Direct Observation of Reaction Intermediates in Debromodecarboxylation Reactions

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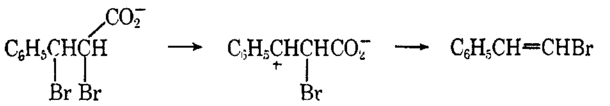
Solvolysis of citraconic acid hydrobromide leads to the formation of a well-defined intermediate which has the properties of a β-lactone. The eventual product is methacrylic acid. The solvolysis of citraconic acid dibromide is very complex, but again involves a β-lactone, and leads to a variety of products including acetone. The lactone resulting from addition of bromine to citraconic acid had a similar spectrum and similar properties as the solvolysis intermediate. A time study of the solvolysis is given which is characteristic of a series of consecutive reactions. Solvolysis of mesaconic acid dibromide exhibits no discernible intermediate. Solvolysis of itaconic acid derivatives lead to five-membered lactones.

Several reaction pathways are open to β-bromocarboxylate anions. The reaction may involve a simple substitution of a solvent fragment for the leaving group. In other systems a dehydrohalogenation is observed. The most striking possibility is debromodecarboxylation, a reaction first observed in the 1870's. This reaction is of considerable utility in preparing pure *cis*- or *trans*-alkenes. Bachman and Farrell[1] have discussed the structural factors in the substrate that favor debromodecarboxylation over the other reaction pathways.

Two main pathways have been postulated for the debromodecarboxylation of 2,3-dibromo-3-phenylpropionate anions.[2-5] One pathway, a stereospecific "E2-like" process yields olefin by a concerted elimination of carbon dioxide and bromine (eq 1).

$$\mathrm{C_6H_5\underset{Br}{CH}\underset{Br}{\overset{CO_2^-}{CH}}} \longrightarrow \mathrm{C_6H_5CH{=}CHBr} \qquad (1)$$

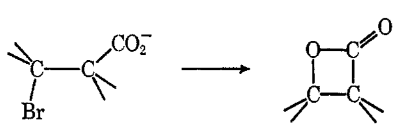
The second pathway is a stereoselective, stepwise "E1-like" process[2-5] (eq 2), which bears some similarity to the acid-catalyzed decarboxylation of substituted cinnamic acids[6] (eq 3).



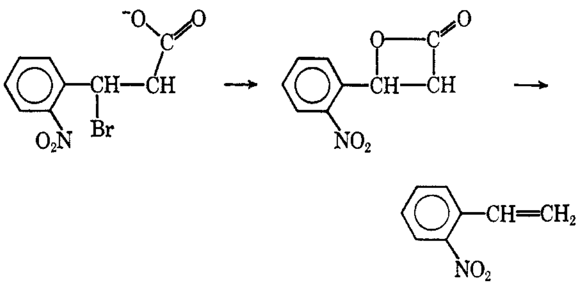
$$\mathrm{C_6H_5\underset{Br}{CH}\underset{Br}{\overset{CO_2^-}{CH}}} \longrightarrow \mathrm{C_6H_5\underset{+}{CH}\underset{Br}{CH}CO_2^-} \longrightarrow \mathrm{C_6H_5CH{=}CHBr} \qquad (2)$$

$$\mathrm{Ar_2C{=}CHCO_2H} \longrightarrow \mathrm{Ar_2\overset{+}{C}CH_2CO_2H} \longrightarrow \mathrm{Ar_2C{=}CH_2} \qquad (3)$$

A second possibility for the reaction of β-bromocarboxylates is solvolysis with neighboring-group participation to form a β-lactone (eq 4).[7]



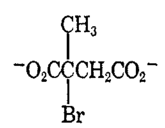
Older workers in fact considered such a ring closure to precede decarboxylation.[8] This idea was supported by the isolation of an intermediate[9-11] from the reaction of β-bromocarboxylate systems (eq 5). This intermediate or side product did not contain bromine and readily decarboxylated to yield olefins. Later Staudinger[12] showed authentic β-lactones were capable of decarboxylation. More recently Noyce and Banitt showed the decarboxylation of β-lactones was stereospecific.[13]



(5)

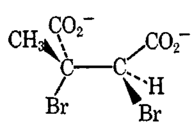
In other cases, epoxide products resulting from reaction of certain β-bromocarboxylate systems were interpreted in terms of a β-lactone intermediate.[3]

In considering a given system it is still not clear if mechanisms as in eq 1 and 2 apply or if ring closure occurs to give a lactone intermediate which subsequently decarboxylates.[14,15] It seems likely that a β-lactone would decompose by a zwitterionic route,[13,15] and the stereochemistry of this process is a question of great interest.[13]



$$\mathrm{{}^-O_2C\underset{Br}{\overset{CH_3}{C}}CH_2CO_2^-}$$

1



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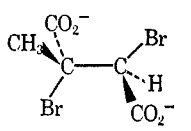

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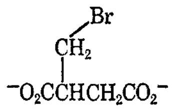
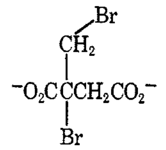


$$\mathrm{{}^-O_2C\overset{CH_2Br}{CH}CH_2CO_2^-}$$

4



$$\mathrm{{}^-O_2C\underset{Br}{\overset{CH_2Br}{C}}CH_2CO_2^-}$$

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The present study involves five substrates, citraconic acid hydrobromide (**1**), citraconic acid dibromide (**2**),

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[1] (a) G. B. Bachman, *J. Amer. Chem. Soc.*, **55**, 4779 (1933); (b) J. Farrell and G. B. Bachman, *ibid.*, **57**, 1281 (1935).

[2] (a) E. Grovenstein and D. Lee, *ibid.*, **75**, 2639 (1953); (b) **77**, 3795 (1955).

[3] (a) S. Cristol and W. Norris, *ibid.*, **75**, 632 (1953); (b) **75**, 2645 (1953).

[4] E. Trumbull, T. Finn, K. Ibne-Rasa, and C. Sauers, *J. Org. Chem.*, **27**, 2339 (1962).

[5] J. F. Bunnett, *Angew. Chem. Intern. Ed. Engl.*, **1**, 225 (1962).

[6] (a) W. S. Johnson and W. Heinz, *J. Amer. Chem. Soc.*, **71**, 2913 (1949); (b) D. S. Noyce, S. Brauman, and F. Kirby, *ibid.*, **87**, 4335 (1965).

[7] (a) J. F. Lane and H. Heine, *ibid.*, **73**, 1348 (1951); (b) E. P. Kohler, and R. Kimball, *ibid.*, **56**, 729 (1934).

[8] R. Fittig and F. Binder, *Ann. Chem.*, **195**, 131 (1897).

[9] A. Einhorn, *Chem. Ber.*, **16**, 2208 (1883).

[10] A. Basler, *ibid.*, **16**, 3001 (1883).

[11] H. Erlenmeyer, *ibid.*, **13**, 303 (1880).

[12] H. Staudinger, *ibid.*, **41**, 1355 (1908).

[13] D. S. Noyce and E. H. Banitt, *J. Org. Chem.*, **31**, 4043 (1966).

[14] H. E. Zaugg, *Org. Reactions*, **8**, 305 (1954).

[15] (a) H. T. Liang and P. D. Bartlett, *J. Amer. Chem. Soc.*, **80**, 3585 (1958); (b) T. L. Gresham, *ibid.*, **76**, 486 (1954), and many related papers.

mesaconic acid dibromide (**3**), itaconic acid hydrobromide (**4**), and itaconic acid dibromide (**5**). The rates of solvolysis of these substrates in their dianion form was studied. In other experiments the course of the solvolysis was monitored by nmr in an effort to observe reaction intermediates.[16,17]

Results and Discussion

Rates of Halide Ion Formation.—The rates of halide ion formation are given in Table I for substrates **1–5** (dianions).[18] Certain activation parameters are also listed. The extreme rapidity of solvolysis of **1** and **4** prevented studies at higher temperatures than 30.1°. The rate solutions were made up to 0.10 ± 0.01 *M* in sodium acetate in an effort to ensure the substrate salts remained predominately in the dianion form. Reactions of these substrates as the monoanion and free acids were approximately 10 and 100 times slower, respectively (**3**, however, was less sensitive to its anionic state).

The relative rates were in the order **4** > **1** > **5** > **2** > **3**. The most reactive material itaconic acid hydrobromide (**4**) was *ca.* 1800 times more reactive than mesaconic dibromide, **3**. In general the monobromides **4** and **1** were substantially more reactive than the dibromides.

The activation parameters are of interest in that **2**, **3**, and **5** show positive entropies. Lane and Heine[7] found positive activation entropies in reactions considered to involve neighboring group participation by carboxylate.

Table I

Rates of Halide Formation by Substrates 1–5 in Water

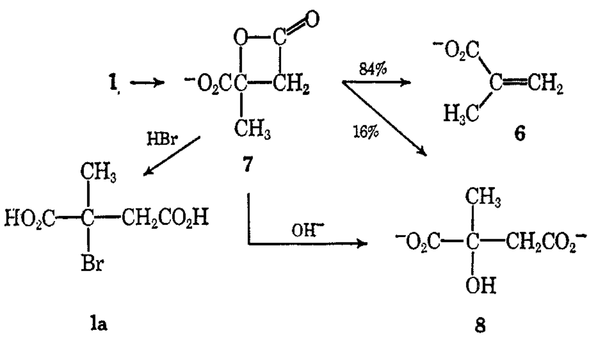
Substrate 1	k_{obsd},[a] sec^{-1} 30.1°	50.1°	k_{rel}	ΔH^*, kcal/mol	ΔS^*, eu
1	$1.5 \pm 0.1 \times 10^{-3}$		250		
2	$3.5 \pm 0.1 \times 10^{-4}$	$5.7 \pm 0.2 \times 10^{-3}$	59	26 ± 1	12 ± 3
3		$9.7 \pm 0.3 \times 10^{-5}$	1	28 ± 1	11 ± 3
4	$1.1 \pm 0.3 \times 10^{-2}$		1800		
5	$3.9 \pm 0.1 \times 10^{-4}$	$5.6 \pm 0.1 \times 10^{-3}$	64	26 ± 1	10 ± 4

[a] No correction was made for the number of bromines which react. For **2** the observed rate is that of loss of one bromide; for **3** and **5** the rate reflects loss of both bromides.

Reaction Products from 1.—In the reaction of citraconic acid hydrobromide (**1**), Fittig and coworkers reported the major product to be methacrylic acid (**6**), which was confirmed in this study. However observation of the course of the reaction by nmr in deuterium oxide showed that an intermediate **7** builds up to high concentration during the period of bromide ion formation. Upon heating, the resonance absorption of the intermediate disappeared, carbon dioxide was emitted in large quantities and the spectrum of methacrylic acid appeared. If the intermediate **7** were treated with excess base, the spectrum of citramalic acid (**8**) appeared, very similar to that of authentic material. When treated with large quantities of bromide ion, little change in the concentration of the intermediate **7** was observed. However when trifluoroacetic acid (plus bromide ion) was added, the spectrum of starting material reappeared.

The decarboxylation of intermediate **7** to form **6** took place smoothly when bromide had been removed with silver. These reactions are summarized in Scheme I, and the pertinent nmr data are given in the Experimental Section. These reactions are consistent with a β-lactone intermediate. The point of interest here is that the decarboxylation step involves the intermediate **7** itself.[19] It does not seem likely that **7** reverts to **1** which subsequently debromocarboxylates by a concerted mechanism.

Scheme I



Reaction Products from 2.—The solvolysis of citraconic dibromide (**2**) is a complex reaction of which only the major sequences can be identified. Fittig and coworkers[20] reported propionaldehyde and bromomethacrylic acid (**9**) as the major products. The nmr results of this study in deuterium oxide confirm **9** as well as its isomer **10** which is formed in part from **9** as the reaction progresses. In our hands acetone (**11**) was apparent, but no propionaldehyde, *per se*, although some small rather diffuse resonance absorptions appeared late in the reaction, possibly owing to decomposition products of propionaldehyde. Similar absorptions were noted when authentic propionaldehyde was allowed to stand in the reaction mixture. Mass balance determinations showed that *ca.* 93% of the original starting material could be accounted for by well-defined products discussed below neglecting possible deuteration of the acetone. It was not possible to isolate propionaldehyde from the runs at 30.1°. However in an attempt to duplicate Fittig's reaction conditions, at *ca.* 80° and using nitrogen to sweep out volatile products, propionaldehyde was indeed obtained in small yield.

In the solvolysis of **2** the kinetic runs showed that the two substrate bromines are lost at markedly different rates. During the period of the first equivalent of bromide ion formation, the starting material resonance absorption decreases monotonically and is replaced in large part by an intermediate, **12** (methyl δ 1.82, methine δ 5.65), plus some of the unsaturated acid **9**. Figure 1 shows a time study of the concentrations of starting material, the intermediate, and the various products. Figure 2 shows a partial nmr spectrum of a typical run in which the major absorptions are identified as shown in Scheme II. The time study of Figure 1 is fairly typical of an A → B → C, D . . . set of consecutive

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[16] R. S. Bly, R. K. Bly, A. Bedenbaugh, and O. Vail, *J. Amer. Chem. Soc.*, **89**, 880 (1967).

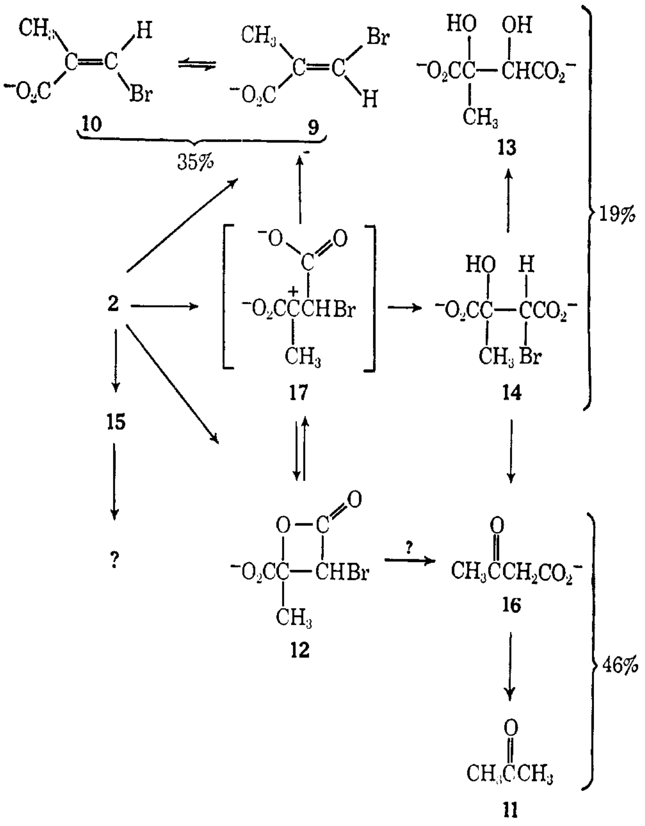
[17] In related systems the presence of an intermediate has been inferred from kinetic evidence, H. Johannson, *Chem. Ber.*, **48**, 1262 (1915), and stereochemical evidence, B. Holmberg, *Svensk Kem. Tidskr.*, **30**, 215 (1918), or by isolation.[7b]

[18] For earlier kinetic studies on **5** see B. Holmberg, *ibid.*, **30**, 190 (1918).

[19] A concerted decarboxylation of a β-lactone is considered unlikely by some workers since this would not be thermally allowed: R. Hoffman and R. B. Woodward, *J. Amer. Chem. Soc.*, **84**, 2046 (1965). A zwitterionic mechanism (ref 15) would be more probable.

[20] R. Fittig and P. Krausemark, *Ann. Chem.*, **206**, 7 (1880); R. Fittig and B. Landolt, *ibid.*, **188**, 77 (1877).

SCHEME II



reactions. A second intermediate **15** is also apparent in low concentration compared to **12**. Due to its low level, it was not possible to determine the eventual fate of **15**.

A group of two products or intermediates **13** and **14** is apparent in rather low yield (19%) at δ 1.3–1.5. The former is also the eventual product of solvolysis of the free acid of **2** and is assigned the diol structure as shown in Scheme II. The latter could be produced by NBS bromination of citraconic acid in aqueous solution or by the base-catalyzed cleavage of **12** and is assigned the bromohydrin structure. The bromohydrin **14** (methyl δ 1.32, eventually reacts to form **13** (methyl δ 1.36), and acetoacetic acid **16** in somewhat variable ratios depending upon pH. The acetoacetic acid **16** in turn slowly produces acetone. The decomposition is faster if the reaction mixture is acidified.

It is clear, however, that the precursor of some of the unsaturated acid **9** and most of the acetoacetic acid **16** is the intermediate **12**. Thus when starting material is nearly gone, **12** reaches a maximum of *ca.* 40% of total material present (at this point **9** is 16% and **16** is 25% of the total). As **12** disappears, **9** plus **10** increase to 35% and **11** plus **16** increase to *ca.* 46% of the total.

In a separate run using excess potassium carbonate (pH *ca.* 8.5), the intermediates **12** and **15** were not apparent. It seems likely that the lactone is rapidly cleaved by base or else it does not form. Under these conditions, the concentration of the diol product **13** is larger (22%) and that of **9** is less (21%) than in runs of neutral pH (**16** was the same (47%)). Thus in these basic solutions the capture of the carbonium ion by solvent, **17** → **14**, is more probable than the decarboxylation reaction **17** → **9**. However the fact that **9** still occurs in substantial yield is suggestive that **9** may be formed in part from other pathways. The direct debromodecarboxylation **2** → **9** is one possibility.[3]

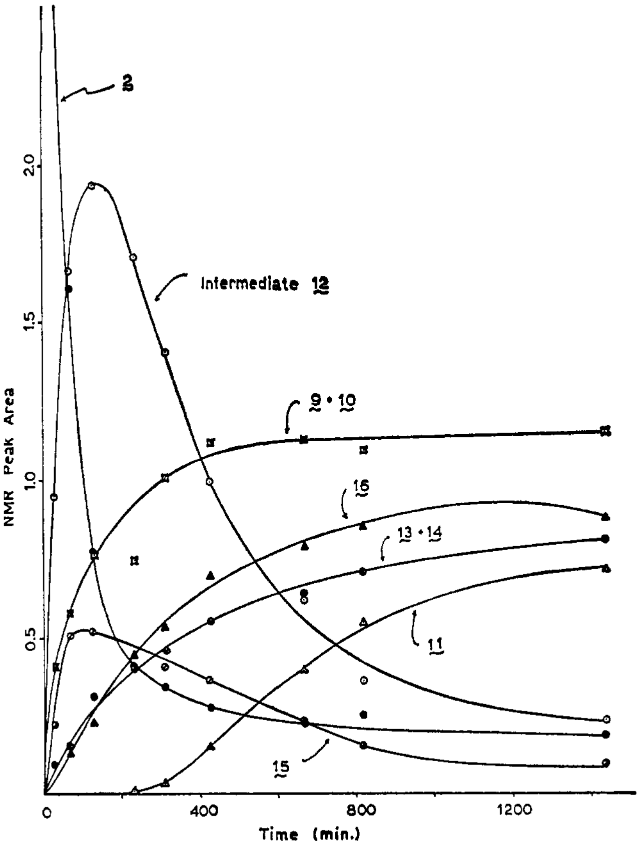


Figure 1.—Time study of the reaction of **2** in D_2O, *ca.* 25°. The nmr peak intensities were determined relative to $(CH_3)_4NBr$.

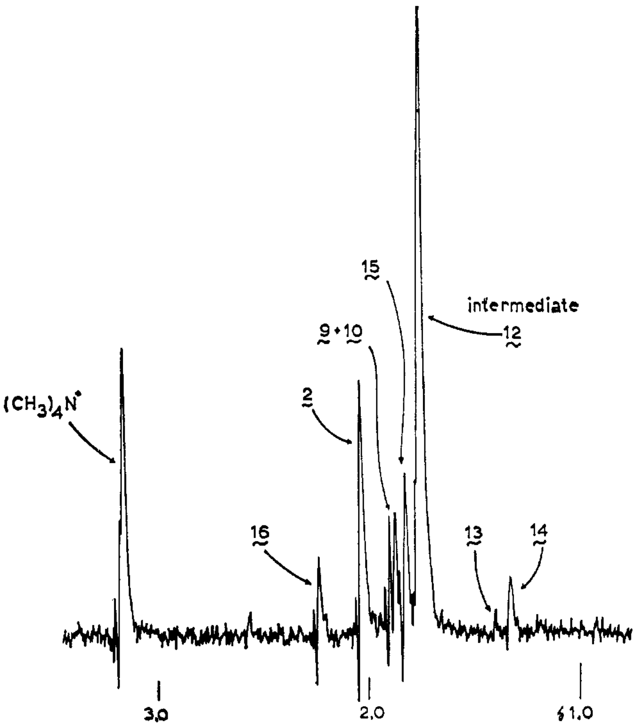


Figure 2.—Partial nmr spectrum of the solvolysis of **2**. Time is 130 min after dissolution.

It was possible to produce **12** by another pathway. Addition of bromine[21] to a cold, neutral aqueous solu-

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[21] D. S. Tarbell and P. D. Bartlett, *J. Amer. Chem. Soc.*, **59**, 402 (1937).

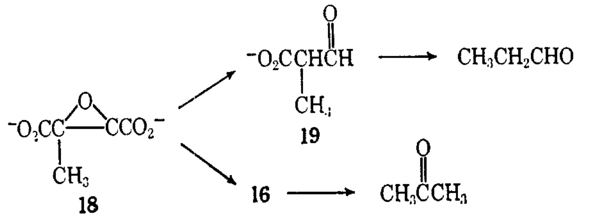
tion of citraconic acid produced a material with a nmr spectrum very similar to **12**. The subsequent reactions of this material were similar to **12**, yielding **9** (40%), **13** plus **14** (6%), and **16** (54%).

In an attempt to isolate intermediate **12**, the solution was acidified to pH 2 with HBr. An oil separated which was mainly **2**. Some **12** remained however, whose infrared spectrum showed an absorption at 1860 cm^{-1}, consistent with its formulation as a β-lactone.[13]

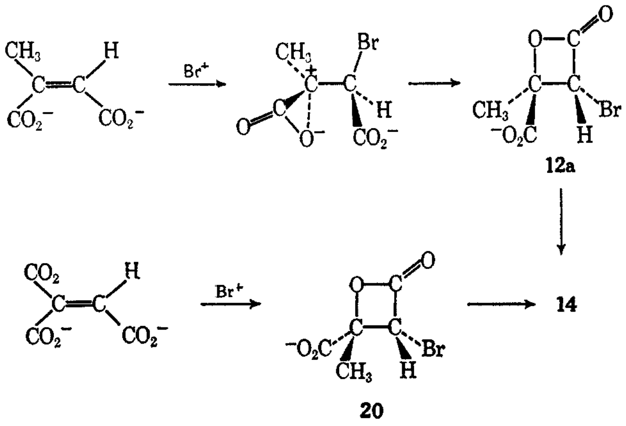
Reaction Products from 3.—The kinetic runs on mesaconic dibromide (**3**) showed that both equivalents of halogen appeared at essentially the same rate. Accordingly the reaction at 30.1° as monitored by nmr showed no intermediate corresponding to **12** in any sizable concentrations. Unfortunately in these runs several small, rather diffuse resonance absorptions appeared at *ca.* δ 0.8–1.3, and accurate product ratios could not be determined. Mass balance determinations were poor (*ca.* 70%) if these diffuse peaks were neglected. In the low temperature runs **9** and **10** amounted to *ca.* 30%; **16** and **11**, *ca.* 25%; and **13** and **14**, *ca.* 10% of the total.

In runs of 75°, the unsaturated acids **9** and **10** amounted to *ca.* 70% of the total. Thus the increase in temperature produced a considerable change in the character of the products.

In the reaction of **3** Fittig and coworkers again reported propionaldehyde, which was verified in cases in which nitrogen was used to sweep out this product. One possible explanation for the production of propionaldehyde as well as acetone centers around a possible epoxide intermediate, **18**. One mode of cleavage of the oxirane ring would yield **19** and eventually propionaldehyde. The other mode of cleavage would produce acetone.



This epoxide was apparent in the low temperature reactions in a maximum yield of 7%. The same material (δ 1.51) as **18** was produced by base-catalyzed ring closure on the bromohydrin **14**.

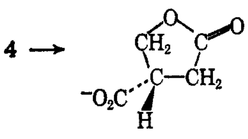


Although a β-lactone was not observed in the solvolysis of **3**, this material **20** (methyl δ 1.74, methine δ 5.57) could be produced by addition of bromine to mesaconic acid. The yield in this case was rather poor (26%), and a plethora of other products included **9**, **10**, **16**, **13**, and mainly **14**. The subsequent reactions of **20** again produced more of these same materials. It is interesting however that both the lactone from citraconic acid (**12**) and the lactone **20** form the same bromohydrin **14** upon hydrolysis, somewhat similar to the results of Tarbell and Bartlett.[21]

Since the lactone **12** can be made from and can be cleaved to citraconic dibromide (**2**), it is assigned the structure **12a**. A tentative structure for **20** is given.

The mode of addition of Br^+ and carboxylate to yield **12a** and **20** is rather unusual, amounting to an over-all *cis* addition. It is felt that participation by the α-carboxyate stabilizes the carbonium ion and allows internal rotation to occur. The β-carboxylate then closes the lactone ring from the same side of the molecule as the original bromine attack.

Reaction Products from 4.—The solvolysis of itaconic acid hydrobromide was a comparatively simple process. The reaction of the "monoanion" was followed instead of the dianion owing to the extreme rapidity of reaction of the latter. Paraconic acid[20] (**21**) appeared to be the sole product. The nonequivalent methylenes of **4** (*ca.* δ 2.70 and 3.7) changed smoothly to the absorptions of product (*ca.* δ 2.9 and 4.6).



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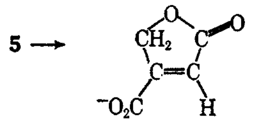
Reaction Products from 5.—The solvolysis of itaconic acid dibromide (**5**) also was straightforward. The only observable product was the unsaturated lactone, aconic acid (**22**) (methylene δ 5.11, vinyl δ 6.42). It was not possible to tell by nmr experiments if ring closure preceded dehydrohalogenation or if the reverse was true.



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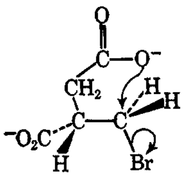
It is clear, however, that debromodecarboxylation does not compete with closure to the stable five-ring lactone.

Since both **4** and **5** have similar structures and both give five-membered lactones, it is interesting to speculate on the *ca.* 30-fold greater reactivity of the monobromide. Part of the slowness of **5** may be due to the electron-withdrawing character of the second bromine. More important are the steric interactions involved. In the transition state the leaving group is *gauche* to both a carboxylate and a bromine, a sterically unfavorable situation. The dianion of **4** has no difficulty in approaching the transition state.



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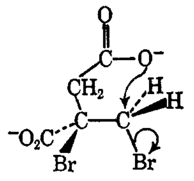

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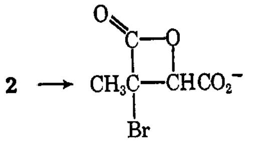
Other Comments.—The solvent isotope effects were measured for the five substrates; k_{H_2O}/k_{D_2O} for **1**, 1.2; **2**, 1.2; **3**, 1.3; **4**, 1.1; **5**, 1.2. These values may be compared to the values from solvolysis of *t*-butyl chloride in water (1.3–1.5) and methyl bromide (1.1–1.2).[22,23] Thus the solvent isotope effect for substrates that form well-defined lactone products is very similar to that of substrates thought to form lactone intermediates but eventually yield other products.

In conclusion the evidence seems quite strong that a β-lactone is a true intermediate in the debromodecarboxylation of **1** and **2**, but probably not of **3**.

In the reactions of **2** it is interesting to note that the lactone closes at the tertiary center to form **12** rather than at the secondary center, which would form **23** (however, **23** and **15** may be the same, but **15** is a minor product). Although a direct displacement of bromide by carboxylate is possible, the sequence most likely involves the carbonium ion **17**. The reactions of **17** appear to be highly stereoselective in that usually just one of two possible stereoisomers is formed.[13] The zwitterion **17** must be a tight internal ion pair.[13]



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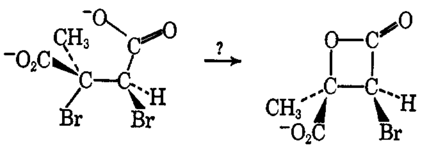
The *ca.* 60-fold greater reactivity of **2** over **3** deserves additional comment. In part this difference is due to the greater thermodynamic stability of **3** ground state. In the solvolysis of the free acids of **2** and **3**, which very likely go by similar mechanisms, **2** is *ca.* sevenfold more reactive. This latter ratio parallels the differences observed with many *erythro–threo* pairs of diastereomers.

In addition to the rather small difference in the solvent isotope effect, other differences between **2** and **3** are thought to reflect a fundamental difference in solvolysis mechanism. The solvent dimethyl sulfoxide (DMSO) has been shown to increase the rates of reactions that involve assistance by carboxylate.[24] Going from water to a solution of 60% DMSO–40% water involves a 15-fold rate increase for **2**, a 12-fold increase for **5** and a fivefold increase for **3**. The addition of ion-pairing cations such as calcium diminish the rate of reaction where carboxylate participation is important. Again the rates of **2** and **5** are rather strongly diminished. The relative ratios of rates of reaction in the absence and presence of 0.16 *M* calcium nitrate are 0.7 for **2** and 0.6 for **5**. On the other hand, **3** shows >0.8 rate ratio (at 70° rather than at 50° for **2** and **5**).

In toto, the *threo* substrate **2** appears rather more sensitive to the state of the carboxylate than does the *erythro* isomer **3**. It does not seem likely that **2** reacts by a direct S_N2-like displacement of bromide by carboxylate. If a S_N2 were in evidence **23** would very likely result rather than the tertiary product **12**. More likely the reaction is an ionization in which the separation of the bromide is materially assisted by a properly oriented β-carboxylate, although a full covalent carbon–oxygen bond is not present.

In the basic aqueous solution the solvated carboxylates are probably very large groups. The conformation needed for assistance by the β-carboxylate in **3** is destabilized by having both carboxylates *gauche* to other sizable groups.



3　　**20**

Furthermore if the substrate **3** did close to the lactone **20** (for which no evidence exists in the solvolysis) the lactone **20** would be destabilized by the carboxylate–bromine interaction (compare the relative stabilities of **9** and **10**).

The substrate **3** may react by other pathways than β-carboxylate participation. A bromonium ion structure is a strong possibility.

Experimental Section

Materials were produced as follows. The starting material **2** and **3** were prepared by Vaughan and Milton's procedure,[25] the procedure of Fittig being worthless.[20] The materials **2** and **3** exhibited melting points of 151–152°, respectively. The material **1** was prepared by the procedure of Fittig and Landolt,[20] mp 143–145° (lit. mp 140°). This material had a slight impurity that was not removed under repeated recrystallization. The resonance absorptions of the impurity occurred at 1.41 and 1.28 ppm and did not change in the course of the hydrolysis.

The substrate itaconic acid dibromide (**4**) was prepared by addition of bromine to itaconic acid, mp 166–168°, and itaconic acid hydrobromide was prepared by the method of Ingold, *et al.*, mp 134–136° (lit. mp 137°).[26]

The nmr product studies were run by dissolving *ca.* 200 mg of substrate in 0.7 ml of deuterium oxide (Columbia Chemical Co.) with *ca.* 10 mg of tetramethylammonium bromide as a standard (the chemical shift was taken as 191 cps). The faster runs were run at probe temperature, *ca.* 35°. The slower runs were stored in a constant temperature bath at 30.1° between readings. Readings were taken on a Varian A-60 instrument. The tubes were usually shaken with CCl_4, the layers were separated, and the organic layer was checked for propionaldehyde (never found).

Product studies were attempted by isolation of the product acids, esterification by diazomethane or by the Fisher procedure, and analysis by vpc. In general these results were not regarded as trustworthy. Apparently some decomposition occurred in the evaporation of the water or in the esterification, particularly in the case of **1**.

The data for a typical nmr run follow. The substrate **1**, 0.150 g, was placed in a small vial and mixed with 0.161 g of lithium bromide, 0.014 g of tetramethylammonium bromide, 0.1045 g of potassium carbonate, and *ca.* 1.0 ml of deuterium oxide. The tetramethylammonium bromide was used as an internal standard, whose integral was compared to the substrate and product integrals. The pH was adjusted to *ca.* 7, and the solution scanned. The starting material absorption (methyl at 2.07 ppm and methylene at 3.19 ppm) changed smoothly to that of the intermediate (1.92 and 3.72 ppm, respectively, ratio 2:1). The change was essentially complete in 90 min. Similar to the run without LiBr only a small amount of olefin was evident at the end of this period. The solution was divided; part was heated on a steam bath for *ca.* 30 min. The spectrum of methacrylic acid (**6**) appeared, very similar to the literature spectrum.[27] The final solution showed 84% **6** and 16% **8**. The remainder of the solution was treated with trifluoroacetic acid to give a solution pH 1. The spectrum of starting material free acid reappeared (methyl, 2.02; nonequivalent methylene, *ca.* 3.34 ppm).

In another experiment, the preformed intermediate was treated

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with base. The spectrum of citramalic acid (**8**) appeared which also was evident in the previous run in small amounts (methyl, 1.48; nonequivalent methylene, 2.41, 2.77 ppm). This spectrum was very similar to that of authentic material (Aldrich).

Product Identification Runs.—Citraconic acid (0.302 g) plus potassium carbonate (320 mg) was heated briefly in deuterium oxide (1.0 ml) plus 10 mg of tetramethylammonium bromide. Bromine was added in small amounts with intermittent cooling. An aliquot was taken and checked by nmr which showed the absorptions of **12**, δ 1.74, 5.71 (53%); unreacted starting material, (21%); **9** and **10** δ *ca.* 1.92 (16%), **13** and **14**, δ 1.38 and 1.31, respectively (10%). The spectrum was rerun at intervals, eventually forming **9** and **10** (38%), **13** and **14** (12%), and **16** (28%).

In another run on large scale the intermediate **12** was carefully treated with HCl in the cold, to pH 2. An oil slowly separated (*ca.* 3.5 g from 10 g of starting material). The infrared spectrum showed a strong absorption at 1860 cm^{-1} plus the carboxylic absorption at 1720 (broad). The nmr of this material showed the material to be 25% of the lactone **12**, 30% **9**, and 45% of a material very similar to **2**. If HBr were used for acidification, the latter gave a spectrum identical with authentic **2**.

In another run, the lactone **12** was formed similarly, then treated with excess potassium carbonate. The spectrum of **12** diminished rapidly and was replaced by the bromohydrin **14** and acetocetic acid (**16**), δ 2.25 (three protons) and 3.47 (two protons). The final solution showed 30% **14**, 13% **13**, and 26% **10**. This solution was basified with potassium hydroxide to pH 13. The bromohydrin changed in large part to **16**, but a new peak appeared δ 1.58, believed to be the epoxide **18**.

The bromohydrin **14** was also produced by treatment of citraconic acid (10.0 g) with N-bromosuccinimide (14.4 g) stirred in 20 ml of H_2O overnight with 0.1 ml of sulfuric acid. The aqueous solution was mixed with 20 g of ammonium chloride and repeatedly extracted with ether. The organic layers were dried over $MgSO_4$, evaporated, and checked by nmr. The product, 5.0 g, was *ca.* 70% **9** and 30% **14**.

Mesaconic acid (320 mg) was treated with potassium carbonate in deuterium oxide until the pH was *ca.* 6.5. Bromine was added dropwise with intermittent cooling. The nmr showed the following absorptions, in addition to **20** (20%), **14** (17%), **13** (8%), unidentified peak δ 1.66 (4%), unreacted mesaconic (11%), unidentified peak δ 2.08 (4%), and **16** (12%) were produced.

Upon acidification with hydrobromic acid **20** rather slowly formed **14**, then **13**. No more than a small quantity of **3** was formed, by comparison of spectra before and after addition of authentic **3**.

In another run **20** was formed as before, then treated with potassium carbonate; **14**, **13**, and **16** were again the major products similar to the experiments with **12**.

To check that **12** and **20** produced the same bromohydrin **14**, 1.0 g of citraconic acid and 1.4 g of mesaconic acid were treated with Br_2 in a neutral, aqueous solution, forming **12** and **20**; upon treatment with K_2CO_3 only a single absorption due to **14** and a single absorption due to **13** was apparent in addition to **16**.

To test for propionaldehyde, **2** or **3** (10.0 g) was added to 50 ml of water plus an equimolar amount of potassium carbonate at *ca.* 80° (steam bath). Two traps were used, one filled with ice, the other with Dry Ice–acetone. Nitrogen was passed through the reaction mixture for *ca.* 30 min. The ice trap contents were analyzed by nmr and vpc and showed water and traces of organic material. The Dry Ice trap contents showed about 1 ml of a liquid, mainly water in the case of **2** with about 20% of an equal mixture of acetone and propionaldehyde. In the case of **3** the trapped material (*ca.* 1 ml) showed equal quantities of water and organic material of which there was 60% propionaldehyde and 40% acetone.

The rate solutions were prepared in volumetric flasks to which *ca.* 20 ml of redistilled water, 200 mg of substrate, and the requisite amount of sodium acetate had been added. This mixture was allowed to come to temperature. The rate was begun by addition of a twofold molar equiv of standard sodium hydroxide, which also had been equilibrated. The evolution of bromide was followed by adding 5-ml aliquots to cooled, pretitrated solutions of standard silver nitrate and sodium thiosulfate. The titration was rapidly completed after addition. Rate constants and activation parameters were calculated by standard procedures.[28]

Registry No.—**7**, 16520-64-2; **9**, 16503-84-7; **10**, 16503-85-8; **11**, 67-64-1; **12**, 16503-86-9; **13**, 16503-87-0; **14**, 16520-63-1; **16**, 141-81-1; **18**, 16503-89-2; **20**, 16503-86-9; **21**, 16503-91-6; **22**, 16503-83-6.

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Conformational Preferences in Diastereomers. IV. 1,2,3 Diastereomers

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The four diastereomers of the 1,2-dibromo-1,3-diphenylbutane system and two of the three diastereomers in the 1,2,3-tribromo-1,3-diphenylpropane system are assigned relative configurations on the basis of nmr studies in deuteriochloroform, dipole moment, and stereospecific reaction data. Iodide-catalyzed debrominations proved to be nonstereospecific. The *erythro* dibromide centers in the former system are nearly conformationally pure, whereas the *threo* centers here conformationally mixed. In the latter system the reverse is true. The results are discussed in terms of possible unfavorability of *gauche* bromine interactions. The importance of 1,3 eclipsing interactions is emphasized. The mechanistic implication of the bromination product yields from the isomeric 1,3-diphenylbutenes is discussed in terms of possible bromonium ions.

The use of nuclear magnetic resonance spectra to aid in the assignment of configurations of acyclic molecules has found increasing application in recent years.[1-8] Most frequently use is made of the Karplus relationship[9,10] which suggests that predominantly *trans* vicinal protons will exhibit large coupling constants (J) in the vicinity of 11–13 cps, whereas predominantly *gauche* protons show low J values of *ca.* 1–3 cps.

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