

dride (50 cc.) containing sulfuric acid (4 drops). The apparatus was flushed with nitrogen and the solution was heated for 12 hr. at 60°. The product (1.14 g.), isolated in the usual way and recrystallized twice from ethyl acetate, melted at 198.5–199.5°.

*Anal.* Calcd. for  $C_{20}H_{18}O_4$ : C, 74.51; H, 5.62. Found: C, 74.39; H, 5.61.

*3-Benzyl-4,6,7-trimethyl-5-acetoxyisocoumaranone* (IV). A solution of III (0.5 g.) in ethyl acetate (150 cc., distilled over phosphorus pentoxide) was subjected at room temperature to action of hydrogen (29 lb.) in the presence of a platinum oxide catalyst (0.1 g.). In an hour the yellow color disappeared and the absorption of hydrogen ceased. The catalyst was removed and ethyl acetate was removed from the filtrate by distillation. The residual yellow oil (0.44 g.) solidified and then melted at 116–119°. The analytical sample, recrystallized twice from ethanol, melted at 118.5–120°.

*Anal.* Calcd. for  $C_{20}H_{20}O_4$ : C, 74.05; H, 6.21. Found: C, 74.40; H, 6.41.

*3-Benzyl-4,6,7-trimethyl-5-hydroxyisocoumaranone* (V). A solution of II (4.4 g.) in dry ethanol (150 cc.) was subjected at room temperature to the action of hydrogen (36 lb.) in the presence of a platinum oxide catalyst (0.22 g.). The amber solution became yellow in 30 min., pale green in an hour, and colorless after 6 hr. After 22 hr., the catalyst was removed by filtration; the filtrate immediately acquired a yellow color in the air. Most of the solvent (142 cc.) was removed, and the dark residue on standing for some time at 0°, deposited an orange solid (2.22 g.). Most of this material melted at 112–121° to a yellow liquid, but complete melting occurred only when the temperature reached 142°. No pure material could be isolated from this solid by repeated crystallization, but when the material (0.4 g.) was acetylated in the usual way by the action of acetic anhydride, there resulted a solid (0.3 g.) which could be separated into two components by crystallization from absolute ethanol. The major component (0.25 g.) was the acetate IV, m.p., and mixed m.p., 119–120°. The other component (0.01 g.) was insoluble in ethanol and melted at 219–220.5° to a yellow liquid. It was not investigated further. Hydrolysis of the acetate V (0.87 g.) by action of a solution of potassium hydroxide (1.25 g.) in ethanol (25 cc.) for 5 hr. at the boiling point led to a minute amount of brown infusible solid, and a dark oil (0.45 g.) which, by crystallization, gave a small amount of orange solid melting indefinitely at 120–140°. No better results were obtained when V (0.3 g.) was subjected to action of sodium methoxide (from sodium, 0.05 g., and dry methanol, 30 cc.) in an atmosphere of nitrogen.

*3-Anisal-4,6,7-trimethyl-5-hydroxyisocoumaranone* (II, R=H; R' =  $p\text{-CH}_3\text{OC}_6\text{H}_4$ ). A solution of I (1.0 g., 0.005 mole), anisaldehyde (0.63 cc., 0.005 mole), and piperidine (5 drops) in dry ethanol (25 cc.) was processed under nitrogen as described above for preparation of II. The product (1.16 g.) formed bright yellow needles which, after crystallization from ethanol, melted at 170.5–172°.

*Anal.* Calcd. for  $C_{19}H_{18}O_4$ : C, 73.53; H, 5.85. Found: C, 72.94; H, 5.96.

*3-Anisal-4,6,7-trimethyl-5-acetoxyisocoumaranone* (III; R' =  $p\text{-CH}_3\text{OC}_6\text{H}_4$ ) was prepared as described above for III. The analytical sample was recrystallized from acetone, when it melted at 222–223° with some sublimation. The compound held water tenaciously and required a long period of drying under vacuum in a pistol before it became anhydrous.

*Anal.* Calcd. for  $C_{21}H_{20}O_5$ : C, 71.57; H, 5.72. Found: C, 71.70; H, 5.91.

*Reaction of cinnamaldehyde with I.* A solution of I (3 g., 0.015 mole), cinnamaldehyde (1.78 cc., 0.015 mole), and piperidine (5 drops) in dry ethanol (75 cc.) was processed under nitrogen as described above for II. The product (4.38 g.) when dried was a reddish solid melting at 155–175°. Recrystallization of this material from 1:1 ethanol-ligroin (b.p. 30–60°) gave three crops of solid materials: (A) rust

colored, melting at 196–206°; (B) brownish, melting at 195–205°; (C) yellow, melting at 170–180°. No pure materials could be obtained from (B) or (C), but (A), after crystallization four times from acetone-ethanol, yielded small yellow needles melting at 271–273° to a red liquid. This material decomposed when heated slowly—even at 150–170° for 10 min.

*Anal.* Found: C, 73.61, 74.52; H, 6.93, 6.21.

*Reaction of butyraldehyde with I.* The above procedure was applied to the reaction of I (1 g.), butyraldehyde (0.44 cc.), and piperidine (12 drops) in dry ethanol (25 cc.). The reaction mixture, when poured into water, deposited an oil which later solidified. Recrystallization of this material several times from ethanol yielded I (0.17 g.) and a yellow solid (0.01 g.) melting at 218.5–221°; which was formed from two moles of I and one mole of isobutyraldehyde.

*Anal.* Calcd. for  $C_{26}H_{30}O_6$ : C, 71.24; H, 6.85. Found: C, 71.34; H, 6.79.

*Reactions of ketones with I.* When either 2-pentanone or acetophenone was used with I and piperidine, the only product isolated was recovered I plus a minute amount of infusible dark solid.

*Reaction of glyoxal with I.* (A) Solution of I (1 g.), aqueous glyoxal (33%, 0.46 g.), and piperidine (3 drops) in ethanol (25 cc.) was processed as described. A black powder (0.55 g.) and tar were the only products. The black material did not melt below 350°; when extracted with ethanol in a Soxhlet apparatus, only a little I was obtained. (B) Substitution of aniline for piperidine gave essentially the same results—recovery of I (0.56 g. from 1 g.) and production of a dark infusible powder. (C) Glyoxal bisulfite (1.035 g.) was dissolved in hydrochloric acid (5%, 53 cc.), the solution was evaporated to dryness, and the residue was extracted with dry ethanol (50 cc.). To this extract, I (1.5 g.) and pyridine (2 drops) were added and the reaction mixture was processed as above. The product consisted of recovered I (0.53 g.) and a small amount (0.02 g.) of dark infusible material. In a duplicate experiment, except that glyoxal was prepared from the bisulfite compound by action of potassium carbonate, I (2.0 g.) yielded only a black solid in small amount, and 0.92 g. of I was recovered.

*Reaction of benzil with I.* A solution of I (1 g.), benzil (0.52 g.), acetic acid (3 drops), and piperidine (9 drops) in dry ethanol (40 cc.) was processed as above. The cooled solution deposited a small amount of black infusible material, and the filtrate from this, when concentrated, gave 0.67 g. of solid. The rest of the product was a black tar. The solid, extracted with hexane, gave only I (insoluble) and benzil (soluble).

SCHOOL OF CHEMISTRY  
UNIVERSITY OF MINNESOTA  
MINNEAPOLIS 14, MINN.

## Convenient Synthesis of Pyrrocoline<sup>1</sup>

V. BOEKELHEIDE AND WAYNE FEELY

Received December 17, 1956

Although pyrrocoline is one of the fundamental aromatic heterocycles, its chemistry has not been extensively investigated nor has a satisfactory synthesis for the parent compound been devised. The most general method of synthesis for this class of compounds is that developed by Chichibabin<sup>2</sup> and

(1) This investigation was aided by a grant from the National Science Foundation.

(2) A. E. Chichibabin, *Ber.*, **60**, 1607 (1927).

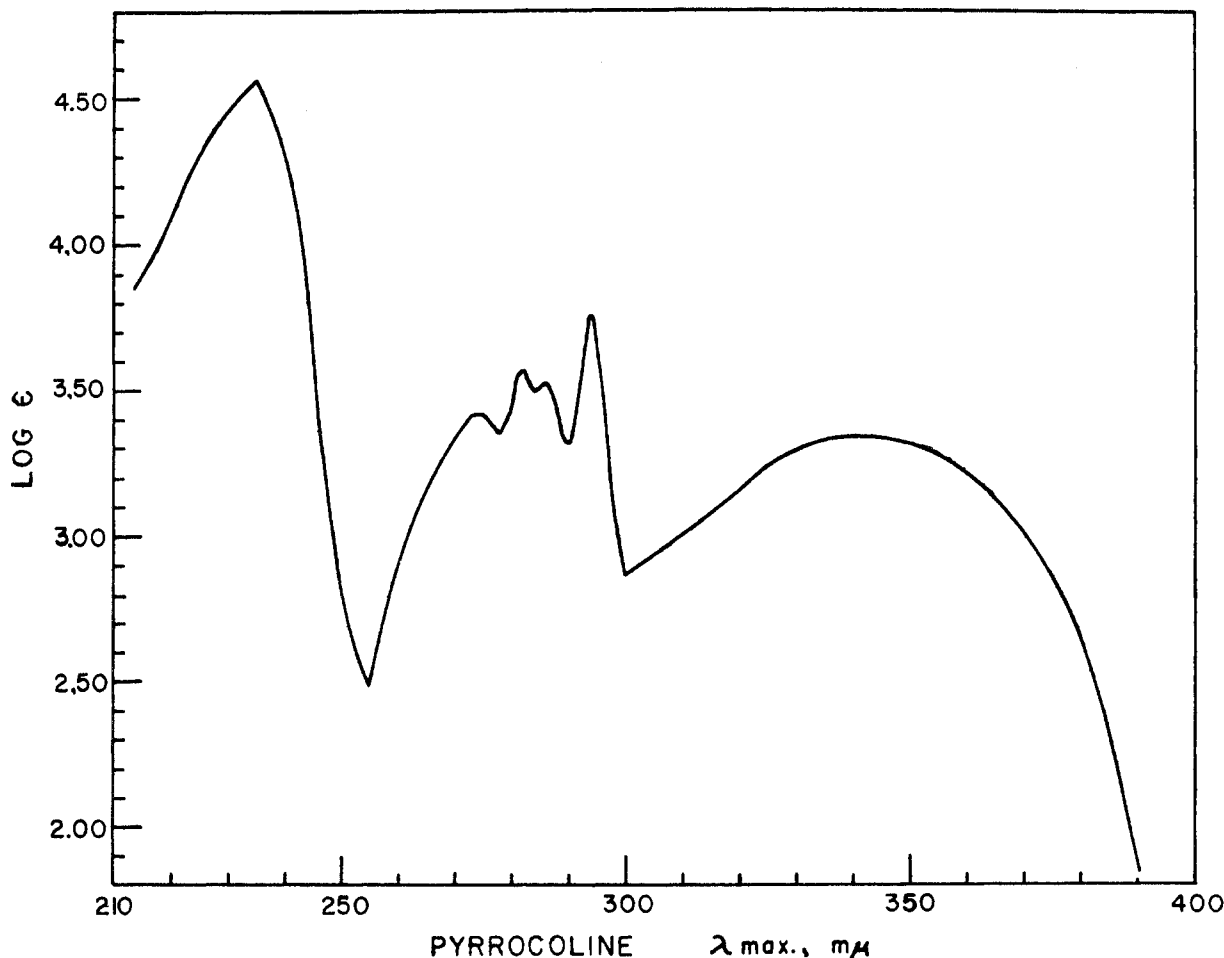
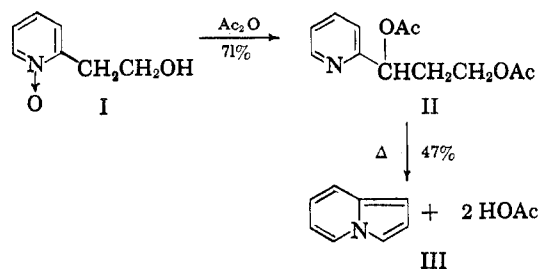


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRUM OF PYRROCOLINE IN 95% ETHANOL (CARY RECORDING SPECTROPHOTOMETER, MODEL 11 MS, QUARTZ CELLS)

this has no practical value for pyrrocoline itself. Borrows and Holland<sup>3</sup> have described the synthesis of 2-carboxy-pyrrocoline in 30% yield by the Chichibabin procedure and presumably<sup>4</sup> this can be decarboxylated to pyrrocoline. Even so, this does not provide an attractive route. Other syntheses of pyrrocoline reported by Diels and Alder and their coworkers,<sup>4</sup> by Wilson,<sup>5</sup> by Krumholtz,<sup>6</sup> and by Brand and Reuter<sup>7</sup> have only incidental or historical interest. Actually the reaction of 2-picoline with acetic anhydride, which led to the original discovery of pyrrocoline by Scholtz,<sup>8</sup> has remained as the best method for its synthesis even though the yield is only about 10%.

In connection with another study on the properties of amine oxides we came into possession of an appreciable quantity of the *N*-oxide of 3-(2'-

pyridyl)propan-1-ol(I) and, because of our continuing interest in pyrrocoline synthesis,<sup>9,10</sup> it was attractive to investigate its usefulness as a precursor for pyrrocoline. We have now found that the 3-(2'-pyridyl)propan-1-ol-*N*-oxide can be converted to pyrrocoline in a two-step process with an over-all yield of 35%. Since the laboratory operations are not difficult and can be adapted to give pyrrocoline on a reasonably large scale, the method represents a marked improvement over earlier procedures.



(3) E. T. Borrows and D. O. Holland, *J. Chem. Soc.*, 672 (1947).

(4) O. Diels, K. Alder, W. Friedrichsen, H. Klare, H. Winkler, and H. Schrum, *Ann.*, **505**, 133 (1933).

(5) C. L. Wilson, *J. Chem. Soc.*, 63 (1945).

(6) P. Krumholtz, *Selecta Chim.*, **8**, 3 (1949); cf. Borrows and Holland, *Chem. Rev.*, **42**, 611 (1948).

(7) K. Brand and K. Reuter, *Ber.*, **72**, 1669 (1939).

(8) M. Scholtz, *Ber.*, **45**, 734 (1912).

(9) V. Boekelheide and J. C. Godfrey, *J. Am. Chem. Soc.*, **75**, 3679 (1953).

(10) E. M. Roberts, M. Gates, and V. Boekelheide, *J. Org. Chem.*, **20**, 1443 (1955).

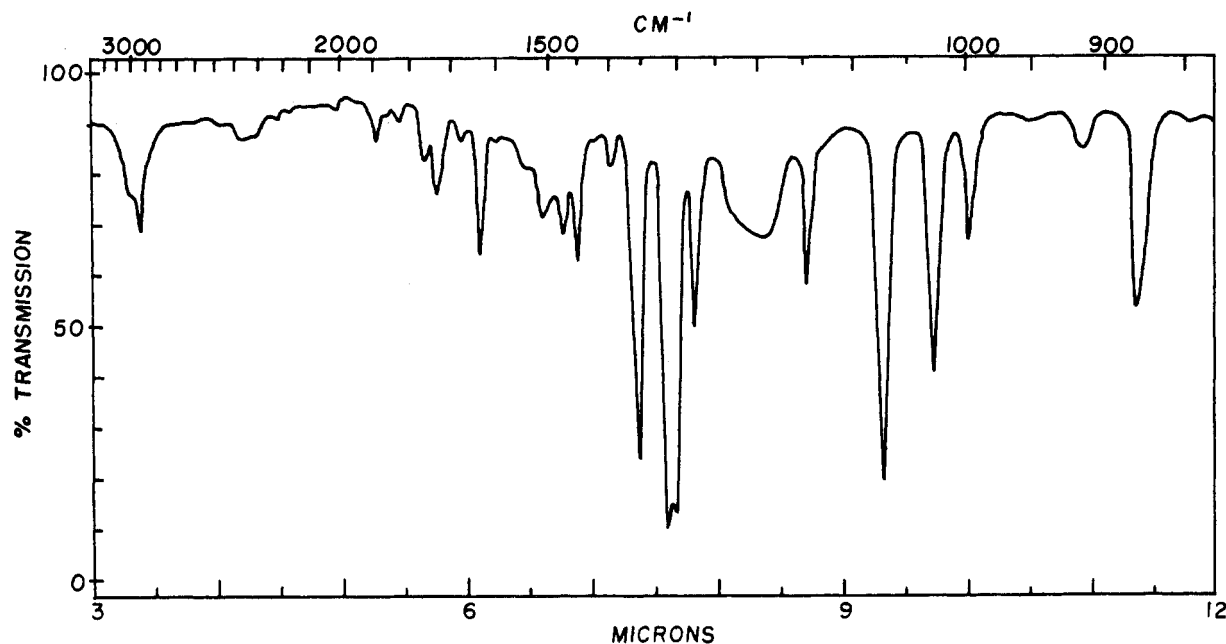


FIG. 2. INFRARED ABSORPTION SPECTRUM OF PYRROCOLINE IN CHLOROFORM USING A PERKIN-ELMER INFRARED SPECTROPHOTOMETER, MODEL 21

As illustrated, the first step in the reaction sequence was the treatment of I with acetic anhydride to give the diacetate, II. This type of rearrangement of pyridine-*N*-oxides has been discussed in detail previously.<sup>11,12</sup> Pyrolysis of the diacetate in a nitrogen atmosphere at 480° then gave pyrrocoline directly. Although the intermediate diacetate could be isolated in a pure state in 71% yield, it was more convenient in most instances to subject the crude reaction product directly to pyrolysis.

In addition to the characterization of pyrrocoline by melting point and analysis, it has been hydrogenated and its octahydro derivative has been shown to be identical with an authentic specimen of octahydropyrrocoline (indolizidine). Since there appears to be no previous record of the ultraviolet and infrared absorption spectra of pyrrocoline in the literature, these are presented in Figs. 1 and 2.

As an alternate method, the diacetate (II) was treated with hydrobromic acid followed by steam distillation of the product from alkali. However, the yield of pyrrocoline by this route was only about 1%.

#### EXPERIMENTAL<sup>13</sup>

**3-(2'-Pyridyl)propan-1-ol-*N*-oxide (I).** To a solution of 137 g. of 3-(2'-pyridyl)propan-1-ol in 1000 ml. of glacial acetic acid there was added slowly 50 ml. of 30% hydrogen peroxide and the resulting mixture was heated at 80° for 2 hr. Then a second addition of 50 ml. of 30% hydrogen peroxide was made and heating at 80° continued for another

2 hr. After a final addition of 100 ml. of 30% hydrogen peroxide, the mixture was heated at 80° for a further 8 hr. The resulting solution was concentrated under reduced pressure, the residue was dissolved in 1 l. of water, and traces of acetic acid were removed by passing the aqueous solution over an ion-exchange column (500 g. of Amberlite-I.R.A.-400-OH<sup>-</sup>). After concentration of the aqueous eluate under reduced pressure, the residual oil was distilled using a short path still, the bulk of the material distilling at 120° at 0.1 mm. The pale yellow distillate was taken up in 1.5 l. of ethyl acetate and crystallization was induced by cooling and seeding the solution. When the solution had been allowed to stand for two days at 0°, the crystals were collected and dried *in vacuo* over phosphorus pentoxide. There was obtained 118 g. (77%) of white crystals, m.p. 52–54°.

*Anal.* Calcd. for C<sub>8</sub>H<sub>11</sub>NO<sub>2</sub>: C, 62.72; H, 7.24. Found: C, 62.87; H, 7.43.

**1-(2'-Pyridyl)-1,3-diacetoxypropane (II).** A solution of 15.3 g. of 3-(2'-pyridyl)propan-1-ol-*N*-oxide (I) in 250 ml. of acetic anhydride was heated on a steam bath for 10 hr. After concentration of the resulting solution under reduced pressure, the residual dark oil was distilled to give 16.8 g. (71%) of a light yellow oil; b.p. 115–118° at 0.7 mm.,  $n_D^{25}$  1.4892.

*Anal.* Calcd. for C<sub>12</sub>H<sub>15</sub>NO<sub>4</sub>: C, 60.75; H, 6.37. Found: C, 60.67; H, 6.36.

**Pyrrocoline (III).** At the top of a tube, 20 mm. in diameter and 250 mm. long and heated at 480°, there was introduced under an atmosphere of nitrogen 65 g. of 1-(2'-pyridyl)-1,3-diacetoxypropane at the rate of 20 drops per min. The pyrolysis products were flushed through the tube with a stream of nitrogen and collected in a three necked flask containing a saturated solution of sodium carbonate. When the pyrolysis was complete, the flask was set for steam distillation and 1 l. of distillate was collected. The product was extracted with ether, dried, and sublimed. This gave 15.0 g. (47%) of white crystals, m.p. 69–71°. Resublimation raised the melting point to 74° (lit.,<sup>8</sup> m.p. 75°). When the crude diacetate (II) was employed without purification by distillation, the over-all yield of pyrrocoline from I was 35%. The product had the typical naphthalene odor and blue fluorescence previously described for pyrrocoline.

*Anal.* Calcd. for C<sub>8</sub>H<sub>7</sub>N: C, 82.01; H, 6.58. Found: C, 81.76; H, 5.90.

(11) V. Boekelheide and W. J. Linn, *J. Am. Chem. Soc.*, **76**, 1286 (1954).

(12) V. Boekelheide and D. L. Harrington, *Chemistry and Industry*, 1423 (1955).

(13) Analyses by Miss A. Smith. All melting points are corrected.

When 117 mg. of these crystals in 10 ml. of ethanol containing a drop of hydrochloric acid and 50 mg. of pre-reduced Adam's catalyst was subjected to hydrogenation at room temperature and atmospheric pressure, there was absorbed 99% of the theoretical amount of hydrogen for 4 moles. Isolation of the product as its picrate derivative gave yellow crystals, m.p. 226°, either alone or mixed with an authentic sample of indolizidine picrate.<sup>14</sup>

DEPARTMENT OF CHEMISTRY  
UNIVERSITY OF ROCHESTER  
ROCHESTER, N. Y.

(14) V. Boekelheide and S. Rothchild, *J. Am. Chem. Soc.*, **70**, 864 (1948).

### Trimethylsilyl Derivatives of Hydroxy Aromatic Acids

CHARLES A. BURKHARD<sup>1</sup>

Received September 27, 1956

Organic chemists have used a number of groups or radicals to protect hydroxyl groups in organic compounds from degradation during distillations, hydrolyses, oxidations, reductions, *etc.* Examples of such protecting groups are illustrated by the use of the methyl or acetyl group to protect the hydroxyl groups of carbohydrates during reaction studies involving the acetal or ketal linkages. In contrast to the ease with which such protecting groups are placed in a carbohydrate, the removal of these groups, especially the methyl group, is difficult. In fact, the reaction conditions required for the removal of these protecting groups may often destroy the compounds during the removal reactions.

The trimethylsilyl group has been used as a protecting group for the hydroxyl groups in the methylolphenols,<sup>2</sup> allyloxy-2,4,6-trimethylolbenzene,<sup>3</sup> and the polyols<sup>4</sup> during separations by distillations. The trimethylsilyl derivatives are thermally stable, *i.e.* they can be distilled without decomposition, and have the added advantage of having either the same or a lower boiling point than that of the original hydroxylic compound. The trimethylsilyl group can be removed very easily by hydrolysis at room temperature to give a mixture of the desired compound and hexamethyldisiloxane. The hexamethyldisiloxane and the excess water can be separated by filtration in the case of solid products or can be removed by evaporation at room temperature at a low pressure.

During a recent study of the carbonation of phenol it became necessary to devise a method for

the separation of salicylic, 4-hydroxybenzoic, and 4-hydroxyisophthalic acid mixtures. Previously this was accomplished by use of selective solvents. It was desirable to effect this separation by a distillation if possible, but it is known that these acids will decarboxylate if heated at elevated temperatures. The previous experience with trimethylsilyl derivatives in separating thermally unstable compounds indicated that the trimethylsilyl derivatives of these acids would be distillable and would be stable during distillation operations.

The trimethylsilyl derivatives of these acids were prepared by the method outlined by Martin.<sup>2</sup> It is of interest to note that while only one derivative was isolated from 4-hydroxybenzoic acid and 4-hydroxyisophthalic acid, salicylic acid always gave two. Salicylic acid gave 2-trimethylsilyloxybenzoic acid and trimethylsilyl 2-trimethylsilyloxybenzoate, while 4-hydroxybenzoic acid gave trimethylsilyl 4-trimethylsilyloxybenzoate and 4-hydroxyisophthalic acid gave bistrimethylsilyl 4-trimethylsilyloxyisophthalate.

In addition to making it possible to separate the phenol carbonation mixture by distillation, these trimethylsilyl derivatives now make it possible to detect and determine the various components of the phenol carbonation mixture. Previously, the analysis of these carbonation mixtures was effected by the determination of the neutral equivalent or by ultraviolet spectroscopy.<sup>5</sup>

The detection and determination of these compounds is aided by several characteristic infrared absorption bands. These bands are tabulated in Table I.

TABLE I  
CHARACTERISTIC INFRARED ABSORPTION BANDS

Compound	Absorption Maxima, $\mu$ .
2-Trimethylsilyloxybenzoic acid	3.18, 5.98, 8.75, 9.15, 9.68, 12.36
Trimethylsilyl 2-trimethylsilyloxybenzoate	5.85, 8.66, 8.87, 9.30, 9.63, 10.87
Trimethylsilyl 4-trimethylsilyloxybenzoate	5.84, 8.60, 8.94, 9.10, 9.87
Bistrimethylsilyl 4-trimethylsilyloxyisophthalate	5.85, 8.74, 8.97, 9.30, 10.67

#### EXPERIMENTAL

*Trimethylsilyl derivatives of salicylic acid.* Trimethylchlorosilane, 50 g., was added dropwise with stirring to a mixture of 20 g. of salicylic acid in 300 ml. of anhydrous pyridine. The mixture was stirred for an additional 3 hr. at room temperature and filtered in the absence of moisture to free the product of the solid pyridine hydrochloride. The pyridine was stripped from the filtrate and the residue that remained was distilled in the Podbielniak spinning-band column giving 2-trimethylsilyloxybenzoic acid, b.p. 62°C. at

(1) Present address: Locomotive & Car Equipment Department, General Electric Co., Erie, Pa.

(2) R. W. Martin, *J. Am. Chem. Soc.*, **74**, 3024 (1952).

(3) C. A. Burkhard, J. V. Schmitz, and R. E. Burnett, *J. Am. Chem. Soc.*, **75**, 5957 (1953).

(4) M. M. Sprung and L. S. Nelson, *J. Org. Chem.*, **20**, 1750 (1955).

(5) O. Baine, G. F. Adamson, J. W. Barton, J. L. Fitch, D. R. Swayampati, and H. Jeskev, *J. Ora. Chem.*, **19**, 510 (1954).