}_{4} 1.090; lit.,[29] b.p. 199.6°, n^{16}_{D} 1.51810 and d^{20}_{4} 1.088. A 0.81-g. quantity of product B was hydrolyzed in 5% sodium hydroxide to give 0.45 g. of benzoic acid, identified by melting point and mixture melting point.

Hydrolytic Cleavage of Methyl Benzoyldiazoacetate.—Methyl benzoyldiazoacetate (0.50 g., 0.0025 mole) was added in one portion to 10 ml. of 5% sodium hydroxide and allowed to stand undisturbed at room temperature for 24 hr. The reaction mixture was a clear yellow solution which evolved nitrogen slowly. Concentrated hydrochloric acid was added dropwise to the mixture, cooled in an ice–water bath, until slightly acid to litmus. There separated a colorless, crystalline solid (benzoic acid), m.p. 122.5–125°, which was recrystallized from water; yield 0.28 g. (93.6%), m.p. and mixture m.p. 122–123°. Bromine in acetic acid test was negative.

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(24) G. Ciamician and P. Silber, *Ber.*, **45**, 40 (1912).

(25) P. Frankland and F. M. Wharton, *J. Chem. Soc.*, **75**, 344 (1899).

(26) L. Schreiner, *Ann.*, **197**, 8 (1879).

(27) A. Karvonen, *Ann. Acad. Sci. Fennicae, Ser. A.*, **10**, 19 (1916).

(28) L. Henry, *Ber.*, **6**, 742 (1873).

(29) "Handbook of Chemistry and Physics," C. D. Hodgman, ed. Chemical Rubber Publishing Co., 1960–1961, p. 848.

The Reaction of *cis*-2,6-Dibromo-4,4-dimethylcyclohexanone with Sodium Acetate in Acetic Acid, a New Elimination–Rearrangement Reaction

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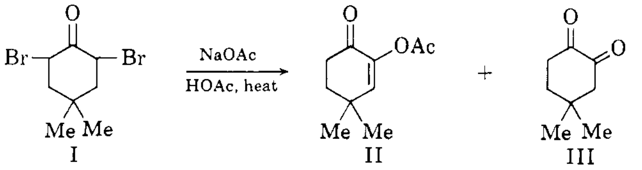
Reaction of *cis*-2,6-dibromo-4,4-dimethylcyclohexanone (I) with sodium acetate in acetic acid gives 2-acetoxy-5,5-dimethylcyclohex-2-enone (VIII) as the major product. Evidence is presented which suggests that VIII is formed by: (1) replacement of one bromine atom by an acetoxy group; (2) abstraction of the proton alpha to the acetoxy group; (3) intramolecular rearrangement of the acetoxy group; and (4) elimination of bromide ion.

It has been reported that 2,6-dibromo-4,4-dimethylcyclohexanone (I) reacts with excess potassium acetate in hot acetic acid to give a compound formulated as 2-acetoxy-4,4-dimethylcyclohex-2-enone (II) plus 4,4-dimethylcyclohexane-1,2-dione (III).[2] Later,[3] the *cis* and *trans* forms of the 2,4-dibromo-9-methyl-3-decalones were described as undergoing comparable reactions. These formulations correspond to that made by Inhoffen[4] for a comparable reaction between 2,4-dibromocoprostan-3-one and potassium benzoate in a mixture of 1-butanol and toluene.



One possible explanation for the conversion of I to II is to assume an initial SN2′ displacement of bromine from the enol of I to form 2-acetoxy-2-bromo-4,4-dimethylcyclohexanone, which then undergoes elimination of hydrogen bromide to form II. Although there are certain seemingly related reactions, such as the formation of 4-α-acetoxycholestan-3-one from the reaction of potassium acetate in acetic acid with 2-α-bromocholestan-3-one, where SN2′ reactions of this type appear to be involved,[5] the postulate of an unusual reaction path applied to an intermediate that is present in only small concentration (the enol) seemed sufficiently novel to warrant further investigation. These re-

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[1] Allied Chemical Corporation Fellow, 1960–1961; Eastman Kodak Company Fellow, 1961–1962.

[2] M. Yanagita and A. Tahara, *J. Pharm. Soc. Japan*, **71**, 1060 (1951).

[3] M. Yanagita and A. Tahara, *J. Org. Chem.*, **18**, 792 (1953); M. Yanagita and K. Yamakawa, *ibid.*, **22**, 291 (1957).

[4] H. H. Inhoffen, *Ann.*, **563**, 135 (1949).

[5] See E. L. Eliel, "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, pp. 97, 98, and K. L. Williamson and W. S. Johnson, *J. Org. Chem.*, **26**, 4563 (1961).

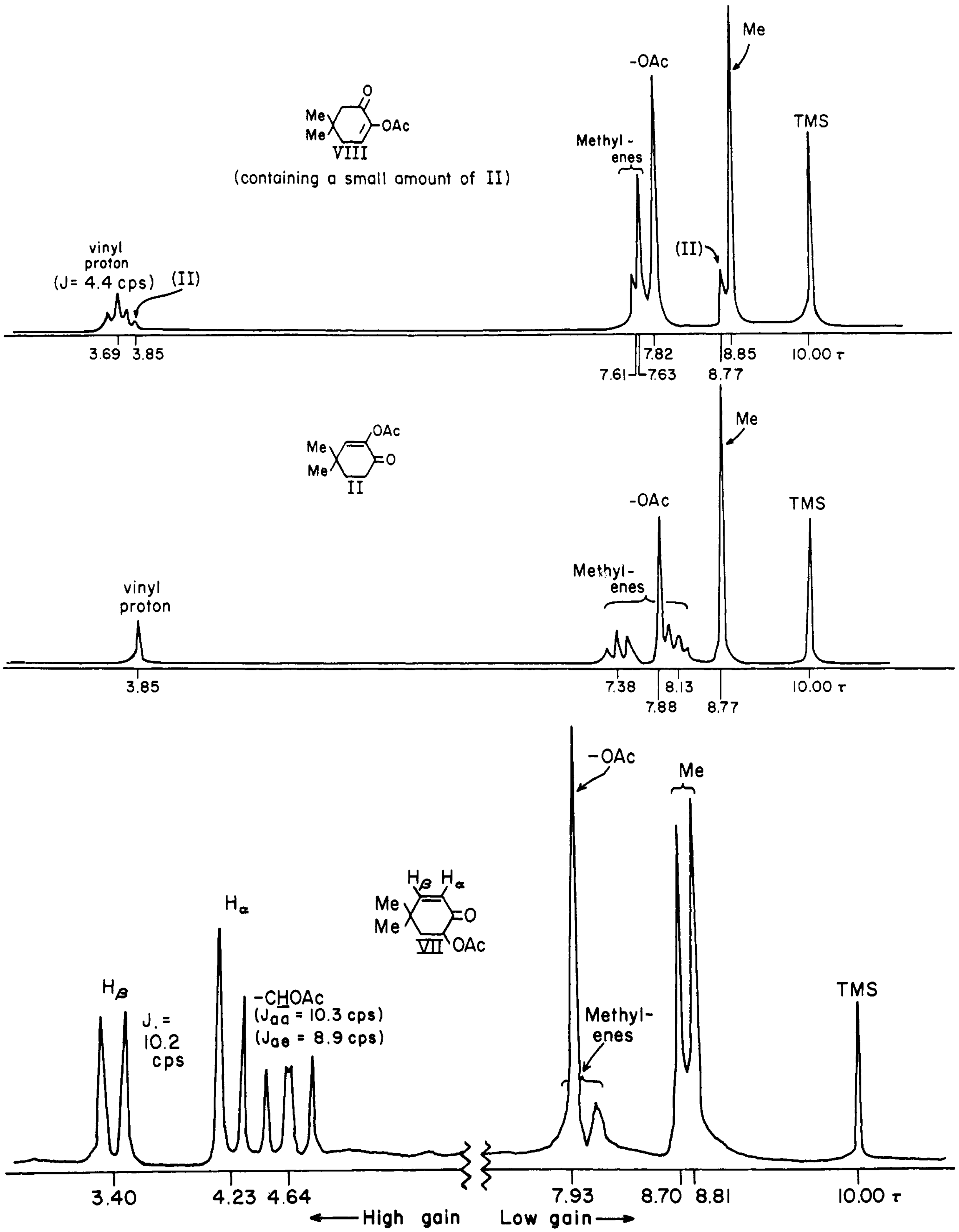

Fig. 1.—The 60-Mc. n.m.r. spectra of II, VII, and VIII in carbon tetrachloride solution with tetramethylsilane (TMS) internal standard.

sults are at possible variance with the report of Inhoffen[6] that 2,4-dibromocholestan-3-one reacts with potassium benzoate in hot toluene–butanol to give two products which he formulated (tentatively) as having structures of a different type, namely, IV and V.

Reinvestigation of the reaction using crude I under the conditions previously described[2] gave about 18% of keto–enol acetates and appreciable amounts of diketone

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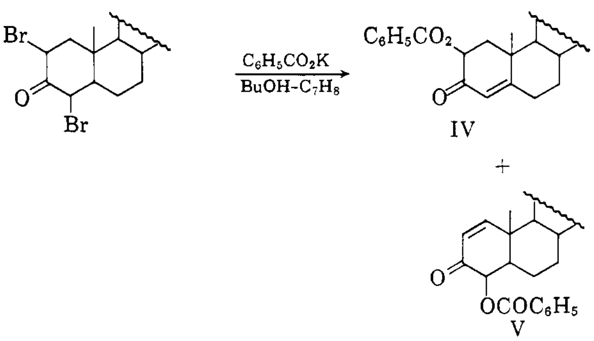
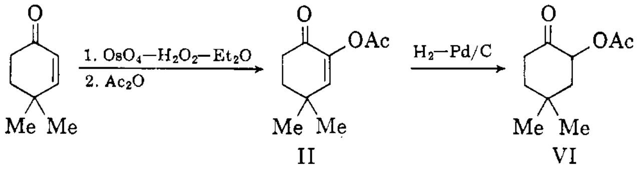
(6) H. H. Inhoffen, *Ber.*, **70**, 1695 (1937).



III. The ratio of these materials was found to depend on the extent to which the keto–enol acetates were hydrolyzed during processing. By using pure *cis* I, strictly anhydrous conditions, and a processing procedure that minimized hydrolysis, the yield of keto–enol acetates was increased to 68% and only a small amount (3%) of diketone was obtained. Gas–liquid chromatographic (g.l.c.) and n.m.r. analysis of the keto–enol acetate fraction revealed the presence of two components, A and B, in a ratio of about 1 to 7, respectively.

An authentic sample of II was prepared by hydroxylation of 4,4-dimethylcyclohex-2-enone with hydrogen peroxide in the presence of osmium tetroxide catalyst, and heating the resulting diol with excess acetic anhydride. The structure of this keto–enol acetate was confirmed as II by hydrogenation to a keto acetate (VI); VI was found to be identical with a sample of 2-acetoxy-4,4-dimethylcyclohexanone prepared by acetoxylation of 4,4-dimethylcyclohexanone with lead tetracetate as described by Cavill and Soloman.[7]



The synthetic sample of II was found to enhance the peak of the minor component (A) of the gas–liquid chromatogram of the keto–enol acetate reaction mixture obtained from I. It is, therefore, a minor product, rather than the principal product, as was previously supposed.[2] The principal product is not formed from II during the reaction, since II was found to be stable under the reaction conditions.

A structure analogous to IV (or V) for B, the major component of the reaction mixture, was also ruled out by synthesis. The analog of IV (or V), 6-acetoxy-4,4-dimethylcyclohex-2-enone (VII), was prepared by acetoxylation of 4,4-dimethylcyclohex-2-enone with lead tetraacetate.[8] It differed in properties from either II or the major reaction product.

The only reasonable structure remaining for B, the major reaction component, is then 2-acetoxy-5,5-dimethylcyclohex-2-enone (VIII). This structure was supported by demonstrating that catalytic hydrogenation of the reaction mixture gave a ketol acetate which formed a phenylhydrazone differing from that of VI. The same 2,4-dinitrophenylosazone was obtained on heating this ketol acetate with excess 2,4-dinitrophenylhydrazine as was obtained from VI, II, or the keto–enol product. This is consistent with the structures assigned.

The structures of II, VII, and VIII were confirmed by n.m.r. spectroscopy (see Fig. 1). The singlet at 3.85 τ in the spectrum of II indicates an uncoupled vinyl hydrogen, whereas coupling of the vinyl hydrogen of VIII with the two equivalent hydrogen atoms of the adjacent methylene group produces a triplet at 3.69 τ. The two vinyl hydrogen atoms of VII give separate doublets at 4.23 τ and 3.40 τ. In II the two adjacent (coupled) methylene groups give rise to two triplets (at about 7.38 and 8.13 τ). The uncoupled methylene group in VIII that is adjacent to the carbonyl group gives a signal at 7.63 τ; the methylene group coupled with the vinyl hydrogen atoms gives rise to a partially hidden doublet at 7.61 τ. In VII the signal for the single hydrogen atom attached to the same carbon atom as the acetoxy group is shifted far downfield (4.64 τ), as expected.

The results described above show that the reaction of *cis*- 2,6-dibromo-4,4-dimethylcyclohexanone (I) with sodium acetate gives VIII as the major product, accompanied by small amounts of II and the dione III (the n.m.r. spectra show that little or no VII is present).

Under mild conditions it is possible to isolate *cis*-2-acetoxy - 6 - bromo - 4,4 - dimethylcyclohexanone (IX)[9] from this reaction mixture. Furthermore, I and IX react with sodium acetate in acetic acid under comparable conditions to give the *same ratio* of II, VIII, and III, as shown by g.l.c. analysis, indicating that IX is an intermediate in the reaction involving I. This all but excludes the possibility that II, VIII, or III is formed from I by a direct reaction not involving IX (such as the S_N2' attack of acetate ion on the enol form of I, which conceivably could lead to II, previously described).

A variety of mechanisms can be imagined by which II, VIII, and III can be formed from IX. Several of these are summarized on p. 1350.

In all of these mechanisms acetate ion is the attacking agent. In mechanisms a and b, acetate ion attacks the carbonyl group with consequent epoxide formation. In mechanism a, a second acetate ion opens the epoxide by attack on one of the acetoxy groups. A proton shift and loss of acetate ion gives the diketone III, which can be reacetylated (by the acetic anhydride released in the previous step) to form II and VIII. In mechanism b, acetate ion removes a proton from the epoxide; 1,4-elimination of acetate ion then leads to VIII directly.

In mechanism c, acetate ion initiates an S_N2' reaction on the enol form of IX. This is followed by intramolecular rearrangement of an acetyl group and loss of acetic acid to give VIII.

In mechanism d, acetate ion removes a proton in the initial step. Intramolecular rearrangement of the acetyl group then gives an intermediate that can form VIII by a 1,4-elimination of bromide ion. Mechanism e differs from d only in the order of the steps following proton abstraction. Here the bromide ion is lost

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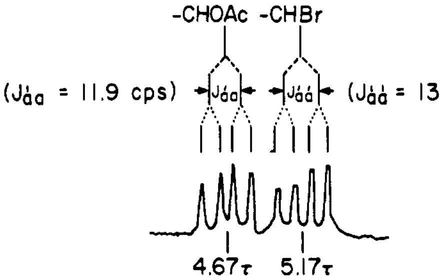
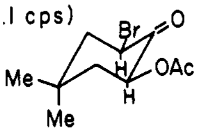
(7) G. N. K. Cavill and D. H. Soloman, *J. Chem. Soc.*, 4426 (1955).

(8) For leading references, see P. Narasimha Rao and L. R. Axelrod, *J. Am. Chem. Soc.*, **82**, 2830 (1960).

(9) The position of the groups in IX and their steric relationship was elucidated by means of its n.m.r. spectrum (Fig. 2). The presence of two clearly resolved quartets with a relative area representing one proton each at 4.67 τ (CHOAc) and 5.17 τ (CHBr) confirm the α and α' positions of the substituents (based on unpublished work of K. M. Wellman). The large coupling constants (of the order of 12 to 13 c.p.s.) indicate axial orientation for the protons (see K. L. Williamson and W. S. Johnson in ref. 5).



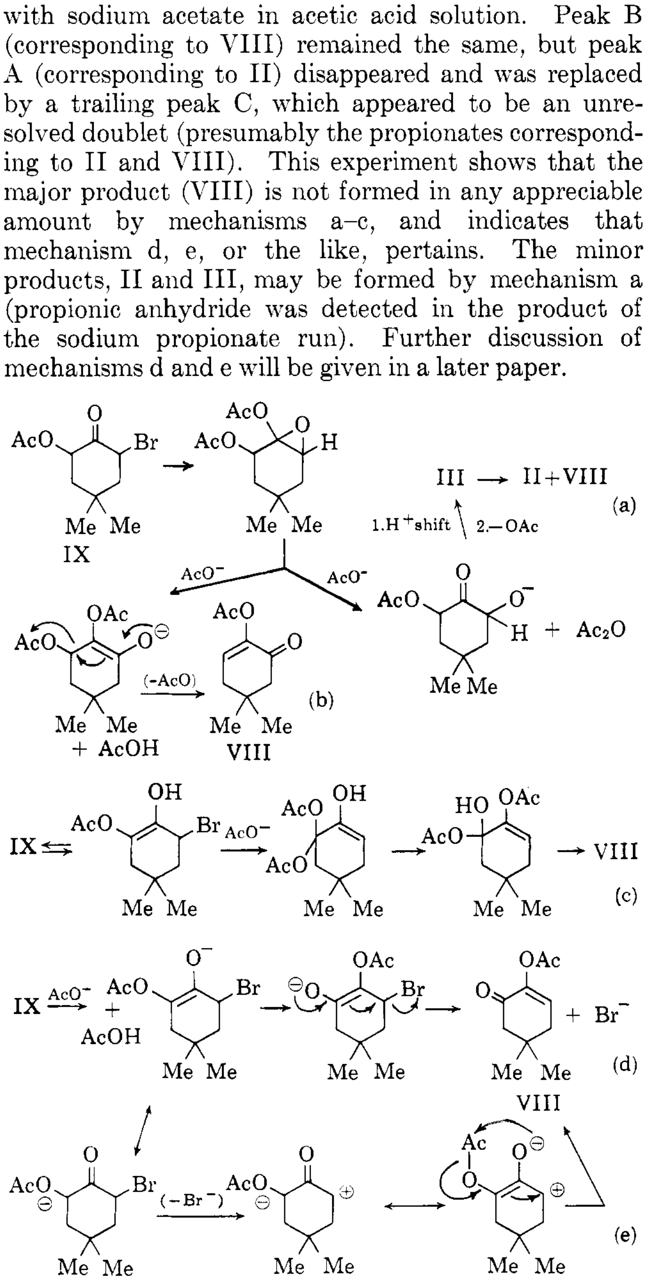


IX

Fig. 2.—The -CHX n.m.r. spectrum for IX.

first to form a dipolar ion. Intramolecular rearrangement of the acetyl group then gives VIII.

A feature common to mechanisms a–c, but not to d and e, is incorporation of external acetate (from acetate ion or the acetic acid solvent) into the product. It was therefore of interest to investigate the reaction of IX with sodium propionate in propionic acid solvent. The g.l.c. pattern of the keto–enol product obtained from this reaction differed in some respects from that of the keto–enol product obtained from the reaction of IX with sodium acetate in acetic acid solution. Peak B (corresponding to VIII) remained the same, but peak A (corresponding to II) disappeared and was replaced by a trailing peak C, which appeared to be an unresolved doublet (presumably the propionates corresponding to II and VIII). This experiment shows that the major product (VIII) is not formed in any appreciable amount by mechanisms a–c, and indicates that mechanism d, e, or the like, pertains. The minor products, II and III, may be formed by mechanism a (propionic anhydride was detected in the product of the sodium propionate run). Further discussion of mechanisms d and e will be given in a later paper.



Reaction of IX with 2,4,6-trimethylpyridine gave VIII as the major product, together with some II, but only a trace of III. The formation of VIII under these circumstances is expected according to mechanism d, or e, since 2,4,6-trimethylpyridine should be able to play the role of acetate ion. (No reaction occurs in the absence of base.) A mechanism other than mechanism a must, however, be used to account for the formation of the small amount of II under these conditions.

The demonstration that VIII, rather than II, is the major product of the reaction of I with sodium acetate in acetic acid casts doubt as to the correctness of the structure assignments made to the products formed under similar conditions from the 2,4-dibromo-9-methyl-3-decalones,[3] 2,4-dibromo-3-coprostanone,[4] and 2,4-dibromo-3-cholestanone.[6] The latter reaction is under current investigation.

Experimental[10]

4,4-Dimethylcyclohex-2-enone was prepared by a modification of an earlier procedure.[11] A solution of 104.3 g. (1.45 moles) of isobutyraldehyde and 118.5 g. (1.70 moles) of methyl vinyl ketone (Chas. Pfizer and Company, Inc., technical grade) was added dropwise with stirring over a period of 45 min. to a solution of 15 ml. of a 40% aqueous (or methanolic) solution of Triton "B" in 300 ml. of *t*-butyl alcohol. The temperature was maintained at 18–22° by cooling during addition. When about 40 ml. of the aldehyde–ketone solution remained, 15 ml. more of the Triton B solution was added, and the addition completed. The solution was warmed to 30°, and allowed to stand for 30 min. The dark red-brown solution was then poured into a mixture of 500 ml. of cold, dilute hydrochloric acid and 1000 ml. of ether. The ethereal layer was washed three times with 500 ml. portions of water, dried, and concentrated by atmospheric distillation to remove *t*-butyl alcohol. The residue was vacuum distilled, and the first fraction [b.p. 50–70° (4 mm.)] was redistilled to give 42 g. (0.339 mole; 23%) of 4,4-dimethylcyclohex-2-enone, b.p. 54–56° (4 mm.); $\lambda_{\max}^{\mathrm{CS_2}}$ 5.95, 12.40 μ; $\lambda_{\max}^{\mathrm{EtOH}}$ 224 mμ (ε 16,000); $n^{25}\mathrm{D}$ 1.4696.

4,4-Dimethylcyclohexanone.—Twenty grams of 4,4-dimethylcyclohex-2-enone were dissolved in 125 ml. of glacial acetic acid and 0.40 g. of 10% palladium on carbon was added. The mixture was shaken under 2–3 atm. of hydrogen for 10 min. after the uptake of hydrogen had ceased. The mixture was filtered twice through diatomaceous earth, and then poured into a mixture of 700 ml. of water and 600 ml. of ether. The acetic acid was neutralized by slow addition of solid sodium bicarbonate. The aqueous layer was separated and washed twice with ether. The ether layers were combined and dried. Concentration gave 18.1 g. of prism-like needles, m.p. 37–39°. Sublimation removed a small amount of residual oil and raised the melting point to 39–40° (reported[12] m.p. 38–41°); $\lambda_{\max}^{\mathrm{KBr}}$ 5.82, 8.67 μ. The semicarbazone melted at 201–202° (reported[12] m.p. 203–204°).

***cis*-2,6-Dibromo-4,4-dimethylcyclohexanone** (I).—Sublimed 4,4-dimethylcyclohexanone (10.05 g.; 0.0798 mole) in 30 ml. of glacial acetic acid was treated dropwise with 25.6 g. (0.16 mole) of bromine over a period of 20 min. with stirring and cooling so as to keep the temperature between 15 and 20°. The slightly yellow-tinged solution was poured into 300 ml. of water and 400 ml. of ether was added to dissolve the precipitated solid. The ethereal layer was washed with water and 125 ml. of pentane was added. After washing with water and dilute sodium bicarbonate, the solution was dried and concentrated to give 23.7 g. of slightly oily solid dibromide ("crude dibromide").

One recrystallization from hexane gave, after washing with 20 ml. of pentane, 14.6 g. of dibromo ketone, m.p. 94–96°, as colorless plates. The filtrate and pentane washings were combined and concentrated to about 10 ml. After a seed crystal of dibromo ketone was added, a small amount of anhydrous hydrogen bromide gas was bubbled through the solution and the flask was

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[10] Microanalyses were determined by Miss Hilda Beck. N.m.r. spectra were obtained by Larry Shadle.

[11] E. L. Eliel and C. A. Lukach, *J. Am. Chem. Soc.*, **79**, 5986 (1957).

[12] E. B. Reid and T. E. Gomp, *J. Org. Chem.*, **18**, 661 (1953).

stoppered and allowed to stand at room temperature overnight. An additional 3.3 g. of product, m.p. 93–95°, was thus obtained; the total yield was 17.9 g. (80%). Further recrystallization gave material melting at 95–96° (reported[2] m.p. 97°).

Reaction of *cis*-2,6-Dibromo-4,4-dimethylcyclohexanone with Sodium Acetate in Acetic Acid.—Repetition of the previous work[2] with 9.00 g. (0.0318 mole) of crude I gave 1.01 g. (0.0056 mole; 18% yield; n^{20}_{D} 1.4750) of liquid keto–enol acetates[13] and 1.89 g. (0.0135 mole; 43%) of solid diketone, m.p. 65–68°. Several recrystallizations from methanol–water gave pure 4,4-dimethylcyclohexane-1,2-dione (III), m.p. 75–76° (reported[2] m.p. 76–77°), as long, glistening, colorless needles.

Freshly distilled glacial acetic acid (56 ml.) and 27.2 g. (0.33 mole) of anhydrous, freshly fused sodium acetate, were heated at 87° for 30 min. I, m.p. 94–96°, (16.5 g.; 0.058 mole) was added and the mixture stirred and heated for 3 hr. at 87–89°. The solidified mixture, obtained on cooling, was broken up and added to 400 ml. of water. The precipitated oil was taken up in 400 ml. of ether, and the aqueous layer was washed with 250 ml. of 1:1 ether–pentane. The combined organic fractions were washed with water and with aqueous sodium bicarbonate. The ethereal layer was dried and concentrated to give 9.18 g. of an oil. A g.l.c. analysis showed three components, the diketone (3%; identified by enhancement of the peak by adding an authentic sample of III to the reaction mixture), and two partially resolved keto–enol acetates. The minor component keto–enol acetate was shown to be II by enhancement of the minor peak (peak A) on addition of authentic II (see below) to the reaction mixture. Vacuum distillation of the reaction mixture gave III as a low boiling fraction (0.228 g; 2.8% yield) which solidified (m.p. 65–68°) in the condenser; its infrared spectrum was identical to that of authentic III. Further distillation gave 7.18 g. (68%) yield of keto–enol acetates, b.p. 74.5–75.0° (0.2 mm.), n^{20}_{D} 1.4740, $\lambda_{\max}^{\mathrm{CS_2}}$ 5.65, 5.89, 6.05, 8.25, 8.45, 8.70, 9.14 μ, $\lambda_{\max}^{\mathrm{EtOH}}$ 232 mμ (ε 10,000). An n.m.r. analysis indicated the ratio of VIII to II to be 5.2 to 1.

***cis*-2,3-Dihydroxy-4,4-dimethylcyclohexanone.**—A mixture of 5.00 g. (0.0323 mole) of 4,4-dimethylcyclohex-2-enone, 100 ml. ether, and 15 ml. of hydrogen peroxide (30% aqueous) was cooled to 0–2° and a solution of 0.25 g. of osmium tetroxide in 10 ml. of ether added. The cold solution turned dark brown; it decolorized slowly when shaken for 20 min. at 0.5°. The cooling bath was removed, and the reaction mixture allowed to stand in the cold room (17°) for 10 hr. After drying, the ether layer became discolored. Two milliliters of aqueous hydrogen peroxide were added, and the mixture shaken until the dark color disappeared. The ethereal fraction was washed with 5 ml. of water, and concentrated to 10 ml. under vacuum at room temperature using a Rinco concentrater. The residue was placed under high vacuum and warmed to 35–45° for 3 hr. giving 5.00 g. of solid dihydroxy ketone. One recrystallization from ether–hexane gave 2.68 g. (0.017 mole; 53% yield) of ***cis*-2,3-dihydroxy-4,4-dimethylcyclohexanone,** m.p. 97–99°, $\lambda_{\max}^{\mathrm{KBr}}$ 2.80, 2.88, 5.83, 8.85, 9.06, 9.42 μ. An analytical sample melted at 100–101° (colorless plates).

Anal. Calcd. for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.89; H, 9.07.

2-Acetoxy-4,4-dimethylcyclohex-2-enone (II).—A solution of 2.507 g. (0.0159 mole) of *cis*-2,3-dihydroxy-4,4-dimethylcyclohexanone in 60 ml. of acetic anhydride was refluxed for 3.5 hr. The reflux condenser was replaced with a Vigreux column, the acetic acid and excess acetic anhydride were removed under vacuum, and the residue (2.43 g.) was distilled; b.p. 100–103° (2 mm.) (1.87 g.; 0.01 mole; 65% yield). A middle cut was taken as an analytical sample of II; b.p. 100.5° (2 mm.); n^{20}_{D} 1.4703; $\lambda_{\max}^{\mathrm{CS_2}}$ 5.65, 5.89, 6.05, 8.25, 9.16 μ. G.l.c. and n.m.r. analyses indicated the absence of any appreciable amount of VIII.

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.34; H, 7.45.

Attempted Rearrangement of II.—Glacial acetic acid (2.5 ml.), sodium acetate (0.62 g.), and II (0.25 g.) were combined and heated at 85–90° (bath temperature) for 2 hr. The infrared spectrum of the resulting oil (0.20 g.) was superimposible on that of the starting material; g.l.c. analysis indicated less than 1% diketone and no appreciable amount of VIII.

6-Acetoxy-4,4-dimethylcyclohexanone (VI). A. By Hydrogenation of II.—Ten milliliters of absolute alcohol, 0.243 g. of II, and 0.024 g. of 10% palladium on carbon were combined and stirred magnetically under 2–3 atm. of hydrogen until the up-take of hydrogen ceased. The reaction mixture was filtered through diatomaceous earth, and the filter cake was washed with 10 ml. of ether. The ether and alcohol were removed by distillation to yield 0.158 g. of crude acetoxy ketone VI. The infrared spectrum was essentially that of pure ketol acetate VI (see below).

B. By Acetoxylation of 4,4-Dimethylcyclohexanone.—According to the general method of Cavill and Soloman,[7] 19.6 g. (0.0432 mole) of lead tetraacetate, which had been dried under vacuum over sodium hydroxide pellets for 24 hr., 5.17 g. (0.041 mole) of 4,4-dimethylcyclohexanone, and 33 ml. of benzene (freshly distilled from over sodium) were heated for 10.5 hr. at 70° in a flask fitted with a condenser and calcium chloride tube. The mixture was filtered and the residue washed with ether. The ether–benzene solution was freed of acetic acid by washing with saturated sodium bicarbonate solution, dried, and concentrated under vacuum to yield 5.79 g. of an oil. Fractionation of the product through a Vigreux column under vacuum gave 3.87 g. (0.0210 mole; 51%) of **6-acetoxy-4,4-dimethylcyclohexanone (VI)**; b.p. 65–68° (0.2 mm.); n^{20}_{D} 1. 4560; $\lambda_{\max}^{\mathrm{CS_2}}$ 5.70, 5.75, 8.08, 9.20, 9.47 μ.

To 243 mg. of VI was added, with stirring, 147 mg. of phenylhydrazine. A yellow-orange solid formed immediately. Recrystallization from ether–hexane gave colorless prisms, m.p. 102° (turning yellow at 97°). This derivative decomposed in 2 hr. at room temperature on the desk. Decomposition occurred in 3 days in a dark cold room (17°).

Anal. Calcd. for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08. Found: C, 69.44; H, 8.11.

6-Acetoxy-3,3-dimethylcyclohexanone Phenylhydrazone.—Crude 6-acetoxy-3,3-dimethylcyclohexanone ($\lambda_{\max}^{\mathrm{CS_2}}$ 5.70, 5.75, 8.08, 9.30 μ) was obtained by hydrogenation of the keto–enol acetate product from I (see above) in the same manner as II was hydrogenated to VI. The infrared absorption spectrum of the crude ketol acetate showed weak absorptions at positions where VI had medium-strong bands (9.20 μ and 9.47 μ). The crude ketol acetate (129 mg.) was stirred with 89.9 mg. of phenylhydrazine until the mixture had completely solidified to the orange-yellow phenylhydrazone. Recrystallization was effected from ether–hexane to give colorless prisms, m.p. 113–114°—dependent on rate of heating—turning yellow at 107°. The phenylhydrazone decomposed overnight at room temperature but was relatively stable in the cold room (17°) or in the dark under vacuum.

Anal. Calcd. for $C_{16}H_{22}N_2O_2$: C, 70.04; H, 8.08. Found: C, 69.84; H, 8.03.

4,4-Dimethyl-1,2-cyclohexadione 2,4-Dinitrophenylosazone.—Brady's reagent was prepared by dissolving 1.925 g. of 2,4-dinitrophenylhydrazine in a solution of 4 ml. of concd. sulfuric acid, 30 ml. of methanol, and 10 ml. of water and decanting the solution from a small amount of dark red residue.

Using this reagent the same osazone (identified by mixture melting points) was obtained from III, II, VIII, VI, and from the crude ketol acetate formed by the catalytic hydrogenation of VIII.

In each instance the procedure was the same. For example, when 0.5053 g. of 2-acetoxy-4,4-dimethylcyclohexanone was added to the freshly prepared reagent at room temperature, a pale yellow precipitate formed immediately. After heating at reflux for 1 hr., the initial colloidal precipitate was transformed to a finely divided dark red precipitate. After drying, the crude osazone (1.36 g.) melted at 190–195°. Two recrystallizations from methanol–chloroform gave small, dark red prisms, m.p. 224–225°.

Anal. Calcd. for $C_{20}H_{20}N_8O_8$: N, 22.39. Found: N, 22.58.

6-Acetoxy-4,4-dimethylcyclohex-2-enone (VII).—A mixture of 5.00 g. (0.0403 mole) of 4,4-dimethylcyclohex-2-enone, 17.84 g. (0.0402 mole) of lead tetracetate and 30 ml. of benzene (freshly distilled from sodium) was heated at reflux for 20 hr. The mixture was filtered and the residue washed with two 50-ml. portions of ether. The ether–benzene solution was washed with water and with dilute sodium bicarbonate, dried, and concentrated to yield 5.5 g. of an oil. Vacuum distillation gave a forerun (0.598 g., 0.0048 mole) of starting material (by infrared analysis) boiling mainly at 60° (5 mm.), a small intermediate fraction [b.p.

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[13] A gas-liquid chromatogram[14] of the keto–enol acetates showed only two partially resolved components. An n.m.r. analysis using the areas under appropriate absorptions indicated the two components to be in the ratio of 1 to 7.3.

[14] Throughout this work an F and M Model 300 vapor phase chromatograph containing a 6-ft. column packed with 20% diisodecyl phthalate on 100–120-mesh firebrick was used at a temperature of about 150°.

65–115° (5 mm.)], and a main fraction consisting of 2.319 g. (0.0128 mole; 36% yield) of **6-acetoxy-4,4-dimethylcyclohex-2-enone**, b.p. 115–116° (5 mm.). An analytical sample had the following characteristics: b.p. 116° (5 mm.), $n^{22}\text{D}$ 1.4736, $\lambda_{\max}^{\text{CS}_2}$ 5, 70, 5.87, 8.08, 8.16, 9.24, 9.49, 12.20 μ.

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.76; H. 7.70.

cis-**2-Bromo-6-acetoxy-4,4-dimethylcyclohexanone (IX)**.—In unsuccessful attempts to isolate IX, the reaction of I with sodium acetate was carried out with excess sodium acetate for varied times at temperatures from 25 to 65°. Success was finally achieved as follows: 5.00 g. (0.0176 mole) of I and 1.44 g. (0.0176 mole) of fused sodium acetate were dissolved in 20 ml. of glacial acetic acid, the reaction vessel stoppered, and placed in an oil bath at 85°. After 125 min. the reaction mixture was cooled, poured into water, and the precipitated oil taken up in ether. The ethereal layer was washed free of acetic acid with concentrated aqueous sodium bicarbonate. After drying, the ethereal solution was concentrated under vacuum to yield 3.10 g. of an oil. The oil was dissolved in hot petroleum ether and the solution cooled slowly, and then placed in the cold room overnight; the resulting large prisms melted at 65–67°. Recrystallization from petroleum ether gave 0.769 g. of pure *cis*-**2-bromo-6-acetoxy-4,4-dimethylcyclohexanone** as large diamond-shaped crystals, m.p. 76.5°, $\lambda_{\max}^{\text{KBr}}$ 5.69, 5.73, 8.08 μ. Chromatography of the mother liquors from the recrystallizations over silica gel (eluting with 10% ether-in-hexane) gave 1.006 g. (m.p. 73–74°) more of the bromoacetoxyketone (total yield: 39%).

Anal. Calcd. for $C_{10}H_{15}BrO_3$: C, 45.64; H, 5.75. Found: C, 45.71; H, 5.61.

Reaction of *cis*-2-Bromo-6-acetoxy-4,4-dimethylcyclohexanone (IX) with Various Bases. A. With Sodium Acetate.—Three milliliters of acetic acid was distilled from acetic anhydride and anhydrous sodium acetate into a reaction vessel containing 0.41 g. (5.0 mmole) of hot, freshly fused sodium acetate. The flask was tightly stoppered and heated at 87° (bath temperature) for about 20 min.; a small amount of the fused sodium acetate remained undissolved. Then 0.2647 g. (1.00 mmole) of IX was added and heating continued for 2.5 hr. at 84–87°. After standing for 20 min. at room temperature, the reaction mixture was poured into a mixture of 50 ml. water and 75 ml. of ether. After vigorous shaking, the aqueous layer was discarded and 25 ml. of pentane was added. The organic solution was washed with water, followed by sufficient sodium bicarbonate to remove the remaining acetic acid. The organic layer was then dried and concentrated under vacuum to yield 0.165 g. (0.91 mmole, assuming pure keto–enol acetates) of slightly yellow colored oil. G.l.c. analysis showed three components (III, II, and VIII) with areas in the ratio of about 0.45:1.0:4.1, respectively. (Since the keto–enol acetates are only partially resolved on the column, the ratio between them is only approximate in this and other runs; the ratio between the acetates and the diketone should, however, be accurate.)

A reaction carried out concurrently and under the same conditions using *cis*-2,6-dibromo-4,4-dimethylcyclohexanone (I) in place of IX gave 0.98 mmole of crude product from 1.06 mmoles of dibromo ketone. The infrared spectra from this and the foregoing run were superimposable, even to small detail. A g.l.c. analysis gave the ratios of III, II and VIII as 0.50:1.0:4.5 in good agreement with the same ratios of products obtained from IX.

B. With Sodium Propionate.—Freshly fused sodium propionate (0.4740 g., 5.0 mmole) and 3 ml. of freshly distilled propionic acid were heated for 20 min. at 84°. Then 0.26 g. (1.0 mmole) of IX was added, and the heating was continued for 2.5 hr. at 84–87°. The reaction mixture was processed as above to give 0.158 g. (0.87 mmole) of oil. The infrared spectrum of this crude product was essentially the same as that of the product from run A above, except for a weak band at 5.53 μ believed to be due to propionic anhydride. The enhancement of one of the peaks in the gas–liquid chromatogram on addition of propionic anhydride gave additional evidence for its presence (to the extent of about 3%).

In contrast to the runs made in acetic acid, no peak A was present in the gas–liquid chromatogram (keto–enol acetate II was absent). Instead, peak B (due to VIII) was followed by two partially resolved components (peak C). These new components are probably the propionates corresponding to II and VIII. The ratio of III to VIII to the propionates was 0.52:4.1:1.0.

C. With 2,4,6-Trimethylpyridine.—A solution of 0.1594 g. (0.6 mmole) of IX and 1.6 ml. of freshly distilled 2,4,6-trimethylpyridine was heated at 98–106° (bath temperature) for 22 hr. The reaction mixture was cooled and poured into a mixture of 50 ml. of 10% hydrochloric acid and 75 ml. of ether. The ethereal layer was separated and washed again with 50 ml. of 10% hydrochloric acid and finally with water. The organic layer was dried and concentrated to yield 0.087 g. of an oil. The infrared spectrum of this product indicated a small amount of starting material remaining. Analysis (g.l.c.) showed only a trace of diketone III; the ratio of VIII to II was at least 11 to 1.0.

Attempted Solvolysis of IX.—A solution of 0.106 g. of IX in 3 ml. of propionic acid and 1 ml. of propionic anhydride was heated at 84–88° (bath temperature) for 2.5 hr. The solution was allowed to stand at room temperature for about an hour and then poured into 50 ml. of concentrated sodium bicarbonate solution. Processing by ether extraction gave back IX, m.p. 71–72°.