tein is negative may well be related to enzyme structural requirements for combination with the highly charged natural substrate molecules. In spite of this difference, future detailed investigations of other enzyme systems may reveal a relationship between micellar properties of detergents and their inactivating action similar to that found for hyaluronidase.[29]

Acknowledgment.—The author would like to express his appreciation to Dr. Albert Dorfman for many helpful discussions.

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[29] The importance of micellar properties of cationic detergents is indicated by observations that the ability of a cationic detergent to accelerate the enzymatic decarboxylation of glutamate and glutamine parallels its ability to form micelles (D. E. Hughes, *Biochem. J.*, **45**, 325 (1949); *ibid.*, **46**, 231 (1950)). It was supposed that the cationic agent removes an inhibitor and thus increases the rate of action of enzyme. The concentration for maximum acceleration approximately coincided with the CMC for each member of a series of detergents.

CHICAGO, ILLINOIS

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

Reactions of Hindered α-Substituted Succinic Acids. III. Mechanism of the Reaction of the Haloacids with Bases[1]

BY WYMAN R. VAUGHAN AND RANDEL Q. LITTLE, JR.[2]

RECEIVED NOVEMBER 9, 1953

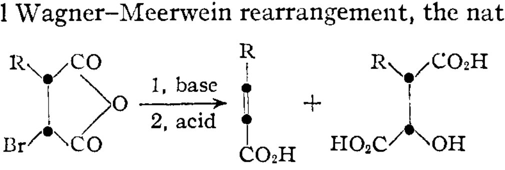
The mechanism of the elimination of the β-carboxyl together with halide ion of hindered α-halosuccinic acids as a consequence of reaction with bases is discussed. The fact that this reaction may occur by a unimolecular process with either the *cis* or *trans* configuration of the two groups is considered, and the nature of the competing reaction in each instance is examined.

In the first paper in this series[3] the general characteristics of the reactions of 2-bromo-3-methyldibenzo[2,2,2]bicyclooctadiene-2,3-*cis*-dicarboxylic anhydride (I), 2-bromodibenzo[2,2,2]bicyclooctadiene-2,3-*cis*-dicarboxylic anhydride (II) and 2-bromodibenzo[2,2,2]bicyclooctadiene-2,3-*trans*-dicarboxylic acid (III) with alkali were described. The elimination of the β-carboxyl with bromide ion was observed with all three compounds, and with I and II the usual formation of the α-hydroxy-acid by β-lactone formation with cleavage on the carbonyl to give the *trans*-configuration was noted. With III the accompanying reaction was an unusual Wagner–Meerwein rearrangement, the nature of which has been considered in the preceding paper of this series.[4]

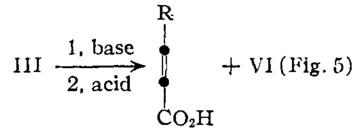
I, R = CH₃
II, R = H

III, X = Br
V, X = OH

Fig. 1.



I and II



The present investigation was designed to shed more light on the general characteristics of the behavior of β-haloacids in alkaline media.

It has been established that in neutral solutions the hydrolysis of both α-haloacids[5] and β-haloacids[6] proceeds with retention of configuration, whereas in acidic or alkaline media the resultant hydroxy acids have the inverted configuration. With the α-haloacids an intermediate α-lactone or lactonic transition state has been proposed, and support for this hypothesis is derived from the observation that the lithium alumino-hydride reduction of optically active 2-chloro-2-phenylpropionic acid affords as a by-product optically active 2-phenyl-1,2-propanediol with complete configurational inversion.[7] The non-inverting hydrolysis follows a first-order path and is pH independent while the alkaline, inverting hydrolysis is first order in the hydroxyl ion.[5]

With the β-haloacids the isolation of the β-lactone has actually been achieved,[8] and the chemistry of the β-lactone system clearly indicates the nature of the inverting and non-inverting reactions.[6] Thus both the α-haloacid and β-haloacid hydrolyses may be described in similar terms.

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[1] Abstracted from a portion of the Ph.D. dissertation of Randel Q. Little, Jr., University of Michigan, 1953. For the preceding paper in this series see THIS JOURNAL, **76**, 1748 (1954).

[2] American Brake Shoe Company Fellow, 1952–1953.

[3] W. R. Vaughan and K. M. Milton, THIS JOURNAL, **74**, 5623 (1952).

[4] W. R. Vaughan, M. V. Andersen, Jr., and R. Q. Little, Jr., *ibid.*, **76**, 1748 (1954).

[5] W. A. Cawdrey, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 1208 (1937); *cf.* L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 175–178.

[6] A. R. Olson and R. J. Miller, THIS JOURNAL, **60**, 2687 (1938); A. R. Olson and J. L. Hyde, *ibid.*, **63**, 2459 (1941); *cf.* P. D. Bartlett and R. N. Rylander, *ibid.*, **73**, 4275 (1951).

[7] E. L. Eliel and J. P. Freeman, *ibid.*, **74**, 923 (1952).

[8] H. Johannson, *Ber.*, **48**, 1262 (1915).

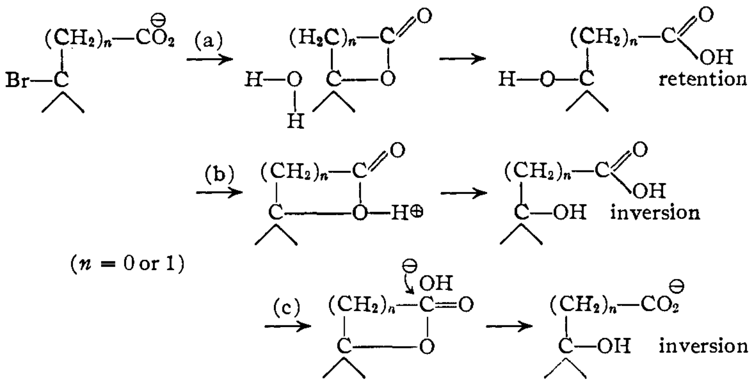

CHART 1

In the present study it is only necessary to consider the third reaction path (c, Chart 1), since it has been established that intermolecular nucleophilic displacement, such as is represented by the neutral hydrolysis of the first reaction path (a, Chart 1), in the present series is highly improbable, if not actually impossible.[3] Consequently it becomes possible to study the reaction in a *p*H range where otherwise a duality of mechanism, with different reaction orders, might be encountered.

The decarboxylation of β-haloacids with loss of halide is one of the oldest known of their reactions,[9] and it was originally suggested that β-lactones were intermediates in the reaction.[9] However, it was subsequently shown that formation of β-lactones and the decarboxylation were *simultaneously* occurring first-order reactions[10]; but not until comparatively recently has any serious consideration been given to the stereochemistry of this reaction. The reasonable assumption that the process occurs by a *trans* elimination is implicit in Woodward's and Loftfield's elucidation of the cantharidin structure,[11] but recent work in this Laboratory has shown that the related *cis* elimination can occur.[3] Most recently the work of Cristol and Norris[12] and of Grovenstein and Lee[13] has shown that *cis*-β-bromostyrene is preferentially produced from the salt of *erythro*-2,3-dibromo-3-phenylpropionic acid (the dibromide of *trans*-cinnamic acid) in acetone solution, with appreciable *trans* isomer arising in absolute ethanol, while in water the *trans* isomer predominates. A duality of mechanism has been proposed to account for the increasing non-stereospecificity of the reaction as the solvating power of the solvent decreases while its ionizing power increases. Thus a concerted elimination similar to that proposed in our first report on this reaction[3] is offered to account for the production of the *cis* isomer by *trans* elimination,[12,13] while the non-stereospecific process which affords the *trans* isomer is held to be either ionization of the halide,[12,13] or possibly isomerization of the *erythro* form of the acid to the *threo* form, followed by *trans* elimination.[12] The advantages of the present system, in which such isomerization is improbable under the conditions of the reaction,[3] and in particular in which the problem of conformational rotation is not a factor, are obvious. Consequently the *cis* elimination may be attributed directly to a difference in mechanism. Inasmuch as the dehalogenative decarboxylation[14] can occur by either a *cis* or *trans* mechanism, it seemed desirable to investigate the kinetics of the two reactions. For this purpose each reaction was initiated by adding a dilute sodium bicarbonate solution to an acetone solution of the reactant. The technique used differs from Cristol's anhydrous acetone–bicarbonate[12] reaction, but since we were not concerned with the possibility of competitive processes for elimination which might be solvent dependent, the presence of water in the reaction medium could be tolerated so long as the system remained homogeneous. Termination of the reaction was accomplished by adding excess dilute nitric acid. Unreacted starting material was removed by washing with chloroform prior to titration of the liberated bromide by the Volhard method.

In both reactions the rate was found to be first order in the haloacid and independent of *p*H in mildly alkaline solutions, in agreement with previous studies.[8,10,15–17] The kinetic data are summarized in Table I, and the rate constants are plotted logarithmically against negative reciprocal absolute temperature in Fig. 2. It should be noted that the rate constants as well as the energies and entropies of activation obtained in this study are composite functions involving more than one reaction: that is, the simultaneous dehalogenative decarboxylation and β-lactone-hydroxyacid formation for the *cis* system II, as in the work of Johannson and Hagman,[10] and simultaneous dehalogenative decarboxylation and rearrangement for the *trans* system III.

TABLE I

Reactant	Temp., °C.	$k \times 10^2$ (min.$^{-1}$)	$E_{act.}$ kcal./mole[a]	S, e.u.[b]
II	19.0	3.38		
	25.2	8.33	24.9	9.9
	29.8	14.93		
III	54.5	1.13		
	59.0	2.15		
	62.5	3.42		
	25.2	0.0126[a]	29.9	13.7

[a] Calculated from the Arrhenius equation.[18] [b] Calculated from the Eyring equation.[19]

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(9) E. Erlenmeyer, *Ber.*, **13**, 305 (1880).

(10) H. Johannson and S. M. Hagman, *ibid.*, **55**, 647 (1922).

(11) R. B. Woodward and R. B. Loftfield, THIS JOURNAL, **63**, 3167 (1941).

(12) S. J. Cristol and W. P. Norris, *ibid.*, **75**, 632, 2645 (1953).

(13) E. Grovenstein, Jr., and D. E. Lee, *ibid.*, **75**, 2639 (1953).

(14) The term "debrominative decarboxylation" has been used by others (*e.g.*, ref 12) to denote simultaneous loss of carboxyl and bromine beta to it. We propose the general term "dehalogenative decarboxylation" for this reaction but caution against confusion with "brominative decarboxylation" which has recently been used to denote the Hunsdiecker silver salt reaction (P. Wilder, Jr., and A. Winston, THIS JOURNAL, **75**, 5370 (1953)).

(15) G. S. Simpson, THIS JOURNAL, **40**, 674 (1918).

(16) A. P. Chadwick and E. Pacsu, *ibid.*, **65**, 392 (1943).

(17) J. F. Lane and H. W. Heine, *ibid.*, **73**, 1348 (1951).

(18) S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, pp. 1, 194.

(19) Ref. 18, p. 199.

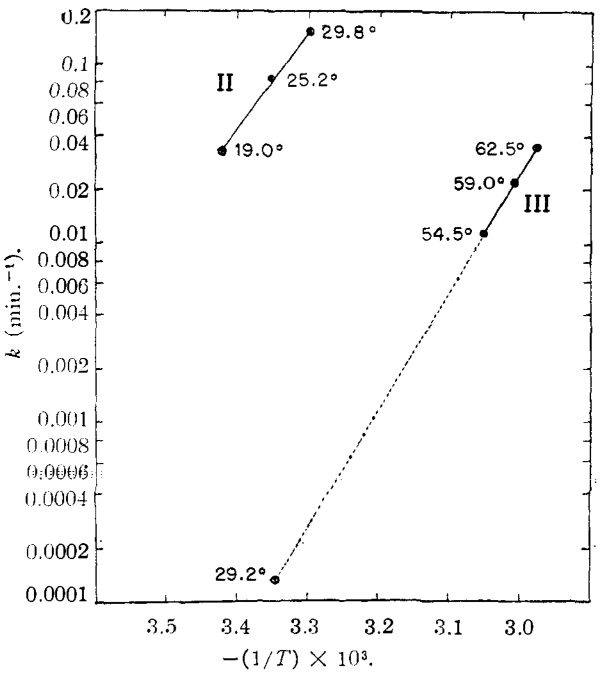


Fig. 2.—First-order base induced reactions of II and III, log k *vs.* $-1/T$.

Furthermore, the over-all reaction of II involves first cleavage of the anhydride followed by the simultaneous reactions of anion of the *cis* acid. That the anhydride opening is rapid and the subsequent simultaneous reactions are rate determining is supported by the observed kinetics and the nature of the reaction products. Further support for this hypothesis is found in the reaction of II with silver nitrate, wherein the anhydride is rapidly opened, with formation of a silver salt, which separates after a few minutes, while several hours are required before the bromide is removed. Complete details of this reaction and the related reaction of II with silver oxide are discussed in the following paper in this series. The reported observation serves to emphasize the greater reactivity of the anhydride system compared with the halide elimination, even in a case where loss of halide should be, if anything, enhanced by electrophilic attack while anhydride opening should be repressed by the non-basic character of the medium.

The work of Lane and Heine[17] on the hydrolysis of aliphatic bromoacids shows that the energies of activation decrease in the order $\alpha > \beta > \gamma$, and that the entropies of activation are positive and similar in magnitude. Thus there appears to be a direct relationship, in agreement with the Baeyer strain theory, between the relative reactivities and the ring size of the intermediate lactone. Inasmuch as there is only a minor variation in the entropy values the processes would appear to be governed chiefly by the energies of activation.

In the present study the formation of a β-lactone intermediate from III by simple intramolecular displacement of bromide is impossible, thus III must be considered as an α-haloacid with respect to internal displacement. The relative reactivities are in agreement with those of Lane and Heine; but there is a considerable difference in the entropy values, such as to facilitate the decomposition of III.

A qualitative examination of the effect of increased hydroxide ion concentration on the decomposition of II shows that the change in the logarithm of the first-order rate constant with respect to time is similar to the change in hydroxide ion concentration of the solution with respect to time (Fig. 3). The linear relationship between the log k and the basicity of the solution is shown in Fig. 4. The dependence of the reaction on the hydroxide ion concentration is in accord with the fact that a bimolecular rate constant was obtained by Olson and Miller[6] for the hydrolysis of β-bromobutyrate ion. In addition to this evidence for a change in order with increasing pH, there is a change in the ratio of dibenzo[2,2,2]bicycloöctatriene-2-carboxylic acid (IV), (Fig. 5) to the second product component (2-hydroxydibenzo[2,2,2]bicycloöctadi-

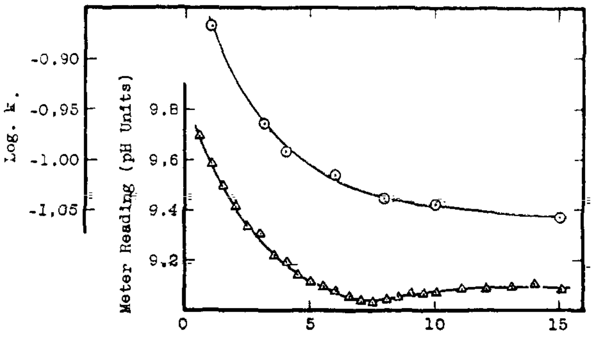


Fig. 3.—Change in logarithm k and pH *versus* time.

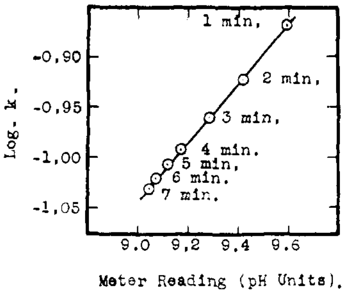
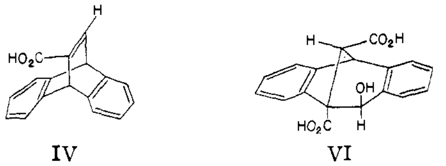


Fig. 4.—Logarithm k *versus* pH at various time intervals.

TABLE II

EFFECT OF INCREASED pH ON PRODUCT RATIOS

Reactant	Reagent	Product ratio (moles) IV:	V:	VI
II	0.25 M NaHCO$_3$	2	3	
	25% KOH[3]	1	2	
III	0.25 M NaHCO$_3$	11		1
	25% KOH[3]	3		2



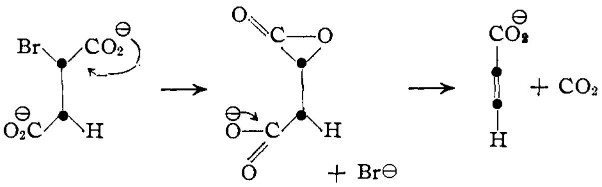
IV VI

Fig. 5.

ene-2,3-*trans*-dicarboxylic acid, V (Fig. 1), from II and the rearranged hydroxyacid,[4] VI (Fig. 5), from III (Table II). Thus since there should be no change in product ratio while the reactions remain within a given kinetic order,[20] one must conclude that different mechanisms are operative at higher *p*H values.

The data from the present study support the concerted type process proposed by Vaughan and Milton[3] for the behavior of II and the similar process proposed by Cristol and Norris[12] and Grovenstein and Lee[13] for the formation of β-bromostyrene.

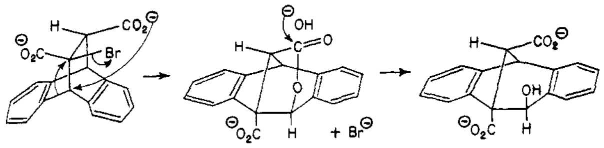
For III, a two-step process reminiscent of the E_1 elimination[21] may satisfactorily describe the reaction leading to IV.



III VII IV

Fig. 6.

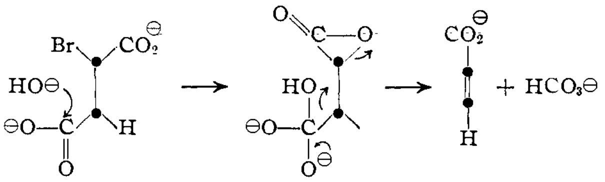
The competitive production of VI by a unimolecular process presents more of a problem, especially since the rearrangement is stereospecific with respect to the configuration of the hydroxyl group.[4] The following series of transformations is suggested as a possible route for the reaction to follow



III VIII VI

Fig. 7.

It is not unreasonable to argue that the rate determining formation of VIII from III is a less probable (*i.e.*, more difficult) reaction than the rate determining formation of VII from III, and the ratio of VI to IV in the unimolecular decomposition would seem to substantiate such an assumption. The decrease in the ratio IV:VI observed at higher *p*H values where the hydroxyl ion concentration appears to be involved may be accounted for by assuming that the reaction III → IV involves a more complex intermediate IX, as suggested in the original investigation of this reaction[3]



III IX IV

Fig. 8.

The formation of VIII remains a unimolecular process, and this would imply that the hydroxyl ion catalyzed decomposition of III to IV is actually slower than the neutral decomposition. It appears more likely that the rate of decomposition of III would increase at a higher *p*H and thus the formation of VI from III also becomes a polymolecular process. However, it is equally possible that at higher *p*H values the lactone never forms, the rearrangement being initiated by attack of hydroxyl ion at carbon-1 instead of the intramolecular carboxylate ion attack at this position. In any case it is clear that regardless of conditions, the mechanism of alkaline decomposition of a *cis*-β-bromoacid is strikingly different from the analogous decomposition of its *trans* isomer where there may be participation from a neighboring carboxyl group. It may be argued that full participation greatly facilitates the *cis* elimination, and the relative magnitudes of the entropies of activation (Table II) would seem to support this hypothesis. The problem of what happens where such neighboring group participation is not possible is currently under investigation in this Laboratory, and preliminary results indicate that the dehalogenative decarboxylation does not occur smoothly in aqueous solutions, and in non-aqueous systems does not occur at all.[22] The greater reactivity of II as revealed in the relative size of the rate constants (Table I) presumably must be attributed to other factors, *e.g.*, the ideally favorable *trans* disposition of halogen and carboxyl.[12,13]

Experimental[23]

Reaction of II with Dilute Sodium Bicarbonate.—To a solution of 0.500 g. (0.00141 mole) of II in 25 ml. of acetone there was added 25 ml. of 0.25 *M* sodium bicarbonate, and the reaction was allowed to stand overnight. The mixture was then acidified with hydrochloric acid and evaporated to dryness. The residual white solid was washed with 2 ml. of 2.5% hydrochloric acid, 1 ml. of water, was filtered and dried. Extraction of the dried product with 12 ml. of boiling chloroform left 0.277 g. (63.4%) of V, m.p. 223.5–225.0° dec. Recrystallization from water afforded a sample of V, m.p. 229.5–231.0° dec., which very slightly depressed the melting point of authentic V,[3] but raised the melting point of the present sample: mixed m.p. 232–234° dec., reported[3] 236.4–236.7° dec., cor.

The chloroform filtrate was evaporated to dryness to give 0.138 g. (39.4%) of crude IV which was extracted with 2 ml. of boiling water, leaving 0.100 g. (28.6%) of IV, m.p. 246–248°. After one recrystallization from acetic acid–water it melted at 248.5–250.0°. No depression in melting point was observed on admixture with authentic IV,[3] reported m.p. 247.1–248.6° dec., cor.

Reaction of II with Silver Nitrate.—A solution of 0.5 *M* silver nitrate (2.9 ml.) was added to 0.502 g. (0.00141 mole) of II in 5 ml. of acetone. After a few minutes a grayish white precipitate appeared, and complete consumption of silver ion was shown by Volhard titration of the supernatant liquor. Subsequent standing of a similar sample in the dark afforded substantially quantitative transformation of the initial precipitate into silver bromide after three hours.

Reaction of III with Sodium Bicarbonate.—A solution of 0.500 g. (0.00134 mole) of III in 25 ml. of acetone and 25 ml. of 0.25 *M* sodium bicarbonate was refluxed overnight. The acidified reaction mixture was evaporated to a volume of about 5 ml. and then was cooled. The precipitated white solid was washed with three 10-ml. portions of water leaving 0.266 g. (80.0%) of IV, m.p. 246–249° dec., which was recrystallized once from acetic acid–water, m.p. 249.5–

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[20] E. D. Hughes and C. K. Ingold, *Trans. Faraday Soc.*, **37**, 663 (1941).

[21] M. L. Dhar, E. D. Hughes, C. K. Ingold, A. M. M. Mandour, G. A. Mau and L. I. Woolf, *J. Chem. Soc.*, **2093** (1948).

[22] W. R. Vaughan and R. L. Craven, unpublished research.

[23] Melting points are uncorrected.

250.8° dec. No depression in melting point was observed on admixture with authentic IV.

The aqueous extracts were evaporated in a cold air stream to leave an amorphous, light brown solid, which was taken up in nitromethane, treated with Norit and allowed to crystallize. A total of 0.029 g. (7.0%) of VI, which melted at 195.5–197.5° dec. (first crop), and on being mixed with authentic VI[3] (201.8–202.4° dec., cor.) the sample melted at 198.0–199.5° dec.

Kinetic Study of the Reactions of II and III with Sodium Bicarbonate.—All runs were made by dissolving and diluting to 50 ml., 1.000 g. of either II or III in acetone. The resulting solution was divided into 5.0-ml. portions which were placed in a constant temperature bath until temperature equilibrium had been reached. The reaction was started by adding 5 ml. of 0.25 *M* sodium bicarbonate. Quenching was effected by adding 25 ml. of 1.14 *M* nitric acid after the appropriate time interval. The reaction mixture was extracted twice with 10- and 5-ml. portions of chloroform, respectively, and the combined chloroform extracts were washed with two 5-ml. portions of 1.14 *M* nitric acid which were then added to the original aqueous solution. Bromide ion was then determined by titration with silver nitrate using the Volhard method. Blank determinations showed no bromide ion to be present. Data are summarized in Table I.

Effect of Change in *p*H on the Hydrolysis of II.—Runs similar to the preceding were made on II using as the alkaline initiator 5 ml. of a mixture which was 0.125 *M* in sodium bicarbonate and 0.125 *M* in sodium carbonate. In addition the change in apparent *p*H as the reaction proceeded was followed by means of a Beckman model H-2 *p*H meter. For this purpose a sample of 0.500 g. of II (0.00141 mole) in 25 ml. of acetone was used with 25 ml. of the alkaline initiator (see Figs. 1 and 2).

ANN ARBOR, MICHIGAN

[CONTRIBUTION FROM THE CHEMICAL AND BIOLOGICAL RESEARCH SECTION, LEDERLE LABORATORIES DIVISION, AMERICAN CYANAMID COMPANY]

$\Delta^{5,7}$-Steroids. XVII.[1] Steroidal Cyclic Ketals. IX.[2] Transformation Products of Reichstein's Substance S

BY ROSE ANTONUCCI, SEYMOUR BERNSTEIN AND ROBERT H. LENHARD

RECEIVED JANUARY 11, 1954

Reichstein's Substance S (I) on reaction with ethylene glycol (benzene, *p*-toluenesulfonic acid) was converted into Δ^{5}-pregnene-17α,21-diol-3,20-dione 3,20-bisethylene ketal (IIa). The 21-acetate (IIb) of the latter on allylic bromination followed by dehydrobromination gave $\Delta^{5,7}$-pregnadiene-17α,21-diol-3,20-dione 21-acetate 3,20-bisethylene ketal (IIIb). This intermediate, in turn, was transformed into $\Delta^{4,7}$-pregnadiene-17α,21-diol-3,20-dione 21-acetate 20-ethylene ketal (IV), $\Delta^{4,7}$-pregnadiene-17α,21-diol-3,20-dione (Va), Δ^{7}-allopregnene-17α,21-diol-3,20-dione (VIII), and $\Delta^{5,7,9(11)}$-pregnatriene-17α,21-diol-3,20-dione 21-acetate 3,20-bisethylene ketal (VII). The latter readily formed a maleic anhydride adduct product (IX).

In this paper we wish to report on the application of certain transformations developed in this Laboratory[1,3] on the important Reichstein's Substance S (I) in which the C3 and 20 carbonyl groups are protected as ethylene ketals.

In a previous publication,[3c] it was shown that Reichstein's Substance S acetate on treatment with ethylene glycol (benzene, *p*-toluenesulfonic acid) afforded the C3-mono-ethylene ketal, Δ^{5}-pregnene-17α,21-diol-3,20-dione 21-acetate 3-ethylene ketal. The condensation of the C20-carbonyl group with ethylene glycol was prevented by the 21-acetate group. A similar finding was observed with desoxycorticosterone acetate[3b] and cortisone acetate.[3c] Moreover, cortisone was converted into its 3,20-bisketal.[3c] Accordingly, Reichstein's Substance S (I) also has now been converted into the 3,20-bisketal (IIa). Acetylation with acetic anhydride–pyridine gave the 21-acetate (IIb). Bromination of IIb with N-bromosuccinimide (NBS) followed by dehydrobromination with *s*-collidine in xylene produced the $\Delta^{5,7}$-diene (IIIb). The 17α,21-diol (IIIa) was obtained on alkaline hydrolysis.

A number of transformations were then carried out with the intermediate, $\Delta^{5,7}$-pregnadiene-17α,21-diol-3,20-dione 21-acetate 3,20-bisethylene ketal (IIIb): *i.e.*, hydrolysis, hydrogenation and dehydrogenation.

Treatment of IIIb with aqueous acetic acid selectively hydrolyzed the C3-ketal group, and $\Delta^{4,7}$-pregnadiene-17α,21-diol-3,20-dione 21-acetate 20-ethylene ketal (IV) was obtained. However, hydrolysis with sulfuric acid–methanol removed both of the ketal groups to afford $\Delta^{4,7}$-pregnadiene-17α,-21-diol-3,20-dione (Va). The 21-acetate (Vb) was obtained by acetylation with acetic anhydride–pyridine.

Hydrogenation of IIIb in alcohol–ethyl acetate or ether–alcohol with W2 Raney nickel catalyst gave Δ^{7}-allopregnene-17α,21-diol-3,20-dione 21-acetate 3,20-bisethylene ketal (VIb). Alkaline hydrolysis removed the C21-acetate group, and VIa was obtained. Hydrolysis of the latter with sulfuric acid–methanol gave Δ^{7}-allopregnene-17α,21-diol-3,20-dione (VIII).

Mercuric acetate dehydrogenation converted IIIb into the $\Delta^{5,7,9(11)}$-acetate bisketal (VII). The latter readily formed a maleic anhydride adduct product.

The structures of the various new compounds described above were supported by the following considerations, other than elemental and infrared spectral analyses, and methods of synthesis.

$\Delta^{5,7}$-Pregnadiene-17α,21-diol-3,20-dione 3,20-bisethylene ketal (IIIa), and its acetate (IIIb) showed the characteristic ultraviolet absorption maxima of a $\Delta^{5,7}$-steroid, namely at 271, 281.5 and 293 mμ.[4] In

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[1] Paper XVI, S. Bernstein, R. Littell and J. H. Williams, *J. Org. Chem.*, **18**, 1418 (1953).

[2] Paper VIII, S. Bernstein, R. Littell and J. H. Williams, THIS JOURNAL, **75**, 4830 (1953).

[3] (a) R. Antonucci, S. Bernstein, R. Littell, K. J. Sax and J. H. Williams, *J. Org. Chem.*, **17**, 1341 (1952); (b) R. Antonucci, S. Bernstein, R. Lenhard, K. J. Sax and J. H. Williams, *ibid.*, **17**, 1369 (1952); (c) R. Antonucci, S. Bernstein, M. Heller, R. Lenhard, R. Littell and J. H. Williams, *ibid.*, **18**, 70 (1953).

[4] W. Huber, G. W. Ewing and J. Kriger, THIS JOURNAL, **67**, 609 (1945); see also, S. Bernstein, L. Binovi, L. Dorfman, K. J. Sax and Y. SubbaRow, *J. Org. Chem.*, **14**, 433 (1949); and R. Antonucci, S. Bernstein, D. Giancola and K. J. Sax, *ibid.*, **16**, 1126 (1951).