2,2',6,6'-Tetramethoxy-3,3',5,5'-tetraacetodiphenyl.—To a solution of 2 g. of tetramethoxydiphenyl in 30 cc. of hot acetic anhydride was added 4 g. of anhydrous aluminum bromide. The solution was gently refluxed for two hours and about 50 cc. of alcohol then added through the condenser. The solution was concentrated to about 30 cc., an equal volume of alcohol was added and the warm solution filtered. The white solid residue was dissolved in hot 10% sodium hydroxide, filtered, and reprecipitated with acetic acid. It was purified from glacial acetic acid, white crystals, m. p. with dec. 340–350°.

Anal. Calcd. for $C_{24}H_{26}O_8$: C, 65.13; H, 5.92. Found: C, 65.15; H, 5.64.

Summary

2,2',6,6'-Tetramethoxy-3,3'-dicarboxydiphenyl and 2,2',6,6'-tetramethoxy-3,3'-diaminodiphenyl have been prepared. The former could not be resolved and no mutarotation of the salts was observed. The latter gave a dicamphorsulfonate that mutarotated at −17°.

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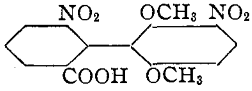
Stereochemistry of Diphenyls. XXXIII.[1] Preparation and Properties of 2,3'-Dinitro-6-carboxy-2',6'-dimethoxydiphenyl and 2-Nitro-6-carboxy-2'-fluoro-6'-methoxydiphenyl

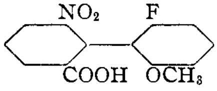
By A. M. VanArendonk,[2] B. C. Becker and Roger Adams

In previous papers a description of the properties of 2,2',6,6'-tetrafluoro-3,3'-dichloro-5,5'-dicarboxydiphenyl;[3] 2,2',6,6'-tetramethoxy-3,3'-dicarboxydiphenyl;[1] 2,2',6,6'-tetramethoxy-3,3'-diaminodiphenyl;[1] and 2,2'-difluoro-6,6'-dimethoxy-3,3'-dicarboxydiphenyl[4] has been given. None of these compounds could be resolved and only in the case of the 2,2',6,6'-tetramethoxy-3,3'-diaminodiphenyl was it possible to observe the mutarotation of a salt at a temperature of −17°.

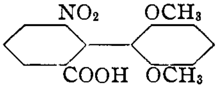
In this investigation two compounds have been prepared in which the 2,6 substituents were represented, respectively, by one fluorine and one methoxyl and by two methoxyls, while the 2',6' groups were nitro and carboxyl. The specific compounds were 2,3'-dinitro-6-carboxy-2',6'-dimethoxydiphenyl (I) and 2-nitro-6-carboxy-2'-fluoro-6'-methoxydiphenyl (II).



I



II



III

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(1) For previous papers in the series see VanArendonk, Cupery and Adams, This Journal, **55**, 4225 (1933). See also Adams and Yuan, *Chem. Rev.*, **12**, 261 (1933).

(2) Submitted as part of a thesis for the Degree of Doctor of Philosophy at the University of Illinois.

(3) Kleiderer and Adams, This Journal, **55**, 4219 (1933).

(4) Becker and Adams, *ibid.*, **54**, 2973 (1932).

Both compounds were readily resolved and the active compounds were racemized only under vigorous conditions. It is apparent that the relatively large size of the nitro and carboxyl groups in place of a fluorine and methoxyl in the non-resolvable compound containing 2,2′-difluoro-6,6′-dimethoxyl groups or in place of two methoxyls in the non-resolvable compound containing 2,2′,6,6′-tetramethoxyl groups has produced sufficient hindrance to prevent free rotation. The 2-nitro-6-carboxy-2′-fluoro-6′-methoxydiphenyl racemized more readily than the 2,3′-dinitro-6-carboxy-2′,6′-dimethoxydiphenyl, again indicating that the fluorine has less effect than the methoxyl.[1,3]

The general assumption has been accepted that in the stereochemistry of diphenyl each ring of the diphenyl must be unsymmetrically substituted in order to make possible resolution, even though restricted rotation is present in the molecule. The non-resolution of *o*-N-carbazylbenzoic acid but resolution of *o*-N-(3-nitrocarbazyl)-benzoic acid[5] confirmed this assumption in the phenylpyrrole series. In the diphenyl series, however, no compounds have been described in which restricted rotation would occur but in which symmetrical substitution was present, and at the same time salt-forming groups which would make possible attempts at resolution. The 2-nitro-6-carboxy-2′,6′-dimethoxydiphenyl (III) formed as an intermediate in the synthesis of I has such properties. Attempts to resolve it resulted in failure.

Experimental

III was produced by condensation of 2-nitro-1-iodo-3-carbethoxybenzene with 2-iodo-1,3-resorcinol dimethyl ether, then saponification, and I by subsequent nitration of III with concd. nitric acid in acetic acid. II was produced by condensing 2-nitro-1-bromo-3-carbethoxybenzene with 2-fluoro-1-iodo-3-methoxybenzene followed by saponification.

2-Nitro-6-carboxy-2′,6′-dimethoxydiphenyl (III).—A mixture of 56 g. of 2-iodo-1,3-resorcinol dimethyl ether and 38 g. of methyl 3-nitro-2-iodobenzoate was heated with stirring under reflux in a Woods metal bath to 240–250°, and 40 g. of finely divided copper was then slowly added (20 min.) the mixture being stirred during the addition. Fifteen minutes after the last addition of copper, 5 g. more of copper was added, and the heating continued for one-half hour with occasional stirring with a rod. At the end of the heating, the temperature was raised to 300° for five minutes. Then the mixture was allowed to cool slowly. The reaction mixture was boiled with 300 cc. of 95% alcohol and filtered. The residue was placed in a Soxhlet extractor, and was extracted overnight with 95% alcohol. The alcoholic solutions were then combined and evaporated to 100 cc. To this was added 200 cc. of 7% sodium hydroxide and the solution was refluxed for six hours. It was then diluted with 100 cc. of water and filtered, thus removing the alkali-insoluble tetramethoxydiphenyl. The filtrate was acidified with concentrated hydrochloric acid and the dark colored precipitate filtered off, washed several times with water and redissolved in sodium bicarbonate solution. A small amount of material remained undissolved and was filtered off. The bicarbonate solution was acidified and a tan precipitate settled out. After washing and drying it was recrystallized from a

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(5) Patterson and Adams, THIS JOURNAL, **55**, 1069 (1933).

minimum amount of boiling glacial acetic acid to which was added a small amount of norite. Yellow crystals of 2-nitro-6-carboxy-2′,6′-dimethoxydiphenyl were obtained, m. p. 248–249° (uncorr.); yield, 5.4 g. (12%).

Anal. Calcd. for $C_{15}H_{13}O_6N$: C, 59.41; H, 4.29; N, 4.62; N. E., 296. Found: (micro) C, 59.60; H, 4.38; N, 4.61; N. E., 303.

The brucine, cinchonine, strychnine and cinchonidine salts were prepared in absolute alcohol and crystallized from the same solvent. Various fractions of each salt gave the same rotation. None showed mutarotation nor gave an active acid on decomposition.

TABLE I

CONSTANTS AND ANALYSES OF THE SALTS OF 2-NITRO-6-CARBOXY-2′,6′-DIMETHOXYDIPHENYL

	Salt	M. p. (uncorr.), °C.	Wt., g.	α_D 15 cc. of dry $CHCl_3$ $l = 2$	$[\alpha]_D^{20°}$
1	Brucine	119–123	0.025	−0.044	− 13.2
2	Cinchonine	176–179	.025	+ .51	+153
3	Strychnine	126–132	.025	− .10	− 30.0
4	Cinchonidine	195–197	.025	− .23	− 69.0

		Analyses (micro), %					
		Carbon		Hydrogen		Nitrogen	
	Formula	Calcd.	Found	Calcd.	Found	Calcd.	Found
1	$C_{38}H_{39}O_{10}N_3$	65.42	65.32	5.59	5.70	6.02	6.07
2	$C_{34}H_{35}O_7N_3$	68.34	68.30	5.86	6.04	7.03	7.06
3	$C_{36}H_{35}O_8N_3$	67.81	67.12	5.49	6.18	6.59	6.61
4	$C_{34}H_{35}O_7N_3$	68.34	68.29	5.86	5.80	7.03	7.07

2,3′-Dinitro-6-carboxy-2′,6′-dimethoxydiphenyl (I).—To 1 g. of III was added a mixture of 10 cc. of acetic anhydride and 0.2 cc. of nitric acid which was prepared by gently heating fuming nitric acid until colorless. The mixture was heated on a hot-plate until all of the solid dissolved and the liquid became orange colored. The solution was allowed to stand for two hours at room temperature and was then heated to incipient boiling for ten minutes. An equal volume of water was added to destroy the acetic anhydride and the solution was placed under an air jet and evaporated to a volume of 10–12 cc. Yellow needle-like crystals separated out. These were recrystallized from

TABLE II

BRUCINE SALTS AND ACTIVE FORMS OF 2,3′-DINITRO-6-CARBOXY-2′,6′-DIMETHOXYDIPHENYL

		Solvent for purif.	M. p., °C.	Solvent for rot.	α_D^{25} made up to 15 cc. $l = 2$	$[\alpha]_D^{25}$
1	Less sol. hydrated	Abs. alc. with a little acetone	146–152	Chloroform	+0.75	+225°
2	More sol. hydrated	Dil. alc.	142–148	Chloroform	− .756	−226.8°
3	*d*-Acid	Alcohol	174–175	Abs. alc.	+ .413	+123.9°
4	*l*-Acid	Alcohol	175–176	Abs. alc.	− .364	−109.2°

		Analyses, %			
		Carbon		Hydrogen	
	Formula	Calcd.	Found	Calcd.	Found
1	$C_{38}H_{38}O_{12}N_4$ (anhydrous)	61.62	61.59	5.14	5.36
2	$C_{38}H_{35}O_{12}N_4$ (anhydrous)	61.62	61.50	5.14	5.25

hot glacial acetic acid containing norite. White crystals of 2,3′-dinitro-6-carboxy-2′,6′-dimethoxydiphenyl separated, m. p. 192–193° (uncorr.); yield, 0.8 g. (70%).

Anal. Calcd. for $C_{15}H_{12}O_8N_2$: C, 51.73; H, 3.44; N, 8.04. Found: (micro) C, 52.25; H, 3.59; N, 7.99.

The salts were made in absolute alcohol and fractionated apart in the same solvent. The free acids were obtained from the salts by treating at 0° with several portions of 6 *N* hydrochloric acid and allowing to stand for several hours.

Racemization Experiments.—0.050 g. made up to 15 cc. in glacial acetic acid gave α_D 1.235, $l = 2$; $[\alpha]^{20}_D$ +185.5°. After refluxing for eight hours the $[\alpha]^{20}_D$ was +32.4°. In boiling absolute ethyl alcohol no racemization in many hours could be observed; in aqueous sodium hydroxide or alcoholic sodium ethylate, decomposition gradually occurred.

2-Nitro-6-carboxy-2′-fluoro-6′-methoxydiphenyl (II).—A mixture of 20 g. of 1-fluoro-2-iodo-3-methoxybenzene[4] and 45 g. of 1-nitro-2-bromo-3-carbomethoxybenzene was stirred and heated under reflux at 210–240° for three hours during which 75 g. of copper bronze was added in small portions. The pasty mass after cooling was extracted with successive 50-cc. portions of hot 95% ethyl alcohol. The extracted solutions were filtered hot and combined, diluted to double volume with water, made strongly alkaline with 25 g. of sodium hydroxide in 150 cc. of water and heated to boiling for two hours in a flask fitted with a reflux condenser. The esters of dinitrodiphenic acid and fluoromethoxynitrocarboxydiphenyl were hydrolyzed by this treatment and upon further dilution stayed in solution as the sodium salts of the respective acids. The water solution of these salts was decanted from the insoluble difluorodimethoxydiphenyl, boiled with norite, filtered, and acidified with concentrated hydrochloric acid. The precipitated mixture of the monobasic and the dibasic acid was filtered off, partially dried by suction, dissolved in hot glacial acetic acid, filtered and cooled. The dinitrodiphenic acid separated while the monobasic acid remained in solution. This solution was evaporated to a small volume and again allowed to cool in order to remove the last traces of the dinitrodiphenic acid which was filtered off. The filtrate was now slowly diluted with water till no more gum precipitated. After decanting the solution further addition of water and concentrated hydrochloric acid caused the formation of light brown crystals which were purified from 50% ethyl or methyl alcohol, then from ethyl ether by the addition of petroleum ether (large crystals), and finally again from 50% ethyl alcohol; m. p. 173–174° (uncorr.); yield, 0.6 g.

Anal. Calcd. for $C_{14}H_{10}FNO_5$: C, 57.5; H, 3.44; N, 4.81. Found: (micro) C, 57.6; H, 3.69; N, 5.37.

Resolution of 2-Nitro-6-carboxy-2′-fluoro-6′-methoxydiphenyl.—The monobrucine salt was made in alcohol and the two diastereoisomers were obtained by fractionation. Both the less soluble and the more soluble salts were purified by recrystallization from alcohol. The salts were decomposed to the active acids by shaking for one hour with 5 cc. of concentrated hydrochloric acid, a little ice and a few drops of chloroform. The free acids precipitated and were recrystallized from 50% alcohol.

CONSTANTS OF SALTS AND ACIDS

		M. p., °C.	Wt. made up to 15 cc. in $CHCl_3$	$l = 2$ α_D	$[\alpha]^{25}_D$
1	Less sol. brucine salt	215	0.0388	+0.538°	+103.9°
2	More sol. brucine salt	207	.047	− .657°	−104.8
3	*d*-Acid	157	.0146 (alc.)	+ .12	+ 61.6
4	*l*-Acid	157	.0120 (alc.)	− .105	− 65.6

CONSTANTS OF SALTS AND ACIDS (*Concluded*)

	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
1	$C_{14}H_{10}FNO_5 \cdot C_{23}H_{26}N_2O_4$	64.8	65.3	5.2	5.5	6.13	6.06
2	$C_{14}H_{10}FNO_5 \cdot C_{23}H_{26}N_2O_4$	..	..	...	...	6.13	6.60
3	$C_{14}H_{10}FNO_5$	..	..	...	...	4.81	5.16
4	$C_{14}H_{10}FNO_5$	..	..	...	...	..	..

Racemization of *l*-acid. Initial α_D −0.36 in C_2H_5OH—Boiling gave the following α_D readings: fifteen minutes, 0.335; forty-five minutes, 0.25; seventy-five minutes, 0.20; one hundred and thirty-five minutes, 0.17. Calcd. half life period, eighty-six minutes. In boiling glacial acetic acid, rotation was zero in less than twenty minutes. In boiling chloroform, half life period was seventy-two minutes. The acids racemized very slowly in aqueous sodium hydroxide or alcoholic sodium ethylate at room temperature.

Summary

2,3′-Dinitro-6-carboxy-2′,6′-dimethoxydiphenyl and 2-nitro-6-carboxy-2′-fluoro-6′-methoxydiphenyl were prepared and resolved. The active forms of the former racemized less readily than those of the latter, showing the fluorine to have less effect in restricting rotation than the methoxyl.

URBANA, ILLINOIS

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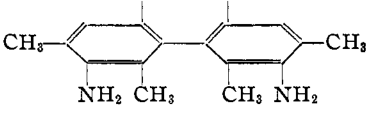
[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY, UNIVERSITY OF WISCONSIN]

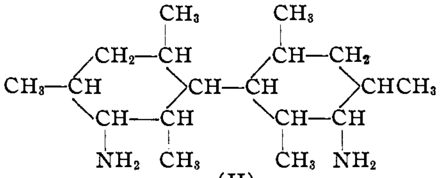
The Hydrogenation of Derivatives of Diphenyl

BY C. R. WALDELAND, WALTER ZARTMAN AND HOMER ADKINS

In connection with the stereochemistry of diphenyl derivatives it would be of interest to ascertain whether or not an optically active dicyclohexyl compound could be obtained by the hydrogenation of an optically active diphenyl compound. For example, if optically active 3,3′-diamino-2,2′,-4,4′,6,6′-hexamethyldicyclohexyl (II) resulted from the hydrogenation of the corresponding *d*- or *l*-diaminodimesityl (I), then the basis for the optical isomerism of compounds of type I is not some "inherent property" of the parent hydrocarbon.[1]



(I)



(II)

It appears that the most feasible way to discover whether derivatives of dicyclohexyl show optical isomerism based upon molecular asymmetry as

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[1] Turner and LeFèvre, *J. Soc. Chem. Ind.*, **45**, 831, 883 (1926); Turner, *Rec. trav. chim.*, **48**, 824 (1929); *cf.* Richter, *Chem. Rev.*, **10**, 368 (1932).