

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]  
**STEREOCHEMISTRY OF DIPHENYLS.<sup>1</sup> XXV. THE RELATIVE  
 INTERFERING EFFECTS OF THE GROUPS F, OCH<sub>3</sub>, Cl, Br AS  
 DETERMINED BY THE RELATIVE RATES OF RACEMIZATION  
 OF THE 2'-SUBSTITUTED 2-NITRO-6-CARBOXYDIPHENYLS**

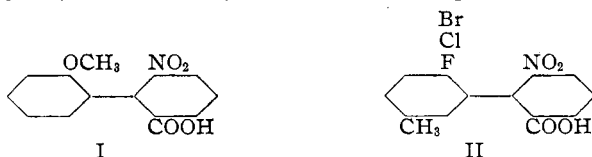
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The observation that 2-nitro-6-carboxy-2',5'-dimethoxydiphenyl racemized readily at room temperature made evident that a study of the rates of racemization of various 2'-substituted 2-nitro-6-carboxydiphenyls might lead to a satisfactory method for determining the relative interfering effects of various groups.

In this investigation the 2-nitro-6-carboxy-2'-methoxydiphenyl (I) and the 2'-fluoro, chloro and bromo derivatives (II) of 2-nitro-6-carboxy-5'-methyldiphenyl have been synthesized and compared.



The 2-nitro-6-carboxy-2'-methoxydiphenyl was of particular interest since it contained the same 2,2',6-substituents as were present in 2-nitro-6-carboxy-2',5'-dimethoxydiphenyl reported by Yuan and Adams.<sup>1b</sup> The only modification is the elimination of the methoxyl group in the 5'-position of the latter compound. Both products showed exactly the same phenomenon in that merely one alkaloidal salt could be isolated and this showed mutarotation. The active forms obtained from the salts racemized with the same half-life period. It is apparent, then, that the additional methoxyl group in the previously reported compound has no appreciable influence on the interference effect of the 2,2',6 groups. The corresponding 2-nitro-6-carboxy-2'-methoxy-5'-methyldiphenyl has also been synthesized, a description of which is published in the succeeding paper and it also showed mutarotation of the single salt which could be isolated and a half-life period for the active acid essentially the same as that for the unsubstituted or 5'-substituted 2-nitro-6-carboxy-2'-methoxydiphenyl. Since the 5'-methyl group had no influence on the molecule, the halogen derivatives, 2'-fluoro, chloro and bromo of the 2-nitro-6-

<sup>1</sup> The last three papers in this series: (a) Roll and Adams, *THIS JOURNAL*, **54**, 2494 (1932); (b) Yuan and Adams, *ibid.*, **54**, 2966 (1932); (c) Becker and Adams, *ibid.*, **54**, 2973 (1932).

<sup>2</sup> This communication is an abstract of a thesis submitted by R. W. Stoughton in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

carboxy-5'-methyldiphenyl were used for comparison since they were considerably simpler to prepare than those not containing the methyl group.

The 2-nitro-6-carboxy-2'-fluoro-5'-methyldiphenyl formed only a single salt. However, unlike the methoxyl derivative, the salt showed no mutarotation at room temperature. Whether this indicated that the fluoro acid was incapable of resolution or that the mutarotation of the salt was so rapid that it could not be observed experimentally, was determined as follows. The brucine salt was dissolved in chloroform, not at room temperature but at 0°, and retained at that temperature in a polarimeter tube. Under these conditions a gradual change in rotation was noted from an initial reading of  $[\alpha]_D^{20} +13^\circ$  to a final constant reading of  $[\alpha]_D^{20} -3.4^\circ$ , which corresponds to a half-life period at 0° of forty-two minutes. If the brucine salt was dissolved at room temperature and then cooled to 0°, a rotation was obtained the same as that of a solution of the salt prepared originally at 0° and allowed to stand till constant rotation resulted. From these experiments it may be concluded that a single form of the brucine salt of the fluoro compound was in hand, but that it mutarotated with such rapidity that only at low temperatures could it be observed in the laboratory. The acid from this salt would certainly be extremely sensitive to racemization and in fact, in spite of all precautions, no active acid could be obtained by decomposition of the salt even at -5°.

The corresponding chlorine and bromine derivatives showed normal properties. Both salts were isolated and both active forms of each compound were obtained. The rates of racemization of the active acids were slow. The chloro compound did not racemize appreciably in hot ethyl alcohol and had a half-life period in boiling butyl alcohol of one hundred and forty-one minutes as compared with seventy hours for the bromo compound under similar conditions. More complete data are given in Table III. In every instance the bromo compound racemized much more slowly than the chloro.

From all these results it appears that the relative interference effects of the four groups studied would be in the following order—bromine > chlorine > methoxyl > fluorine, with marked differences between each. It is unlikely that any other factors in the molecule could modify the rates of racemization to such a degree that these groups would fall out of the order indicated. The corresponding methyl, carboxyl and nitro derivatives are now under investigation.

The average interference on each side of the molecule from x-ray data, based on the values previously assigned to the individual groups (with the exception that 1.45 Å. was substituted for 1.54 Å. for the methoxyl group)<sup>1c</sup> was as follows: for the F, OCH<sub>3</sub>, Cl, Br: +0.01 Å., +0.04 Å.,

+0.25 Å., +0.37 Å. Assuming the rings to be coaxial at all times, the minimum interference value in each molecule would be, respectively, as follows: 0.05 Å., 0.11 Å., 0.55 Å., 0.78 Å. As the order from the two methods of computation is the same, either method might be adopted. The authors at present favor the second and recognize the fact that any calculated interferences in the 2,2',6-trisubstituted diphenyls have less influence on racemization rates in these compounds than the same interference in the 2,2',6,6'-tetrasubstituted diphenyls.

The compounds were prepared by condensing 1-nitro-2-bromo-3-carbomethoxybenzene with the intermediates *o*-iodoanisole, 1-methyl-3-iodo-4-chlorobenzene, 1-methyl-3-iodo-4-bromobenzene and 1-methyl-3-iodo-4-fluorobenzene by means of copper, saponification of the reaction product and isolation of the desired diphenyls. The salts of the acids showed a marked tendency to retain water, possibly in the form of water of crystallization. The anhydrous salts were hygroscopic and consequently the rotations were taken on the hydrated salts which had been analyzed for water content.

### Experimental

**1-Nitro-2-bromo-3-carbomethoxybenzene.**—A solution of 130 g. of 1-nitro-2-bromo-3-carboxybenzene<sup>3</sup> in one liter of dry methyl alcohol was saturated with dry hydrogen chloride and refluxed for eight hours. This solution was poured into 6 liters of ice water, filtered, washed with sodium carbonate solution and recrystallized from a liter of 30% alcohol. A yield of 131 g. (95%) of white plates melting at 78.0–78.5° was obtained.

*Anal.* Calcd. for  $C_8H_6BrNO_4$ : Br, 30.76. Found: Br, 30.3.

**1-Methyl-3-iodo-4-chlorobenzene.**—A solution of 50 g. of 1-methyl-3-iodo-4-aminobenzene hydrochloride<sup>4</sup> in 350 cc. of glacial acetic acid, 90 cc. of water and 30 cc. of concentrated hydrochloric acid was cooled in an ice-salt bath and to it was added with constant stirring a solution of 17.5 g. of sodium nitrite in 90 cc. of water. At the same time a cuprous chloride solution was prepared by refluxing a mixture composed of 80 g. of potassium chloride, 44 g. of crystallized copper sulfate, 30 cc. of concentrated hydrochloric acid, 17 cc. of concentrated sulfuric acid, 50 g. of copper turnings and 250 cc. of water until it turned colorless. After the diazotized solution had stood for one and one-half hours in the cold, it was added to the hot cuprous chloride solution and the reaction mixture was immediately steam distilled. The distillate was extracted with ether and purified by vacuum distillation. The product amounted to 36 g. (76%) boiling at 157–159° at 50 mm. Ullmann and Glenck<sup>5</sup> prepared it by diazotizing chloro-*m*-toluidine and replacing with iodine. They give the boiling point at 249° at atmospheric pressure.

**1-Methyl-3-iodo-4-bromobenzene.**—A solution of 90 g. of 1-methyl-3-iodo-4-aminobenzene<sup>4</sup> in 600 cc. of glacial acetic acid, 90 cc. of water and 18 cc. of concentrated sulfuric acid was cooled in an ice-salt bath and to it was added with constant stirring

<sup>3</sup> "Organic Syntheses," John Wiley and Sons, Inc., New York City, 1927, Vol. VII, p. 12.

<sup>4</sup> Wheeler and Liddle, *Am. Chem. J.*, **42**, 445 (1909).

<sup>5</sup> Ullmann and Glenck, *Ber.*, **49**, 2493 (1916).

a solution of 26 g. of sodium nitrite in 150 cc. of water. At the same time a cuprous bromide solution was prepared by refluxing a mixture composed of 192 g. of sodium bromide, 90 g. of crystallized copper sulfate, 70 cc. of concentrated sulfuric acid, 70 g. of copper turnings and 500 cc. of water until it turned light yellow. After the diazotized solution had stood for one and one-half hours in the cold it was added to the hot cuprous bromide and the reaction mixture was immediately steam distilled. The distillate was extracted with ether and purified by vacuum distillation. A yield of 46 g. (40%) of a yellow oil was obtained boiling at 145–150° at 20 mm.

*Anal.* Calcd. for  $C_7H_5BrI$ : Br + I, 69.68. Found: Br + I, 69.39.

**1-Methyl-3-iodo-4-fluorobenzene.**—To a solution of 100 g. of 1-methyl-3-iodo-4-aminobenzene<sup>4</sup> hydrochloride in 50 cc. of concentrated hydrochloric acid and 80 cc. of water, cooled in an ice-salt bath, 35 g. of sodium nitrite was added slowly over a period of three hours. After standing for two hours in the cold, the diazotized solution was filtered and to it was added 90 cc. of fluoroboric acid solution. This solution was prepared according to the directions of Balz and Schiemann<sup>6</sup> by adding slowly 73 g. of boric acid to 190 g. of a cold 48% hydrogen fluoride solution in a copper flask. The solution was kept in a wax bottle. Upon the addition of the fluoroboric acid a heavy yellow crystalline precipitate of diazonium borofluoride separated. This was filtered and washed first with alcohol and then with a little ether. A yield of 90 g. (70%) was obtained. This substance decomposes at 110° and upon standing for several weeks becomes dark colored.

The diazonium borofluoride was decomposed by placing in a distilling flask, loosely fitted with a cork stopper and connected to a condenser and receiver. A stream of air was drawn through the apparatus by a suction pump through a water trap. The flask was heated gently with a free flame until decomposition started. A large amount of boron trifluoride was liberated and if heated too strongly escaped into the room in spite of the suction. After the salt was decomposed, the flask was heated more strongly in order to distil over the iodofluorotoluene. As soon as iodine vapors appeared in the flask the heating was discontinued. Some of the product was always carried over to the water trap. This was added to the main product and washed with sodium hydroxide and water. It was finally vacuum distilled. A yield of 45 g. (70% based on the borofluoride) of a colorless liquid was obtained: b. p. (30 mm.) 122–125°,  $d_{20}^{20}$  1.8337,  $n_D^{18}$  1.5757.

*Anal.* Calcd. for  $C_8H_6FI$ : I, 53.8. Found: I, 53.0.

**Condensation of 1-Nitro-2-bromo-3-carbomethoxybenzene with Halogenated Benzenes to Form Substituted 2-Nitro-6-carboxydiphenyls.**—In a 200-cc. 3-necked flask fitted with a mechanical stirrer and reflux condenser was placed 20–30 g. of 1-nitro-2-bromo-3-carbomethoxybenzene and an excess of half a mole of the aryl halide. The mixture was heated in a metal bath and as soon as the contents began to boil 40–60 g. of copper bronze was added slowly over a period of three-quarters of an hour. During the addition of the copper, the bath temperature was maintained just below the refluxing point and then raised 25° for fifteen minutes. After cooling, the mixture was thoroughly extracted with 200–300 cc. of hot alcohol and filtered. To this alcohol extract 100–150 cc. of 10% sodium hydroxide was added, the solution diluted to 500–750 cc. and refluxed for five hours. At the end of this time an oil remained which consisted of a mixture of unreacted halide and any diphenyl formed from its symmetrical coupling. This was recovered by steam distillation.

The aqueous layer was then acidified with dilute hydrochloric acid. The brown solid that separated was collected and dissolved in 150–200 cc. of hot glacial acetic acid.

<sup>6</sup> Balz and Schiemann, *Ber.*, **60**, 1186 (1927).

On cooling, any 2,2'-dinitro-6,6'-dicarboxybenzene that had been formed, separated. This was removed and the filtrate was diluted to 400–500 cc. with water and heated until solution was complete. On cooling, the crude acid was deposited. It was then recrystallized from a suitable solvent. The pure acid may also be obtained by extracting the crude product from the saponification with warm benzene as the 2,2'-dinitro-6,6'-dicarboxybenzene is nearly insoluble in benzene even when warm. The benzene solution is then extracted with sodium hydroxide and recrystallized.

TABLE I  
PROPERTIES OF DIPHENYLS

The products were purified by dissolving in hot alcohol and adding water up to the point of cloudiness. The 2-nitro-6-carboxy-2'-bromo-5'-methyldiphenyl, however, was crystallized from either alcohol or glacial acetic acid.

Acid	Aryl halide condensed with 1-nitro-2-bromo- 3-carbomethoxy- benzene	Temp. of coupling bath, °C.	Yield, pure, %	Form and color	M. p. (corr.), °C.	Analyses, %	
						Calcd.	Found
2-Nitro-6-carboxy- 2'-fluoro-5'- methyldiphenyl	1-Methyl-3-iodo- 4-fluorobenzene	200–210	18	Yellow plates	187–188	C, 61.10 H, 3.64	61.19 3.69
2-Nitro-6-carboxy- 2'-chloro-5'- methyldiphenyl	1-Methyl-3-iodo- 4-chlorobenzene	230–240	11	Yellow plates	234–234.5	C, 57.63 H, 3.62	57.89 3.57
2-Nitro-6-carboxy- 2'-bromo-5'- methyldiphenyl	1-Methyl-3-iodo- 4-bromobenzene	240–250	10	Yellow plates	228–229	Br, 23.78	23.59
2-Nitro-6-carboxy- 2'-methoxydiphenyl	1-Iodo-2-methoxy- benzene	240–250	21	Yellow needles	196.5–197	C, 61.53 H, 4.08	61.73 3.88

**2,2'-Dichloro-5,5'-dimethyldiphenyl.**—The oil recovered from the saponification process in the preparation of 2-nitro-6-carboxy-2'-chloro-5'-methyldiphenyl was steam distilled. At first the unreacted chloriodotoluene came over but near the end of the distillation a white solid was obtained. This was recrystallized from dilute alcohol. It melted at 85–86°.

*Anal.* Calcd. for  $C_{14}H_{12}Cl_2$ : Cl, 28.25. Found: Cl, 28.35.

**Resolution of 2-Nitro-6-carboxy-2'-methoxydiphenyl.**—To a warm solution of 1.86 g. of 2-nitro-6-carboxy-2'-carboxydiphenyl in 150 cc. of alcohol was added a solution of 2.79 g. of brucine in 75 cc. of alcohol and the mixture filtered. Upon standing overnight at 0°, 1.2 g. of yellow solid deposited. Due to the instability of this salt no attempt was made to purify it by recrystallization. It melted at 219–220°. This salt contained water which corresponded to one-half a molecule of water of crystallization. The anhydrous form melts at 223–224°. (See Table II for rotations and mutarotations of the hydrated salt.)

The mother liquors were evaporated under an air jet in the cold and 1.5 g. more obtained with the same melting point and rotation.

*Anal.* Calcd. for  $C_{27}H_{27}N_3O_9$ : C, 66.54; H, 5.59. Found: C, 66.85; H, 5.65.  
Calcd. for  $C_{27}H_{27}N_3O_9 \cdot 0.5H_2O$ :  $H_2O$ , 1.33. Found: 1.57.

**d-2-Nitro-6-carboxy-2'-methoxydiphenyl.**—The active acid was obtained by treating 1 g. of the salt with 50 cc. of ice cold 6 *N* hydrochloric acid in a flask cooled in an ice-salt bath for one hour. It was filtered, treated with a second portion of hydrochloric acid and allowed to stand in an ice box overnight. It was then filtered and washed, first with dilute acid and then with water until the washings gave no test for brucine. Until the acid was obtained in the solid state the temperature was kept at 0°. A yield of 0.3 g. was obtained melting at 196–197°. (See Table II for rotations and racemization experiments.)

TABLE II

ROTATIONS OF *d*-2-NITRO-6-CARBOXY-2'-METHOXYDIPHENYL AND ITS BRUCINE AND SODIUM SALTS

Compound	Wt., <sup>a</sup> g.	Solvent	Temp., °C.	Rotations in degree <sup>b</sup>				Average K	Average deviation of K	Half-life period in min.
				Initial $\alpha_D$	[ $\alpha$ ] <sub>D</sub>	Final $\alpha_D$	[ $\alpha$ ] <sub>D</sub>			
Brucine salt <sup>c</sup>	0.1827	Chloroform	0	+1.08	+88.7	-0.11	-9.0	0.0010	=0.001	301.0
Brucine salt	.1016	Chloroform	26	+0.40	+29.5	- .11	-8.1	.025	= .002	12.0
<i>d</i> -Acid	.2057	Alcohol	26	+ .81	+29.5	Not carried to completion <sup>d</sup>		.032	= .003	9.4
Sodium salt	.1260	0.1 N NaOH	26	+ .80	+47.5	Not carried to completion <sup>d</sup>		.015	= .002	20.0
Sodium salt	.1414	Dil. Na ethylate <sup>c</sup>	26	+ .94	+49.9	Not carried to completion <sup>d</sup>		.091	= .005	3.3

<sup>a</sup> Made up to 15 cc. <sup>b</sup>  $l = 2$ . <sup>c</sup> Solution of 0.5 g. of sodium in 50 cc. of absolute alcohol was used. <sup>d</sup> Six to eight readings were taken during the period of partial racemization and from these half-life periods were calculated. <sup>e</sup> The brucine salt at 0°:  $l = 1$  but all the others  $l = 2$ .

**Resolution of 2-Nitro-6-carboxy-2'-chloro-5'-methyldiphenyl.**—To a warm solution of 3.0 g. of 2-nitro-6-carboxy-2'-chloro-5'-methyldiphenyl in 125 cc. of ordinary ethyl alcohol was added a solution of 4.15 g. of anhydrous brucine in 75 cc. of alcohol. Upon standing for five hours 4.2 g. of white plates was deposited. These were collected and after three recrystallizations from alcohol 1.5 g. of salt of constant rotation was obtained melting at 200° with previous softening at 150°. This less soluble salt was found to contain water which corresponded to three-fourths of a molecule of water of crystallization. The melting point of the anhydrous form is 215–217°.

**Rotation.** Hydrated less soluble salt: 0.1270 g. made up to 15 cc. with chloroform at 20° gave  $\alpha_D -0.32^\circ$ ;  $l = 2$ ;  $[\alpha]_D^{20} -25.3^\circ$ .

**Anal.** 0.2681 g. lost 0.0052 g. on drying. Calcd. for  $C_{17}H_{13}ClN_2O_5 \cdot 0.75H_2O$ :  $H_2O$ , 1.85. Found:  $H_2O$ , 1.94. Calcd. for  $C_{17}H_{13}ClN_2O_5$ : C, 64.75; H, 5.29. Found: C, 64.75, H, 5.39.

The mother liquors were evaporated under an air jet and the solid obtained was recrystallized three times from *n*-butyl alcohol. This yielded 2.0 g. of more soluble salt. It melted at 220–221°.

**Rotation.** More soluble salt: 0.1398 g. made up to 15 cc. with chloroform at 20° gave  $\alpha_D +0.43^\circ$ ;  $l = 2$ ;  $[\alpha]_D^{20} +22.8^\circ$ .

**Anal.** Calcd. for  $C_{17}H_{13}ClN_2O_5$ : C, 64.75; H, 5.29. Found: C, 65.52; H, 5.47.

***l*- and *d*-2-nitro-6-carboxy-2'-chloro-5'-methyldiphenyl.**—The active acids were liberated from their salts by treatment with hydrochloric acid in the cold as previously described. The organic acids were obtained as fine cream-colored powders.

The active acids were recrystallized from dilute alcohol. The *l*-acid from the less soluble salt was obtained melting at 234.5° with slight softening at 180°. The *d*-acid from the more soluble salt melted at 234° with slight softening at 180°. (See Table III for rotations and racemization experiments on *l*-acid.) The rotation of the *l*-acid in boiling ethyl alcohol remained constant.

**Rotation.** *d*-Acid: 0.1213 g. made up to 15 cc. with ethyl alcohol at 20° gave  $\alpha_D +0.30$ ;  $l = 2$ ;  $[\alpha]_D^{20} +18.6^\circ$ .

**Resolution of 2-Nitro-6-carboxy-2'-bromo-5'-methyldiphenyl.**—To a warm solution of 1.68 g. of 2-nitro-6-carboxy-2'-bromo-5'-methyldiphenyl in 50 cc. of alcohol was added a solution of 1.97 g. of anhydrous brucine in 50 cc. of alcohol and the mixture filtered. Upon standing overnight 1.6 g. of white plates was deposited. These were collected

and after two recrystallizations from alcohol 1.0 g. of salt of constant rotation remained. It melted at 203° with previous softening at 150°. This salt on drying was found to contain water which corresponded to one molecule of water of crystallization. The anhydrous form melted at 219°.

*Rotation.* Hydrated less soluble salt: 0.1226 g. made up to 15 cc. with chloroform at 20° gave  $\alpha_D -0.52^\circ$ ;  $l = 2$ ;  $[\alpha]_D^{20} -31.8^\circ$ .

*Anal.* 0.3424 g. lost 0.0088 g. on drying. Calcd. for  $C_{37}H_{36}BrN_3O_8 \cdot H_2O$ :  $H_2O$ , 2.47. Found:  $H_2O$ , 2.57. Calcd. for  $C_{37}H_{36}BrN_3O_8$ : Br, 10.95. Found: Br, 10.88.

The mother liquors were evaporated under an air jet and the solid obtained was recrystallized three times from *n*-butyl alcohol. This yielded 0.5 g. of pure more soluble salt. It contained no water and melted at 228–229°.

*Rotation.* Anhydrous more soluble salt: 0.1463 g. made up to 15 cc. with chloroform at 20° gave  $\alpha_D +0.75^\circ$ ;  $l = 2$ ;  $[\alpha]_D^{20} +38.4^\circ$ .

*Anal.* Calcd. for  $C_{37}H_{36}BrN_3O_8$ : Br, 10.95. Found: Br, 11.17.

*l*- and *d*-2-Nitro-6-carboxy-2'-bromo-5'-methyldiphenyl.—The active acids were liberated from their salts by treatment with hydrochloric acid in the cold. The organic acids were obtained as fine cream-colored powders. The active acids were purified from dilute alcohol. The *l*-acid from the less soluble salt melted at 227–228° with very distinct softening at 177°. The *d*-acid from the more soluble salt melted at 226.5–228° with softening at 177°. (See Table III for rotations and racemization experiments on *l*-acid.)

*Rotation.* *d*-Acid: 0.1337 g. made up to 15 cc. with ethyl alcohol at 20° gave  $\alpha_D +0.49^\circ$ ;  $l = 2$ ;  $[\alpha]_D^{20} +27.5^\circ$ .

TABLE III  
RACEMIZATION EXPERIMENTS OF *l*-2-NITRO-6-CARBOXY-2'-CHLORO-5'-METHYLDIPHENYL  
AND *l*-2-NITRO-6-CARBOXY-2'-BROMO-5'-METHYLDIPHENYL

Wt., <sup>a</sup> g.	Solvent	Temp., °C.	Rotations in degrees <sup>b</sup>				Average age K × 10 <sup>3</sup>	Average deviation of K × 10 <sup>3</sup>	Half-life period in min.	
			Initial $\alpha_D$	Partially racemized $[\alpha]_D^{30}$ Time, min.	$\alpha_D$	$[\alpha]_D^{30}$				
2-Nitro-6-carboxy-2'-chloro-5'-methyldiphenyl										
0.1868	Butyl alcohol	117	-0.61	-40.8	360	-0.10	-6.7	2.14	±0.03	141
.2342	Acetic acid	118	-1.29	-68.9	340	-0.29	-15.5	1.95	±.03	154
.1604	0.1 N NaOH	80	+1.61	+125	390	+1.41	+110	0.12	±.03	2510
.1190	0.1 N NaOH	100	-0.93	-97.6 <sup>c</sup>	330	-0.39	-41.0	1.4	±.2	218
.1505	Dil. Na ethylate <sup>d</sup>	78	+1.4	+116	240	+1.27	+105	0.17	±.01	1770
2-Nitro-6-carboxy-2'-bromo-5'-methyldiphenyl										
0.2495	Butyl alcohol	117	-0.74	-37.1	1500	-0.58	-29.1	0.69	±0.001	4350
.1478	Acetic acid	118	-0.69	-58.4	1080	-.55	-46.5	.88	±.005	3240
.1816	0.1 N NaOH	100	+1.20	+82.6	1080	+.97	+66.8	.85	±.002	3540
.1094	Dil. Na ethylate <sup>d</sup>	78	+0.76	+85.9	300	+.66	+75.3	.13	±.01	2340

<sup>a</sup> Made up to 25 cc. <sup>b</sup>  $l = 2$ . <sup>c</sup> Partially active. <sup>d</sup> Solution of 0.5 g. of sodium in 50 cc. of absolute alcohol was used.

**Resolution of 2-Nitro-6-carboxy-2'-fluoro-5'-methyldiphenyl. Brucine Salt.**—To a warm solution of 2.75 g. of 2-nitro-6-carboxy-2'-fluoro-5'-methyldiphenyl in 50 cc. of ordinary ethyl alcohol was added a solution of 3.94 g. of anhydrous brucine in 100 cc. of alcohol. Upon standing overnight in an ice box 5.1 g. of a white solid was deposited. Upon evaporation of the mother liquors in the cold 1 g. of a yellow viscous oil remained which solidified on standing. On recrystallization, a salt of similar rotation to the first fraction was obtained.

The salt gave a constant rotation at 20° but if made up at 0° a rotation was at first

observed which gradually decreased through mutarotation until a constant value resulted. This final constant value was the same as that obtained by cooling to 0° the sample that had been first dissolved at 20°. Recrystallization of this salt did not change the rotation. It melted at 213–214.5° with slight softening at 150°. This salt retained water which corresponds to one-fourth of a molecule of water of crystallization. The melting point of the anhydrous form is 214–215°.

*Rotation.* Hydrated salt: 0.2846 g. made up to 15 cc. with chloroform at 20° gave  $\alpha_D -0.12^\circ$ ;  $l = 2$ ;  $[\alpha]_D^{20} -3.2^\circ$ . 0.1464 g. made up to 10 cc. with chloroform at 0° and allowed to remain at 0°;  $l = 1$ .

Time in minutes	$\alpha_D$	$[\alpha]_D^{20}$	$k$	Av. $k$
0	...	+15.0° (calcd.)	....	
10	+0.19°	+13.0°	....	
30	+ .10°	+ 6.8°	0.0093	
60	+ .05°	+ 3.4°	.0072	0.0083
115	- .02°	- 1.4°	.0084	
5 hours	- .05°	- 3.4°	....	

Half-life period, 42 minutes.

*Anal.* 0.2154 g. lost 0.0015 g. on drying. Calcd. for  $C_{37}H_{36}FN_3O_8 \cdot 0.25H_2O$ :  $H_2O$ , 0.68. Found:  $H_2O$ , 0.70. Calcd. for  $C_{37}H_{36}FN_3O_8$ : C, 66.34; H, 5.42. Found: C, 66.41; H, 5.45.

**Quinine Salt.**—To a warm solution of 3.24 g. of quinine in 30 cc. of ordinary ethyl alcohol was added a solution of 2.75 g. of 2-nitro-6-carboxy-2'-fluoro-5'-methyldiphenyl in 30 cc. of alcohol and the mixture filtered. At the end of four hours 2.6 g. of yellow crystals was deposited. Upon standing overnight 2.5 g. more was obtained which gave the same rotation as the first fraction. This salt behaved as did the brucine salt in showing a constant rotation at 20° but mutarotation at 0°. Likewise recrystallization did not affect the rotation. This salt melts at 135–140°. It was found to contain solvent of crystallization which corresponds to two molecules of water. The anhydrous form melts at 138–140°.

*Rotation.* Hydrated salt: 0.114 g. made up to 15 cc. with chloroform at 20° gave  $\alpha_D -1.40^\circ$ ;  $l = 2$ ;  $[\alpha]_D^{20} -94.5^\circ$ .

*Mutarotation.* Hydrated salt: 0.0703 g. was made up to 10 cc. with chloroform at 0° and allowed to stand at 0°;  $l = 1$ .

Time in minutes	$\alpha_D$	$[\alpha]_D^{20}$	$k$	Av. $k$
0	...	-125.0° (calcd.)	....	
5	-0.82°	-116.6°	....	
35	- .65°	- 92.4°	0.0178	0.0187
60	- .60°	- 85.3°	0.0196	
5 hours	- .58°	- 82.5°	....	

Half-life period, 16 minutes.

*Anal.* 0.3099 g. lost 0.0173 g. on drying. Calcd. for  $C_{34}H_{34}FN_3O_8 \cdot 2H_2O$ :  $H_2O$ , 5.67. Found:  $H_2O$ , 5.58. Calcd. for  $C_{34}H_{34}FN_3O_8$ : C, 68.08; H, 5.71. Found: C, 67.12; H, 5.81.

**Strychnine Salt.**—A mixture of 2.26 g. of 2-nitro-6-carboxy-2'-fluoro-5'-methyldiphenyl and 3.18 g. of strychnine was dissolved in 100 cc. of ordinary ethyl alcohol. Upon standing for two days 4.4 g. of white crystals was deposited. This salt showed no mutarotation at 0° and recrystallization did not change the rotation. The melting point is 194–196°.



*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  $C_{28}H_{22}FN_2O_6$ : 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  $-5^\circ$  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  $-5^\circ$ . Three-tenths of a gram obtained in this manner melted at 185–186°. 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°.

*Anal.* Calcd. for  $C_{14}H_8FNO_3$ : 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<sub>3</sub> > F.

URBANA, ILLINOIS

## [CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS] STEREOCHEMISTRY OF DIPHENYLS.<sup>1</sup> 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

<sup>1</sup> 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).

<sup>2</sup> 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.