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

STEREOCHEMISTRY OF DIPHENYL COMPOUNDS. VI. PREPARATION AND RESOLUTION OF 2,4,6,2',4'-PENTANITRO-3-CARBOXYDIPHENYL[1]

BY H. A. STEARNS[2] AND ROGER ADAMS

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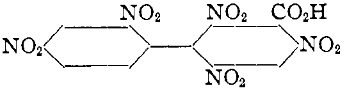
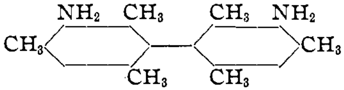
Only two 2,2',6-trisubstituted derivatives of diphenyl have as yet been prepared and resolved. Both of these compounds were readily racemized in alkaline solution. Pertinent information concerning the phenomenon of optical activity in the diphenyl series should be obtained more readily by a study of 2,2',6-trisubstituted compounds than from the 2,2',6,6'-tetrasubstituted compounds.

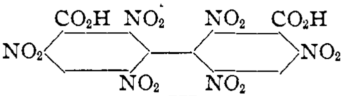
In this communication is given the description of 2,4,6,2',4'-pentanitro-3-carboxydiphenyl (I), the first trisubstituted derivative prepared with the 2,2',6-positions filled with the same groups and with each of the rings unsymmetrical in itself. As might be anticipated after the preparation and resolution of 2,2',6,6'-tetramethyl-3,3'-diaminodiphenyl (II) and 2,4,6,2',4',6'-hexanitro-3,3'-dicarboxydiphenyl (III), this trisubstituted compound was readily resolved. Further evidence is thus submitted that the mechanical interference of the groups is preventing free rotation of the rings.



I



II



III

The active forms of 2,4,6,2',4'-pentanitro-3-carboxydiphenyl are stable to racemization. Eight hours of boiling in ammonium carbonate solution or six hours of boiling in glacial acetic acid, or several days' standing in cold sodium carbonate solution failed to change the rotation, and eight hours of boiling in 95% acetic acid saturated with hydrogen chloride failed to change the rotation more than slightly. Hot sodium carbonate solution caused a deep reddening of the solution so that possible racemization could not be determined.

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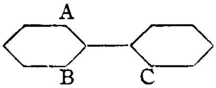
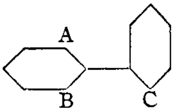
[1] For previous papers in this field see (a) Hyde and Adams, THIS JOURNAL, **50**, 2499 (1928); (b) Moyer and Adams, *ibid.*, **51**, 630 (1929); (c) Stanley and Adams, *Rec. trav. chim.*, **48**, 1035 (1929); (d) This JOURNAL, **52**, 1200 (1930); (e) Bock, Moyer and Adams, *ibid.*, **52**, 2054 (1930).

[2] This communication is a portion of an abstract of a thesis submitted by H. A. Stearns in partial fulfilment of the requirement for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

The probable effects within these trisubstituted molecules should be considered. If it is assumed that the two rings remain symmetrically placed toward each other when they arrive in or approach the same plane, then all that should be required for a substance to be capable of resolution is to have in the general formula (IV), group C large enough to interfere materially with B and with A.



IV



V

If the interference at either or both points is small, the compound should racemize more or less readily. If, however, the two rings may be assumed to bend toward each other when the same plane for both rings is approached closely (in the manner represented in V), it is conceivable that non-resolution of certain compounds which should otherwise be capable of resolution might be expected. Though during the process of resolution much distortion of this kind seems unlikely, it might well occur under the conditions used in racemization experiments and consequently racemization of certain compounds might readily take place.

A 2,2′,6-trinitro compound from this standpoint would give the following results. Using the values[1d] $C–NO_2$, 1.92 Å; C–H, 0.92 Å.; C–C (2,2′), 2.90 Å, the interference of two nitro groups will be as follows: $1.92 \text{ Å.} + 1.92 \text{ Å.} = 3.84 \text{ Å.} - 2.90 \text{ Å.} \longrightarrow +0.94 \text{ Å.}$, a large difference compared to what was found necessary for interference in the tetrasubstituted compounds. At the same time on the other side of the molecule the nitro and the hydrogen would not collide at all; $1.92 \text{ Å.} + 0.92 \text{ Å.} = 2.84 \text{ Å.} - 2.90 \text{ Å.} \longrightarrow -0.06 \text{ Å.}$ If the molecules were distorted so that the nitro and the hydrogen pulled toward each other more than 0.06 Å., collisions would occur on both sides of the molecule simultaneously, without reducing to any great extent the interference between the two nitro groups. In such a molecule racemization would not be expected and does not occur.

On the other hand, such a compound as 2,6-diamino-2′-methyldiphenyl presents other possibilities. Using the values, $C–NH_2$, 1.56 Å.; $C–CH_3$, 1.73 Å.; C–H, 0.92 Å., on the side of the molecule holding the amino and methyl groups the interference would be as follows: $1.73 \text{ Å.} + 1.56 \text{ Å.} = 3.29 \text{ Å.} - 2.90 \text{ Å.} \longrightarrow +0.39 \text{ Å.}$ On the other side of the molecule $1.56 \text{ Å.} + 0.92 \text{ Å.} = 2.48 \text{ Å.} - 2.90 \text{ Å.} \longrightarrow -0.42 \text{ Å.}$ Upon the assumption of a symmetrical position for the two rings at all times, resolution of the compound should take place readily and the active compounds should not racemize at all or at least not readily. On the other hand, if the amino and the hydrogen are pulled toward each other to the extent of 0.39 Å., then the groups could pass by each other without collisions on either side of the molecule. Although it is improbable that such a distorted position would exist so as to prevent resolution, it is likely that under certain conditions it might be approached to an extent which would allow easy racemization of the active compounds. The extent to which the possible distortion might occur in various molecules will, of course, depend upon the character of the groups present. It is of little value to speculate further with the x-ray data until more facts are available.

In connection with the assumptions just made, it is necessary to consider the 2,4′-dinitro-6,6′-dicarboxydiphenyl[3] and the 2,4,4′-trinitro-6,6′-dicarboxydiphenyl,[4] both of which have two carboxyls and one nitro group in the critical positions. Using the values given previously and in addition C–COOH, 1.56 Å., the side with two carboxyls would give the following results: 1.56 Å. + 1.56 Å. = 3.12 Å. − 2.90 Å. ⟶ +0.22 Å. On the other side, 1.92 Å. + 0.92 Å. = 2.84 Å. − 2.90 Å. ⟶ −0.06 Å. It is obvious, then, that not much distortion would be necessary in such a molecule to reduce the interference to the point where racemization would take place. These substances do racemize slowly by heating at 100° with sulfuric acid. On the other hand, if the size of the carboxyl groups is decreased, as happens when ionized, racemization should be comparatively rapid. Results have shown these compounds to racemize readily in alkaline solution.

The 2,4,6,2′,4′-pentanitro-3-carboxydiphenyl was prepared by condensing, under carefully specified conditions, 2,4,6-trinitro-3-bromotoluene and 2,4-dinitrochlorobenzene by means of copper. The resulting compound, 2,4,6,2′,4′-pentanitro-3-methyldiphenyl was oxidized with a mixture of fuming nitric acid, fuming sulfuric acid and sodium dichromate to the corresponding carboxylic acid. This latter compound was resolved readily through the strychnine salt.

Experimental

2,4,6,2′,4′-Pentanitro-3-methyldiphenyl.—In a 1-liter flask equipped with a mechanical stirrer were placed 133 g. of 2,4-dinitrochlorobenzene, 100 g. of 2,4,6-trinitro-3-bromotoluene,[5] 240 cc. of nitrobenzene and 3 g. of copper bronze. The mixture was stirred and heated on an oil-bath until the contents of the flask had reached a temperature of 160°, at which temperature brown copper halides began to form. The oil-bath was then removed, and 230 g. of copper bronze was added at such a rate that the reaction mixture remained at a temperature of 160–165° during the addition. Exterior heating was then continued so that the mixture remained within this temperature range for a total period of one hour.

The hot reaction mixture was filtered, the copper residues extracted with acetone and the extract added to the filtrate. Acetone and nitrobenzene were then removed from the products by means of a steam distillation. The product was next washed with

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[3] Christie and Kenner, *J. Chem. Soc.*, **121**, 614 (1922); 470, 671 (1926).

[4] Kuhn and Albrecht, *Ann.*, **455**, 272 (1927); **458**, 221 (1927).

[5] Bentley and Warren, *Am. Chem. J.*, **12**, 4 (1890).

alcohol to remove traces of nitrobenzene, dissolved in acetone and this solution refluxed with norite for one-half hour. After filtration, the acetone was evaporated off and the residue washed twice with alcohol, then recrystallized from glacial acetic acid until a melting point of 200–201° was reached. Finally, the product was dissolved in a minimum of boiling acetone, and thrown out of solution as a fine, white, granular powder by the addition of a large excess of alcohol; melting point, 200–201°. The yield was about 52 g. (40%).

Anal. Calcd. for $C_{13}H_7O_{10}N_5$: C, 39.69; H, 1.80. Found: C, 39.74; H, 2.08.

2,4,6,2′,4′-Pentanitro-3-carboxydiphenyl.—In a 1-liter flask provided with a mechanical stirrer and cooled by means of a salt–ice-bath was placed 20 g. of pure 2,4,6,2′,4′-pentanitro-3-methyldiphenyl dissolved in 220 cc. of fuming nitric acid[6] (sp. gr. 1.52). Eighty cubic centimeters of fuming sulfuric acid (20%) was added to the stirred mixture at such a rate that the temperature did not rise above 20° during the addition. To the stirred and cooled solution, 40.4 g. of powdered potassium dichromate was added at such a rate that the temperature of the solution did not rise above 10° during the addition (about three-quarters of an hour). Stirring was continued for twenty-four hours, and the bath was permitted to rise slowly to room temperature during this period. The reaction mixture was then poured into a large excess of ice and the free acid obtained by filtration. The acid was purified by recrystallization from benzene and formed a fine, white, crystalline powder of m. p. 205–206°. The yield was 7 g. (32.5%).

The yield from this reaction varied from 30 to 50% for successive runs, apparently because of a difference in purity of the crude acid obtained. The crude acid varies considerably in purity depending upon conditions which have not been defined. If, upon one crystallization from benzene, the melting point of the crude acid rises, further recrystallization will readily purify it; on the other hand, if the melting point lowers or if, for any other reason, the acid acts peculiarly, it is advisable to purify through the pyridine salt. This was precipitated from a saturated alcoholic solution of the acid by the slow addition of its chemical equivalent of pyridine. The salt was extracted twice with small amounts of boiling benzene, then dissolved in a minimum of acetone, and the free acid obtained by the addition of excess concentrated hydrochloric acid to this solution. The acetone solution was cooled and stirred during the hydrochloric acid addition, and the acid so obtained was recrystallized from benzene.

Anal. Calcd. for $C_{13}H_5O_{12}N_5$: C, 36.88; H, 1.19; N, 16.55. Found: C, 36.98; H, 1.83; N, 16.88.

Resolution of **2,4,6,2′,4′-Pentanitro-3-carboxydiphenyl.**—To a solution of 10.2 g. of 2,4,6,2′,4′-pentanitro-3-carboxydiphenyl in 700 cc. of methyl alcohol was added slowly and with stirring 800 cc. of a solution of 8.08 g. of strychnine in 2 liters of methyl alcohol. The solution was cooled to 0° and allowed to stand for one hour. A crop (7.5 g.) of pale yellow, needle-like crystals (A) was obtained. To the mother liquor from (A) was added an additional 300-cc. portion of the strychnine–methyl alcohol solution. The resulting mixture was evaporated to about 700 cc. under diminished pressure and a second crop (3 g.) of yellow crystals (B) was filtered off. To the mother liquor from (B) was added the remainder of the strychnine solution. This mixture was evaporated to a volume of about 300 cc., cooled overnight at 0°, and a third crop (7.8 g.) of orange-colored, granular crystals (C) obtained.

Crystals (A) were purified by dissolving them in a minimum of warm acetone and adding to this stirred solution petroleum ether until the solution was slightly opaque. Upon standing overnight at 0°, the salt separated as fine, pale yellow needles. The

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[6] A good grade of fuming nitric acid is important. Inferior grades give much poorer results.

purified salt turns red at 265° and melts with decomposition at some point between 270 and 280°. Two successive recrystallizations of salt (A) sufficed to bring the salt to a constant rotation.

Rotation. 0.1373 g. of salt made up to 15 cc. with pyridine at 20° gave α_D −1.13°; $l = 1$, $[\alpha]^{20}_D$ −123.5°.

Anal. Calcd. for $C_{34}H_{27}O_{14}N_7$: C, 53.88; H, 3.59. Found: C, 53.75; H, 4.06.

Strychnine salt (C) was purified by dissolving it in boiling alcohol, evaporating this solution down to such a volume that crystals started to appear in the hot solution, then allowing the solution to stand at 0° overnight. Crystals of (C) were obtained as a light orange colored powder. This material turns red at 203–205° and apparently melts at 222–226°. Two successive recrystallizations brought the rotation to a constant value.

Rotation. 0.1319 g. made up to 15 cc. in pyridine at 20° gave α_D +0.74°, $l = 1$, $[\alpha]^{20}_D$ +84.4°.

Anal. Calcd. for $C_{34}H_{27}O_{14}N_7$: C, 53.88; H, 3.59. Found: C, 53.52; H, 4.35.

***l*-2,4,6,2′,4′-Pentanitro-3-carboxydiphenyl.**—To 2.19 g. of the pure strychnine salt (A) was added 20 cc. of acetone. Solution was not complete. The beaker was cooled with an ice-bath, and 50 cc. of concentrated hydrochloric acid added with stirring, at such a rate that the temperature of the mixture was always kept below 20°. The cooled mixture was permitted to stand for fifteen minutes so as to assure complete crystallization of the free acid, then filtered. The acid was completely redissolved in 10 cc. of acetone and again thrown out of solution by the addition of 50 cc. of concentrated hydrochloric acid in the manner just described. The acid was dried *in vacuo* at room temperature and then purified further by recrystallizing twice from benzene to a constant rotation and melting point. The pure acid was obtained as white, granular crystals of melting point 233°. The yield was 0.87 g. (71.3%).

Rotation. 0.1165 g. of acid made up to 15 cc. in acetone at 20° gave α_D −0.82°, $l = 1$, $[\alpha]^{20}_D$ −105.3°.

***d*-2,4,6,2′,4′-Pentanitro-3-carboxydiphenyl.**—To 1.19 g. of the strychnine salt (C) dissolved in 5 cc. of acetone and cooled with an ice-bath, slowly and with stirring was added 50 cc. of concentrated hydrochloric acid. The cooled mixture was permitted to stand for one-half hour so as to assure complete crystallization of the liberated acid, then filtered. The acid was redissolved in 9 cc. of acetone and reprecipitated by the addition of another 50-cc. portion of concentrated hydrochloric acid in the manner just described. It was recrystallized twice from benzene and formed a white, granular powder of melting point 229–231°. It gave a negative strychnine test when dissolved in sulfuric acid and treated with manganese dioxide. The yield of recrystallized acid was 0.4 g.

Rotation. 0.1116 g. of acid made up to 15 cc. in acetone at 20° gave α_D +0.73, $l = 1$, $[\alpha]^{20}_D$ +98.8°.

Racemization Experiments

(a) A 0.1357-g. sample of *d*-2,4,6,2′,4′-pentanitro-3-carboxydiphenyl was made up to 25 cc. in glacial acetic acid at 20° and the following rotation found for the solution: α_D +0.53, $l = 1$, $[\alpha]^{20}_D$ +98.3°. The entire solution was transferred to a 50-cc. flask equipped with a glass-fitted reflux condenser and refluxed for one and one-half hours. The solution was then evaporated to a volume of about 10 cc., transferred to a volumetric flask, and its volume again made up to 25 cc. with glacial acetic acid at 20°. The rotation of the solution was then α_D +0.53°; $l = 1$, $[\alpha]^{20}_D$ +98.3°. The solution was refluxed for an additional two and one-half hours and its rotation again taken: α_D +0.52°, $l = 1$, $[\alpha]^{20}_D$ +95.8°.

(b) A 0.1268-g. sample of *l*-2,4,6,2′,4′-pentanitro-3-carboxydiphenyl, $[\alpha]^{20}_D$ −105.3° in acetone, was refluxed with 20 cc. of 5% ammonium carbonate solution for a period of eight hours. The solution was then cooled with an ice-bath and 30 cc. of concentrated hydrochloric acid added slowly and with stirring. The precipitated acid was filtered from this mixture, dried *in vacuo* at room temperature, and its rotation taken as follows: 0.1073 g. of acid made up to 15 cc. in acetone at 20° gave α_D $-0.76°$, $l = 1$, $[\alpha]^{20}_D$ $-105.8°$.

(c) A 0.1236-g. sample of the *l*-acid, $[\alpha]^{20}_D$ $-105.3°$ in acetone, was dissolved in 20 cc. of a solution that had been prepared by saturating an acetic acid solution, which contained 5% of water, with hydrogen chloride. The resulting solution was refluxed for eight hours, then cooled in an ice-bath and 50 cc. of concentrated hydrochloric acid added. After permitting the cooled mixture to stand for one-half hour, the precipitated acid was filtered from it, dried *in vacuo* at room temperature, and its rotation taken as follows: 0.0967 g. of acid made up to 15 cc. in acetone at 20° gave α_D $-0.54°$, $l = 1$, $[\alpha]^{20}_D$ $-83.4°$.

(d) A 0.1535-g. sample of the *l*-acid was made up to 15 cc. in a 5% sodium carbonate solution at 20° and its rotation taken: α_D $-2.13°$, $l = 1$, $[\alpha]^{20}_D$ $-208.0°$. This pale yellow solution was permitted to stand in a sealed tube at room temperature for seven days, during which period it developed an amber color. Its rotation was then taken and found to be: α_D $-2.11°$, $l = 1$, $[\alpha]^{20}_D$ $-206.3°$.

An attempt was made to heat the solution in a sealed tube to a temperature of 50–60°, but after eight hours of this treatment the solution had developed such a deep red color that its rotation could not be taken.

Summary

1. The compound 2,4,6,2′,4′-pentanitro-3-carboxydiphenyl has been prepared and resolved. This is the first diphenyl derivative with three of the same groups in the 2,2′,6-positions which has been resolved.

2. The active forms could not be racemized in acid, neutral or alkaline solution.

3. Discussion is given of what properties may be anticipated of various 2,2′,6-trisubstituted diphenyls.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT AT OHIO STATE UNIVERSITY]

NATURAL AND SYNTHETIC RUBBER. IV. 4-METHYL-4-OCTENE BY ISOPRENE ETHYLATION

BY THOMAS MIDGLEY, JR., AND ALBERT L. HENNE

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In preceding papers[1] it has been shown that when isoprene accepts hydrogen, or when two molecules of isoprene link together, the reaction affects only the 1- and 4-positions. This behavior has been regarded as a general property, and it has been used to explain the polymerization of isoprene to synthetic rubber.

The present paper offers one more evidence of the 1,4-addition. Two ethyl groups have been attached to an isoprene molecule

$$H_2C{=}C(CH_3)CH{=}CH_2 + 2C_2H_5Br \xrightarrow{Na} CH_3CH_2CH_2C(CH_3){=}CHCH_2CH_2CH_3$$

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[1] Midgley and Henne, THIS JOURNAL, **51**, 1215, 1293, 1294 (1929).