

from which the benzonitrile had been removed, was acidified and again extracted with ether. The dried extract left an oil when evaporated, but a solution of this oil in petroleum ether deposited a solid melting at 75°. This was identified as phenylacetic acid by comparison with a sample.

Summary

1. When a ketonic isoxazoline oxide $\begin{array}{c} \text{R}-\text{CHCH}-\text{COR} \\ | \quad \diagup \text{O} \\ \text{R}-\text{C}=\text{NO} \end{array}$ is hydrogenated

it first takes up two atoms of hydrogen at the carbonyl group and forms a new oxide.

2. The reduction of isoxazoline oxides in which there is no carbonyl group doubtless always gives an open-chained hydroxy oxime as the first product; but in catalytic hydrogenations these oximes are reduced to amines.

3. 3,4-Disubstituted isoxazoles, heretofore unknown, can be prepared by cleaving ketonic isoxazoles with bases. When these 3,4-disubstituted isoxazoles undergo further cleavage, they behave like those mono-substituted isoxazoles which have no substituent in the 5-position.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

STEREOCHEMISTRY OF PHENYLPYRIDINE COMPOUNDS: THE PREPARATION AND INVESTIGATION OF 2-(2-CARBOXY- 6-CHLOROPHENYL)-PYRIDINE-3-CARBOXYLIC ACID AND 3-(2-CARBOXYPHENYL)-6-PHENYLPYRIDINE-2,4- DICARBOXYLIC ACID, X.¹

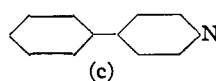
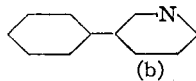
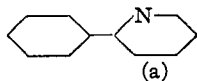
BY CATHERINE CASSELS STEELE² AND ROGER ADAMS

RECEIVED AUGUST 14, 1930

PUBLISHED NOVEMBER 5, 1930

A natural corollary to the development of the study of the optical isomerism exhibited by certain types of substituted diphenyl compounds is an investigation of binuclear compounds similar to diphenyl, and of these the dipyridines and the phenylpyridines resemble diphenyl most closely.

In the case of the phenylpyridines, only one ring—the pyridine nucleus—is different, and they may be divided into three classes; (a) where the N is "ortho," (b) where it is "meta" and (c) where it is "para" to the carbon atom linked to the phenyl nucleus.



Type (a) differs from (b) and (c) in the fact that there cannot be four

¹ For the last two papers in this series, see (a) Stanley and Adams, *THIS JOURNAL*, **52**, 4471 (1930); (b) Browning and Adams, *ibid.*, **52**, 4098 (1930).

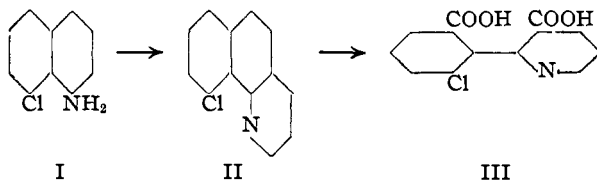
² Commonwealth Fund Fellow.

substituent groups in the "ortho" position, and any trisubstituted phenylpyridine of the type (a) will not be directly comparable with the corresponding trisubstituted diphenyl, as the fourth position is not occupied by a hydrogen atom. If the obstacle theory^{1a,3} is correct and on the assumption that a pyridine ring resembles in structure a benzene ring, this difference would be unlikely to affect resolution except in so far as a blocking group of size 0.94 to 1.04 Å.⁴ is eliminated. If, however, Bell and Kenyon's⁵ modified view that the electrical character of the substituting groups has an added influence besides the effective size of the electrical field of force of these groups, then the substituted phenylpyridines though conforming to all the requirements for resolution of the correspondingly substituted diphenyls, may exhibit a marked divergence in behavior.

Trisubstituted phenylpyridines of all three types and tetrasubstituted compounds of types (b) and (c) must be investigated, and various groups used to determine whether or not the calculated amount of interference⁴ between such groups will give the same experimental results as the corresponding diphenyls. Neither has it been established that the five carbon atoms and the nitrogen are coplanar in pyridine. If the nitrogen is bent away from the plane of the five carbons, or if the whole ring is distorted, then in the (a) type the distances between the ortho positions in the two rings will be very different from those between identical groups in a diphenyl, and therefore the interference values will also differ.

The methods available for preparing ortho-substituted phenylpyridines of types (a) and (b) are very limited; in fact, the only satisfactory method yet found is the synthesis of substituted naphthoquinolines and then their oxidation to the corresponding phenylpyridine-dicarboxylic acids.

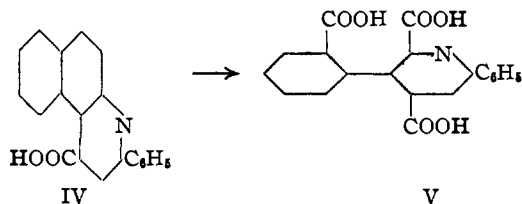
In this work, two acids were prepared: 2-(2-carboxy-6-chlorophenyl)pyridine-3-carboxylic acid (III), which is of type (a), and 3-(2-carboxyphenyl)-6-phenylpyridine-2,4-dicarboxylic acid (V), of type (b). The first was obtained through a Skraup synthesis of 10-chloro- α -naphthoquinoline (II) from 8-chloro-1-naphthylamine (I), and subsequent oxidation with neutral permanganate, and the second by the oxidation of α -phenyl- β -naphthoquinoline- γ -carboxylic acid (diapurin IV).



³ Mills, *J. Soc. Chem. Ind.*, **45**, 884 (1926); Stanley and Adams, *THIS JOURNAL*, **52**, 1200 (1930).

⁴ Stanley and Adams, *ibid.*, **52**, 1201 (1930).

⁵ Bell and Kenyon, *J. Soc. Chem. Ind.*, **45**, 864 (1926).



It was found impossible to resolve either acid; of the chloro acid the following salts were investigated: di-strychnine, di-brucine, di-morphine, mono-cinchonine, di-cinchonine and mono-quinine, and of the tricarboxylic acid, the mono-strychnine, di-strychnine, mono-brucine, di-brucine and mono-cinchonine salts were prepared.

If x-ray data are taken into consideration using the values C-Cl, 1.89 Å.; C-COOH, 1.56 Å.; and C-C (2,2' for the diphenyl system), 2.90 Å.;⁴ in the case of the 2-(2-carboxy-6-chlorophenyl)-pyridine-3-carboxylic acid it is obvious that either the chlorine or carboxyl in the benzene ring should collide with the carboxyl in the pyridine ring and free rotation should be prevented (two carboxyls, 1.56 Å. + 1.56 Å. = 3.12 Å. - 2.90 Å. → + 0.22 Å.; one chlorine and one carboxyl, 1.56 Å. + 1.89 Å. = 3.45 Å. - 2.90 Å. → + 0.55 Å.). In the case of the 3-(2-carboxyphenyl)-6-phenylpyridine-2,4-dicarboxylic acid, similar conditions exist; the carboxyl in the phenyl ring should collide with either of the carboxyls in the pyridine nucleus.

These results may indicate distortion within the molecule with subsequent free rotation, due to the electrical attraction of the basic nitrogen and acid carboxyl groups. Two diastereoisomeric salts were in no case isolated. More types of phenylpyridines must be studied before speculation in regard to the stereochemical character of this class of compounds is extended. Other phenylpyridines and dipyridyls are under investigation in this Laboratory.

It should be noted that the di-brucine salt of the chloro acid gave zero rotation, while all the salts of the tricarboxylic (except the monochinchonine) gave zero rotations. These substances obviously fall into a group which show abnormalities similar to those compounds which Haworth believed demonstrated the existence of labile optical isomers.⁶ Such a phenomenon is so general among alkaloidal salts⁷ of many types that the authors believe such conclusions as were drawn by Haworth to be misleading.

Experimental Part

8-Chloro-1-naphthylamine.—The preparation was carried out in two steps. 8-Chloro-1-nitronaphthalene was prepared according to Ullmann and Consonno⁸ by the

⁶ "Annual Reports," **24**, 101 (1928).

⁷ Hyde and Adams, *THIS JOURNAL*, **50**, 2502 (1928).

⁸ Ullmann and Consonno, *Ber.*, **35**, 2808 (1902); see also German Patent 99,758.

chlorination of 1-nitronaphthalene in 100-g. lots. The yield of the pure 8-chloro-1-nitro isomer after crystallization from benzene-ligroin was 23 g., m. p. 94–95°. The reduction of 8-chloro-1-nitronaphthalene by tin and hydrochloric acid described by Ullmann was very tedious and good results were not obtained. 8-Chloro-1-naphthylamine was, however, prepared in 97% yield by the following method.

An intimate mixture of 20 g. of 8-chloro-1-nitronaphthalene with 60 g. of iron powder and 30 cc. of water in a 500-cc. round-bottomed flask fitted with a reflux condenser was heated for ten minutes on the steam-bath and a few drops of concd. hydrochloric acid added through the condenser, the flask being well shaken. Heating was thereafter continued for seven hours with occasional shaking. With longer heating decomposition of the molecule becomes a factor, and with less time unreduced nitro compound is recovered. The mixture was cooled and the amine extracted with ethyl alcohol until the filtrate gave no precipitate with water. The alcoholic filtrate was poured into a large excess of water and the precipitate filtered. The latter was then dissolved in dilute hydrochloric acid, filtered from any nitro compound and the amine precipitated with ammonia. The amine separates from ligroin in small colorless needles which turn dark purple in color on exposure to the air; m. p. 95–96° (various values for the melting point are given in the literature; Ullmann, 89°; Atterberg, 93–94°).⁹

Anal. Calcd. for $C_{10}H_8NCl$: (Parr bomb) Cl, 20.00. Found: Cl, 19.93.

10-Chloro- α -naphthoquinoline.—The Skraup synthesis was carried out using arsenic acid as the oxidizing agent in the proportions given by Claus¹⁰ for the conversion of α -naphthylamine to α -naphthoquinoline. To 59.5 g. of 8-chloro-1-naphthylamine in a 1-liter, 3-necked flask fitted with a mechanical stirrer, condenser and dropping funnel, were added 54.2 g. of arsenic acid (sp. gr. 2) and 178.7 g. of glycerol in the order named. Then 113.8 g. of concd. sulfuric acid was added gradually from the dropping funnel, the stirrer being started whenever the mixture became sufficiently liquid. The mixture was heated for one and one-half hours at 100° in an oil-bath, and then for nine hours at 170–180°. The material was poured while hot into a large excess of water and the precipitate allowed to settle overnight. The resinous precipitate was removed by filtration through an ordinary filter funnel and washed with water. The combined filtrates were placed in a 3-liter separatory funnel and a layer of ether followed by an ice-cold solution of 44 g. of potassium hydroxide (one-third the calcd. amount to neutralize the sulfuric acid used) in about 220 cc. of water was added. This ethereal extract consists almost entirely of resinous material. The aqueous layer was then treated similarly with a concd. solution of 88 g. of potassium hydroxide (the remaining two-thirds necessary for neutralization) and the precipitate extracted thoroughly with ether. The ether layer was dried over anhydrous magnesium sulfate and the ether removed. The yield of crude material was 47.5 g. A second run of 27.5 g. of chloronaphthylamine was made and the 17.5 g. of crude material obtained was added to the first product; the resulting 65 g. of crude material after two crystallizations from ligroin gave 26.8 g. with the constant, m. p. 81–82°. The insoluble material was re-extracted with boiling ligroin and 3.7 g. with a melting point of 81.5–82° was obtained. The total yield of pure 10-chloro- α -naphthoquinoline was 30.5 g. (20%). It crystallized from ligroin in small, hard, bright yellow prisms, m. p. 81.5–82°.

Anal. Calcd. for $C_{11}H_8NCl$: Cl, 16.63. Found: Cl, 16.44.

2-(2-Carboxy-6-chlorophenyl)-pyridine-3-carboxylic Acid.—Skraup and Cobenzl¹¹ found that oxidation of α -naphthoquinoline with chromic acid gave α -naphthoquinoline-

⁹ Ullmann, *Ber.*, 35, 2809 (1902); Atterberg, *ibid.*, 9, 1731 (1876).

¹⁰ Claus, *J. prakt. Chem.*, [2] 57, 68 (1898).

¹¹ Skraup and Cobenzl, *Monatsh.*, 4, 463 (1883).

quinone, while oxidation with permanganate at 40–50° gave a 70% yield of α -phenylpyridine-dicarboxylic acid. It was found possible to oxidize chloronaphthoquinoline to the dicarboxylic acid with permanganate but the higher temperature of 100° was necessary. The difficulty with such oxidations is the isolation of the acid, as there is no general method suitable for all the acids. After several attempts, the following method gave the best results. A mixture of 10 g. of chloronaphthoquinoline and 800 cc. of water was heated to 100° in a 3-liter, 3-necked flask fitted with a mechanical stirrer, condenser and dropping funnel. To the boiling mixture was added gradually from the dropping funnel a cold saturated solution of 21.8 g. of potassium permanganate (10% excess) in water. Decolorization of the permanganate was almost immediate and the addition was complete in forty-five minutes. The hot liquid was filtered from the manganese dioxide, the latter washed thoroughly with boiling water and the united filtrates allowed to cool. A small amount of unoxidized quinoline usually separated at this point and was removed by filtration. The solution was then made slightly acid with hydrochloric acid and evaporated to a very small volume on the steam-bath, when crystals of the dicarboxylic acid separated. The yield was 5 g. The acid was slightly colored and was purified by dissolving in alcohol, decolorizing with norit, and after concentration of the solution, diluting the latter with hot water until a slight cloudiness appeared. On cooling, the solution deposited small, colorless crystals of 2-(2-carboxy-6-chlorophenyl)-pyridine-3-carboxylic acid. They showed no sharp melting point, but turned dark around 240°, and completely melted at 252–256° with decomposition.

Anal. Calcd. for $C_{13}H_8O_4NCI$: Cl, 12.86. Found: Cl, 13.04.

The yields obtained in the synthesis of this acid may be summarized as follows:
 450 g. nitronaphthalene \rightarrow 121.6 g.; 8-chloro-1-nitronaphthalene \rightarrow 87 g.;
 8-chloro-1-naphthylamine \rightarrow 30.5 g.; 10-chloro- α -naphthoquinoline \rightarrow 15 g.;
 chlorophenylpyridine-dicarboxylic acid.

Alkaloid Salts of Chlorophenyl-pyridine-dicarboxylic Acid

Di-strychnine Salt.—Warm methyl alcohol solutions of 1.2 g. of acid and 2.87 g. of strychnine were mixed and evaporated to dryness. The hard amorphous solid so obtained crystallized slowly from hot water in large, translucent parallelogram plates. These on exposure to the air effloresced to give a white powder which was dried in a desiccator, m. p. 171–173°. The first fraction, consisting of 1 g. (one-fourth of the total salt) had the specific rotation $[\alpha]_D -21.37^\circ$ in chloroform, and on a second crystallization had $[\alpha]_D -25.45^\circ$. A second fraction from the original mother liquors gave $[\alpha]_D -25.3^\circ$, and the final mother liquor on evaporation to dryness gave a salt with $[\alpha]_D -21.16^\circ$.

Rotation. 0.3041 g. made up to 25 cc. with chloroform at 20° gave $\alpha_D = -0.52^\circ$; $l = 2$; $[\alpha]_D -21.37^\circ$.

Anal. Calcd. for $C_{65}H_{62}O_8N_6Cl$: neut. equiv., 472.7. Found: 473.6.

One gram of the salt was decomposed with dilute ammonia and the strychnine removed by extraction with chloroform. The aqueous solution of the ammonium salt of the acid was evaporated to dryness and showed no optical activity in aqueous solution.

Di-brucine Salt.—The di-brucine salt was made in and crystallized from methyl alcohol. Clusters of long, slender, colorless needles separated and effloresced in air. They were powdered and dried in air; m. p. 168–170°. All the fractions isolated as well as the mother liquors had zero rotation. The salt also crystallized from ethyl acetate in small hard prisms, but no change in rotation was observed.

Anal. Calcd. for $C_{69}H_{60}O_{12}N_6Cl$: Cl, 3.33. Found: Cl, 3.53.

Di-morphine Salt.—This salt was made in methyl alcohol and did not crystallize readily from any of the ordinary solvents. Crystals were obtained by dissolving the

salt in the minimum amount of hot ethyl alcohol and adding hot ethyl acetate until one more drop turned the solution cloudy. On cooling, small, colorless crystals separated, m. p. 200–204°. Six fractions in all were isolated, and had the same rotation in absolute methyl alcohol.

Rotation. 0.1067 g. made up to 25 cc. with methyl alcohol at 20° gave $\alpha_D = -0.589^\circ$; $l = 2$; $[\alpha]_D -69.06^\circ$.

Anal. Calcd. for $C_{47}H_{46}O_{10}N_3Cl$; Cl, 4.19. Found: Cl, 4.26.

Mono-cinchonine Salt.—This was prepared in methyl alcohol, and crystallized from a large volume of ethyl acetate in small colorless prisms, m. p. 154–156°. Three fractions were isolated and the salt in the mother liquors recovered. All gave the same rotation.

Rotation. 0.1014 g. made up to 20 cc. with absolute methyl alcohol at 20° gave $\alpha_D = +0.763^\circ$; $l = 2$; $[\alpha]_D +75.2^\circ$.

The first fraction, consisting of a gram of salt, was decomposed by shaking with dilute ammonia and chloroform in a separatory funnel. The ammonium salt solution was evaporated to dryness. It gave zero rotation.

Di-cinchonine Salt.—Methyl alcohol solutions of the acid and alkaloid were mixed, evaporated to small bulk and water added to the precipitation point. On cooling small crystals separated, m. p. 194–196°. They could not be recrystallized from any single solvent. All the fractions obtained had the same rotation, and this was not altered by three precipitations of the first fraction.

Rotation. 0.1060 g. made up to 20 cc. with absolute methyl alcohol at 20° gave $\alpha_D = +1.25^\circ$; $l = 2$; $[\alpha]_D +117.8^\circ$.

Anal. Calcd. for $C_{51}H_{50}O_6N_5Cl$; Cl, 4.1. Found: Cl, 4.26.

A 1-g. portion of the purified first fraction was decomposed with ammonia and the ammonium salt of the acid isolated. It gave a zero rotation.

Mono-quinine Salt.—This salt could not be recrystallized readily, but three fractions of microscopic, colorless crystals were obtained from benzene containing a little ethyl alcohol, m. p. 152–155°. The fractions and the salt recovered from the mother liquor all gave the same rotation.

Rotation. 0.1060 g. made up to 20 cc. with absolute methyl alcohol at 20° gave $\alpha_D = -0.624^\circ$; $l = 2$; $[\alpha]_D -58.89^\circ$.

Anal. Calcd. for $C_{33}H_{32}O_6N_3Cl$; Cl, 6.13. Found: Cl, 5.91.

α -Phenyl- β -naphthoquinoline- γ -carboxylic Acid.—This was prepared and purified according to the method of Döbner and Kuntze¹² and was obtained in 50% yield, m. p. 290° (Döbner, 53% yield, m. p. 296°).

Anal. Calcd. for $C_{20}H_{13}NO_2$; neut. equiv., 299. Found: 299.3.

3-(2-Carboxyphenyl)-6-phenylpyridine 2,4-dicarboxylic Acid.—Dobner¹² reports that α -phenyl- β -naphthoquinoline- γ -carboxylic acid could not be oxidized to a tricarboxylic acid, while the corresponding α -naphthoquinoline compound was oxidized to the tricarboxylic acid with alkaline permanganate at 50°. Immerheiser¹³ reported the oxidation of β -naphthoquinoline-8-sulfonic acid by dissolving the potassium salt of the acid in water and using a neutral solution of potassium permanganate at ordinary temperatures. It was found that by this latter method α -phenyl- β -naphthoquinoline- γ -carboxylic acid could be oxidized very rapidly at ordinary temperatures to the corresponding tricarboxylic acid, and by using a large excess of permanganate until a permanent purple color remained in the reaction mixture, no unoxidized material was ob-

¹² Döbner and Kuntze, *Ann.*, **249**, 129 (1889).

¹³ Immerheiser, *Ber.*, **22**, 405 (1889).

tained. No ketone acid was isolated corresponding to those reported by Immerheiser¹¹ and Dobner.¹²

A solution of 14.5 g. of α -phenyl- β -naphthoquinoline- γ -carboxylic acid in 600 cc. of warm water was treated with a concd. solution of potassium hydroxide until the resulting solution was just alkaline to phenolphthalein. The solution was cooled and placed in a 2-liter, 2-necked flask fitted with a mechanical stirrer and a dropping funnel. A concentrated aqueous solution of potassium permanganate (25 g., 20% excess) was added gradually with rapid stirring. The mixture warmed up considerably and the decolorization was instantaneous. The manganese dioxide was allowed to coagulate overnight, the clear solution decanted off, and the manganese dioxide extracted thoroughly with boiling water. The combined filtrates, on being made strongly acid to methyl orange with sulfuric acid, gave a white oily precipitate which did not crystallize on standing. This was extracted with ether and dried over anhydrous magnesium sulfate. On removal of the solvent, 16.5 g. of crystalline material was obtained, m. p. 123–129°. It was recrystallized by dissolving it in the minimum amount of hot ethyl acetate and adding ligroin to the point of precipitation. On cooling, 13 g. (74%) of small colorless crystals was obtained. Recrystallization from ethyl acetate gave a constant melting point of 202°.

Anal. Calcd. for $C_{20}H_{13}NO_4$: C, 66.1; H, 3.58; neut. equiv., 121. Found: C, 59.9; H, 3.32; neut. equiv., 122.7.

Alkaloid Salts of 3-(2-Carboxyphenyl)-6-phenylpyridine-2,4-dicarboxylic Acid

Mono-strychnine Salt.—The salt was made in methyl alcohol, and would not crystallize readily from any solvent. The crude material gave zero rotation with sodium light, and so did a small crystalline fraction obtained from a mixture of chloroform and ethyl acetate.

Di-strychnine Salt.—This separated in small, colorless prisms from benzene containing a little ethyl alcohol; m. p. about 238° with decomposition.

Anal. Calcd. for $C_{62}H_{57}O_{10}N_6$: neut. equiv., 344.3. Found: neut. equiv., 341.7.

A constant rotation was shown by all fractions; *rotation*: 0.2022 g. made up to 20 cc. with chloroform at 20° gave $\alpha_D = -0.173^\circ$; $l = 2$; $[\alpha]_D = -8.57^\circ$.

The first fraction and the salt recovered from the mother liquors were both decomposed with ammonia and the ammonium salt isolated in the usual manner. Neither showed rotation.

Mono-brucine Salt.—This salt could not be recrystallized readily from any solvent. A few crystals were obtained from water, and they, as well as the crude material, gave zero rotation.

Di-brucine Salt.—The salt was crystallized from a small volume of absolute ethyl alcohol. It separated in small, regular prisms and all the fractions obtained showed no rotation. The salt had no definite melting point; it partially melted at 204° with decomposition, and was completely melted by 225°.

Anal. Calcd. for $C_{65}H_{65}O_{14}N_5$: neut. equiv., 383.6. Found: neut. equiv., 383.6.

Mono-cinchonine Salt.—The crude salt had a rotation of $+75.46^\circ$.

Rotation. 0.2068 g. made up to 25 cc. with absolute methyl alcohol at 20° gave $\alpha_D = +1.249^\circ$; $l = 2$; $[\alpha]_D = +75.46^\circ$.

Four fractions were isolated by crystallization from water containing a little ethyl alcohol and none showed any change in rotation; the crystals melted and resolidified at 174–176°, and finally melted with further decomposition at 200–204°. The

first fraction, after two recrystallizations rotated as follows: *rotation*, 0.2016 g. made up to 25 cc. with methyl alcohol at 20° gave $\alpha_D = -1.214^\circ$; $l = 2$; $[\alpha]_D +75.26^\circ$.

This fraction and the salt from the original mother liquor were decomposed and the ammonium salts isolated. Neither showed rotation.

Esters of 3-(2-Carboxyphenyl)-6-phenylpyridine-2,4-dicarboxylic Acid

It was thought that the *ortho*-substituted groups might be enlarged by esterification of the three acid groups with an alcohol of comparatively large size. If a crystalline tri-ester could be obtained, then resolution might be possible by forming salts of the pyridine nitrogen. Alternatively, a tri-ester of an optically active alcohol might separate into two diastereoisomers on recrystallization.

Tricarboxylic Acid Trichloride.—The acid was treated with an excess of thionyl chloride in a flask fitted with a ground-in water condenser until there was no further reaction. This required about two hours. The acid chloride was then washed out with ligroin and the latter decanted. The acid chloride was dried in a vacuum desiccator; *m. p.* 127–130°. It was found impossible to recrystallize it from any of the ordinary solvents.

Anal. Calcd. for $C_{20}H_{10}NO_4Cl_3$: Cl, 25.47. Found: Cl, 24.7.

Tri-*n*-butyl Ester of the Tricarboxylic Acid.—One mole of the acid trichloride was treated with 3 moles of *n*-butyl alcohol and warmed on the water-bath until the mass was homogeneous. The product was poured into water, made slightly alkaline with sodium carbonate and extracted with ether. The ethereal layer, after being washed with water and dried, gave a thick sirup which could not be crystallized.

Trimethyl Ester of the Tricarboxylic Acid.—This was prepared in an analogous manner to the tributyl ester. The sirup so obtained could not be recrystallized.

Rotation. 0.2559 g. made up to 20 cc. with acetone at 20° gave $\alpha_D -0.97^\circ$; $l = 2$; $[\alpha]_D -38^\circ$.

Summary

1. The possibilities of optical isomerism in the phenylpyridines as compared with the diphenyl series is discussed.

2. 10-Chloro- α -naphthoquinoline and 2-(2-carboxy-6-chlorophenyl)-pyridine-3-carboxylic acid were prepared. Salts of this acid with several alkaloids were made, but no separation into diastereoisomers was observed.

3. 3-(2-Carboxyphenyl)-6-phenylpyridine-2,4-dicarboxylic acid was prepared; its alkaloid salts appeared to exist in only one form.

URBANA, ILLINOIS