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THE OPTICAL ACTIVATION OF RACEMIC BROMCAMPHOR CARBOXYLIC ACID BY MEANS OF CATALYSTS: THE SPECIFICITY OF CATALYSTS.

—BY HENRY JERMAIN MAUDE CREIGHTON, M. A., M. Sc., DR. Sc., *Lecturer on Physical Chemistry,* Dalhousie University, Halifax, N. S.*

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INTRODUCTION.

Methods for the resolution of racemic bodies into their optically active components date back to the time of *Pasteur.* In an investigation on the salt formed by racemic tartaric acid with cinchonicine, he found that at first almost pure cinchonicine l- tartrate *cyrstallised out* from solutions of the racemate, while most of the cinchonicine d- tartrate remained behind in the mother liquid. *Pasteur* also found, when yeast was added to a solution of ammonium racemate, that the inactive solution became laevo-rotatary after a time, and that finally it was possible to separate l- tartaric acid from the liquid. In this case the d- component is consumed *by the ferment.* By means of yeast and other ferments, *LeBel*[1] was able to obtain amyl- and several other alcohols in an active condition;

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1. Le Bel, J. A.; Compt. rend., **87**, 213, (1878); **89**, 312, (1879); Bull. soc. chim., **7**, (3), 551.

Bremer[1] has split up inactive malic acid into its active components by means of cinchonine; and *Lewkowitsch*[2] has decomposed mandelic acid into its active isomers by different methods. The reverse of the method used *Pasteur* was employed by *Ladenburg*[3] in the synthesis of conine. Here a racemic base *a*- normal propyl piperidine, prepared by the reduction of *a*- allyl piperidine, was split up into its antipodes by means of an active acid. *E. Fischer*[4] in his researches in the sugar group has split up many compounds by the foregoing method of *Pasteur*.

It is well known that the majority of the properties of antipodes are the same; for example, both generally react at the same rate. When, however, antipodes unite with another optically active body, they lose their antipode character and acquire different solubilities, rates of reaction, etc. Much use has been made of this in separating a racemic body into its optically active components. For instance, on account of the *different rates* at which an active body reacts with a racemate, it is possible to obtain a product which shows optical activity, by stopping the reaction before completion. In this manner *Markwald* and *Meth*[5] effected a partial separation of r- mandelic acid by l- menthylamine, the amide being formed by the reaction. The converse of this method has been used successfully by *McKenzie* and *Thompson*[6], who prepared optically active products by submitting the partially racemic esters, formed by the complete esterification of different acids externally compensated by optically active alcohols, to fractional hydrolysis with an inactive base.

An *asymmetric synthesis* of an active compound from a symmetric substance, whereby an optically active solvent should

1. Bremer, G. J. W.: Ber. d. deutsch. chem. Ges., **13**, 351, (1880).
2. Lewkowitsch, J.: Ber. d. deutsch. chem Ges., **16**, 1573, (1883).
3. Ladenburg, A.: Ber. d. deutsch. chem. Ges., **19**, 429, and 2518, (1881)
4. Fischer, E.: ibid. **23**, 2114, (1890).
5. Markwald, W., and Meth, R.: ibid., **38**, 801, (1905).
6. McKenzie, A., and Thompson, H. B.: Trans. Chem. Soc., **91**, 789, (1907).

play the part of a *catalyst,* was first suggested by *van't Hoff*[1]. This was an important suggestion for, in the plant and animal organisims, asymmetric bodies are being built continually from symmetric substances, the synthesis probably being brought about *by the actions of enzymes or other catalysts.*

It is well known that different substances are only acted on by particular enzymes, it being supposed that the enzyme associates itself with a particular molecular grouping of the substrate. This *"specificity"* of the *enzymes* is well seen in the action of various yeasts on disaccharides, an investigation carried out by *E. Fischer*[2], and one which led him to formulate his simile of the "lock and key" relationship. As this implies a close relationship between enzyme and substrate, such as is found in optically active opposites, it has been suggested that enzymes themselves are optically active bodies. *Dakin's*[3] investigation on the hydrolysis of optically active esters by the lipase of the liver affords support to this suggestion. He found that when an optically inactive mixture of the two esters of mandelic acid was acted on by lipase, the dextro component hydrolysed more rapidly than the laevo component; and further, that if the hydrolysis were incomplete, the residual mixture was laevo rotatary. The unequal rates of reaction of the two components can only be explained *if the enzyme is assumed to be optically active.* The work of *Fischer* and *Abderhalden*[4] on the relation of trypsin to the polypeptides, shows that trypsin, too, exhibits a marked affinity for certain optically active groups.

Attention was first called to the marked similiarity between enzymes and inorganic catalysts by *Berzelius*[5] in 1837. He pointed out that: "We have reasons, well founded on fact, to make the assertion, that in living plants and animals there take

1. van't Hoff, J. H.: "Die Lagerung der Atome im Raum."
2. Fischer, E.: Ber. d. deutsch. chem. Ges., **27**, 29 and 92, (1894).
3. Dakin, H. D.: Journ. of Physiol., **30**, 253, (1904).
4. Fischer, E., and Abderhalden, E.: Zeit. f. physiol. Chem., **46**, 52, (1905).
5. Berzelius, J. J.: Lehrb. d. Chem., 3. Aufl., 20-25 (1837).

place thousands of catalytic processes between tissues and fluids"; and also, "when compared with known phenomena in the inorganic world, it resembles nothing else so much as the decomposition of hydrogen peroxide under the influence of platinum, silver, or fibrin." In recent times, *Bredig*[1] has shown many striking resemblances between the enzymes and certain inorganic catalysts, such as colloidal solutions of the metals. Indeed, all recent investigations *point to the action of enzymes being catalytic.*

The asymmetric division of an inactive mixture by means of enzymes, which we may look on as catalysts, suggests the possibility of such a division being brought about with the help of *a catalyst of known chemical structure.*

Several attempts have already been made to accomplish an asymmetric division by means of a catalyst. *F. S. Kipping*[2] carried out the synthesis of benzion from benzaldehyde (with potassium cyanide), and of mandelic acid nitrile from benzaldehyde and potassium cyanide in concentrated alcoholic camphor solutions; but in these and other cases the compounds obtained were inactive. E. and O. *Wedekind*[3] allowed *menthyl*-benzly-aniline to unite with allyl-iodide in optically active solvents such as d-limonene, l-menthol, and l-chlor-methyl-menthyl-ether, but in every case the products were inactive. At *Bredig's* suggestion, the rate of decomposition of d- and l-camphorcarboxylic acid in d- and l-limonene was investigated by *Balcom*[4] who found that the isomers decomposed at the same rate.

It remained for Professor G. *Bredig* to find a *stereochemical specific catalyst.* At his suggestion *Fajans*[5] measured the *rate of decomposition of the isomeric camphorcarboxylic acids in*

1. Bredig, G.: Biochem. Zeit., **6**, 283, (1907).
2. Kipping, F. S.: Proc. Chem. Soc., **16**, 283, (1901).
3. Wedekind, E. and O.: Ber. d. deutsch. chem. Ges., **41**, 456, (1908).
4. Balcolm, R. W.: Diss. Heidelberg 1905. Bredig and Balcolm: Ber. d. deutsch. chem. Ges., **41**, 740, (1908).
5. Fajans, K.: Diss. Heidelberg 1910. Zeit. f. phys. Chem., **73**, 25, (1910).

the presence of optically active bases, such as certain alkaloids. It was found *that not only was the rate of decomposition of the acid greatly accelerated by the different alkaloids,* but that the d- and l-acids decomposed at different rates. By acting on the *racemic acid* with quinine, and quinidine, and by stopping the reaction at the point where the excess of one component over the other was greatest, *Fajans was able to prepare optically active solutions of the isomeric camphors and the camphorcarboxylic acids.* This result is similar to that obtained by *Dakin*[1] through the catalytic *enzyme action* of lipase (a catalyst of unknown structure) on mandelic acid ester, and *constitutes the first example of an asymmetric division by means of a catalyst of definite structure.*

Recently, in the physical chemical institute of this place, *Bredig* and *Fiske*[2] have further brought about an *asymmetric synthesis* of a nitrile by the use of optically active catalysts. The reaction

$$C_6H_5CHO + HCN = C_6H_5CH\ OH\ CN$$

is catalysed by bases, and when *alkaloids* (in this case quinine and quinidine) are used *as catalysts* the resulting nitrile is optically active (that is the d- and l-nitrile are formed in unequal amount), and the mandelic acid produced by the saponification of the nitrile is also active. This asymmetric synthesis is analogous to that of *L. Rosenthaler's*[3] with the help of emulsin.

When solutions of *bromcamphor-carboxylic acid* are heated it is found that the acid decomposes much more rapidly than similar solutions of camphor-carboxylic acid. The decomposition takes place according to the equation:

$$C_8H_{14}\begin{cases}CBrCOOH\\ |\\ CO\end{cases} = C_8H_{14}\begin{cases}CrBH\\ |\\ CO\end{cases} + CO_2$$

It was suggested by Professor Bredig that I should study the catalytic influence of alkaloids on the above reaction, and

1. Dakin, H. D.: loc. cit.
2. Bredig, G.: Chem. Zeitung, xxxv, 36, 324, (1911).
3. Rosenthaler, L.: Biochem. Zeit., **14**, 238, (1908).

prepared by catalysis, if possible, the optically active isomeric bromcamphors and bromcamphor-carboxylic acids, from the racemic bromcamphor-carboxylic acid. This acid is found to be *much better suited* for *catalytic asymmetric division* than camphor-carboxylic acid, for which the former acid the quantity of catalyst, calculated in equivalents, can be *very much smaller* than that of the decomposed *substrate.*

PREPARATIONS.

Inactive solvent: Acetophenone was obtained from C. F. *Kahlbaum,* and before being used it was dried over anhydrous sodium sulphate and redistilled.

Acids: d-, l-, and in-bromcamphor-carboxylic acids. These acids were prepared from the corresponding camphor-carboxylic acids. As difficulties had been experienced in obtaining perfectly pure bromcamphor-carboxylic acids, it was thought best to start with absolutely pure camphor-carboxylic acids. These were prepared according to the sodium amide[1] method of *Bruhl*[2]. The inactive acid was prepared from synthetic camphor, (very kindly presented by the chemischen Fabrik auf Aktien vorm. E. Schering, Berlin), after its slight dextro rotation had been compensated by the addition of the requisite amount of l-camphor. The best yields of camphor carboxylic acid were obtained when the sodium amide was finely divided, the temperature high (110° — 140°), and the stirring as rapid as possible. It was found that the sodium amide could be conveniently ground up in an ordinary mortar under toluene. By using toluene or xylene for the reaction liquid, a favourable temperature was obtained. In order to stir the mixture rapidly, and also to lessen the chance of breakage, owing to the tendency of the sodium amide to adhere to the sides of the glass flask, the use of an iron vessel was tried. It was found, however, that the amide acted on the iron to a certain extent, a substance resembling Prussian Blue being formed, and that it required several crystallisations to obtain

1. For the fresh sodium amide I am indebted to the Deutschen Gold- und Silberscheideanstalt, Frankfort, a/M.
2. Brühl, J. W.: Ber. d. deutsch. chem. Ges., **36**, 1305, (1903).

a pure acid. The impure acids were twice recrystallised from water at 60°. In agreement with *Fajans,* the melting points of the d- and l- acids were 127° — 128°; while that of the inactive acid was higher, 136° — 137°, from which it may be concluded that the acid, prepared as above, is a racemic acid.

Analysis by titration with barium hydroxide solution and phenolphthalein gave the following degrees of purity:

	d – acid		l – acid		in - acid
I	100,07%	I	100,12%	I	100,07%
II	100,11%	II	99,88%	II	100,10%
III	99,78%	III	99,98%	III	— —
Mean:	99,99%		99,99%		100,09%

The optical rotation of these camphor-carboxylic acids was determined at 25°:

3.7743 g. d- acid, dissolved to 25 ccm. in absolute alcohol, gave a rotation of + 23°.02 in a 2.5 dcm. tube.

0.4302 g. l- acid, dissolved to 10 cc. in absolute alcohol, gave a rotation of - 2°.63 in a 1 dcm. tube.

These rotations correspond to a specific rotation of ± 61°.1.

The acid prepared from the inactive camphor was completely inactive.

Besides these tests of purity the affinity constant of the d- and l- acid was measured, and the results obtained at 25° are given below[1]:

d – Camphor-carboxylic acid.			$\lambda \infty = 374$		l – Camphor-carboxylic acid.		
v lit.	Mol. Cond. λ	Degree Diss. 100 γ	100 k	v lit.	Mol. Cond. λ	Degree Diss. 100 γ	100 k
31,32	26,56	7,10	0,0173	31,32	26,60	7,11	0,0174
62,64	36,96	9,88	0,0173	62,64	37,65	10,07	0,0180
93,97	44,92	12,01	0,0175	156,64	57,65	15,41	0,0174
156,61	57,63	15,41	0,0179	250,49	70,24	18,78	0,0173
250,58	70,91	18,96	0,0177	814,35	117,21	31,34	0,0176
		Mean:	0,0175			Mean:	0,0175

1. One half of the specific conductivity of the water was subtracted from that obtained for the solution. In the case of the d- acid $\frac{1}{2}$. 4×10^{-6}; and in the case of the l- acid $\frac{1}{2}$. 2.7×10^{-6}.

The value 0.0174×10^{-2} was obtained by Ostwald for the affinity constant of d- camphor-carboxylic acid at 25°.

The bromcamphor-carboxylic acids were prepared according to *Aschan's*[1] method of brominating the corresponding camphor-carboxylic acids, in acetic acid solution at room temperature. Aschan obtained a pure acid by crystallising once from ligroin. In spite of a large number of experiments, in which a variety of solvents were employed, I have been unable to obtain a perfectly pure bromcamphor-carboxylic acid. In ligroin the acid appeared to be almost insoluble. The purest preparations were obtained by recrystallisation from a mixture containing a large quantity of ether to a small quantity of alcohol. About 25 grams of acid were shaken up with almost sufficient ether to dissolve it, and then alcohol was added, a few drops at a time, until the acid dissolved. The acid was then allowed to slowly crystallise out from this solution. Especially good crystals were obtained with one of the preparations of l- acid. These were examined and found to consist of a combination of the following three forms of the monoclinic system:

(i) Vertical Prisms. $a : mb : \infty c$
(ii) Klinodoma $\infty a : b : mc$
(iii) Orthopinakoid $a : \infty b : \infty c$

The orthopinakoid was very well developed.

Two different preparations A and B of the d- and l- acids were made and in the kinetic experiments which follow, measurements were, as a rule, made with both these preparations. Only one inactive preparation was prepared. The melting points and optical rotation of the different acids were determined; also analyses were made of the acids, both by titration with barium hydroxide solution and by estimation

1. Aschan, O.: Ber. d. deutsch. Chem. Ges., **27**, 1445, (1894).

of the bromine content. The results obtained are given in the following table:

Preparations:	d-acid A	d-acid B	l-acid A	l-acid B	in acid
Melting Point:	111,5°	111,0°	111,0°	110,5°	122°
$[\alpha]_D^{20°}$:	+ 77,78°	+ 78,00°	− 77,80°	− 77,79°	0,00°
Analysis with $Ba(OH)_2$:	97,41%	96,62%	97,36%	96,89%	96,99%
Analysis by Bromine Estimation:	97,56%	96,90%	96,94%	97,42%	96.97%

Bases: Quinine and quinidine were obtained from C. F. Kahlbaum, and were identified by their melting points. Before being used they were dried at 110° — 120°[1].

Apparatus.

In order to *determine the velocity of decomposition of the bromcamphor-carboxylic acids* in solution, both with and without catalysts, the progress of the reaction with time was followed by *weighing the amount of carbon dioxide* that was liberated from the acid. The apparatus for this consisted essentially of a small glass flask, with a capacity of about 30 ccm., which was connected to two sets of soda-lime tubes by means of a three way tap. The small reaction flask was closed with a ground glass stopper through which passed two tubes, the one going within 2 mm. of the bottom of the flask; attached to the second tube was a small cooler through which tap water flowed. During the reaction the small reaction flask was immersed in a thermostat, the temperature of which was kept constant within ± 0°.05. The liberated CO_2 was carried off by a stream of nitrogen which bubbled through the solution. The complete apparatus is shown in fig. 1. The nitrogen was contained in the gas-holder G and in the bomb B, from either of which it passed to the purifying apparatus through the three-way tap T_1. The gas was freed from traces of oxygen by means of alkaline sodium hydrosulphite in the wash bottles W_1 and W_2; then washed with potassium hydroxide solution in the wash

1. Lenz, W.: Zeit. f. anal. Chemie, **27**, 551, (1888).

bottles W_3 and W_4; and dried with concentrated sulphuric acid in W_5. The last traces of carbon dioxide were removed with soda-lime in the tube U_1. From this the nitrogen passed into the reaction flask R, where it mixed with the carbon dioxide liberated from the acid. On passing out of the reaction flask most of the solvent vapour that was carried along with the nitrogen condensed in the cooler K_1 and ran back again into the flask; the last traces of solvent vapour condensed in the three small condensors K_2, which were immersed in a freezing mixture of ice and salt. After leaving K_2 the gas passed through the three way tap T_2 to either of the sets of soda-lime tubes U_2U_3 and U_4U_5, where the carbon dioxide was absorbed. Each of these sets of tubes was connected with a soda-lime tube R_1 or R_2 and a bubble counter b_1 or b_2. The reaction flask, the coolers, and the soda-lime tubes were all attached to a small wooden frame. To immerse the reaction flask in the thermostat it was simply necessary to lower the wooden frame. At fixed times the current of gas was cut off from one set of U-tubes and passed through the second set by means of the three way tap; during the interval the first set of tubes was weighed. This operation was repeated as often as was necessary. The influence of the rate of the nitrogen stream on the velocity of decomposition of the bromcamphor-carboxylic acid was investigated, and it was found that the velocity of evolution of CO_2 apparently increased slightly with increase in the velocity of the nitrogen stream up to four liters per hour, probably owing to small traces of carbon dioxide remaining in supersaturated solution; but when the nitrogen stream was over four liters per hour, however, no further increase in the velocity of CO_2 evolution, with increase in the velocity of the nitrogen steam, was observed to occur. In the experiments which follow the current of nitrogen was usually 6-8 liters per hour. A more rapid current of gas was not used on account of the evaporation of the solvent. With a nitrogen stream of 8 liters per hour traces of acetophenone vapour were usually carried over into the first two tubes of the cooler K_2; but seldom was a trace of acetophenone ever found in the third

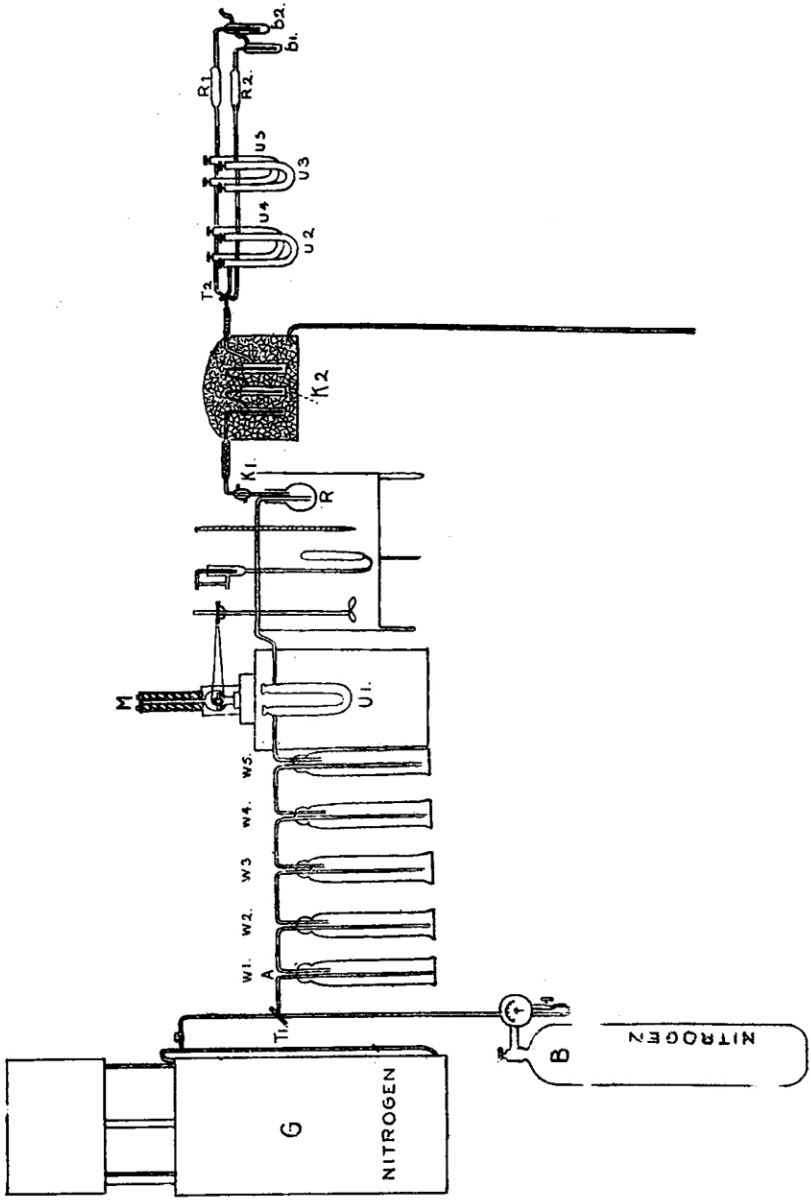
B2.
B1.
R1.
R2.
U5
U3
U4
U2
T2
K2
K1.
R
M
U1.
W5.
W4.
W3
W2.
W1.
A
T1.
B
NITROGEN
G
NITROGEN

FIG 1.

tube of the cooler. Owing to the fact that carbondioxide results from the oxidation of acetophenone, it was necessary to remove every trace of oxygen from the nitrogen. Oxidation of acetophenone was found to take place with small traces of oxygen at as low a temperature as 40°. I assured myself that the apparatus worked properly by means of a blank experiment made every few days. This consisted in passing a current of purified nitrogen through some solvent contained in the reaction flask, and then through the soda-lime tubes. At the end of 1/2 — 1 hour the tubes were weighed and it was seen whether they had increased in weight.

The efficiency of the apparatus was tested by decomposing a known weight of Na_2CO_3 with pure dilute sulphuric acid, and the evolved CO_2 carried off with a current of dry pure nitrogen into the soda-lime tubes, after having been dried with concentrated sulphuric acid. The results obtained were:

0.3428 g. Na_2CO_3 liberated 0.1419 g. CO_2; calculated 0.1423 g. Error: — 0.3%.

As a further test of the efficiency of the apparatus the velocity constant of decomposition of d- and l-camphorcarboxylic acids was measured. As *Fajans* has found, the reaction follows the first order. k has been calculated from the formula:

$$k = \frac{1}{t \cdot 0{,}4343} \lg \frac{A}{A - x},$$

where t is the time in minutes, A the original amount of acid calculated as CO_2 and A — x the amount present at the time t, both expressed in milligrams.

TABLE I.

Each gram of acid in 10 ccm[1]. acetophenone. Temperature 80°

d--acid			l—acid		
t	A — x	k	t	A — x	k
0	225,1	—	0	225,1	—
60	210,3	0,00113	58	211,2	0,00114
154	189,5	0,00112	180	183,7	0,00113
268	166,8	0,00112	268	166,6	0,00112
455	136,9	0,00112	420	139,1	0,00114
620	112,8	0,00111	1320	50,7	0,00113
1335	50,9	0,00111	1620	36,1	0,00113
1890	27,6	0,00111			
	Mean	0,00112		Mean	0,00113

For the d- acid Fajans[2] found $k = 0.00114$, and for the l- acid $k = 0.00115$.

On account of the relatively high rate of decomposition of bromcamphor-carboxylic acid in the presence of bases, solutions of the acid and the base were prepared saparately; on starting an experiment the solution of the acid was placed in the reaction flask, nitrogen bubbled through so as to remove any carbon-dioxide and air from the apparatus, and then 1 ccm. of the solution of base, containing the required amount of the substance, was added to the acid solution in the reaction flask. The two solutions were thoroughly mixed by shaking and the flask immediately lowered into the thermostat.

1. The liquid was measured at room temperature.
2. Fajans, K.: loc. cit.

Decomposition of Bromcamphor-carboxylic Acid.

1. *Experiments Without Catalysts and Temperature Coefficient.*

The decomposition of bromcamphor-carboxylic acid in acetophenone, in the absence of alkaloids, was found to follow the first order of reaction, the velocity constant being calculated from the equation

$$k = \frac{1}{t} \cdot \frac{1}{0{,}4343} \cdot \lg \frac{A}{A - x}$$

The symbols here have the same meaning as previously indicated.

The values obtained for k at 80°, 70°, and 60° are as follows:

Table II.

Each gram of acid in 10 ccm. acetophenone. Temperature 80°.

d—acid			l—acid		
t	A — x	k	t	A — x	k
0	155,8	—	0	144,0	—
10	138,2	0,0120	10	127,5	0,0122
20	122,2	0,0121	20	112,9	0,0122
30	108,2	0,0122	30	100,1	0,0121
40	95,8	0,0122	40	88,9	0,0121
50	84,8	0,0122	60	70,3	0,0120
60	75,2	0,0121	85	52,7	0,0118
75	62,7	0,0121	115	35.8	0,0121
			140	27,1	0,0119
	Mean	0,0121		Mean	0,0121

TABLE III.

Each gram of acid in 10 ccm. acetophenone. Temperature 70°.

d-acid			l-acid		
t	A—x	k	t	A—x	k
0	160,0	—	0	160,0	—
10	152,0	0,00513	30	137,1	0,00515
30	137,3	0,00510	60	118,6	0,00499
50	124,2	0,00506	90	102,0	0,00500
80	107,1	0,00502	120	87,9	0,00499
120	88,2	0,00496	170	68,1	0,00503
240	48,5	0,00497	240	48,0	0,00502
300	35,8	0,00499			
	Mean	0,00503		Mean	0,00503

TABLE IV.

Each gram of acid in 10 ccm. acetophenone. Temperature 60°.

d-acid			l-acid		
t	A—x	k	t	A—x	k
0	160,0	—	0	80,0	0
10	156,7	0,00207	30	75,1	0,00211
20	153,4	0,00208	60	70,3	0,00215
30	150,3	0,00208	90	65,9	0,00215
40	147,3	0,00207	150	57,7	0,00218
85	133,8	0,00210	210	50,5	0,00219
110	128,2	0,00201	380	34,9	0,00218
180	109,5	0,00211			
	Mean	0,00207		Mean	0,00216

The mean value for k is 0.0121 at 80°, 0.00503 at 70°, and 0.00212 at 60°. From these numbers the temperature coefficient for two intervals of ten degrees each may be calculated. Between 60° and 70° it is 2.37 and between 70° and 80° it is 2.40.

From the van't Hoff-Arrhenius equation

$$\frac{d\ln k}{dT} = \frac{A}{T^2},$$

we obtain by integration the equation

$$\frac{1}{0{,}4343} \log \cdot \frac{k_1}{k_2} = \frac{A\,(T_1 - T_2)}{T_1\,T_2},$$

and from this the value for A may be calculated. By substituting the value of the ratio $\frac{k_{80°}}{k_{70°}}$ in the foregoing equation, A is found to be 10600, while with the ratio $\frac{k_{70°}}{k_{60°}}$ A is found to be 9854. The mean difference between these two values is 3.5 per cent.

2. *Decomposition of Bromcamphor-carboxylic Acid at 40° in the Presence of Quinine and Quinidine.*

a. Quinine.

Pure quinine was obtained from C. F. Khalbaum. After being dried for two hours its melting point was taken and found to be 171°.5 — 172°.

In the following tables $\frac{dx}{dt}$ represents the rate of decomposition of the acid, and C_m the mean concentration of the acid; the other symbols have the same meaning previously indicated.

Table V.

1 g. l-acid and 0.0200 g. quinine in 11ccm. acetophenone. (0.3305 mole acid and 0.0056 mole quinine per liter).

Experiment 1l.

t	A − x	$\frac{dx}{dt} = \frac{x_2 - x_1}{t_2 - t_1}$	$C_m = A - \frac{x_1 + x_2}{2}$	$\frac{\frac{dx}{dt}}{C_m} \cdot 10^2$	% Decomposition
0	160,0	—	—	—	—
10	147,9	1,21	154,0	0,79	7,6
20	134,2	1,37	141,1	0,97	16,1
30	118,9	1,53	126,6	1.21	25,5
40	101,8	1,71	110,3	1,55	36,4
50	82,1	1,97	92,0	2,14	48,7
60	60,6	2,15	71,3	3,01	62,1
70	32,5	2,81	46,6	6,03	79,7
80	27,4	0,51	30.0	1,70	82,9
100	24,3	0,15	25,9	0,51	84,8
140	21,6	0,07	22,9	0,30	86,6

Experiment 2l.

0	160,0	—	—	—	—
5	154,9	1,02	157,5	0,64	3,2
15	142,9	1,20	148,9	0.80	10,7
25	128,3	1,46	135,6	1,08	19,8
35	112,0	1,63	120,1	1,35	30,0
45	93,8	1,82	102,9	1,77	41,1
55	72,2	2,16	83,0	2,60	54,9
65	47,7	2,45	60,0	4,08	70,2
75	24,6	2,31	36,2	6,38	84,6
85	22,7	0,19	23,6	0,80	85,8
115	21,8	0,03	22,2	0,14	86,4

TABLE VI.

1. g. d-acid and 0.0200 g. quinine in 11 ccm. acetophenone. (0.3305 mole acid and 0.0056 mole quinine per liter).

Experiment 31.

t	A − x	$\frac{dx}{dt} = \frac{x_2-x_1}{t_2-t_1}$	$C_m = A - \frac{x_1+x_2}{2}$	$\frac{\frac{dx}{dt}}{C_m} \cdot 10^2$	% Experiment.
0	160,0	—	—	—	—
10	151,6	0,84	155,8	0,54	5,3
20	138,4	1,32	145,0	0,92	13,5
30	124,9	1,35	131,6	1,02	22,2
40	111,5	1,34	118,2	1,13	30,3
50	97,6	1,39	104,5	1.33	39,0
60	83,9	1,37	90,7	1,50	47,6
70	68,0	1,59	75,9	2,08	57,5
80	49,6	1,84	58.8	3,13	69,0
90	32,8	1,68	41,2	4,08	79,5
100	27,2	0,56	30,0	1,87	83,0
110	24,7	0,25	26,0	0,96	84,6
140	21,6	0,10	23,2	0,43	86,5
170	19,1	0,08	20,4	0,39	88,1

Here it is observed that the velocitv of the reaction increases with time, reaches a maxium, and then falls off rapidly to nothing; also that the ratio of the velocity of decomposition to the mean concentration C_m of the undecomposed acid behaves in the same way. As should be expected, since quinine is a laevo-rotatary substance, the rate of decomposition of the two isomers is different. At the end of 70 minutes, when the difference between the percentage decomposition of the two acids is greatest (almost 25 per cent), the velocity of decomposition of the l-acid is almost double that of the d-acid. The progress of the reaction with time is shown in fig. 2.

b. Quinidine.

The quinidine used in the following experiments was obtained from C. F. Kahlbaum. After heating for two hours at 110° — 120° it melted at 170°.

Table VII.

1 g. d-acid and 0.0200 g. quinidine in 11 ccm. acetophenone. (0.3305 mole acid and 0.0056 mole quinidine per liter).

Experiment 2b.

t	A — x	$\frac{dx}{dt} = \frac{x_2 - x_1}{t_2 - t_1}$	$C_m = A - \frac{x_1 + x_2}{2}$	$\frac{\frac{dx}{dt}}{C_m} \cdot 10^2$	% Decomposition.
0	160,0	—	—	—	—
5	155,0	1,00	157,5	0,63	3,1
15	141,7	1,33	148,4	0,89	11,4
25	128,9	1,28	135,4	0,94	19,4
35	111,9	1,70	120,4	1,42	30,1
45	94,2	1,77	103,1	1,71	41,1
55	74,8	1,94	84,5	2,29	53,3
65	54,4	2,04	64,6	3,16	66,0
75	30,6	2,38	42,5	5,60	80,9
85	18,5	1,21	24,6	4,92	88,5
115	12,4	0,20	15,5	1,29	92,3

Experiment 3b.

0	160,0	—	—	—	—
9	149,6	1,14	154,8	0,73	6,5
20	134,2	1,54	141,9	1,08	16,1
30	119,2	1,50	126,7	1,18	25,9
40	103,1	1,61	111,1	1,45	35,6
50	85,1	1,80	94,1	1,91	46,8
60	66,1	1,90	75,6	2,51	58,7
70	43,2	2,29	54,7	4,19	73,0
80	21,4	2,18	32,3	6,75	86,5
90	16,6	0,48	19,0	2,52	89,6
100	12,1	0,45	14,4	3,12	92,5
130	8,9	0,11	10,5	1,05	94,5

FIG. 2.

Quinine as Catalyst.

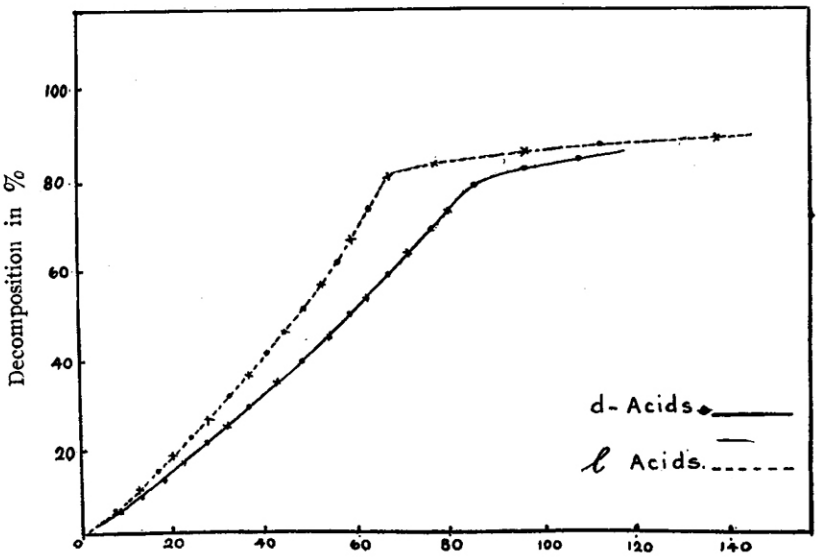

FIG. 3.

Quinidine as Catalyst.

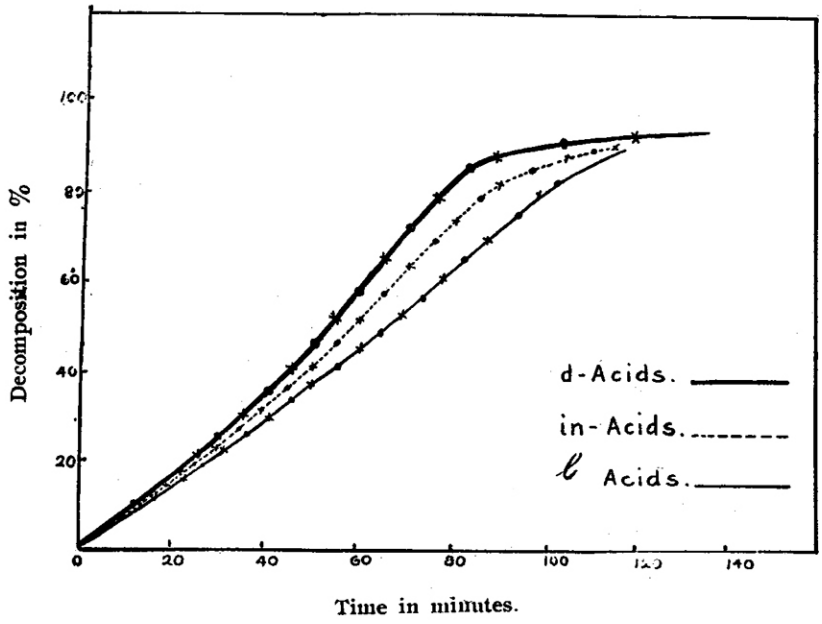

Table VIII.

1 g. l-acid and 0.0200 g. quinidine in 11 ccm. acetophenone. (0.3305 mole acid and 0.0056 mole quinidine per liter).

Experiment 4b.

t	A — x	$\frac{dx}{dt} = \frac{x_2 - x_1}{t_2 - t_1}$	$C_m = A - \frac{x_1 + x_2}{2}$	$\frac{\frac{dx}{dt}}{C_m} \cdot 10^2$	% Decomposition.
0	160,0	—	—	—	—
10	148,9	1,11	155,4	0,72	6,9
20	137,9	1,10	143,4	0,76	13,8
30	125,7	1,22	131,8	0,92	21,5
40	112,7	1,29	119,2	1,08	29,5
50	99,5	1,33	106,1	1,21	37,8
60	86,4	1,31	93,0	1,41	46,0
70	72,3	1,41	79,4	1,78	54,8
80	57,7	1,46	65,0	2,24	63,9
90	40,6	1,71	49,2	3,48	74,6
100	24,0	1,66	32,3	5,14	85,0
110	9,9	1,41	17,0	8,29	93,8
120	6,6	0,33	8,3	4,00	95,9
130	5,2	0,14	5,9	2,37	96,8
175	3,7	0,03	4,4	0,68	97,8
		Experiment 5b.			
0	160,0	—	—	—	—
5	154,3	1,14	157,1	0,73	3,6
15	144,5	0,98	149,4	0,66	9,7
25	132,5	1,20	138,5	0,87	17,2
35	119,6	1,29	126,1	1,02	25,2
45	104,1	1,55	111,9	1,39	34,9
55	91,1	1,30	97,6	1,32	43,1
65	78,1	1,30	84,6	1,54	51,2
75	63,7	1,44	70,9	2,03	60,2
85	46,5	1,72	55,1	3,12	71,1
95	30,4	1,61	38,4	4,19	81,0
105	14,7	1,57	20,5	7,66	90,8
125	6,8	0,40	10,8	3,70	95,8

Table IX.

1 g. in- acid and 0.0200 g. quinidine in 11 ccm. acetophenone. (0.3305 mole and 0.0056 mole quinidine per liter).

Experiment 6b.

t	A — x	$\frac{dx}{dt} = \frac{x_2 - x_1}{t_2 - t_1}$	$C_m = A - \frac{x_1 + x_2}{2}$	$\frac{\frac{dx}{dt}}{C_m} \cdot 10^2$	% Decomposition.
0	160,0	—	—	—	—
10	148,3	1,17	154,2	0,75	7,3
20	136,2	1,21	142,2	0,84	14,9
30	123,0	1,32	129,6	1,02	23,1
40	107,7	1,53	115,3	1,34	32,7
50	92,3	1,54	99,0	1,55	42,3
60	75,8	1,65	84,1	1,99	52,6
79	57,3	1,85	66,6	2,77	64,2
80	39,5	1,78	48,4	3,69	75,3
90	28,2	1,13	33,9	3,33	82,4
100	19,4	0.88	23,8	3,70	87,9
110	9,0	1,04	14,5	7,32	94,4
120	3,5	0,55	6,2	8,87	97,8
130	3,0	0,05	3,3	1,51	98,1

Experiment 7b.

0	160,0	—	—	—	—
5	153,9	1,21	157,0	0,77	3,8
15	143,5	1,04	148,7	0,70	10,3
25	130,8	1,27	137,2	0,93	18,3
35	116,5	1,43	123,7	1,15	27,2
45	100,1	1,64	108,3	1,51	37,4
55	84,6	1,55	92,3	1,68	47,1
65	67,0	1,76	78.8	2,32	58,1
75	48,2	1,88	57,6	3,27	69,9
85	33,1	1,51	40,7	3,70	79,3
95	23,7	0,94	28,4	3,33	85,2
115	6,7	0,90	14,7	6,12	96,3

An examination of the numbers in the foregoing tables shows that the influence of quinidine on the decomposition of d- and l- bromcamphor-carboxylic acid is almost identical with the effect produced by its isomer, quinine, on the decomposition of l- and d- bromcamphor-carboxylic acids. The rate of decomposition of the inactive acid lies about midway between the rates for the d- and l- acids. Further, the velocity of the reaction and the ratio given in column five of the tables show the maxium to which mention has already been made. The progress of the reaction with time is shown graphically in Fig. 3.

Optical Activation by Catalysis.

In the foregoing *kinetic measurements* on the decomposition of bromcamphor-carboxylic acid in the presence of quinine and quinidine, it has been found that *there is a difference between the rates of reaction of the two optical isomers.* It should be expected therefore, when the *optically inactive* acid *is decomposed under the catalytic influence of an alkaloid and the reaction stopped before the end, that the two antipodes would not be present in equivalent amounts,* and that also the *newly formed* bromcamphor, as well as the *remaining undecomposed bromcamphor-carboxylic acid, would show optical activity.* In order to test whether optical activation could be brought about by this means, *quinine* in one experiment, and *quinidine* in another were used as catalysts.

As the curves (fig. 2 and 3) illustrating the progress of the reaction with time show, the difference between the already decomposed (or still undecomposed) acid content of the two isomers grows steadily for a time; reaches a maximum, and then falls off until, when the acid is all decomposed, it is nothing as at the beginning of the reaction. In order to obtain the greatest rotation it is evident that the *reaction must be stopped at the moment when this difference is greatest.* This is readily calculated from the curves.

Synthetic camphor, the weak dextro-rotation of which was compensated with the necessary amount of l-camphor, was used to prepare a *bromcamphor-carboxylic acid* which was *completely inactive*. This acid was used for the following activation experiments.

1. With *quinine*. Since with this alkaloid the l-acid decomposes more rapidly than the d-acid, one should expect that the undecomposed acid on the one hand would be laevo-rotatary, and on the other the bromcamphor, which is formed by the reaction, would be dextro-rotatary.

From the decomposition curve it is found that the most favourable moment for stopping the reaction is at the end of 68 minutes. Two parallel experiments were made. 5.0000 grams of inactive bromcamphor-carboxylic acid were dissolved in 50 ccm. of acetophenone and mixed with 5 ccm. of acetophenone which contained 0.1000 gram of quinine. The mixture was placed in a thermostat and kept at 40° for 68 minutes, at the end of which time it was mixed with 10 ccm. of a dilute solution of hydrochloric acid and buried in a freezing mixture of salt and ice. The hydrochloric acid was previously saturated with common salt so as to cause the layer of the acid solution to separate from the acetophenone solution more quickly. The addition of the hydrochloric acid solution served the double purpose of stopping the reaction and removing the quinine The optical rotation of the hydrochloric acid solution, after separation from the acetophenone layer, was measured is a 1 dcm. tube and found to be: —1°99. The acteophenone solution was shaken up twice again with 10 ccm. of the hydrochloric acid. The second HCl extract when polarised in a 1 dcm. tube was found to give a rotation of —0°.02; while the third extract gave a rotation of: 0°.00. 0.1000 gram of quinine was dissolved in 10 ccm. of the above HCl solution that was used for extracting the quinine from the reaction mixture; this when polarised in a 1 dcm. tube and was found to give a rotation of —1°.96, thus showing that one shaking with 10 ccm. of the HCl solution

was sufficient to remove the 0.1000 gram of chinin used for the activation. As further proof of the complete removal of the quinine, no green colouration was obtained on shaking the last HCl extract with bromine water and ammonia (a very delicate test for quinine). The undecomposed acid was then removed from the acetophenone by shaking with dilute potassium hydroxide solution. As water solutions separate only very slowly from acetophenone (the sp. g. is almost the same for the two), in most cases they were separated by means of a centrifugal machine. After removal of the acid the acetophenone solution was dried with anhydrous sodium sulphate. Its volume was 50 ccm., 5 ccm. having been lost in the separation operations. 16 ccm. of this solution were placed in a 2 dcm. tube and its rotation was found to be: $a = -0°.71$*. In order to calculate the amount of active bromcamphor in the acetophenone solution, the specific rotation of bromcamphor in acetophenone was measured. 0.5000 gram of d-bromcamphor, dissolved to 10 ccm. in acetophenone, gave, in a 1 dcm. tube, a rotation of: $+6°.94$, corresponding therefore to $[a]_D^{18°} = 138°.8$. The weight of bromcamphor contained in $v = 55$ ccm. of the above acetophenone is

$$g = v \frac{a}{[a] \cdot l} = 55 \frac{0{,}71}{138{,}8 \cdot 2} = 0{,}141 \text{ g.}$$

From the kinetic data it is found that, at the end of 68 minutes from the commencement of the reaction, 1.569 g. of l-bromcamphor and 1.176 g. of d-bromcamphor should be found. The excess of l-bromcamphor over d-bromcamphor being, therefore 0.420 g. Perhaps the difference between the amount of active bromcamphor calculated from the kinetic data and that actually found, may be due to the occurrence of racemization.

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*The mean error in reading the polariscope was $0°.01 - 0°.02$.

The undecomposed bromcamphor-carboxylic acid was precipitated from the potassium hydroxide solution with dilute hydrochloric acid, and then purified by recrystallising from ether. 1.485 grams of the acid were obtained. This amount, dissolved to 16 ccm. in absolute alcohol, gave a rotation of: $\alpha = 1°.29$, corresponding to $[\alpha]_D^{18°} = +\ 6°.92$ when measured in a 2 dcm. tube. The specific rotation of the pure active acid in absolute alcohol is $+ 77°.8$, so therefore this preparation contains 9% active acid, whereas it should contain 27% active acid. This difference is probably due to loss during the crystallisation, or possibly to racemization. It would have been better to have polarised the potassium hydroxide solution of the acid.

2. With *quinidine*. In this case the undecomposed acid should rotate to the left and the bromcamphor, formed by the reaction, to the right. The most favourable point for stopping the reaction is found from the curve (fig. 3) to be at the end of 75 minutes, at which moment 80.9% of the d-acid and 60.2% of the l-acid has decomposed. As before two parallel experiments with 5.0000 grams of inactive acid and 0.1000 gram of quinidine, dissolved in 55 ccm. of acetophenone, were carried out at 40°. The method and procedure were the same as in the foregoing experiments.

52 ccm. of the acetophenone solution of bromcamphor were obtained, and 16 ccm. of this solution when polarised in a 2 dcm. tube gave a rotation of $+ 0°.99$, corresponding therefore to 0.196 g. of active bromcamphor in the initial 55 ccm. Calculations from the kinetic data show that 0.44 g. should have been formed. In case of no other experimental error, this difference between the experimental and theoretical quantities of bromcamphor may be regarded as caused by racemization.

The undecomposed bromcamphor-carboxylic acid was removed from the potassium hydroxide solution with dilute hydrochloric acid, and then purified. The acid obtained weighed 1.535 grams. This was dissolved to 16 ccm. in

absolute alcohol and polarised in a 2 dcm. tube. This solution gave a rotation of $-1°.59$ corresponding to $[a]_D^{18°} = -8°.2$, whereas from kinetic calculations it should have been $[a]_D^{18°} = -23°.2$. The excess of active acid is therefore 0.180 gram or *0.00066 mole*, whereas it should be 0.513 gram or *0.00150 mole*. In this experiment *0.00066 equivalent of acid has been made active by the catalytic influence of 0.00060 equivalent or 0.00030 mole of quinidine.*

In order to make certain that the optical activity obtained was due to a specific catalytic action of the base and not to any error in the method employed, a controll experiment was carried out in the same manner as the activation experiment. In this experiment the quantity of materials used were the same as in the activation experiment, except that here no base was used. It was found that *neither the potassium hydroxide or acetophenone solutions showed the slightest optical activity on being polarised.*

We see then from these experiments that, *by means of an optically active base, it is possible to produce catalytically both active bromcamphor and bromcamphor-carboxylic acid from the inactive acid,* for 4 equivalents or 4 moles of acid have been made optically active by the help of 4 equivalents or 2 moles of base. According to the kinetic curves 2 moles of base should activate about 10 equivalents or moles of acid. But for a lack of a sufficient quantity of the inactive acid, further activation experiments would have been carried out with the object of obtaining a quantitative yield of the active bromcamphor and bromcamphor-carboxylic acid.

Is the Action of the Base Catalytic?

The question of whether the acceleration of the decomposition of bromcamphor-carboxylic acid by optically active bases is due to a catalytic influence or not, is of interest, and has been

discussed at length by Fajans[1]. In order to answer this question the exact definition of catalysis and catalyst must be considered. Ostwald, who has done so much work in this region, has defined[2] catalysis as follows: "Katalyse ist die Beschleunigung eines langsam verlaufenden chemischen Vorgangs durch die Gegenwart eines fremden Stoffes." This definition is independent of what the cause of what catalysis may be. A catalyst he defines[3] as "jeden Stoff, der ohne im Endproducte einer chemischen Reaktion zu erscheinen, ihre Geschwindigkeit verändert." This definition has been broadened by Bredig[4]: "Die Katalysatoren sind Stoffe, welche die Geschwindigkeit einer Reaktion verändern, ohne stets eine stöchiometrische äquivalente Beziehung der eventuell umgewandelten Menge des sogenannten Katalysators zu der Menge der anderen umgewandelten Substanzen, der sog. Substrate, besteht." This last definition, which includes the former, is accepted to-day by most investigators in the field of catalysis.

There has been some doubt expressed as to whether the decomposition of camphor-carboxylic acid as carried out by Fajans is a catalytic process. Objections have been made to the use of equivalent quantities of acid and base on the one hand, and to the mechanism of the reaction on the other. These criticisms have been fully answered by Fajans[5].

In our reaction it has been found that the decomposition of bromcamphor-carboxylic acid is *greatly accelerated* by the presence of *very small* quantities of base. It has further been shown[6], that the base used to catalyse the decomposition of the acid is in the same condition and present in the same amount at the end of the reaction as at the beginning; and also that it is capable of decomposing *a new quantity of acid with the same velocity as at first.*

1. Fajans, K.: loc. cit. p. 59-65.
2. Ostwald, W.: Zeit. f. phys. Chemie, **15**, 705, (1894); Lehrb. d. allgem. Chemie, 2. Aufl. (1), 2, 515, (1893).
3. Ostwald, W.: Zeit. f. Elektrochem, **7**, 998, (1901).
4. Bredig, G.: ibid., **9**, 735, (1903).
5. Fajans, K.: loc. cit.
6. Creighton, H. J. M.: Dissertation, Zürich, 1911, p. 30 und 74.

In the reaction under investigation, we have good reasons[1] for supposing that the acceleration in the presence of a base depends on the formation of a salt, which is much less stable than the acid itself, and which readily breaks up again into CO_2, bromcamphor, and free base, the latter being free to unite with more acid. With regard to any objections that may be raised to the theory of a catalytic action by the base, on the grounds of the mechanism of the reaction, it may be emphasized that an intermediate reaction between the acid and catalyst constitutes one of the oldest and commonest types of catalytic processes. With truth it may be held that our reaction is just as much a catalytic process as, for example, the accelerating influence of molybdic acid on the velocity of oxidation of hydriodic acid by hydrogen peroxide[2], in which reaction there takes place the following steps:

$$\text{I.}\quad MoO_2 \begin{matrix} OH \\ OH \end{matrix} + H_2O_2 = MoO_2 \begin{matrix} OH \\ O-OH \end{matrix} + H_2O$$

$$\text{II.}\quad MoO_2 \begin{matrix} OH \\ O-OH \end{matrix} + 2\,HI = H_2O + I_2 + H_2MoO_4$$

We see then that the action of quinine and quinidine conforms in every way to the above definitions of catalysis, and that therefore we are justified in claiming that *our reaction is a catalytic process;* and further, *that the optical activation of the inactive bromcamphor-carboxylic acid has been accomplished by means of optically active catalysts.*

Specificity of Catalysts.

The analogies between enzyme action and the action of ordinary catalysts are so numerous that the former bodies also are now generally looked on as a *type of catalyst*[3]. One of the most interesting of recently discovered analogies between these substances is to be found in their *behavior towards certain*

1. Creighton, H. J. M.: Dissertation, Zürich, 1911, p. 58 et seq.
2. Brodie, J.: Zeit. f. phys. Chemie, **37**, 257, (1901).
3. Creighton, H. J. M.: Dissertation, Zürich, 1911, p. 88 et seq.

poisons. The poisonous influence of many substances towards inorganic catalysts has been thoroughly investigated by Bredig and his pupils in the last few years. The effect of a number of different poisons on inorganic catalysts and enzymes is illustrated in the accompaning table, in which is shown the concentration of the different poisons that is necessary to entirely destroy the catalytic influence of colloidal platinum[1] and of catalase[2] on hydrogen peroxide:

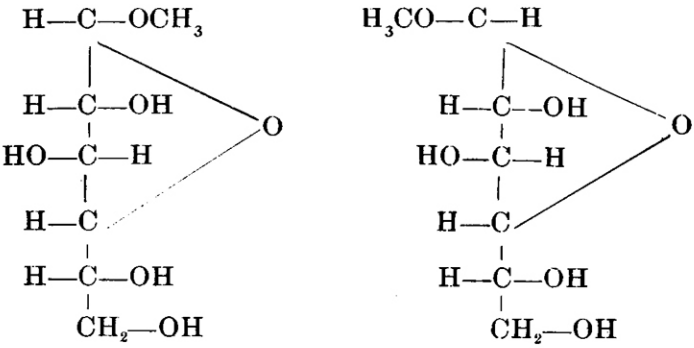
Poison	Colloidal Platinum	Catalase
H_2S	1 : 300 000 molar	1 : 1 000 000 molar
HCN	1 : 20 000 000 "	1 : 1 000 000 "
$HgCl_2$	1 : 2 000 000 "	1 : 2 000 000 "
$Hg(CN)_2$	1 : 200 000 "	1 : 300 "
I in KI	1 : 5 000 000 "	1 : 50 000 "
$NH_2(OH)HCl$	1 : 25 000 "	1 : 80 000 "
Aniline	1 : 5 000 "	1 : 40 000 "
As_2O_3	1 : 50 "	1 : 2 000 "
CO	very poisonous	no paralysis
HCl	1 : 3 000 molar	1 : 100 000 "
NH_4Cl	1 : 2 000 "	1 : 1 000 "
HNO_3	no paralysis	1 : 250 000 "

That enzymes exhibit a *stereochemical specificity* has long been known. The principle here involved is that one of the antipodes of the substrate is changed much quicker by the enzyme than the other, which very often remains practically unchanged. Pasteur[3] observed, for instance, that with racemic ammonium tartrate only the dextro antipode was attacked by mould enzyme (penicillium glaucum), the solution becoming laevo-rotatary. Our fundamental knowledge in this field, however, is due to the researches of E. Fischer. He has shown that a particular enzyme is able to attack certain stereochemical

1. Bredig, G., and Müller v. Berneck: Zeit. f. phys. Chem., **31**, 258, (1899).
2. Senter, G.: Zeit. f. phys. Chem., **44**, 257, (1903).
3. Pasteur: Compt. rend., **51**, 298, (1860).

isomers which, on account of their configuration, belong to one group. Thus, for example, he has found[1] that d-glucose, d-mannose, d-galactose, and d-fructose all undergo fermentation with yeast, while the laevo isomers of these substances do not. Not only, however, are the micro-organisms able to distinguish between isomers of entirely opposed activity, but the transposition of two groups, attached to a single one of a number of asymmetric carbon atoms, is of importance to them. Fischer and Thierfelder[2] have shown that although the above mentioned sugars are fermentable by various yeasts, d-talose, which differs from d-mannose and d-galactose only by the transposition of the groups attached to a single asymmetric carbon atom, is not attacked by the same yeast species. To insure enzyme action, then, the substrate and enzyme must have their configurations adjusted to one another like lock and key; and it may be possible that they may act on one another to their mutual distruction if the keys turn opposite ways. However, experiments made by Eiloart showed no such destruction in the case of human and pig pepsins.

The relation between the substrate molecule and that of the enzyme is illustrated[3] by the splitting of α — and β — methyl



1. Fischer, E.: Zeit. f. physiol. Chem., **26**, 60, (1898).
2. Fischer, E., and Thierfelder: Ber. d. deutsch .chem. Ges., **27**, 2031, (1894); see also Fischer, ibid. **27**, 2985, 3228, 3479.
3. Fischer, E.: ibid. **32**, 3617, (1899).

glucoside into their antipodes by means of emulsin. Of these two isomers only the β- form is attacked by emulsin, which conversely this form is not changed by yeast and the α- antipode is split up into grape sugar and methyl alcohol. This "lock and key" relationship between enzyme and substrate has been confirmed by Pottevin[1] and others[2].

This *stereochemical specificity* of enzymes has been held to be a fundamental difference between the *ordinary catalysts* and the enzymes, and an important reason why the latter should not be looked on as catalysts. Very recently, however, this argument has been broken down by the investigations of Bredig and Fajans[3] whose results show *that ordinary catalysts of asymmetric structure may, like enzymes, also possess a stereochemical specificity.* The results, which I have obtained in the present investigation, *confirm and strengthen this new and important relationship between enzymes and ordinary satalysts.*

Summary.

1. The decomposition of bromcamphor-carboxylic acid in acetophenone solution has been investigated kinetically, and it has been found that the presence of small quantities of alkaloids accelerate this decomposition enormously.

2. Optically active bases catalyse the decomposition of the *antipodes* of the acid in *different degrees.* The difference between the *velocities of decomposition* of the two optical-isomeric acids is as much as 30% in some cases (Tables V and VI).

3. *This catalytic behaviour of optical active bases suggests an analogy to the stereochemical specificity of the enzymes.*

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1. Pottevin, H.: Compt. rend., **136**, 169, (1903).
2. For an account of the numerous investigations in this field, see Fajans, K., loc. cit.
3. Fajans, K.: loc. cit.

4. *By means of the stereochemical specific catalytic influence of optically active bases, optically active bromcamphors, as well as optically active bromcamphor-carboxylic acids, have been prepared from inactive bromcamphor-carboxylic acid.*

5. In conclusion the specificity of catalysts has been discussed.

Laboratorium für electro und physikalische Chemie,
Eidgenössisches Technischen Hochschule,
Zürich, Switzerland, July, 1911.