ions.[7] It is therefore reasonable to employ other metals forming distinctive precipitates with 8-quinolinol as indicators in the titration of copper with a standard solution of 8-quinolinol in a manner analogous to the Mohr method for determining halide. The procedure was tried using both iron and aluminum as the indicating ion; with ferric ion the end-point is observed as the appearance of a black color; with aluminum a fluorescence marks the end-point. Results of fair accuracy (Table I) on prepared samples could be obtained after a little practice by both methods. Similar titrations using zinc as a fluorescent indicator were also tried but did not give good results.

TABLE I

MOHR-TYPE TITRATIONS OF COPPER WITH 8-QUINOLINOL

Indicator	Mg. Cu taken	Mg. Cu found	No. of trials
Fe^{+3}	6.58	6.59 ± 0.05	15
Al^{+3}	6.66	6.68 ± .02	20
Zn^{+2}	6.63	6.8 ± .3	10

(7) Mellor and Maley, *Nature*, **159**, 370 (1947).

Acknowledgment.—This work was supported in part by a grant from the Cottrell Research Corporation.

Summary

1. A procedure for the estimation of the relative stabilities of the chelates formed by several substituted 8-quinolinols with copper has been described, and a conductometric titration method for determining copper with 8-quinolinol has been developed.

2. A volumetric method of analysis for copper based on the relative stabilities of the various metal chelates of 8-quinolinol has been shown to be satisfactory.

LOUISVILLE, KENTUCKY RECEIVED JUNE 26, 1950

[CONTRIBUTION FROM THE FRICK CHEMISTRY LABORATORY, PRINCETON UNIVERSITY]

A Polarographic Investigation of the Alkaline Decomposition of Streptomycin

BY CLARK E. BRICKER AND W. AUBREY VAIL

A rapid polarographic method for assaying streptomycin has been reported by Levy, Schwed and Sackett.[1] These authors suggest a 3% solution of tetramethyl ammonium hydroxide for the supporting electrolyte for the polarographic determination of this compound. They also state that the wave height is a function of the *p*H of the medium and that the wave height is not constant until a *p*H of 13.6 is reached in the supporting solution. No reference was made to the polarographic behavior of the similar compound, mannosidostreptomycin.

In this investigation a more thorough study has been made of the effect of *p*H on the diffusion current obtained from streptomycin (to be called streptomycin A hereafter) and from mannosidostreptomycin (to be called streptomycin B).

Since streptomycin A or B which has been decomposed by heating an alkaline solution of these compounds was found to be non-reducible at the dropping mercury electrode, it was decided to study the rate of decomposition of these compounds polarographically. From these decomposition studies, it has been possible to calculate the energy of activation for these reactions and by comparing these values with that obtained from a similar study with α-hydroxyisobutyraldehyde, the rate determining step in the decomposition of the streptomycins has been deduced.

Experimental

Apparatus and Materials.—A Leeds and Northrup Model E Electrochemograph was employed for recording all polarograms. A polarographic cell assembly similar to that described by Furman, *et al.*,[2] was used throughout this study. This assembly was modified according to the apparatus described by Lingane[3] so that the mass of mercury flowing per second could be measured easily at any applied potential. In addition a constant temperature jacket was used to maintain the temperature of the solution being polarographed. With this jacket, the temperature of the solution was maintained to ±0.2° at as high a temperature as 75° and to ±0.05° at 25°.

Two capillaries were used in this study. All of the kinetic studies were made with a capillary that delivered 2.39 mg. of mercury per second. Those polarograms which were taken to illustrate the effect of *p*H on the reduction of streptomycin were recorded with a capillary that delivered 2.00 mg. of mercury per second. Whenever it was necessary to calculate I_D, the actual values of m and t were measured at the potential which was used for measuring i_d.

A saturated calomel electrode was used as the anode for all polarograms recorded at 25°. For the higher temperatures, a quiet pool of mercury was used. The potential of this anode was measured against a saturated calomel electrode with a Leeds and Northrup student type potentiometer. All *p*H measurements were made with a Leeds and Northrup research model *p*H meter using a No. 1199-30 glass electrode.

Tank nitrogen for removing dissolved oxygen from all solutions prior to the polarographic analysis was purified by passing it through vanadous sulfate solution as described by Meites and Meites.[4] All solutions were deaerated for 10 minutes with a slow stream of nitrogen prior to recording the polarograms. In the kinetic studies, the buffer solutions alone were deaerated ten minutes and then two minutes more after the solution of the reducible material was added.

The phosphate buffer solutions were prepared by mixing NaH_2PO_4 and Na_2HPO_4 or by mixing Na_2HPO_4 and NaOH so that the total available phosphate concentration was 0.25 M in all cases. The borate buffers were prepared from boric acid and sodium hydroxide with a resulting available borate concentration of 0.1 M.

A 1.0% gelatin solution containing a trace of mercuric iodide was used as a maximum suppressor throughout this study. This solution was perfectly stable and showed no evidence of mold growth over a period of several months.

The streptomycin A and streptomycin B were specially purified and were obtained from the Heyden Chemical Corporation.

Experiments with Streptomycin A and Streptomycin B.—A 1.53 millimolar solution of streptomycin A trihydrochloride and a 1.54 millimolar solution of streptomycin B sulfate

(1) G. B. Levy, P. Schwed and J. W. Sackett, THIS JOURNAL, **68**, 528 (1946).

(2) N. H. Furman, C. E. Bricker and E. B. Whitesell, *Anal. Chem.*, **14**, 333 (1942).

(3) J. J. Lingane, *ibid.*, **16**, 329 (1944).

(4) L. Meites and T. Meites, *ibid.*, **20**, 984 (1948).

were prepared. Polarograms were recorded from solutions which contained 2.00 ml. of the streptomycin solution, 0.10 ml. of the gelatin solution and 10.0 ml. of the appropriate buffer or 10.0 ml. of a sodium hydroxide solution. A saturated calomel electrode was used as the reference anode in all of these runs. The pertinent data from the polarograms recorded from streptomycin A are tabulated in Table I. Streptomycin B gave the same results as streptomycin A with the exception that a *p*H of 8 and higher, the I_D values for the streptomycin B were slightly lower than those given in Table I.

TABLE I

DATA FROM THE POLAROGRAPHIC REDUCTION OF STREPTOMYCIN AT VARIOUS *p*H

*p*H	I_D ($i_d/Cm^{2/3}t^{1/6}$) for 1st wave	I_D ($i_d/Cm^{2/3}t^{1/6}$) for Total waves	$E_{1/2}$ *vs.* S.C.E. for 1st wave
14.0	1.56	1.56	−1.69
13.0	2.28	2.28	−1.55
12.4	1.92	2.05	-1.53_5
11.2	1.35	1.68	-1.47_5
9.93	1.01	1.49	−1.40
9.40	0.98	1.48	−1.38
8.68	.79	1.16	−1.32
8.43	.61	1.00	−1.31
8.00	.55	0.79	−1.28
7.73	.39	.58	-1.26_5
7.38	.29	.41	-1.24_5
7.13	.28	.40	-1.22_5
5.92	.26	.34	−1.16
4.20	.15	.15	−1.04

The $E_{1/2}$ values from Table I show a linear relationship with *p*H and can be represented by the equation, $E_{1/2} = -0.806 - 0.059_5$ *p*H. When the I_D values for the first wave are plotted against *p*H, a graph is obtained which is very similar to the actual titration curve of streptomycin trihydrochloride with sodium hydroxide. It was also observed that the second polarographic wave from streptomycin appeared to coalesce with the first wave when the polarograms were recorded from solutions at higher temperatures. These facts can be interpreted on the basis that the first wave is due to the reduction of the essentially free (probably hydrated in solution as an aldehydrol) aldehydic group and the second wave is caused by reduction of a partially bound aldehydic group. (In streptomycin trihydrochloride solutions at *p*H's less than 12.5, the carbonyl group appears to be bound by either or both the protonated guanidino groups or the protonated secondary amine.) This latter reduction is probably not quantitative and therefore the I_D values in Table I for the total of the two waves are not constant. In other words, the two I_D values for streptomycin at a certain *p*H depend on the relative quantities of essentially free and partially bound aldehydic groups that exist at this *p*H.

Kinetic Study with Streptomycin A and Streptomycin B at Various Temperatures and *p*H.—A 10.00-ml. portion of a buffer solution and 0.10 ml. of 1% gelatin were placed in a clean, dry, thermostated polarographic cell and deaerated for ten minutes. Then 2.00 ml. of approximately 1.5 millimolar streptomycin A or B solution was added and the deaeration was continued for two minutes more. As soon as the streptomycin solution was added, a stop watch was started. At various time intervals after the additional two minutes of deaeration, polarograms were recorded from this solution.

The Leeds and Northrup Model E Electrochemograph was especially suitable for this study since the instrument is synchronized so that it requires 30.0 seconds to transverse 0.100 volt. Thus by starting the polarogram at a definite time, it was very simple to calculate the elapsed time between the addition of the streptomycin solution to the buffer medium and the time when i_d was reached. In order to record a sufficient range of a polarogram to facilitate the measurement of the i_d values and in order to rewind the chart paper and reset the polarizing unit and zero adjustment on the recorder, polarograms could not be recorded more frequently than every five minutes. For very fast rates of decomposition, it is possible to stop the polarizer at a potential which produces the diffusion current and then follow the change in i_d continuously from the recorder.

The polarograms from the decomposition study on streptomycin A in a phosphate buffer of *p*H 10.65 and at a temperature of 65° are shown in Fig. 1. A similar series of polarograms were recorded from streptomycin A at 35, 45, 55 and 75° with the same buffer. In addition, decomposition studies were made at most of these same temperatures using 1 *N* sodium hydroxide and other phosphate buffers having *p*H's of 10.3, 11.2 and 11.65, respectively.

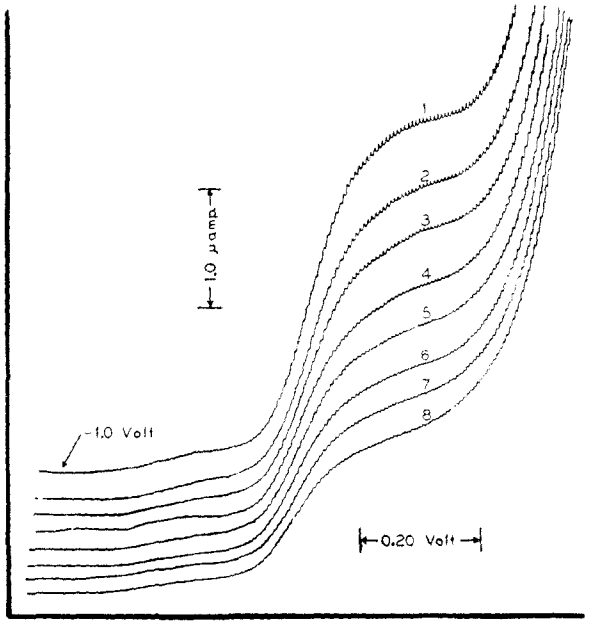


Fig. 1.—Polarograms of streptomycin A in phosphate buffer *p*H 10.6 at 65°; the i_d for polarogram 1 was recorded 10.0 minutes after the addition of the streptomycin A to the phosphate buffer solution; the time interval between polarograms was 5.0 minutes.

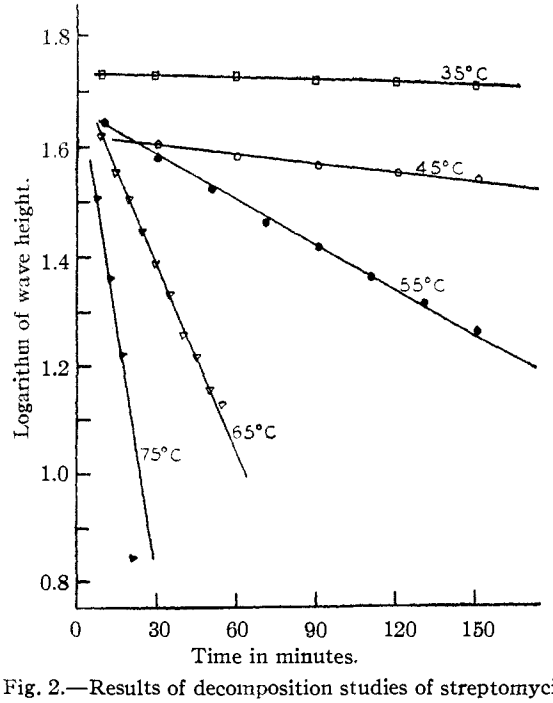


Fig. 2.—Results of decomposition studies of streptomycin A in phosphate buffer of *p*H 10.6 plotted as logarithm of wave height *versus* time.

After it was proved that i_d at a given *p*H and temperature was proportional to the concentration of streptomycin, it seemed valid to use the wave heights directly to interpret the decomposition data. From each series of polarograms, the logarithm of the wave height was plotted against the time elapsed between the addition of the streptomycin solution and the time at which i_d was recorded. The plot of the logarithm of the wave height against time for all of the decomposition studies made on streptomycin A with the phosphate buffer of *p*H 10.65 are shown in Fig. 2. Since this figure shows that the logarithm of the concentration of streptomycin varies linearly with time, the decomposition of streptomycin A must follow a first order reaction. The slopes of these lines as well as those for all of the decomposition studies made on streptomycin A were calculated and are tabulated in Table II as the velocity constant, k, of the reaction (measured slope $\times$ 2.303 = k).

Decomposition studies were also made on streptomycin B in two of the phosphate buffers and in 1 *N* sodium hydroxide. The velocity constants for all of these experiments are also listed in Table II. It is apparent from the velocity constants where the same conditions were used for both streptomycins that both compounds decompose at essentially the same rate.

TABLE II

VELOCITY CONSTANTS FOR THE DECOMPOSITION OF STREPTOMYCINS

Medium	Temp., °C.	Velocity constant, k min.$^{-1}$ for Streptomycin A	Streptomycin B
1 *N* NaOH	25.0	0.0062	0.0068
	30.0	.0131	.0136
	35.0	.0378	.0355
	40.0	.0627	.0635
Phosphate buffer	35.0	.0026	.0027
*p*H 11.65	40.0	.0054	.0053
	45.0	.0101	.0111
	50.0	.0216	....
	55.0	.0437	.0461
Phosphate buffer	35.0	.0010	....
*p*H 11.20	45.0	.0044	....
	55.0	.0198	....
	65.0	.0695	....
Phosphate buffer	35.0	.00026	.00023
*p*H 10.65	45.0	.00124	.00128
	50.0	....	.00445
	55.0	.00629	.00668
	65.0	.0363	.0327
	75.0	.0723	....
Phosphate buffer	35.0	.00014	....
*p*H 10.30	45.0	.00069	....
	55.0	.00262	....
	65.0	.0138	....
	75.0	.0485	....
Borate buffer	45.0	.00107	.00099
*p*H 10.70	55.0	.00442	.00374
	59.0	.00781	.00760
	62.0	.0134	.0127
Borate buffer	55.0	.00031	.00030
*p*H 9.60	59.0	.00058	.00056
	65.0	.00130	.00127

One of the objectives of this study was to determine if the decomposition was only *p*H dependent on whether it was affected by the buffer anion. Since streptomycin B contains more hydroxyl groups than streptomycin A and since polyhydroxy compounds form complexes with borate ions, a borate buffer should show more effect than any other buffer solution. For this reason the decomposition of streptomycin A and B was studied over a temperature range using borate buffers of *p*H 9.6 and 10.7. The velocity constants from these studies are also presented in Table II. These data when compared with those from phosphate buffers at the same *p*H and temperature indicate that the streptomycin decomposes at a slower rate in borate media than in phosphate media. Furthermore, the velocity constants for streptomycin B appear to be consistently lower (from 2 to 15%) than those for streptomycin A under the same conditions. Such a difference was not observed in phosphate buffers. Although the differences in velocity constants observed for streptomycin A and B in borate buffers are probably larger than experimental error, they are not sufficiently different to utilize for analyzing mixtures of these two compounds in the presence of each other.

In order to calculate the experimental energy of activation ($E_{exp.}$) for the decomposition of the streptomycins, the

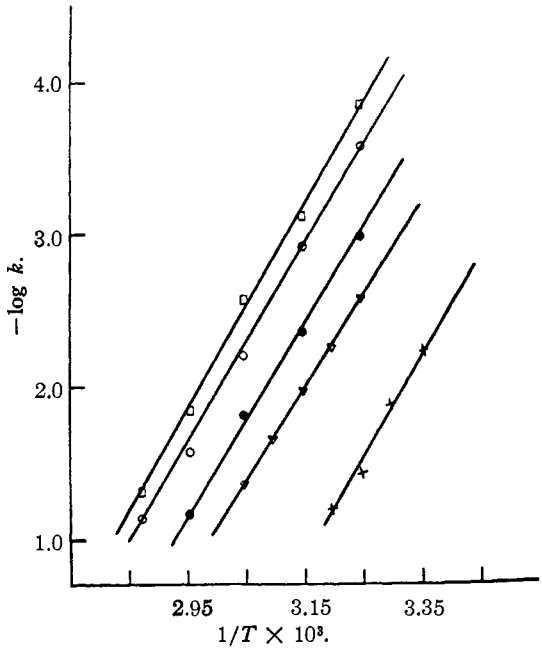


Fig. 3.—Logarithm of rate constant for decomposition of streptomycin A in various media *versus* the reciprocal of the absolute temperature; squares, results at *p*H 10.3; open circles, *p*H 10.65; closed circles, *p*H 11.2; triangles, *p*H 11.65; crosses, *p*H 14.0.

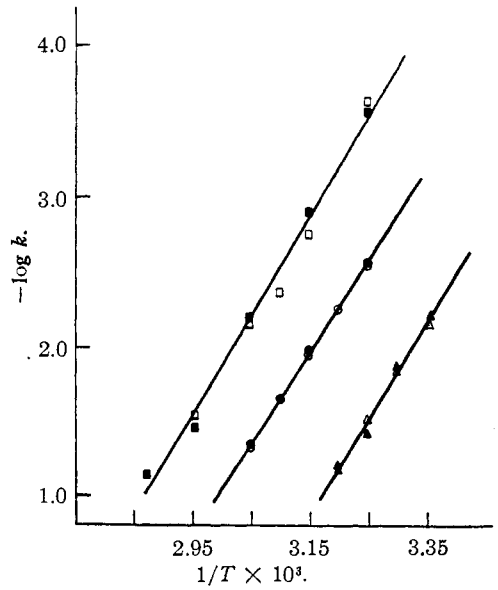


Fig. 4.—Logarithm of rate constant for streptomycin A and B in various media *versus* the reciprocal of the absolute temperature; streptomycin A, open symbols; streptomycin B, closed symbols; squares, *p*H 10.65; circles, *p*H 11.65; triangles, *p*H 14.0.

logarithms of the velocity constants were plotted against the reciprocal of the absolute temperature. These data for streptomycin A in phosphate buffers and 1 *N* sodium hydroxide are shown in Fig. 3. This figure shows that the slopes of the straight lines are practically identical which indicates that the energy of activation is a constant value and independent of *p*H. Furthermore, since the energy of activation remains so nearly constant over the comparatively wide *p*H range, it is likely that the same mechanism for the decomposition of streptomycin occurs in all cases. That is, the reaction is probably not a pseudo first order reaction involving hydroxyl ions as well as streptomycin. The average value of $E_{exp.}$ which was calculated from the slopes of the lines in Fig. 3 was 30.2 ± 0.7 kcal.

To illustrate the great similarity of the decomposition of streptomycin A and B, the logarithm of the velocity constants for the decomposition of both of these compounds where they were studied in the same media are plotted against the reciprocal of the absolute temperature in Fig. 4. This figure shows very clearly that these two compounds decompose at the same rate and that they both apparently require the same energy of activation.

The velocity constants for the decomposition of streptomycin B in borate buffers were found to be somewhat lower than those for streptomycin A. However, when the logarithms of these velocity constants for both streptomycins were plotted against the reciprocal of the absolute temperature, a pair of parallel straight lines was found for each borate buffer. These lines also had the same slope as those shown in Figs. 3 and 4. It is necessary to conclude that, although the two streptomycins probably form complexes of different stability with borate ions which affect their rate of reaction, the decomposition which actually takes place requires the same energy of activation and must proceed by the same mechanism.

The various thermodynamic quantities, ΔH^*, ΔF^* and ΔS^*, were calculated for the decomposition of the two streptomycins in the various media and their average values are given in Table III.

TABLE III

THERMODYNAMIC QUANTITIES FROM DECOMPOSITION STUDIES ON THE TWO STREPTOMYCINS

A refers to streptomycin; B to mannosidostreptomycin.

Medium	ΔH^*, kcal. A	ΔH^*, kcal. B	ΔF^*, kcal. A	ΔF^*, kcal. B	ΔS^*, e.u. A	ΔS^*, e.u. B
1 *N* NaOH	29.2	29.2	22.8	22.8	20.8	21.0
Phosphate buffer						
*p*H 11.65	27.8	27.8	20.7	20.7	21.8	22.2
11.20	28.7	..	20.2	..	25.9	..
10.65	29.1	29.1	20.3	20.3	26.6	25.9
10.30	29.8	..	20.3	..	29.4	..
Borate buffer						
*p*H 10.70	29.4	29.4	20.5	20.6	26.9	26.7
9.60	30.9	31.0	20.5	20.5	31.2	31.3

Experiments with α-Hydroxyisobutyraldehyde.—Schenck and Spielman[5] observed that maltol was formed from streptomycin when this compound was treated with aqueous alkali under relatively mild conditions. Kuehl, *et al.*,[6] stated that maltol must be derived from the streptose moiety of the streptomycin. They also proved that a group must be attached glycosidically at carbon-1 in streptose and that a free or potentially free streptose aldehydic group is necessary in order to get maltol. Lemieux and Wolfrom[7] have suggested a possible series of reactions for the alkaline degradation of streptomycin to maltol. The first reaction in this degradation is similar to the rearrangement of α-hydroxyisobutyraldehyde to form acetoin which was studied by Danilov and Venus-Danilova.[8] Since it seemed likely that the α-hydroxyisobutyraldehyde would be reducible at the dropping mercury electrode and that the acetoin would not undergo reduction at the same potential, it was decided to investigate the kinetics of this rearrangement so a comparison could be made with the data from the streptomycins.

The α-hydroxyisobutyraldehyde was made from α-bromoisobutyraldehyde by hydrolyzing the latter compound and neutralizing the resulting solution with barium carbonate.[9] Because of the difficulty of separating and preserving the pure α-hydroxyisobutyraldehyde, the hydrolyzed solution of α-bromoisobutyraldehyde was filtered and used without further purification. All kinetic measurements were made in the same manner as described previously.

From the rate of rearrangement of α-hydroxyisobutyraldehyde, which was measured at several temperatures in phosphate buffers of *p*H 10.3, 10.65 and 11.2, respectively, the velocity constants and various thermodynamic quantities were calculated. These values are listed in Table IV.

TABLE IV

DATA FROM KINETIC STUDIES WITH α-HYDROXYISOBUTYRALDEHYDE

Phosphate buffers *p*H	Temp., °C.	*k*, min.$^{-1}$	$E_{exp.}$, kcal.	ΔH^*, kcal.	ΔF^*, kcal.	ΔS^*, e.u.
10.30	45.0	0.00375	31.1	30.5	19.4	34.6
	50.0	.00972	31.1	30.5	19.1	35.0
	55.0	.0180	31.1	30.5	19.1	34.8
	60.0	.0336	31.1	30.4	18.3	35.7
	65.0	.0778	31.1	30.4	18.7	34.7
10.65	47.0	.0119	30.8	30.2	19.3	33.7
	50.0	.0174	30.8	30.2	19.3	33.4
	55.0	.0368	30.8	30.2	19.1	33.7
11.20	35.0	.0195	31.1	30.5	19.7	35.1
	37.0	.0245	31.1	30.5	19.5	35.3
	45.0	.0974	31.1	30.5	18.7	37.0

Discussion

The average ΔH^* values for the decomposition of the streptomycins (Table III) are only 1.1 kcal. different from the average ΔH^* value obtained from the rearrangement of α-hydroxyisobutyraldehyde (Table IV). This would suggest that the rate determining step in the decomposition of streptomycin must be similar to the rearrangement observed in the isobutyraldehyde and therefore must involve a change of the aldehyde group in the streptomycin. This indicates that the first step in the mechanism proposed by Lemieux and Wolfrom[7] for the production of maltol from streptomycin is probably the rate determining step in the alkaline decomposition of this compound.

It has been shown that the buffer anion exerts some effect on the rate of decomposition of the different streptomycins but this effect is very small in proportion to the *p*H effect. The decomposition of the two streptomycins and the rearrangement of α-hydroxyisobutyraldehyde show essentially the same *p*H dependence. The logarithm of the velocity constants for all three of these compounds changes about one unit for every unit change in *p*H between 9.6 and 11.6. The fact that these compounds show the same *p*H dependence provides additional evidence that the same general reaction must be responsible for the rate determining step in both the decomposition of streptomycin and rearrangement of α-hydroxyisobutyraldehyde.

The velocity constant for the rearrangement of α-hydroxyisobutyraldehyde was observed to be considerably higher than that for either of the strepto-

(5) J. R. Schenck and M. A. Spielman, THIS JOURNAL, **67**, 2276 (1945).

(6) F. A. Kuehl, Jr., E. H. Flynn, N. G. Brink and K. Folkers, *ibid.*, **68**, 2679 (1946).

(7) "Advances in Carbohydrate Chemistry," edited by W. W. Pigman and M. L. Wolfrom, Vol. 3, Academic Press, Inc., New York, 1948. Chapter entitled "The Chemistry of Streptomycin" by R. U. Lemieux and M. L. Wolfrom.

(8) S. Danilov and E. Venus-Danilova, *Ber.*, **67**, 84 (1934).

(9) A. Franke, *Monatsh.*, **21**, 231 (1900).

mycins under similar conditions. This is not surprising if it is assumed that an essentially free carbonyl group is necessary for the rearrangement. The aldehyde group in the streptomycin molecule at a *p*H of 12.5 or less is apparently partially bound. Thus, in solutions of these *p*H's, every streptomycin molecule does not produce an essentially free aldehyde group which is capable of rearrangement. Consequently, the rate of decomposition of streptomycin should be slower than the rearrangement of α-hydroxyisobutyraldehyde where all the aldehyde groups are essentially free.

Acknowledgment.—The authors wish to thank the Heyden Chemical Corporation for supplying all of the streptomycin that was used in this investigation.

Summary

1. A study has been made of the polarographic reduction of streptomycin and mannosidostreptomycin over the *p*H range of 4.2 to 14.

2. The rate of decomposition of streptomycin has been followed polarographically in various alkaline phosphate and borate buffers and in 1 *N* sodium hydroxide.

3. In the *p*H range 9.6 to 14, the rate of decomposition of both streptomycins has been shown to be identical in phosphate buffers and to follow a first order reaction. The rate of decomposition for these compounds differs slightly in borate buffers. The energy of activation, free energy of activation and entropy of activation were calculated for this reaction.

4. The rate of rearrangement of α-hydroxyisobutyraldehyde to form acetoin was measured and compared with the rate of decomposition of streptomycin. Both of these reactions are first order, require essentially the same energy of activation, and show the same *p*H dependence. It was concluded that the rate determining step in the alkaline decomposition of streptomycin is probably the rearrangement of the streptose moiety to form a six-membered ring.

5. Because of the great similarity of the two streptomycins in their polarographic behavior and in their rates of decomposition, it is unlikely that a simple polarographic technique can be used to determine these compounds in the presence of each other.

PRINCETON, NEW JERSEY RECEIVED AUGUST 7, 1950

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK & CO., INC.]

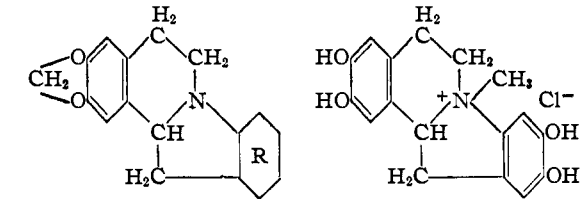
Erythrina Alkaloids. XVIII. Studies on the Structure of Erysopine, Erysodine, Erysovine and Erythraline

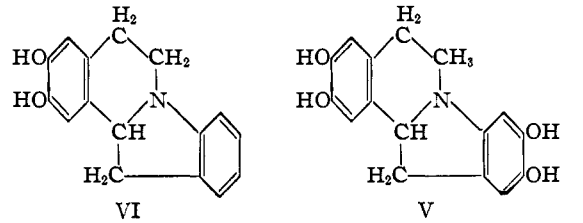
BY KARL FOLKERS, FRANK KONIUSZY AND JOHN SHAVEL, JR.

It was established[1] that erysopine, erysodine and erysovine have the same four-nuclei ring system and that each has three oxygen atoms at the same positions on the ring system. However, these three alkaloids differ in the number and position of O-methyl groups. These deductions are based on analytical, hydrogenation, and methylation experiments, and provided a basis for the new Hofmann degradation and other reactions which are described herein.

The structures[2] of erythramine (I), erythraline (II) and erythratine (III) also provided a basis for further work on erysopine, erysodine and erysovine since all of these alkaloids seemed to have related structures. The conversion of laudanosoline into dehydrolaudanosoline chloride (IV) and then into 2,3,11,12-tetrahydroxydibenzotetrahydropyrrocoline (V) has been discovered by both Robinson[3] and Schöpf[4] and their coworkers. The properties of the pyrrocoline derivative (V) and the Hofmann and Emde degradations of it were promising precedents for these new Erythrina alkaloid studies.

Erysodine and erysovine have the formula $C_{18}H_{21}NO_3$, and have two methoxyl groups and one hydroxyl group; erysopine has the formula $C_{17}H_{19}NO_3$, and one methoxyl group and two





hydroxyl groups.[5] Each of these alkaloids has two double bonds in addition to the benzenoid nucleus and yields tetrahydro derivatives.[1,6] It was desirable to aromatize the ring containing the two double bonds before attempting a Hofmann degradation. This aromatization was accomplished by treatment of the alkaloid with hydrobromic acid which resulted in a decrease of CH_4O in composition. The reaction of erysopine with

(1) Koniuszy, Wiley and Folkers, THIS JOURNAL, **71**, 875 (1949).
(2) Folkers, Koniuszy and Shavel, *ibid.*, **64**, 2146 (1942).
(3) Robinson and Sugasawa, *J. Chem. Soc.*, 789 (1932).
(4) Schöpf and Thierfelder, *Ann.*, **497**, 22 (1932).
(5) Folkers and Koniuszy, THIS JOURNAL, **62**, 1677 (1940).
(6) Folkers and Koniuszy, *ibid.*, **72**, 1832 (1950).