protons of near 90°.[8] In contrast, the spectrum of the *cis* compound did show coupling between the C-4 and C-5 protons. The C-5 proton appeared as two overlapping quartets at τ 5.35 ($J \sim 8$ c.p.s.) indicating the dihedral angle is approximately 0° as expected for *cis* IIId. The downfield shift for the C-5 proton from the *trans* to the *cis* compound can be explained in terms of more effective shielding by the methyl groups in the former. This downfield shift also occurs for the C-4 protons. The C-4 proton appears as a multiplet at τ 6.35 in the *trans* oxazoline and at τ 5.95 in the *cis*. Again, in both cases, the C-4 proton couples with the α-methylene protons in the 2-position. Each of the five oxazolines had a strong infrared absorption peak at 1650 cm.$^{-1}$ (C═N) and was transparent in the region 3100–3600 cm.$^{-1}$.

Experimental Section[9]

Butyramidine.[10]—A mixture of 39 g. (1 mole) of sodamide in 250 ml. of *p*-xylene was stirred under N_2 while 69 g. (1 mole) of butyronitrile was added over a 30-min. period. The mixture was then stirred and heated at 105–110° for 3 hr. After cooling, 250 ml. of toluene was added to reduce the freezing point of the solvent, and the reaction flask was fitted with a Dry Ice condenser, and liquid ammonia was added until the mixture became slushy. Ammonium chloride (53 g., 1 mole) was then carefully added to the stirred mixture over a 2-hr. period. The ammonia was allowed to evaporate and the mixture stood for 3 days under N_2 with occasional stirring. The mixture was filtered, the solids were washed with benzene, and the combined filtrate and washings were distilled under reduced pressure. The pressure was periodically adjusted to keep the distillation temperature below 50° until the solvents had been removed. The product was then distilled, b.p. 83–87° (3 mm.). The yield was 60 g. (70%), and the product had a melting point of 26–27°. An analytical sample was obtained by fractionation, b.p. 96° (10 mm.).

Anal. Calcd. for $C_4H_{10}N_2$: C, 55.80; H, 11.71; N, 32.53. Found: C, 55.66; H, 11.74; N, 31.71.

The product formed a hydrochloride[11] with m.p. 107–109° (ethyl acetate–isopropyl alcohol).

Anal. Calcd. for $C_4H_{11}ClN_2$: C, 39.18; H, 9.04; N, 22.86. Found: C, 39.38; H, 9.22; N, 22.57.

Reaction of Butyramidine with Ethylene Oxide (Ia).—A mixture of 8.6 g. (0.1 mole) of butyramidine and 13 g. (0.3 mole) of ethylene oxide was allowed to stand for 3 days at room temperature in a pressure bottle. There was no increase in pressure. Removal of the excess epoxide left a viscous liquid with an infrared spectrum consistent[3a] with the structure IIa, showing peaks at 1610, 1570, and 3340 (broad) cm.$^{-1}$. Attempts to distil this product at reduced pressure resulted in decomposition to form 2-propyl-2-oxazoline (IIIa). The distillation temperature gradually rose from 53 to 165° (0.8 mm.). The distillate was then redistilled at atmospheric pressure to give 4.6 g. (40% yield) of IIIa, b.p. 135–145°. Fractionation gave an analytical sample b.p. 141°.

Anal. Calcd. for $C_6H_{11}NO$: C, 63.69; H, 9.79; N, 12.39. Found: C, 63.70; H, 9.86; N, 12.45.

The product gave 2-(3,5-dinitrobenzamido)ethyl butyrate, m.p. 75–77° (ethanol–water), on reaction with 3,5-dinitrobenzoyl chloride in $NaHCO_3$ solution.[12]

Anal. Calcd. for $C_{13}H_{15}N_3O_7$: C, 48.00; H, 4.65; N, 12.92. Found: C, 48.05; H, 4.83; N, 13.05.

Reaction with Propylene Oxide (Ib).—A mixture of 0.1 mole of butyramidine and 0.2 mole of propylene oxide in a pressure bottle was allowed to stand at room temperature for 3 days. An infrared spectrum of the product corresponded to the intermediate IIb; however, a peak at 1650 cm.$^{-1}$ indicated the presence of some 2-propyl-5-methyl-2-oxazoline (IIIb) also. The material evolved NH_3 on distillation under reduced pressure, and the distillation temperature gradually rose from 30 to 53° (3 mm.). Redistillation at 40 mm. gave 10.6 g. (83% yield) of IIIb, identical with an authentic sample.[6]

Reaction with 1,2-Butylene Oxide (Ic).—A mixture of 0.1 mole of butyramidine and 0.2 mole of 1,2-butylene oxide was heated on an oil bath at 50° for 8 hr. The excess epoxide was then removed, and the product distilled at reduced pressure, b.p. 65–75° (15 mm.). The yield was 11.5 g. (82%) of 2-propyl-5-ethyl-2-oxazoline (IIIc). An analytical sample was obtained by Todd column fractionation, b.p. 76° (20 mm.).

Anal. Calcd. for $C_8H_{15}NO$: C, 68.09; H, 10.71; N, 9.92. Found: C, 67.55; H, 10.35; N, 10.48.

1-(3,5-Dinitrobenzamido)-2-butyl butyrate from the oxazoline and 3,5-dinitrobenzoyl chloride melted at 90–91° (alcohol).

Anal. Calcd. for $C_{15}H_{19}N_3O_7$: C, 51.00; H, 5.42; N, 11.90. Found: C, 51.26; H, 5.57; N, 11.02.

When the reaction was repeated and the reactants allowed to stand 3 days at room temperature, the infrared spectrum indicated a mixture of the oxazoline IIIc and the intermediate IIc.

Reaction with *cis*-2,3-Butylene Oxide (Id).—A mixture of 8.6 g. (0.1 mole) of butyramidine and 14.4 g. (0.2 mole) of *cis*-2,3 butylene oxide underwent no change on standing 3 days at room temperature and was therefore heated on an oil bath at 75° for 20 hr. The excess epoxide was removed and the product was distilled. Six grams (42% yield) of *trans*-2-propyl-4,5-dimethyl-2-oxazoline (IIId) was obtained, b.p. 60–66° (27 mm.). The analytical sample, obtained by fractionation of the product on a Todd column, had a boiling point of 69° (30 mm.), $n^{20}D$ 1.4262.

Anal. Calcd. for $C_8H_{15}NO$: C, 68.05; H, 10.71; N, 9.92. Found: C, 67.74; H, 10.50; N, 10.42.

The derivative with 3,5-dinitrobenzoyl chloride, *threo*-3-(3,5-dinitrobenzamido)-2-butyl butyrate, melted at 131–132° (alcohol).

Anal. Calcd. for $C_{15}H_{19}N_3O_7$: C, 50.99; H, 5.42; N, 11.89. Found: C, 51.05; H, 5.32; N, 12.03.

Reaction with *trans*-2,3-Butylene Oxide (Id).—A mixture of 0.1 mole of butyramidine and 0.2 mole of *trans*-2,3-butylene oxide remained unchanged after heating 20 hr. on an oil bath at 75°. The mixture was then placed in a pressure bottle and heated at 100° for 5 hr. until there was no more pressure increase. The excess epoxide was removed and the product was distilled. *cis*-2-Propyl-4,5-dimethyl-2-oxazoline (IIId, 9.5 g., 60% yield) was obtained, b.p. 70–75° (30 mm.). Fractionation gave an analytical sample, b.p. 77° (32 mm.), $n^{20}D$ 1.4362.

Anal. Calcd. for $C_8H_{15}NO$: C, 68.05; H, 10.71; N, 9.92. Found: C, 67.68; H, 10.58; N, 10.27.

Reaction of the oxazoline with 3,5-dinitrobenzoyl chloride in $NaHCO_3$ solution gave an oil which did not crystallize.

Acknowledgment.—Appreciation is expressed to Dr. Richard Anderson of Utah State University for determination of the n.m.r. spectra and assistance with their interpretation.

Baeyer–Villiger Oxidation of Cyclopropyl Ketones

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Although a great deal of data has been published concerning migratory aptitudes in the Baeyer–Villiger reaction,[2] very little is known about the behavior of

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[8] R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1963, p. 79.

[9] Microanalyses were by Huffman Laboratories, Wheatridge, Colo. N.m.r. spectra were run at 60 Mc. in deuteriochloroform with tetramethylsilane as an internal standard. Infrared spectra were on neat material.

[10] This preparation is a modification of that described by E. F. Cornell, *J. Am. Chem. Soc.*, **50**, 3311 (1928).

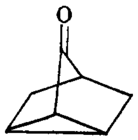
[11] H. R. Henze and S. O. Winthrop [*J. Am. Chem. Soc.*, **79**, 2230 (1957)] report m.p. 95–98° for a crude product.

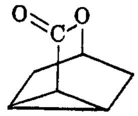
[12] Preparation of oxazoline derivatives by reaction with acid chlorides in aqueous base is described by E. M. Frey, *J. Org. Chem.*, **15**, 802 (1950).

[1] Henry Rutgers Scholar, 1964–1965; National Science Foundation Undergraduate Research Fellow, 1964–1965.

[2] For a recent review, see P. A. S. Smith in "Molecular Rearrangements," Vol. I. P. DeMayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp. 577–591.

cyclopropyl systems. Emmons and Lucas[3] reported that methyl cyclopropyl ketone gave cyclopropyl acetate on treatment with trifluoroacetic acid. Yukawa and Yokoyama reported that phenyl cyclopropyl ketone was converted by perbenzoic acid to an 84:16 mixture of esters with phenyl migration predominating.[4] Nortricyclanone (I) reacts with peracetic acid with preferential migration of the cyclopentyl moiety to give II.[5]


I


II

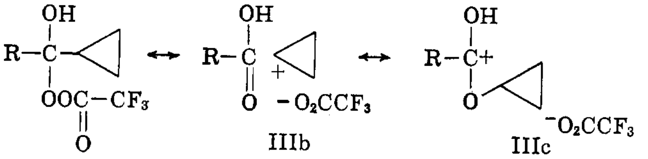
It seemed appropriate to carry out a more systematic study of cyclopropyl systems in an effort to correlate the isolated cases listed. With this in mind, the following ketones were subjected to oxidation with trifluoroperacetic and *m*-chloroperbenzoic acids[6]: methyl cyclopropyl, ethyl cyclopropyl, isopropyl cyclopropyl, and phenyl cyclopropyl. Table I lists the results.

TABLE I

BAEYER–VILLIGER PRODUCT DISTRIBUTIONS

Ketone, $R\overset{O}{\overset{\|}{C}}C_3H_5$ R	*m*-Chloroperbenzoic acid		Trifluoroperacetic acid	
	ROOC—◁, %	RCOO—◁, %	ROOC—◁, %	RCOO—◁, %
CH_3	5	95	4	96
C_2H_5	..	..	79	21
i-C_3H_7	99	1	94	6
C_6H_5	97	3	97	3

From these results it can be seen that the migratory sequence observed, $C_6H_5 \sim i\text{-}C_3H_7 > C_2H_5 > C_3H_5 > CH_3$, is consistent with earlier work.[2,7] The position of the cyclopropyl group in this series is presumably a reflection of the instability of resonance structures such as IIIb in the transition states.



IIIa IIIb IIIc

Note should be made of the fact that in this study a small amount of methyl cyclopropanecarboxylate was found in the product of oxidation of methyl cyclopropyl ketone in contrast to literature reports.[3,8] The only disturbing aspect of these results is the contrast between this work and that of Yukawa and Yokoyama with phenyl cyclopropyl ketone. Although the peracids used were different, it does not seem reasonable to attribute the discrepancy to this aspect since we find very little difference between trifluoroperacetic acid and *m*-chloroperbenzoic acid.

It is interesting that the isopropyl group appears to be a slightly poorer migrating group than phenyl in the runs with trifluoroperacetic acid. This is probably a result of the difference in methods of determining the ratio. The reported ratio,[7] 1.9:1, was determined by direct competition, but the positions of the transition states may be slightly different in the two cases.

Experimental Section

The gas chromatographic equipment used was an Aerograph A-90-P2 and a Barber Colman Model 5000 with flame-ionization detector. The analysis was by G. Robertson, Florham Park, N. J.

Ketones.—Methyl cyclopropyl ketone and phenyl cyclopropyl ketone were used as purchased from Aldrich Chemical Corp.

Ethyl cyclopropyl ketone was prepared by addition of cyclopropyl cyanide to ethylmagnesium bromide.[9] The ketone was obtained in 88% yield and had b.p. 132°, $n^{27}D$ 1.4270 (lit.[10] b.p. 131.8°, $n^{20}D$ 1.42986). Isopropyl cyclopropyl ketone was prepared in a similar manner and had b.p. 139–146° (lit.[10] b.p. 141–141.4°).

Baeyer–Villiger Reactions. A. Trifluoroperacetic Acid.—In all cases, these were run essentially according to directions given by Emmons and Lucas.[3]

B. *m*-Chloroperbenzoic Acid.—A 1.2 molar excess of the peracid was used in all cases. The general procedure was to dissolve the ketone and peracid in methylene chloride and allow the solution to stand at 25° for 35 days. The precipitated *m*-chlorobenzoic acid was removed by filtration and the filtrate was washed with aqueous sodium bisulfite and sodium carbonate solutions. The dried (Na_2SO_4) solution was evaporated and the crude products were analyzed by gas chromatography.

In all cases, ketone remained at the end of the reaction periods and attempts were not made to isolate pure products. The methyl and ethyl systems were especially unreactive, with *ca.* 80 and 50% unreacted ketone remaining, respectively.

Esters.—All of the cyclopropanecarboxylates were synthesized for spectral comparison and the gas chromatographic work. The method of Spassow[11] was used in all cases. Methyl cyclopropanecarboxylate had b.p. 116–118° (lit.[12] b.p. 117.5° at (763 mm.). Ethyl cyclopropanecarboxylate had b.p. 131–133° (lit.[12] b.p. 133° at 763 mm.). Phenyl cyclopropanecarboxylate had b.p. 136° at 33 mm. (lit.[13] b.p. 117–118° at 13 mm.). Isopropyl cyclopropanecarboxylate had b.p. 63° at 46 mm.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.43. Found: C, 65.25; H, 9.33.

Cyclopropyl acetate was prepared by the method of Emmons and Lucas.[3] The remaining esters were not synthesized owing to experimental difficulties.[8] Their presence in the reaction products was proved by reduction of the crude oxidation products with lithium aluminum hydride and gas chromatographic analysis of the alcohols.

Gas Chromatographic Analyses.—The methyl system was analyzed on a 150 ft. × 0.01 in. column coated with Ucon 50-HB-2000 at 68°. The ethyl system was not completely resolved by any of the available columns. Reduction to the alcohols proved satisfactory and the analysis was carried out on a 25 ft. × 1/8 in. column of 5% Carbowax 20M on Chromosorb G at 115°. The areas were calibrated against a weight mixture of *n*-propyl alcohol and cyclopropylcarbinol. The isopropyl system was likewise best analyzed by conversion to the alcohols. Analysis could be made by a comparison of the areas of isobutyl alcohol and cyclopropylcarbinol against a standard mixture. The phenyl system was reduced to a mixture in which the benzyl alcohol

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[3] W. D. Emmons and G. B. Lucas, *J. Am. Chem. Soc.*, **77**, 2287 (1955).

[4] Y. Yukawa and T. Yokoyama, *Mem. Inst. Sci. Ind. Res., Osaka Univ.*, **13**, 171 (1956).

[5] R. R. Sauers, *Tetrahedron Letters*, 1015 (1962).

[6] We are indebted to the FMC Corp., New York, N. Y., for a generous gift of *m*-chloroperbenzoic acid.

[7] M. F. Hawthorne, W. D. Emmons, and K. S. McCallum, *J. Am. Chem. Soc.*, **80**, 6393 (1958).

[8] C. H. DePuy and L. R. Mahoney, *ibid.*, **86**, 2653 (1964).

[9] R. B. Moffett and R. L. Shriner, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 562.

[10] P. Bruylants, *Bull. soc. chim. Belges*, **36**, 519 (1927).

[11] A. Spassow, *Ber.*, **75**, 779 (1942).

[12] G. Jeffery and A. Vogel, *J. Chem. Soc.*, 1804 (1948).

[13] S. Skroup and O. Binder, *Ber.*, **62**, 1127 (1929).

and phenol were assayed by calibration against a weighed mixture on a 9-ft. Carbowax 20M packed column at 190°.

In general, the errors are probably large in the case of the runs in which a minor product was formed to the extent of 5% or less. These results are probably good to only ±1%.

The infrared and n.m.r. spectra of the pure esters were checked against these runs also and found to be essentially identical in all cases.

The Cyclization of Some β-Ferrocenylpropionic Acids

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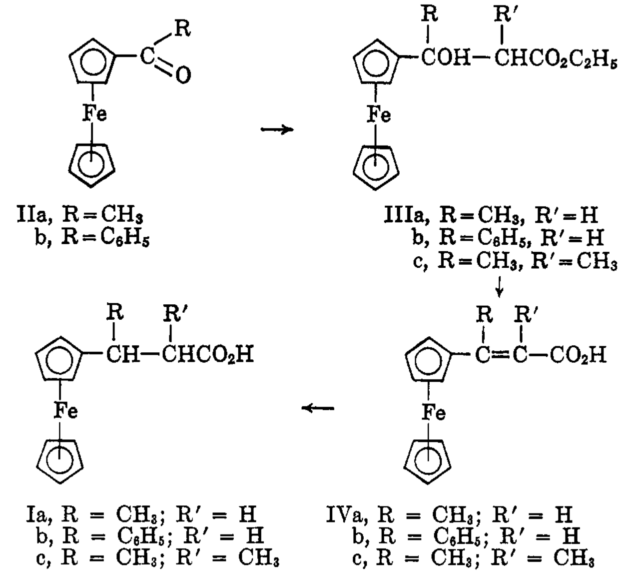
It has been found that cyclization of a variety of β-ferrocenylpropionic acids under Friedel-Crafts gives rise to heteroannularly substituted ("bridged") ketones,[2] rather than the homoannular indanone analogs. Although there are a few examples where a heavily substituted ferrocenylpropionic acid derivative gives the homoannular ketone,[2d,3] there appears to be little known about the effect of substitution in the propionic acid side chain upon the course of these cyclizations. It was initially felt that by suitable modifications of the alkyl portion of the molecule it might be possible to obtain acids which would undergo cyclization to give significant quantities of the homoannular products.[4] In addition, it was felt that such a study would give some insight into the steric factors governing the course of these cyclizations.

The acids chosen for this work were β-methyl- (Ia), β-phenyl- (Ib), and α,β-dimethyl-β-ferrocenyl propionic acids (Ic). Acids Ia and Ic were prepared from acetylferrocene[5] (IIa) in four steps. Reaction of the ketone with ethyl bromoacetate or ethyl α-bromopropionate under standard Reformatsky conditions gave the hydroxy esters IIIa and IIIc, respectively. Dehydration with toluenesulfonic acid in benzene followed by saponification gave the unsaturated acids IVa and IVc. Although ferrocenylcrotonic acid (IVa) was obtained as a crystalline solid, the α-methylcrotonic acid (IVc) could not be solidified and may well be a mixture of stereoisomers. β-Ferrocenylcinnamic acid (IVb) was prepared from benzoylferrocene[6] (IIb) by a similar sequence of reactions. The substituted β-ferrocenylpropionic acids were readily obtained from the unsaturated compounds by hydrogenation. Although β-ferrocenylbutyric and β-ferrocenyldihydrocinnamic acids were solids, the α,β-dimethyl acid Ic was an oil, presumably a mixture of the *erythro* and *threo* isomers.



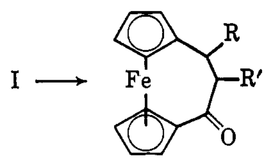
IIa, $R = CH_3$
b, $R = C_6H_5$

IIIa, $R = CH_3$, $R' = H$
b, $R = C_6H_5$, $R' = H$
c, $R = CH_3$, $R' = CH_3$

Ia, $R = CH_3$; $R' = H$
b, $R = C_6H_5$; $R' = H$
c, $R = CH_3$; $R' = CH_3$

IVa, $R = CH_3$; $R' = H$
b, $R = C_6H_5$; $R' = H$
c, $R = CH_3$; $R' = CH_3$

Cyclization of β-ferrocenylbutyric acid by either polyphosphoric acid or trifluoroacetic anhydride gave a single, crystalline ketone in yields of 32 and 75%, respectively. This compound was a monomer of formula $C_{14}H_{14}FeO$ and showed infrared absorption at 6.06 μ and no high-intensity ultraviolet maximum above 230 mμ. These data are all consistent with the published spectra of 1,1'-(α-ketotrimethylene)ferrocene[2e,7] (Vd), and when coupled with the absence of infrared bands at 9 and 10 μ[8] indicate that this compound is 1,1'-(α-keto-α'-methyltrimethylene)ferrocene (Va). The cyclization products of ferrocenylhydrocinnamic acid (Ib) and the α,β-dimethyl acid Ic also had properties consistent with bridged structures Vb and Vc. It is thus apparent that, at least in the relatively simple substituted ferrocenylpropionic acid derivatives studied, the intramolecular Friedel-Crafts reaction gives heteroannular cyclization.



Va, $R = CH_3$; $R' = H$
b, $R = C_6H_5$; $R' = H$
c, $R = CH_3$; $R' = CH_3$
d, $R = H$; $R' = H$

Experimental Section[9]

β-Ferrocenylcrotonic Acid.—To a mixture of 5.00 g. (2.19×10^{-2} mole) of acetylferrocene in 150 ml. of anhydrous benzene, and 65.38 g. of metallic zinc (previously activated by treatment with 5% hydrochloric acid, successive washings with water,

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[1] Abstracted from the Ph.D. Thesis of R. L. Asbury, Clemson University, Jan. 1965.

[2] (a) K. L. Rinehart and R. J. Curby, *J. Am. Chem. Soc.*, **79**, 3290 (1957); (b) K. Schlögl and H. Seiler, *Tetrahedron Letters*, **No. 7**, 4 (1960); (c) M. Rosenblum, A. K. Banarjee, N. Danieli, R. W. Fish, and V. Schlatter, *J. Am. Chem. Soc.*, **85**, 316 (1963); (d) K. L. Rinehart, D. E. Bublitz, and D. H. Gustafson, *ibid.*, **85**, 970 (1963); (e) K. L. Rinehart, R. J. Curby, D. H. Gustafson, H. G. Harrison, R. E. Bozak, and D. E. Bublitz, *ibid.*, **84**, 3263 (1962); (f) E. A. Hill and J. H. Richards, *ibid.*, **83**, 4216 (1961).

[3] D. E. Bublitz and K. C. Rinehart, *Tetrahedron Letters*, 827 (1964).

[4] While this work was in progress, it was reported (ref. 2c) that α,α-dimethyl-β-ferrocenylpropionic acid does in fact give both homoannular and heteroannular ketones on cyclization with trifluoroacetic anhydride.

[5] P. J. Graham, R. V. Linsey, G. N. Parshall, M. L. Peterson, and G. M. Whitman, *J. Am. Chem. Soc.*, **79**, 3416 (1957).

[6] N. Weliky and E. S. Gould, *ibid.*, **79**, 2742 (1957).

[7] Although Rinehart, *et al.*,[2e] report the carbonyl band of Vd at 5.95 μ, their spectrum was determined in carbon disulfide solution, while ours were run as Nujol mulls. The carbonyl absorption of Vd in Nujol appears at 6.02 μ (R. L. Asbury, Ph.D. Thesis, Clemson University, 1965).

[8] M. Rosenblum and R. B. Woodward, *J. Am. Chem. Soc.*, **80**, 5443 (1958).

[9] All melting points were taken on a Hershberg melting point apparatus and are uncorrected. Infrared spectra were recorded as liquid films or as Nujol mulls using a Perkin-Elmer Model 137 spectrophotometer. Microanalyses were carried out by either Galbraith Laboratories, Knoxville, Tenn., or Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.