

Rotation. 0.2030 g. made up to 15 cc. with chloroform at 20° gave $\alpha_D -0.67^\circ$; $l = 2$; $[\alpha]_D^{20} -24.5^\circ$. 0.1342 g. made up to 10 cc. with chloroform at 0° gave $\alpha_D -0.42^\circ$; $l = 1$; $[\alpha]_D^0 -31.2^\circ$.

Anal. Calcd. for $C_{35}H_{35}FN_3O_6$: C, 68.93; H, 5.29. Found: C, 67.84; H, 5.67.

Attempt to Obtain Active 2-Nitro-6-carboxy-2'-fluoro-5'-methyldiphenyl.—The organic acid was obtained by treating one gram of the brucine salt with 50 cc. of dilute hydrochloric acid at -5° for twelve hours. This was filtered and washed, first with dilute hydrochloric acid and then with cold water. Until the acid was obtained in the pure state, the temperature was kept at -5° . Three-tenths of a gram obtained in this manner melted at $185-186^\circ$. However, this acid showed no rotation when dissolved in ethyl alcohol at 0°. Similar results were obtained from the quinine and strychnine salts.

1-Methyl-4-fluoro-5-nitrofluorenone.—A solution of 0.5 g. of 2-nitro-6-carboxy-2'-fluoro-5'-methyldiphenyl in 10 cc. of concentrated sulfuric acid was warmed on the steam cone for ten minutes. The solution turned red as soon as the diphenyl dissolved. This was poured into ice water. The solid that separated was recrystallized from alcohol. A quantitative yield of yellow needles was obtained melting at $204-205^\circ$.

Anal. Calcd. for $C_{14}H_9FNO_3$: C, 65.35; H, 3.11. Found: C, 65.60; H, 3.27.

Summary

1. 2-Nitro-6-carboxy-2'-methoxydiphenyl and the 2'-fluoro, chloro and bromo derivatives of 2-nitro-6-carboxy-5'-methyldiphenyl have been prepared and resolved. The rates of racemization of the active forms have been compared.

2. The differences between the individual compounds are very marked and lead to the conclusion that the interfering effect of the 2'-substitution is in the following order: $Br > Cl > OCH_3 > F$.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]
STEREOCHEMISTRY OF DIPHENYLS.¹ XXVI. THE EFFECT OF SUBSTITUTION ON THE RATE OF RACEMIZATION OF CERTAIN OPTICALLY ACTIVE DIPHENYLS

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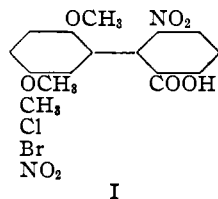
It is generally accepted that the two phenyl rings in diphenyl compounds have a common axis of rotation, and that the phenomenon of stereoisomerism in variously substituted 2,2',6,6' derivatives is due to restriction of free rotation of one ring with respect to the other by those groups, thus causing the two rings to be non-coplanar and giving the molecule a spatial asymmetric configuration. No experimental evidence is as yet available

¹ For the last three papers in this series see (a) Yuan and Adams, *THIS JOURNAL*, **54**, 2966 (1932); (b) Becker and Adams, *ibid.*, **54**, 2973 (1932); (c) Stoughton and Adams, *ibid.*, **54**, 4426 (1932).

² This communication is a portion of a thesis submitted by H. C. Yuan in partial fulfillment of the requirements for the Degree of Doctor of Philosophy in Chemistry at the University of Illinois.

in regard to the effect of substituents at positions other than 2,2',6,6' on the resolvability of certain diphenyl compounds or on the stability of the active molecules. The present investigation had the object in view of getting information on this problem. Since the ortho tetrasubstituted derivatives, with the exception of a few types, present molecules which cannot be racemized at all or only with great difficulty, the 2,2',6-tri-substituted diphenyls offer the most promising field for this study.

The specific compounds prepared were four substituted 2-nitro-6-carboxy-2'-methoxydiphenyls with the groups methyl, chloro, bromo and nitro in position 5' (I). Together with the 2-nitro-6-carboxy-2',5'-dimethoxydiphenyl described in a previous article,^{1a} five analogous diphenyls are available for comparison with the unsubstituted 2-nitro-6-carboxy-2'-methoxydiphenyl.^{1c} Conclusions may thus be drawn in regard to the effect of different types of groups in the 5'-position.



As observed in the case of 2-nitro-6-carboxy-2',5'-dimethoxydiphenyl and 2-nitro-6-carboxy-2'-methoxydiphenyl, only one brucine salt could be isolated for each of the diphenyls prepared. The second salt was apparently converted through mutarotation to the less soluble form during the process of concentration of the solution. Moreover, all the salts mutarotated and the active acids obtained from the salts racemized readily in organic solvents at room temperature. On the assumption that the size of the ortho substituents was the only factor involved, the rates of mutarotation of the various salts should be identical and the rates of racemization of the active acids should be the same. Experimentally, however, this was found not to be true. The half-life periods calculated from the velocity constants were taken as a means for comparison of the stabilities. The half-life periods are given in Table I. For complete data see Table III.

TABLE I
HALF-LIFE PERIODS AT 26° OF THE ACTIVE FORMS OF SUBSTITUTED 2-NITRO-6-CARBOXY-2'-METHOXYDIPHENYLS AND THEIR SALTS

Compound group at 5'	Half-life period in minutes			
	Free acid in alcohol	Brucine salt in chloroform	Sodium salt in water	Sodium salt in alcohol
—OCH ₃ ^{1a}	10.8	16.7	27.4	3.7
—CH ₃	11.5	15.8	30.1	3.8
—Cl	31.0	16.7	40.2	9.7
—Br	32.0	16.7	43.6	11.5
—NO ₂	35.4	7.7	35.0	16.7

The average deviation of the individual velocity constants was less than 10%. The values could be readily duplicated.

The following conclusions may be drawn from these data. (1) A comparison of the rates of racemization of the free acids indicates that the

stabilities of 5'-methoxy and 5'-methyl derivatives are practically the same, the stabilities of the 5'-chloro and 5'-bromo are also identical and they are more stable than the first two. The 5'-nitro is the stablest of all the derivatives. This can be seen more clearly from Fig. 1. Line A is parallel to B and C to D and line E has the smallest slope. (2) The brucine salts, which, unlike the acids, contain an additional asymmetric influence, have essentially similar stability with the exception of the nitro derivative. The brucine salt of the 5'-nitro mutarotates twice as fast as the others (Fig. 2). (3) The brucine salts of the 5'-methoxy and the 5'-methyl derivatives in chloroform are more stable than the corresponding acids in alcohol while the salts of the 5'-chloro, bromo or nitro derivatives in chloroform are less stable. (4) The sodium salts in water racemize less readily but in alcohol more readily than the free acids in organic solvents.

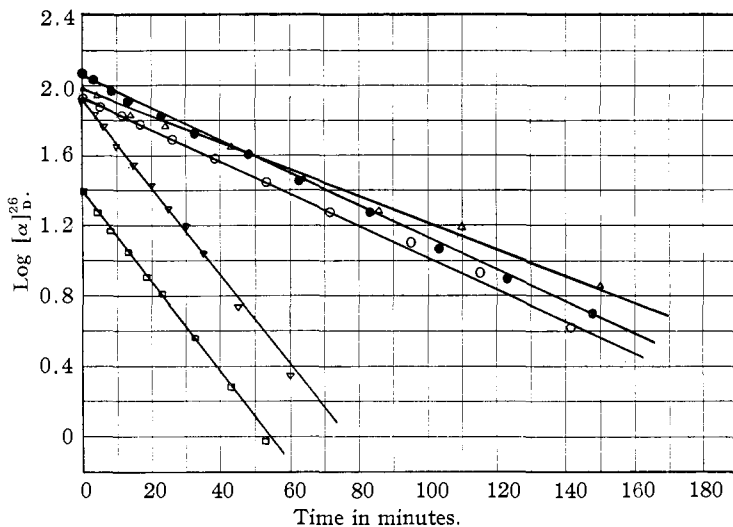


Fig. 1.—Rates of racemization of five 5'-substituted 2-nitro-6-carboxy-2'-methoxydiphenyls: \square , CH_3 ; ∇ , OCH_3 ; \circ , Br; \bullet , Cl; \triangle , NO_2 .

The first point constitutes the main theme of the present investigation, the effect of substituents on the rate of racemization of the active acids when determined under similar conditions. Although the exact mechanism of this phenomenon is still obscure, there are several factors, any or all of which may influence the molecules.

First, it has been demonstrated by Ingold,³ Debye⁴ and Smyth⁵ and many others through different methods that the valence angle of carbon

³ Ingold, *J. Chem. Soc.*, 121, 2676 (1922), and other papers.

⁴ Debye, *Z. Elektrochem.*, 36, 612 (1930).

⁵ Smyth, "Dielectric Constant and Molecular Structure," Chemical Catalog Company, New York, 1931, p. 112.

is not a constant value 109.5° , but varies with the nature of atoms or groups present in the molecule. The introduction of the 5' groups into the diphenyl molecules may be sufficient to change the valence angles of the groups in the 2,2',6-positions and thus diminish or increase the interference in a molecule.

Second, the 5' groups may cause the linkage between the two rings to bend in such a way that the rings are no longer coaxial. The interference of the 2,2',6 groups would certainly be affected by such a change.

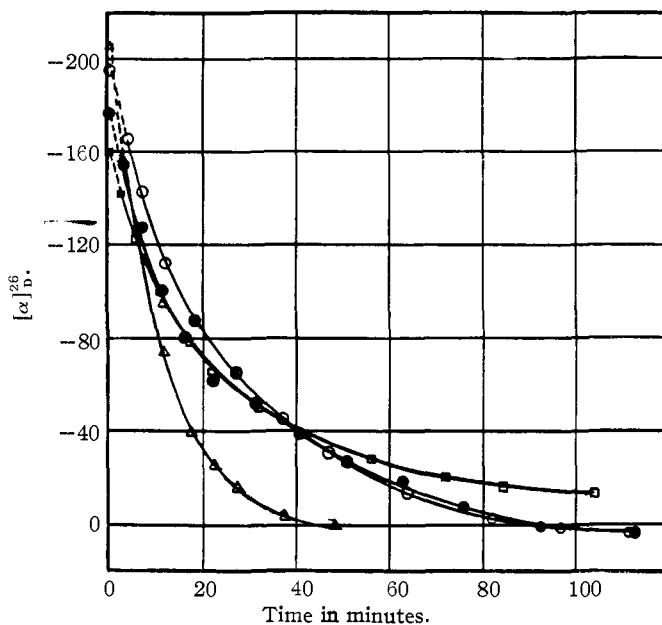


Fig. 2.—Mutarotation curves of the brucine salts of four 5'-substituted 2-nitro-6-carboxy-2'-methoxydiphenyls: □, CH₃; ○, Br; ●, Cl; △, NO₂.

Third, the frequency of semi-circular oscillation of the two rings may vary with the nature of the substituents and hence may change the rate of racemization. It is reasonable to expect that heavy substituents might slow down the oscillation, and thus diminish the rate of racemization. In the compounds under investigation, however, this factor apparently cannot play more than an unimportant role since both 5'-chloro and 5'-bromo derivatives racemize at the same rate.

Fourth, the distance between 1,1' carbon atoms may vary with the nature of the substituents. The vertical distance between the 2,2' carbon atoms in the phenyl rings was estimated as 2.90 Å. based upon the x-ray measurement of the distance between two carbon atoms. In the study of

the stereoisomerism of diphenyls, this value of 2.90 Å.⁶ was assumed to be essentially constant for all substituted diphenyls. This assumption can only be approximately true, since much evidence⁷ is available that the interatomic distance does vary more or less with the nature of the compound. For substituted diphenyls it is very probable that the distance between the 1,1'-carbon atoms varies by at least a few hundredths of an Å. due to the nature of the substituents. Such a change, though small, may affect considerably the rate of racemization if the groups in the 2,2',6-positions are of such a size as barely to permit restricted rotation.

There appears to be some parallelism between the dipole moments and the rates of racemization.⁸ No data are available on the dipole moments of resolvable diphenyls and it is questionable whether these values would be significant on account of the complicated structure of such molecules. The dipole moment, however, is more or less an additive property in a molecule. One half of each of the diphenyls under investigation remains the same, 2-nitro-6-carboxyphenyl, which may be assumed to have a constant moment. In regard to the other half of the molecules, it is of interest to consider moments of the corresponding substituted anisoles (Table II).

TABLE II
DIPOLE MOMENTS OF SUBSTITUTED ANISOLES AND HALF-LIFE PERIODS OF ANALOGOUS
DIPHENYLS

Substituted anisole	Moment $\times 10^{16}$	5'-Substituted 2-nitro-6-carboxy-2'-methoxydiphenyls	Half-life period in minutes
No subs.	1.2	No subs. ^{1c}	9.4
<i>p</i> -CH ₃	1.2 ⁹	CH ₃	11.5
<i>p</i> -OCH ₃	1.8	OCH ₃	10.8
<i>p</i> -Cl	2.24	Cl	31.0
<i>p</i> -Br	2.24	Br	32.0
<i>p</i> -NO ₂	4.3	NO ₂	35.4

⁶ The value 2.90 Å. originally adopted as the approximate distance between the 2,2' carbon atom in diphenyl should perhaps have been more accurately considered to be 2.96 Å. by the addition of the linkage of the diphenyls 1.54 Å. and 1.42 Å. (the aromatic C—C distance).

⁷ The distance between two carbon atoms was found to be 1.54 Å. in diamond, 1.6 Å. in solid ethane, 1.55 Å. in the side-chains of hexamethylbenzene, 1.58 Å. in long-chain paraffins, 1.42 Å. in graphite, 1.45 Å. in naphthalene, 1.35 Å. in solid stilbene.

⁸ Dr. C. P. Smyth has kindly calculated the energy differences involved in the different reaction rates as given by the half-life periods in Table II. He has found that the energies involved are of the same magnitude as the potential energies which must exist between the dipoles in the two halves of the molecule. This offers the possibility of explaining the variation in rate of racemization (at least semi-quantitatively) in terms of the mutual potential energies of the dipoles.

⁹ Smyth, "Dielectric Constant and Molecular Structure," Chemical Catalog Company, New York, 1931, p. 196; see also Bergmann and Engel, *Z. physik. Chem.*, **15B**, 94 (1931); Smyth in a private communication reports a value of 2.24×10^{18} for *p*-bromoanisole.

The rate of racemization diminishes as the dipole moment becomes larger. If this is approximately true, prediction can be made concerning other substituted 2-nitro-6-carboxy-2'-methoxydiphenyls. *p*-Anisidine, for example, has a moment of 1.8, then the half-life period of the active 2-nitro-6-carboxy-2'-methoxy-5'-aminodiphenyl should be between ten and fifteen minutes at room temperature. Substituted anisoles always decrease in moment from para to meta to ortho. Therefore, the 3' or 4' substituted 2-nitro-6-carboxy-2'-methoxydiphenyls should racemize more readily than those in the 5'-position, if dipole moments are significant.

Apart from this semi-quantitative consideration, there appears to be some correlation between the polarity and the relative rate of racemization. The 5'-methyl- and 5'-methoxydiphenyls have the same stability and the two groups are practically non-polar. The chloro and bromo are two groups with the same polarity and the corresponding substituted diphenyls racemized at the same rate. The nitro is more strongly polar and the 5'-nitro derivative was the stablest of the five.

The rate of mutarotation of the brucine salts, as pointed out above, does not parallel the rates of racemization of the active acids. The presence of other points of asymmetry adds materially to the complexity of the molecule and no attempt to explain the facts will be made at this

TABLE III
ROTATIONS OF FOUR SUBSTITUTED 2-NITRO-6-CARBOXY-2'-METHOXYDIPHENYLS AND OF THEIR BRUCINE SALTS AND SODIUM SALTS

Compound group at 5'	Wt. ^a in g.	Temp. °C.	Rotations in degrees ^b						Average K	Average Half-life deviation of K	Half-life period in min.	
			Max. $[\alpha]_D$ by extrap.	Min.	Initial α_D	$[\alpha]_D$	Min.	Final α_D				$[\alpha]_D$
Brucine salts in chloroform												
-CH ₃	0.0378	26.5	-160	3	-1.07	-142	104	-0.10	-13	0.019	±0.001	15.8
-Cl	.0320	26.5	-177	3	-1.00	-156	113	+0.02	+ 3.1	.018	± .002	16.7
-Br	.0402	26.5	-196	4	-1.33	-166	112	+0.03	+ 3.7	.018	± .001	16.7
-NO ₂	.0381	26.5	-206	3	-1.20	-157	45	0.0	0.0	.039	± .004	7.7
Free acids in absolute alcohol												
-CH ₃	0.1532	26	- 26	4	-0.62	- 20	68	0	0	0.026	±0.002	11.5
-Cl	.0440	27	-125	3	- .99	-115	193	0	0	.0097	± .0004	31.0
-Br	.0449	26	- 93	5	- .76	- 84	191	0	0	.0094	± .0006	32.0
-NO ₂	.0270	26.5	-101	4	- .50	- 93	195	0	0	.0085	± .0006	35.4
Sodium salts in water ^c												
-CH ₃	0.0525	26	- 33	3	-0.32	- 30.5	130	0	0	0.010	±0.0006	30.1
-Cl	.0342	26.5	-173	6	-1.07	-156	260	0	0	.0075	± .0005	40.2
-Br	.0491	26	-262	6	-1.25	-127	264	0	0	.0069	± .0005	43.6
-NO ₂	.0300	27	-196	3	-1.09	-183	246	0	0	.0086	± .0004	35.0
Sodium salts in absolute alcohol ^d												
-CH ₃	0.0502	26	- 46	3	-0.24	- 24	25	0	0	0.079	±0.002	3.8
-Cl	.0328	26.5	-316	4	-1.58	-241	59	0	0	.031	± .001	9.7
-Br	.0408	26	-262	2	-1.90	-233	87	0	0	.026	± .002	11.5
-NO ₂	.0275	26.5	-291	2	-1.50	-273	102	0	0	.018	± .001	16.7

^a Made up to 10 cc. ^b $l = 2$. ^c 0.1 N NaOH solution used. ^d Solution of 0.1 g. of sodium in 100 cc. of absolute alcohol was used.

time. The greater rates of mutarotation of the brucine salts of 5'-chloro, 5'-bromo and 5'-nitrodiphenyls than the rates of racemization of the corresponding active acids is also puzzling. This is not without precedent, however, as Mills and Elliott¹⁰ made the same observation in regard to N-benzenesulfonyl-8-nitro-1-naphthylglycine and its salts.

From the data in this and in previous communications the axially asymmetrical diphenyls may be classified into four groups: (1) resolvable and non-racemizable; (2) resolvable but racemizable at higher temperatures; (3) resolvable but racemizable at room temperature (the alkaloidal salts of these compounds mutarotate in solution); (4) non-resolvable. To which group a diphenyl belongs is primarily determined by the number and size of the 2,2',6,6' substituents. In the second or the third classes, differences in rate of racemization are due not only to the number and size of the ortho groups but to the nature of other substituents also. For those compounds on the border line, the nature of other substituents may be a deciding factor.

The compounds in this investigation were prepared by condensing 1-nitro-2-bromo-3-carbomethoxybenzene by means of copper with the proper halogen compounds, 1-iodo-2-methoxy-5-methylbenzene, 1-iodo-2-methoxy-5-chlorobenzene, 1-iodo-2-methoxy-5-bromobenzene, 1-iodo-2-methoxy-5-nitrobenzene, saponification of the condensation products and separation of the desired acids from the by-products.

Experimental

2-Nitro-6-carboxy-2'-methoxy-5'-methyldiphenyl.—A mixture of 30 g. of 1-iodo-2-methoxy-5-methylbenzene¹¹ and 18 g. of 1-nitro-2-bromo-3-carbomethoxybenzene was placed in a 200-cc., three-necked flask fitted with a mechanical stirrer and a reflux condenser. The flask was heated in a metal bath and as soon as the bath temperature reached 240°, 45 g. of copper bronze was introduced in portions. The addition of copper took about one-half to three-quarters of an hour and during this period the bath temperature was held between 240 and 260°. About fifteen minutes after all the copper had been added, the flask was removed from the bath and cooled to room temperature. The product was then extracted from the copper and copper halides with 100 cc. of warm alcohol and filtered. The filtrate was transferred to a 2-liter flask, concentrated to about 50 cc. and refluxed with 500 cc. of 5% sodium hydroxide for four hours. After cooling, the aqueous solution was decanted from the unsaponified oil and acidified slowly with dilute hydrochloric acid. A brownish-black tar separated which solidified upon standing.

The crude product was dissolved in sodium bicarbonate solution, filtered and reprecipitated with dilute hydrochloric acid. The precipitate weighed 11 g. It was then dissolved in 50 cc. of warm glacial acetic acid and treated with norite. Less than 1 g. of 2,2'-dinitro-6,6'-dicarboxydiphenyl crystallized out upon standing. The mother liquor was diluted with an equal amount of water, warmed to bring all the precipitate into solution and treated further with norite. Crystals of 2-nitro-6-carboxy-2'-meth-

¹⁰ Mills and Elliott, *J. Chem. Soc.*, 1291 (1928).

¹¹ Davis, Magers and Steiner, *THIS JOURNAL*, 52, 1570 (1930).

oxy-5'-methyldiphenyl were obtained after standing at room temperature overnight. They were collected and recrystallized twice from 50% alcohol. The yield was 3.5 g.

The pure 2-nitro-6-carboxy-2'-methoxy-5'-methyldiphenyl forms greenish-yellow plates melting at 182–183°, soluble in the common organic solvents, but insoluble in water.

Anal. Calcd. for $C_{15}H_{13}NO_5$: neut. equiv., 287.1; N, 4.88. Found: neut. equiv., 288.7; N (micro Dumas), 4.92.

Resolution of 2-Nitro-6-carboxy-2'-methoxy-5'-methyldiphenyl. Brucine Salt.—A solution of 1.200 g. of 2-nitro-6-carboxy-2'-methoxy-5'-methyldiphenyl in 30 cc. of warm alcohol was mixed with a solution of 1.647 g. of anhydrous brucine in 40 cc. of warm alcohol. No salt was obtained after standing in the ice box for three days. After addition of 20 cc. of water and further cooling, small white crystals were obtained. The first fraction weighed 0.985 g. The mother liquor was concentrated *in vacuo* to 50 cc. A second fraction of 0.816 g. of the brucine salt resulted. Further concentration of the solution to about 10 cc. yielded a third fraction of 0.648 g. The different fractions of the brucine salt had the same appearance, the same melting point, 146–150°, and the same rotation (see Table III and Fig. 2).

Anal. Calcd. for $C_{35}H_{33}N_3O_9$: N, 6.16. Found: N (micro Dumas), 6.31.

A mixture of 0.2014 g. of the racemic acid and 0.2765 g. of anhydrous brucine was made up to 25 cc. with chloroform at 26°. After the solid had been wetted for eight minutes, it gave the initial rotation $\alpha_D -0.36^\circ$, $l = 2$, $[\alpha]_D^{25} -9.6^\circ$ and in thirty minutes a final value $\alpha_D -0.28^\circ$, $[\alpha]_D^{25} -7.4^\circ$. The final specific rotation is a little lower than the final value obtained from the *l*-salt. This is due, possibly, to the higher concentration of this solution.

***l*-2-Nitro-6-carboxy-2'-methoxy-5'-methyldiphenyl.**—One and four-tenths grams of the brucine salt was ground to a fine powder in an agate mortar and transferred to a 125-cc. Erlenmeyer flask surrounded with ice. Then 50 cc. of 6 *N* ice-cold hydrochloric acid was added. The flask was immersed in an ice-water bath with occasional shaking. In three to four hours the hydrochloric acid was filtered off and replaced by fresh acid of the same strength. After standing overnight in an ice box the active acid was filtered by suction and washed thoroughly with ice-cold water until both the filtrate and the precipitate showed a negative test for brucine. The dried acid weighed 0.56 g. It melted at 180–182° (see Table III and Fig. 1 for rotation).

2-Nitro-6-carboxy-2'-methoxy-5'-chlorodiphenyl.—A mixture of 36 g. of 1-iodo-2-methoxy-5-chlorobenzene¹² and 18 g. of 1-nitro-2-bromo-3-carbomethoxybenzene was heated to 240° and then 40 g. of copper bronze was introduced in small portions. The reaction product was extracted with two portions of 250 cc. of warm alcohol. The alcoholic solution was transferred to a 2-liter flask and the alcohol was distilled. The residue was then saponified with 5% sodium hydroxide solution, the unsaponified oil separated from the water solution, and the solution acidified with dilute hydrochloric acid. A light yellow precipitate formed which weighed 13 g.

The crude product was dissolved in 60 cc. of warm glacial acetic acid and treated with some norite. Upon standing for several hours, 2 g. of 2,2'-dinitro-6,6'-dicarboxy-diphenyl crystallized out. The mother liquor was diluted with 50 cc. of water and the solution was warmed on a hot-plate to bring all the precipitate into solution. Pale yellow leaflets were obtained after standing at room temperature for a few hours. The crude product, which amounted to 8.5 g., was recrystallized twice from 70% alcohol. The yield of pure 2-nitro-6-carboxy-2'-methoxy-5'-chlorodiphenyl was 6.5 g., m. p. 174–175°.

¹² Ingold, Smith and Vass, *J. Chem. Soc.*, 1248 (1927).

Anal. Calcd. for $C_{14}H_{10}ClNO_3$: neut. equiv., 307.5; Cl, 11.52; N, 4.55. Found: neut. equiv., 309.1; Cl, 11.64; N (micro Dumas), 4.67.

The unsaponified oil solidified upon standing. It was washed with water and then cold methanol and recrystallized three times from 95% alcohol. About 6 g. of pure product was obtained. It was 2,2'-dimethoxy-5,5'-dichlorodiphenyl, one of the symmetrical coupling products.

The pure 2,2'-dimethoxy-5,5'-dichlorodiphenyl forms colorless needles melting at 144.5–145.5°.

Anal. Calcd. for $C_{14}H_{12}Cl_2O_2$: C, 59.33; H, 4.27. Found: C, 59.24; H, 4.37.

Resolution of 2-Nitro-6-carboxy-2'-methoxy-5'-chlorodiphenyl. Brucine Salt.—A solution of 1.6847 g. of 2-nitro-6-carboxy-2'-methoxy-5'-chlorodiphenyl in 40 cc. of warm absolute alcohol was mixed with a solution of 2.16 g. of anhydrous brucine in 40 cc. of warm absolute alcohol and then filtered. Upon standing, crystals began to deposit and in five hours 2.81 g. of brucine salt was obtained. The mother liquor was placed in an ice box overnight and a second fraction of 0.858 g. of the salt crystallized. These two fractions together amounted to 98% of the theoretical yield. They were both the same salt.

The product forms light yellow leaflets melting at 148–153°. It contains one molecule of water of crystallization (see Table III and Fig. 2 for rotations).

Anal. Calcd. for $C_{27}H_{20}ClN_3O_9 \cdot H_2O$: H_2O , 2.50; N, 5.84. Found: H_2O , 2.42; N (micro Dumas), 5.89.

l-2-Nitro-6-carboxy-2'-methoxy-5'-chlorodiphenyl.—The salt was finely pulverized and decomposed in a similar manner as the brucine salt of 2-nitro-6-carboxy-2'-methoxy-5'-methyldiphenyl. The product was dried over phosphorus pentoxide and weighed 0.62 g., m. p. 173–175° (see Table II and Fig. 1 for rotations).

2-Nitro-6-carboxy-2'-methoxy-5'-bromodiphenyl.—A mixture of 26 g. of 1-iodo-2-methoxy-5-bromobenzene¹³ and 16 g. of 1-nitro-2-bromo-3-carbomethoxydiphenyl was heated at 200–215°, then 40 g. of copper bronze was introduced by portions. The reaction product was extracted with two 100-cc. portions of boiling alcohol. Upon cooling of the alcoholic solution, 5.8 g. of white crystals of 2-nitro-6-carbomethoxy-2'-methoxy-5'-bromodiphenyl melting at 148–149° separated. The ester was saponified by refluxing with 200 cc. of 5% aqueous sodium hydroxide solution for four hours. The solution was filtered and acidified with dilute hydrochloric acid. The crude product was recrystallized twice from 50% alcohol.

The pure 2-nitro-6-carboxy-2'-methoxy-5'-bromodiphenyl forms pale yellow plates melting at 186–187°.

Anal. Calcd. for $C_{14}H_{10}BrNO_3$: neut. equiv., 352; N, 3.98. Found: neut. equiv., 354.4; N (micro Dumas), 4.02.

Resolution of 2-Nitro-6-carboxy-2'-methoxy-5'-bromodiphenyl. Brucine Salt.—A solution of 1.3305 g. of the diphenyl in 30 cc. of alcohol was treated with a solution of 1.4910 g. of anhydrous brucine in 30 cc. of warm alcohol. The solution was diluted with 40 cc. of water. After standing for several hours 1.14 g. of the brucine salt deposited. By concentrating the mother liquor to 60 cc., 0.97 g. more of the salt was obtained. Further concentration gave a third fraction of 0.62 g. They were the same in melting point and rotation.

The brucine salt of 2-nitro-6-carboxy-2'-methoxy-5'-bromodiphenyl forms pale yellow needles, m. p., 162–165° (see Table III and Fig. 2 for rotations).

Anal. Calcd. for $C_{27}H_{20}BrN_3O_9$: N, 5.63. Found: N (micro Dumas), 5.51.

¹³ Hirtz, *Ber.*, 29, 1410 (1896).

l-2-Nitro-6-carboxy-2'-methoxy-5'-bromodiphenyl.—One and four-tenths grams of the finely powdered brucine salt was decomposed by the ice-cold hydrochloric acid in the manner previously described. The product weighed 6.2 g., m. p. 185–187° (see Table III for rotations and Fig. 1).

2,5'-Dinitro-6-carboxy-2'-methoxydiphenyl.—The procedure was similar to that for the other three diphenyls. The bath temperature was carefully controlled between 230 and 240°. (In the first run when the temperature was raised higher than 250°, all of the 1-iodo-2-methoxy-5-nitrobenzene decomposed.) Since the coupling product was not very soluble in alcohol, it was extracted with acetone and the acetone was distilled off before saponification. The separation of 2,2'-dinitro-5,5'-dicarboxydiphenyl was carried out as usual through the fractional crystallization from acetic acid. From 30 g. of 1-iodo-2-methoxy-5-nitrobenzene,¹⁴ 18 g. of 1-nitro-2-bromo-3-carbomethoxybenzene and 40 g. of copper bronze, 3.5 g. of the crude 2,5'-dinitro-6-carboxy-2'-methoxydiphenyl was obtained. It was purified by recrystallizing twice from 70% alcohol. The yield was 2.5 g.

The pure 2,2'-dinitro-6-carboxy-2'-methoxydiphenyl forms pale yellow prisms melting at 202–203°.

Anal. Calcd. for $C_{14}H_{20}N_2O_7$: neut. equiv., 318; N, 8.80. Found: neut. equiv., 316.8; N (micro Dumas), 8.69.

Resolution of 2,5'-Dinitro-6-carboxy-2'-methoxydiphenyl. Brucine Salt.—A solution of 1.0528 g. of 2,5'-dinitro-6-carboxy-2'-methoxydiphenyl in 20 cc. of warm alcohol was treated with a solution of 1.3052 g. of anhydrous brucine in 30 cc. of warm alcohol. No salt was obtained after standing for several days. Then 40 cc. of water was added and the solution was allowed to stand at room temperature overnight. One and twenty-four hundredths grams of brucine salt separated as golden yellow crystals. When the mother liquor was concentrated to 30 cc., a second fraction of 0.61 g. of the brucine salt was obtained. A resinous residue was left after the mother liquor evaporated to dryness. The residue was dissolved in 50 cc. of boiling water and more crystalline brucine salt was obtained.

Different fractions of the brucine salt had the same appearance, the same melting point, 179–183° and the same rotation (see Table III for rotations and Fig. 2). Its chloroform solution is colorless.

Anal. Calcd. for $C_{37}H_{36}N_4O_{11} \cdot 3H_2O$: H_2O , 7.05; N, 7.31. Found: H_2O , 6.89; N (micro Dumas), 7.25.

l-2,5'-Dinitro-6-carboxy-2'-methoxydiphenyl.—One and five-tenths grams of the finely powdered brucine *l*-salt was decomposed in the usual manner with ice-cold hydrochloric acid. The dried *l*-acid weighed 0.61 g. It melted at 201–202° (see Table III for rotations and Fig. 1).

Summary

1. Five 5'-substituted 2-nitro-6-carboxy-2'-methoxydiphenyls have been prepared containing the OCH_3 , CH_3 , Cl, Br and NO_2 groups. These have been resolved and the rates of racemization of the active acids compared with the results on 2-nitro-6-carboxy-2'-methoxydiphenyl.

2. The rates of racemization have been shown to be affected. A discussion is given of the possible mechanism of the changes produced by the 5'-substitution.

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¹⁴ Reverdin, *Ber.*, 29, 997 (1896).