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The Dissociation Constants of Some of the Terpene Acids

BY HILDA HOWELL AND G. S. FISHER

RECEIVED MARCH 17, 1958

Using Speakman's equation, the dissociation constants in aqueous solutions have been determined for the terpene acids: *d*-pinononic, *dl*-pinonic, *dl*-pinolic, nopinic, *cis*-norpinic, *trans*-norpinic, *dl*-pinic (m.p. 101°), *l*-pinic (m.p. 135°), *sym*-homopinic, *cis*-*d*-camphoric and camphenic. The interprotonic distances have been calculated for *sym*-homopinic, pinic and the norpinic acids by Bjerrum's formula, by the Westheimer equations and on the basis of the geometry of the assigned parameters. In contrast to many other acids previously reported, the *cis*-pinic and *cis*-norpinic acids showed K_1/K_2 ratios which were very close to the ratios for the corresponding *trans* forms. Also, the interprotonic distances calculated by the various methods do not provide an adequate basis for assignment of configuration or conformation for these 1,3-cyclobutanedicarboxylic acids.

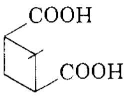
Recent investigations[2-4] of the production and utilization of acids obtained from α-pinene have revealed the lack of reliable values for the ionization constants of these acids. Values have been reported in the literature for *cis*- and *trans*-norpinic (I),[5] camphoric (IV)[6] and pinonic (VII)[7] acids. However, the constants for both camphoric and pinonic acids were determined in solutions with a concentration significantly higher than that recommended by Speakman[8] for the elimination of error in the calculation of the ionic strength. Abichandani and Jatkar, who reported the values for *cis*- and *trans*-norpinic acids, also in the same article reported values for *cis*- and *trans*-caronic acids which were widely different from the values reported elsewhere.[9] In addition, the material designated as *trans*-norpinic acid was probably the *cis–trans* mixture which until quite recently[10] was erroneously identified as the *trans*-norpinic acid.

Consequently, the dissociation constants of these acids have been redetermined using the method of Speakman[8] and are presented with the constants determined in the same way for pinic, *sym*-homopinic (III), camphenic (V), pinononic (VI), pinolic (VIII) and nopinic (IX) acids.

By utilizing dilute solutions of acids and rigorous exclusion of foreign salts, the method of Speakman permits the activities of the various ions to be calculated from the usual potentiometric titration data. A first-order equation

$$X = K_1 + K_1K_2Y$$

where X and Y are functions of pH, initial acid concentration and titrant added, can be derived from the equations defining the thermodynamic dissociation constants of a dibasic acid. A comparable derivation gives the value for monobasic acids. Thus, absolute values of K_1 and K_2 can then be calculated from a single titration without need for extrapolation to zero ionic strength. Furthermore, the relationship is much less cumbersome than other derivations in common use such as the one by Gane and Ingold.[11]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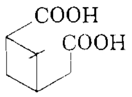
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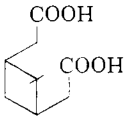
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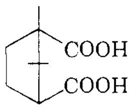
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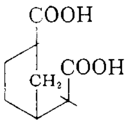
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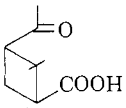
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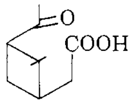
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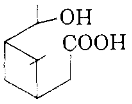
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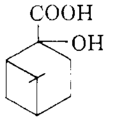
IX

Five to nine points in each titration were observed for calculation and fell very close to the line fitted by the method of least squares. If the equation is reduced to the form for monobasic acids, individual pK values for each observed pH value are obtained and the result reported for each acid is an average of the points within the interval of 25 to 75% of complete titration. In a typical titration, such as titration 1 for pinonic acid, the standard deviation of pK for eight individual points was ±0.03.

Table I gives the pK values obtained for the monobasic acids. The pK_1, pK_2 and ΔpK values for the dibasic acids are listed in Table II.

Adipic acid was included as a check on the technique used and, as indicated in Table II, an excellent check with the literature values was obtained. The constants determined for camphoric acid agree well with those reported by the authors indicated; but in the case of the norpinic acids only the value for pK_2 of the *cis* form agrees at all with the reported values.

The extremely high ratio of K_1/K_2 as found in maleic, malonic, disubstituted malonic, tetra-

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[1] One of the laboratories of the Southern Utilization Research & Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article not copyrighted.

[2] J. S. Stinson and Ray V. Lawrence, *J. Org. Chem.*, **19**, 1047 (1954).

[3] R. N. Moore, C. Golumbic and G. S. Fisher, THIS JOURNAL, **78**, 1173 (1956).

[4] F. Holloway, H. J. Anderson and W. Rodin, *Ind. Eng. Chem.*, **47**, 2111 (1955).

[5] C. T. Abichandani and S. K. K. Jatkar, *J. Indian Inst. Sci.*, **21A**, 373 (1938).

[6] W. Ostwald, *Z. physik. Chem.*, **3**, 369 (1889); P. Walden, *Ber.*, **29**, 1692 (1896); E. E. Chandler, THIS JOURNAL, **30**, 694 (1908); W. Dieckmann and Albin Hardt, *Ber.*, **52B**, 1134 (1919).

[7] W. A. Roth and G. J. Ostling, *ibid.*, **46**, 309 (1913).

[8] J. C. Speakman, *J. Chem. Soc.*, 855 (1940).

[9] Values of 2.42×10^{-4} and 4.76×10^{-6} for *cis*-caronic acid and 2.52×10^{-4}, 5.60×10^{-6} for *trans*-caronic acid are reported. I. Jones and F. G. Soper, *J. Chem. Soc.*, 133 (1936), report 4.59×10^{-3} and 4.94×10^{-9} for *cis*-caronic acid and 1.52×10^{-3} and 4.78×10^{-7} for *trans*-caronic acid.

[10] Unpublished work.

[11] R. Gane and C. K. Ingold, *J. Chem. Soc.*, 1594 (1928); 1691 (1929).

TABLE I

Acid	Titration no.	pK_1	Acid	Titration no.	pK_1
Pinononic	1	4.64	Pinolic	1	4.83
	2	4.63		2	4.83
	3	4.61		Mean	4.83
	4	4.63			
	Mean	4.63	Nopinic	1	4.61
Pinonic	1	4.83			
	2	4.81			
	Mean	4.82[a]			

[a] Lit. value 4.67; reference 7.

TABLE II

Acid	Titration no.	pK_1	pK_2	ΔpK	ΔpK-0.6 log $K_1/4K_2$[d]
Adipic	1	4.41	5.41	1.00	0.40
	2	4.42	5.41	0.99	.39
Means		4.42	5.41	1.00	0.40
Lit. value[a]		4.43	5.42		
cis-Norpinic	1	4.36	5.52	1.16	0.56
	2	4.30	5.50	1.20	.60
	3	4.34	5.51	1.17	.57
Means		4.34	5.51	1.18	0.58
Lit. value[b]		3.83	5.55		
trans-Norpinic	1	4.45	5.56	1.11	0.51
	2	4.44	5.56	1.12	.52
	3	4.44	5.57	1.13	.53
Means		4.44	5.56	1.12	0.52
Lit. value[b]		3.57	5.24		
dl-Pinic	1	4.47	5.47	1.00	0.40
	2	4.44	5.48	1.04	.44
	3	4.53	5.46	0.93	.33
Means		4.48	5.47	0.99	0.39
d-Pinic	1	4.48	5.49	1.01	0.41
	2	4.48	5.46	0.98	.38
Means		4.48	5.48	1.00	0.40
Homopinic	1	4.57	5.48	0.91	0.31
	2	4.59	5.50	.91	.31
	3	4.60	5.50	.90	.30
	4	4.55	5.50	.95	.35
Means		4.58	5.49	0.92	0.32
cis-*d*-Camphoric	1	4.73	5.83	1.10	.50
	2	4.70	5.82	1.12	.52
	3	4.69	5.83	1.14	.54
Means		4.71	5.83	1.12	0.52
Lit. value[c]		4.71, 4.62	5.86, 5.89		
Camphenic	1	4.78	5.69	0.91	0.31
	2	4.73	5.65	.92	.32
	3	4.68	5.65	.93	.33
Means		4.73	5.65	0.92	0.32

[a] Reference 8. These values for adipic acid are also in good agreement with those from other sources quoted by Speakman. [b] Reference 5. [c] Reference 6. [d] Deviation from expected statistical ratio of K_1/K_2.

methylsuccinic, *cis*-cyclopropanedicarboxylic and caronic acids[12] was not encountered in any of the terpene acids used. It must be concluded, then, that the carboxyl groups, even of *cis*-norpinic acid, are either in sterically hindered positions or are too far apart to permit hydrogen bonding between the groups. Hence, it was of interest to attempt to calculate the interprotonic distances for the various dicarboxylic acids. The two equations most commonly used for this purpose are those of Bjerrum[13] and Westheimer.[14] The final equation used in both methods has the general form $r = Ne^2/RT\ D \ln (K_1/4K_2)$ in which N, e, R and T have their usual significance, r is the interprotonic distance in cm. and D is the dielectric constant of the medium between the protons. Bjerrum uses the dielectric constant of water while Kirkwood and Westheimer attempt to include transmission of part of the electrostatic effect through the molecule itself by calculating an effective dielectric constant. These methods are described in detail in the original articles, so it will be sufficient here simply to point out that the Bjerrum approximation has been found to give satisfactory values for long chain acids while the more elaborate equation of Westheimer and Kirkwood is superior for shorter ones.

Estimation of the effective dielectric constant, D_E, requires rather detailed assumptions with regard to the geometry of the molecule. It must be decided whether the molecule should be treated as a prolate ellipsoid or a spheroid, and in the latter case it is also necessary to estimate the angle, θ between the lines joining the protons with the center of the molecule. This in turn involves assumptions regarding bond lengths, bond angles and conformation of the molecule. Having assigned reasonable values to these parameters, they can be used to calculate interprotonic distances directly by simple trigonometry as well as to calculate D_E for use in the Westheimer equation. The interprotonic distances calculated by the two methods, one based on assumptions of geometry and the other based on these assumptions plus an experimentally determined dissociation constant, should check if the geometry is correct and the equations are valid.

In the case of the cyclobutyl acids involved in the present investigation, problems in the choice of the parameters to be used involve those encountered by Westheimer and additional ones due to (1) uncertainty of the bond angles and bond lengths in the unsymmetrically substituted cyclobutane rings, (2) the degree of pucker of the ring (if any), (3) the *cis* or *trans* configuration of specific isomers and (4) the orientation of the carboxyls with respect to the other substituents.

Although the bond lengths, bond angles and ring symmetry with respect to substituted cyclobutane have not been established rigidly, reasonable limits can be placed on the basis of values quoted by various authors for unsubstituted cyclobutane, octachlorocyclobutane, octafluorocyclobutane and tetraphenylcyclobutane.[15] The values used for the calculation of the "geometrical interprotonic dis-

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[12] D. H. McDaniel and H. C. Brown, *Science*, **118**, 370 (1953).

[13] Niels Bjerrum, *Z. physik. Chem.*, **106**, 219 (1923).

[14] J. G. Kirkwood and F. H. Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); F. H. Westheimer and J. G. Kirkwood, *ibid.*, **6**, 513 (1938); F. H. Westheimer and M. W. Shookhoff, THIS JOURNAL, **61**, 555 (1939).

[15] J. D. Dunitz and Verner Schomaker, *J. Chem. Phys.*, **20**, 1703 (1952); T. B. Owen and J. L. Hoard, *Acta Cryst.*, **4**, 172 (1951); G. W. Rathjens, Jr., N. K. Freeman, W. D. Gwinn and K. S. Pitzer, THIS JOURNAL, **75**, 5634 (1953).

tances" were C–C 1.568 Å., RCH (external to the cyclobutane ring) 114°, and the proton 1.45 Å. beyond the terminal carbon atom and on the extension of the last carbon-to-carbon bond. To indicate the extreme range of the effect of a pucker in the cyclobutane ring, a dihedral angle of 33° was assumed for the puckered conformations. Actually, much smaller angles have been used and the distortion also seems to be highly dependent upon the substituents added to the ring.[16]

In order to calculate θ, it also becomes necessary to choose a center of the molecule and, as indicated by Westheimer and Shookhoff, this is difficult to accomplish without ambiguity. Although the assignment is not strictly correct, except perhaps in the cases of the *trans*-norpinic and certain forms of *trans*-homopinic acids, the center of the molecule was chosen as the midpoint between carbon atoms 1 and 3 of the cyclobutane ring. The angle θ then is the angle between the lines joining this center to the protons.

The choice between an ellipsoidal and a spherical model for the computation of the interprotonic distances, R_W, according to Westheimer, *et al.*, was based on the relative length of a line joining the two protons and the perpendicular distance from this line to the extreme point of the *gem*-dimethyl group. Configurations in which the trigonometric interprotonic distance was less than twice the perpendicular distance were treated as spherical.

Orientation of the carboxyl groups of a *cis* compound in the axial positions on a puckered ring was not considered because of the repulsion of the carboxyl groups as well as the spatial requirements involved with the methyl groups. The difficulty with which the anhydrides are formed and the failure, so far, to prepare the lactone of a hydroxy pinic acid would substantiate this. In the *trans* compounds, an examination of the models shows that the necessary assignment of one of the acid groups to the axial position does not give unreasonably hindered configurations and such conformations cannot be excluded on this basis.

For homopinic acid, only three of the infinite number of orientations of the carboxyl substituents with respect to the perpendicular plane bisecting the cyclobutane ring were considered: (a) the carboxyls lie in the plane and opposed to the tertiary hydrogens; (b) the carboxyls are rotated 45° in the same direction from the plane; (c) the carboxyls are rotated as in (2) but are on opposite sides of the plane. Rotation in either direction to accomplish (b) would give the same interprotonic distance. Rotation toward the methylene carbon would give less steric hindrance. Conformation (a) gives the maximum separation of the two carboxyls, but is an opposed conformation. The 45° angle of rotation was used arbitrarily because the small internal bond angle of the cyclobutane ring prevents perfect staggering of the groups. Conformation (c) retains the maximum separation of the carboxyls in rotated position, but the group turned toward the *gem*-dimethyl group is in a sterically unfavorable position. Conformation (b) is most favorable sterically but brings the carboxyls closer together.

The *cis* and *trans* configuration of the specific isomers is still open to question in some cases. As stated above, the *cis*- and *trans*-norpinic acids have been identified. This identification voids the argument of Guha, *et al.*,[17] for the structures of the pinic acids. Stinson and Lawrence[2] did not state whether their homopinic acid was assumed to be the *cis* or the *trans* compound, but if it were pure then it must have been *trans* because it was optically active. However, both *cis* and *trans* forms were considered in the calculations.

In Table III the results of the calculations of interprotonic distance for the various assumed conformations of norpinic, pinic and homopinic acids using Westheimer's and Bjerrum's formulas are compared with those calculated trigonometrically; R_T is the interprotonic distance calculated from the assigned bond lengths, bond angles and steric conformation; R_W is the distance calculated from the Westheimer equation using the same assigned values as those from which R_T was calculated; R_B is the distance obtained by the application of Bjerrum's formula. The exact degree of uncertainty of the values is not known, but is unlikely to be less than ±3%. With this in mind, the data indicate that ionization constants of the 1,3-cyclobutanedicarboxylic acids have only limited value in determining the configuration or conformation of the isomers.

TABLE III

Acid	log (K_1/ $4K_2$)	Assumed isomer	Molecular form	Cosine θ	R_T	R_W	R_B
Planar ring							
Norpinic	0.58	*cis*	Sphere	−0.088	5.48	5.25	5.16
	.52	*trans*	Ellipse	.....	7.44	7.32	5.75
Pinic	.39	*cis*	Sphere	− .651	7.83	6.70	7.67
	.39	*trans*	Ellipse	.....	8.22	8.19	7.67
Homopinic	.32	*cis*[a]	Ellipse	.....	9.72	8.98	9.35
		trans[a]	Ellipse	.....	9.80	8.98	9.35
		cis[b]	Sphere	− .527	8.38	6.86	9.35
		trans[b]	Sphere	− .650	8.63	7.12	9.35
		cis[c]	Ellipse	.....	9.28	8.98	9.35
		trans[c]	Ellipse	.....	9.50	8.98	9.35
Puckered ring, dihedral angle 33°							
Norpinic	0.58	*cis*	Ellipse	....	7.88	7.17	5.16
	.52	*trans*	Sphere	− .600	6.36	6.10	5.75
Pinic	.39	*cis*	Ellipse	.....	8.69	8.19	7.67
	.39	*trans*[d]	Ellipse	.....	8.47	8.19	7.67
		trans[e]	Sphere	− .002	5.70	5.68	7.67
Homopinic	.32	*cis*[a]	Ellipse	.....	9.48	8.98	9.35
		trans[a]	Sphere	− .610	8.38	7.05	9.35
		cis[b]	Sphere	− .577	8.30	7.02	9.35
		trans[b]	Sphere	− .336	7.37	6.55	9.35
		cis[b]	Ellipse	.....	9.21	8.98	9.35
		trans[c]	Ellipse	.....	9.38	8.98	9.35

[a] Carboxyls are assumed to be extended and coplanar with C_1, C_3 and the hydrogens of the ring. [b] Carboxyls are turned 45° from the positions in (a) and located on the same side of the plane. [c] Carboxyls are turned 45° from the position in (a) and located on opposite sides of the plane. [d] COOH axial. [e] CH_2COOH axial.

In the case of the norpinic acids, where the *cis* and *trans* configurations are known, there are significant differences in the interprotonic distances calculated for the two isomers, but if less pucker were assumed even this difference would disappear.

In the case of homopinic acid conformations, (b) can probably be rejected on the basis of the poor

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[16] J. D. Dunitz, *Acta Cryst.*, **2**, 1 (1949).

[17] P. C. Guha, K. Ganapathi and V. K. Subramanian, *Ber.*, **70**, 1505 (1937).

agreement of R_T with either R_W or R_B. Conformation (c) gives better agreement than conformation (a) but planar and puckered conformations and *cis* and *trans* configurations are indistinguishable.

On the basis of infrared spectra the two samples of pinic acid used had different *cis–trans* configurations, but both gave the same dissociation constants. The better agreement of R_T with R_W would favor the puckered conformation of the *cis* form over the planar one; but no choice can be made for the *trans* form.

As might be anticipated the values for R_B agree well with R_T values for homopinic acid, but less well for pinic and norpinic acids.

Experimental

The terpene acids were obtained by appropriate reactions with α- and β-pinene.

Nopinic Acid.—β-Pinene was oxidized with permanganate in an ammonium sulfate-buffered solution and the crystalline product recrystallized from benzene; m.p. 125–126°.

***dl*-Pinonic Acid.**—α-Pinene was oxidized in the same way[18] and the solid product was recrystallized from water and then from acetone; m.p. 104°.

***dl*-Pinolic Acid.**—*dl*-Pinonic acid with 1% by weight of platinum oxide catalyst was placed in a rocking-type hydrogenator and an excess of aqueous alkali was added. The system was flushed with hydrogen in the usual manner and the addition of hydrogen at forty pounds pressure was begun without delay. Complete reduction at room temperature usually took from 2 to 5 days. The product was recovered from the acidified solution with chloroform which was evaporated under vacuum with little or no heat. The residue was recrystallized from acetonitrile to m.p. 100°.

***dl*-Pinic Acid.**—*dl*-Pinonic acid was oxidized with hypobromite by the conventional procedure.[19] The product was recrystallized from water; m.p. 99–101°.

***l*-Pinic Acid.**—The dimethyl ester of crude pinic acid, obtained from α-pinene having $\alpha^{25}\text{D}$ +23°, was refluxed with sodium methylate[20] followed by saponification. The product when recrystallized from water melted 135°, $[\alpha]\text{D}$ in ether −3°.

***sym*-Homopinic Acid.**—The homopinic acid was obtained by the Willgerodt reaction with pinonic acid according to Stinson and Lawrence[2] and was supplied by these authors; m.p. 113–117°.

***cis-dl*-Camphenic Acid.**—Camphene was oxidized with permanganate by the procedure of Aschan[21] to give *cis-dl*-camphenic acid, m.p. 136–137°.

***d*-Pinononic Acid.**—α-Pinene was oxidized with air[3] and distilled to give a cut rich in verbenone and verbenol. This fraction was then oxidized with permanganate in an ammonium sulfate-buffered solution to give pinononic acid. The crude acid was recrystallized to give a product, m.p. 131°, $[\alpha]\text{D}$ +42.5° in ether.

***cis*-Norpinic Acid.**—Pinononic acid was oxidized with hypochlorite and the product purified by recrystallization from dilute hydrochloric acid; m.p. 176°.

***trans*-Norpinic Acid.**[10]—*cis*-Norpinic acid was heated at 180° in a sealed tube with 6 N HCl for two hours which gave a mixture of *cis*- and *trans*-norpinic acid. The *trans*-norpinic acid was separated from the *cis* compound by recrystallization from ether. The purified product melted 179°; admixed with *cis*-norpinic acid, m.p. 137–144°.

***cis-d*-Camphoric Acid.**—The sample of this material was obtained commercially and melted 186–188°.

Adipic Acid.—This sample also was obtained commercially and recrystallized to give m.p. 152–153°.

Procedure.—The dissociation constants were determined, with a few minor alterations, according to the method of Speakman.[8] The titrations were made at room temperature (held between 25 and 30°) using a *p*H meter. Measurements were made with a glass electrode which was inserted directly into the sample solution, and a saturated calomel electrode which dipped into a saturated potassium chloride solution and was connected to the sample solution by means of a capillary tube filled with saturated potassium chloride. As indicated by Speakman, it was necessary that the capillary be drawn to a very small diameter and then bent into several loops or waves in order to avoid contamination of the sample solution with potassium chloride. The sample solution was checked and found negative for chloride ion after each titration.

The system was standardized before and after each titration with buffers recommended by Taylor and Hitchcock.[22] Potassium acid phthalate, 0.05 M, was used for *p*H 4.01 and 0.025 M K_2HPO_4 + 0.025 M KH_2PO_4 for *p*H 6.86. Usually an additional check was made with the needle marker for the neutral position of the instrument settings when the titration had progressed to the point of about *p*H 7.

All solutions were made up with distilled water which had been swept free of carbon dioxide with a stream of nitrogen. The sample solution was prepared by pipetting 50 ml. of water into the titrating cup which contained a known amount of acid to give a molar concentration ranging from 0.727×10^{-3} to 1.348×10^{-3} for monobasic acids and from 0.386×10^{-3} to 0.691×10^{-3} for dibasic acids. Titrations were made with 0.106 N carbonate-free sodium hydroxide using a mercury-operated micro-buret of 1-ml. capacity reading to 0.0001 ml. The solution was stirred during the titration with a stream of water-saturated nitrogen, both to keep the solution free of carbon dioxide and to avoid the *p*H meter fluctuation encountered when using magnetic stirrers for agitation.[23] Several readings of *p*H value were taken between 25 and 75% of neutralization and again toward complete neutralization to check the concentration of the acid.

Acknowledgment.—The authors are indebted to Dr. C. Golumbic for his helpful suggestions during the early part of this work. We also wish to express our appreciation to Mr. J. S. Stinson and Mr. Ray V. Lawrence for the sample of *sym*-homopinic acid, to Dr. Bernard H. Braun for the sample of camphenic acid and to Mr. A. A Sekul for the samples of pinononic and *cis*-norpinic acid which were used in these experiments.

OLUSTEE, FLA.

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[18] M. Delépine, *Bull. soc. chim.*, [5] **3**, 1369 (1936).

[19] Conrad Weygand, "Organic Preparations," Interscience Publishers, Inc., New York, N. Y., 1945, p. 459.

[20] E. R. Buchman, A. O. Reims and M. J. Schlatter, THIS JOURNAL, **64**, 2703 (1942).

[21] Ossian Aschan, *Ann.*, **383**, 52 (1911).

[22] D. I. Hitchcock and A. C. Taylor, THIS JOURNAL, **59**, 1812 (1937).

[23] G. F. Livingston, *Chemist-Analyst*, **43**, 106 (1954).