Cobaltous hexapyridine cyanate yields a blue solution in chloroform which turns lilac-colored or pink if the temperature is lowered or if pyridine is added. By adjusting the amount of excess pyridine in such a solution, a liquid may be secured which changes color with very moderate changes of temperature.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF ILLINOIS]

STUDY OF THE POSSIBLE ISOMERISM OF CERTAIN ANALOGS OF RESOLVABLE DIPHENYL COMPOUNDS[1]

BY J. F. HYDE AND ROGER ADAMS

RECEIVED JUNE 18, 1928 PUBLISHED SEPTEMBER 5, 1928

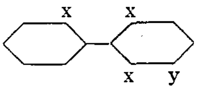
A configuration in which the two aromatic nuclei are coaxial and not in the same plane apparently accounts for all of the known facts concerning the optical activity in certain diphenyl compounds. It is generally accepted that the asymmetry arises from the influence which the groups located in the ortho position to the connecting bond have in preventing free rotation of the two nuclei. The exact nature of the interference to free rotation remains still to be determined.

Mills[2] considers it to be entirely mechanical in nature. The groups are unable to get by each other due to their size and proximity in space. Meisenheimer[3] has offered additional evidence to favor mechanical interference and has pointed out that spacings of the groups from the nucleus as well as between the two rings must be considered.

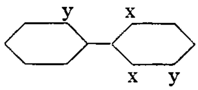
Turner and Le Fèvre[4] consider the problem from the point of view of residual affinity on each ring and the influence of the electrical nature of the ortho substituted groups.

It seems reasonably certain that the isomerism is not due to the specific effect of any particular group on the nuclei.[5]

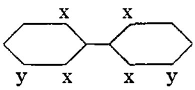
Diphenyl derivatives of the general types Ia, Ib, Ic, in which the ortho



Ia



Ib



Ic

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[1] This communication is a portion of a thesis submitted by J. F. Hyde in partial fulfilment of the requirements for the Degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[2] Mills, *Chemistry Industry*, **45**, 883, 905 (1926).

[3] Meisenheimer and Höring, *Ber.*, **60**, 1425 (1927).

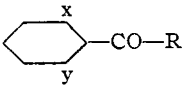
[4] Turner and Le Fèvre, *Chemistry Industry*, **45**, 831 (1926).

[5] Christie and Kenner, *J. Chem. Soc.*, **121**, 614 (1922); *ibid.*, **123**, 779 (1923); Christie, James and Kenner, *ibid.*, **123**, 1948 (1923); Christie, Holderness and Kenner, *ibid.*, **129**, 671 (1926); Bell and Kenyon, *Chemistry Industry*, **45**, 864 (1926); Turner and Le Fèvre, *ibid.*, **46**, 218 (1927).

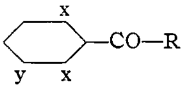
substituting groups may be the same and in which the individual rings are asymmetric should be capable of resolution. The free rotation is prevented in these cases by groups in the ortho positions which are identical. The asymmetry is introduced by the same or different groups in another part of the molecule. If the restricted rotation is due simply to mechanical interference, these substances should be resolvable. If, on the other hand, the influence is entirely electrical, the two rings might assume a coplanar position resulting in a compound that is non-resolvable. While the resolution of such a compound might not make the cause of steric hindrance clearer, it would certainly establish the present mechanical theory more firmly.

This investigation had as one of its objects the preparation and resolution of an individual compound falling in one of the types mentioned. Although this part of the work is not completed, the publication of Mascarelli[6] setting forth in detail the views just given, though without any experimental evidence, has made it advisable to publish the completed results on closely related compounds.

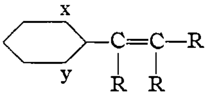
If the prevention of free rotation is entirely a matter of the space occupied by interfering groups and does not require a direct association of two aromatic rings, then it should be possible to resolve still other types of compounds which could become asymmetric due to steric hindrance. Such types are represented by the general formulas IIa, IIb, IIIa, IIIb, where **R** stands for groups of the proper size.



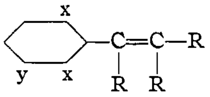
IIa



IIb



IIIa



IIIb

In such compounds as IIa, IIb, IIIa and IIIb, any effect due to the direct joining of two rings to each other is eliminated. The carbon–carbon double bond and possibly the carbon–oxygen double bond adjacent to the ring should have more or less of a directive influence on the valencies of that carbon as is the case with a rigid ring structure. The molecules would undoubtedly be less rigid, but if the free rotation around the bond joining the unsaturated linkage to the substituted ring is prevented, any position of the olefin or carbonyl group and the unsubstituted ring in space should give an asymmetric molecule. The possibility of this occurring in the case of the carbonyl compounds as in types IIa and IIb seems much less probable than in the olefins IIIa and IIIb. If the carbonyl group itself will not interfere with free rotation, it is possible that the R groups in the molecules, if large enough, might cause interference.

Although the syntheses of representatives of types I, II and III are

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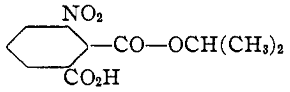
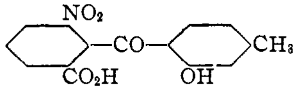
[6] Mascarelli, *Atti. accad. Lincei,* [6] **6,** 60 (1927).

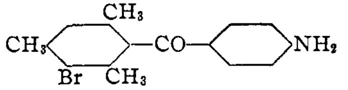
under way, in this paper merely compounds falling into group II will be described and discussed. The following four compounds were prepared



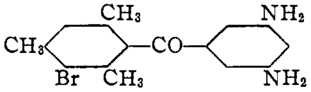
IV



V



VI



VII

The one numbered IV was made directly by the action of *iso*propyl alcohol on 3-nitrophthalic anhydride, the one numbered V by the condensation of nitrophthalic anhydride with *m*-cresol, and those numbered VI and VII by the condensation of nitro- and dinitro-benzoyl chloride with bromomesitylene followed by subsequent reduction. The resolution of IV and V was attempted with brucine and of VI and VII with camphorsulfonic acid.

In carrying out the fractional crystallization of the salts there was no definite separation, nor did the relative size of the fractions give any indication of salts of different solubilities. In order to prove the possibility of the existence of optical isomerism, it was considered essential to isolate a sample of the material which should show at least momentary rotatory power and be entirely free from optically active reagent. In no case were optically active compounds obtained by decomposition of the salts.

It was shown that the carbonyl group in such ketones as VI was very unreactive, as indicated by failure of all attempts to reduce it or to cause it to react with the Grignard reagent. The carbonyl group is, therefore, protected from influences outside of the molecule and it must be that the volume of the carbonyl group is not sufficient to interfere (on rotation) with the ortho groups of the substituted ring. Moreover, the *o*-hydroxy substituted phenyl group apparently has no effect.

Certain anomalies appeared in the rotation of the salts. The brucine salt of 2-(2-hydroxy-4-methylbenzoyl)-3-nitrobenzoic acid, V, has an α_D $+18.3°$, while under the same conditions brucine has an α_D $-119°$. Kuhn and Albrecht[7] noticed a similar phenomenon in the case of the quinine salt of 4,4'-dinitrodiphenic acid, which had an α_D $+110°$, whereas in the same solvent quinine had an α_D $-117°$. No active acids, however, were isolated. They also observed that the quinine salts of *m*-nitrobenzoic acid and of phthalic acid have, under the same conditions, a rotation similar to that of quinine. A possible explanation for such abnormal rotations in the salts would be the assumption that a complete transformation to one form of two possible diastereoisomers had occurred

[7] Kuhn and Albrecht, *Ann.*, **455**, 272 (1926).

upon the addition of the optically active reagent. Haworth[8] in reviewing the work of Kuhn on diphenyl compounds, has accepted this observation of abnormal rotation as conclusive evidence of the existence of labile optical isomers in diphenyl compounds with only one ortho substituting group in each ring. He suggests that this behavior serves to distinguish these compounds from those diphenyl derivatives with three ortho substituting groups of proper size and character which make possible the isolation of the two diastereoisomeric salts and the two enantiomorphic diphenyl compounds. These conclusions of Haworth cannot be considered of more than passing interest as they are based on far too few facts. He has made no mention of the extensive work of Hilditch,[9] who has studied a large variety of salts of various alkaloids and has observed just such anomalous effects as have appeared in this investigation and in the investigation of Kuhn and Albrecht. Hilditch has shown that if there are conjugated systems in proximity to the optically active part of the molecule, the rotatory power is markedly influenced. He has also observed that the nature of the groups, particularly in the ortho position to the one combined to the active reagent, may induce anomalous rotations. These latter types are quite similar in character to the diphenyl compounds studied by Kuhn and to the substances described in this research, though the anomalies could hardly be attributed to the same cause as that assigned by Haworth to 4,4′-dinitrodiphenic acid and its salt.

The camphorsulfonic acid salts of amino and diamino-benzoylbromomesitylene led to negative results as far as optically active amines were concerned. The salts, however, showed a curious behavior. In certain solvents the substances changed in rotation upon standing. At first this was assumed to be a gradual change of one salt to the diastereoisomer. However, it is significant that this was observed only in chloroform. The camphorsulfonate of aminobenzoylbromomesitylene had an α_D +13.8° at first and an α_D +7.6° after several hours' standing. Upon evaporation of the solution after determining the second rotation, the solid salt was obtained. If this was redissolved in chloroform, however, the original rotation was again observed, and only after standing did it diminish. Apparently other salts of camphorsulfonic acid show this same phenomenon. The aniline salt was studied and showed an even greater variation in rotation on standing in chloroform solution. It appears to be due to a change in the character of the molecule either by tautomerism or by combination with a solvent.[10] Whatever the change may be, it does not appear to be a permanent one and is not characteristic of the base used.

The synthesis of compounds of the type I has been attempted by diazo-

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[8] Haworth, "Annual Reports," Gurney and Jackson, London, **24**, 101 (1928).

[9] Hilditch, *J. Chem. Soc.*, **93**, 1388 (1908); **95**, 335, 1570 (1909); **99**, 224 (1911).

[10] Pope and Read, *ibid.*, **105**, 800 (1914).

tizing methyl anthranilate and other analogous amines and coupling with bromomesitylene in order to produce diphenyl derivatives. Amino bromomesitylene has also been diazotized, and attempts to couple it with various benzene derivatives in order to produce the proper diphenyl compound have all resulted as yet in failure. Now, however, it seems possible to get a diphenyl compound of the type desired through dimesityl.

Experimental Part

Benzoylbromomesitylene.—A mixture of 0.33 mole of bromomesitylene and 0.3 mole of benzoyl chloride was dropped very slowly into a reaction flask containing 0.47 mole of aluminum chloride and 260 g. of carbon disulfide. This took about an hour and the stirring was continued for about two hours longer. Finally, part of the carbon disulfide was distilled off, using a water-bath. The reaction mixture was then decomposed by pouring into ice water containing some hydrochloric acid. The product distilled as a light yellow, viscous oil at 173–175° at 1 to 2 mm., which was practically colorless on redistillation. The yield was 91 g. (92%). This viscous liquid on stirring and allowing to stand for several hours solidified to a white, granular, crystalline mass with a melting point of 48–49°. No attempt was made to recrystallize the compound.

Anal. (Parr Bomb). Subs., 0.2101: 7.05 cc. of 0.1005 N $AgNO_3$. Calcd. for $C_{16}H_{15}OBr$: 26.40. Found: 26.76.

An attempt was made to condense benzoylbromomesitylene with ethyl bromoacetate in the presence of zinc. After several trials it was found that no reaction had taken place and merely the original product was obtained. Phenylmagnesium bromide also would not react with this compound.

An attempt to oxidize the benzoylbromomesitylene to the benzoylbromodimethylbenzoic acid resulted in the formation of a neutral, viscous liquid. The reaction was accompanied by the evolution of carbon dioxide.

A Clemmensen reduction to the corresponding hydrocarbon gave negative results.

***p*-Nitrobenzoylbromomesitylene.**—This was prepared in exactly the same way as that described for benzoylbromomesitylene except that the bromomesitylene had to be heated in order to make the acid chloride dissolve in it and it was necessary to continue the heating during the reaction (about four hours) to prevent crystallization. Upon decomposing, some chloroform was added so that the solvent was a mixture of carbon disulfide and chloroform. The resulting ketone, after removing the carbon disulfide and chloroform, was crystallized by dissolving in acetone, filtering and adding twice the volume of ethyl alcohol to the hot solution. After recrystallizing once more from the same combination of solvents, the product consisted of light yellow plates, melting at 154–155°. The yield was 29.5 g. (85%).

Anal. (Parr Bomb). Subs., 0.2269: 6.44 cc. of 0.1005 N $AgNO_3$. Calcd. for $C_{16}H_{14}O_3NBr$: 22.98. Found: 22.86.

3,5-Dinitrobenzoylbromomesitylene.—This was prepared in an analogous way to the mononitro. Very poor results were obtained unless the reaction mixture was warmed somewhat and stirred for at least four or five hours. The product was not distilled but merely crystallized from acetone. It formed light yellow plates melting at 160–161.5°. The yield was 9.5 g. (24%).

Anal. Subs., 0.2366: 11.74 cc. of 0.0502 N $AgNO_3$. Calcd. for $C_{16}H_{13}O_5N_2Br$: 20.35. Found: 20.09.

***p*-Aminobenzoylbromomesitylene.**—A suspension of 21 g. of nitrobenzoylbromomesitylene in 50 cc. of alcohol was reduced with 0.1 g. of platinum-oxide platinum black[11] and hydrogen. When the theoretical amount of hydrogen was absorbed, the catalyst was filtered and the solvent evaporated. The product was purified by dissolving in carbon disulfide and by adding gradually an equal amount of benzene. It crystallized in fine, white needles; melting point, 138°.

Anal. Subs., 0.1735: 10.66 cc. of 0.0502 *N* $AgNO_3$. Calcd. for $C_{16}H_{16}ONBr$: 25.15. Found: 24.67.

p-Aminobenzoylbromomesitylene Hydrochloride.—This was prepared by dissolving the free base in ethyl acetate and treating with hydrogen chloride. The hydrochloride crystallized out rather slowly in white, needle-like crystals and was recrystallized from the same solvent.

Anal. Subs., 0.1291: 3.66 cc. of 0.1005 *N* $AgNO_3$. Calcd. for $C_{16}H_{17}ONBrCl$: 10.01. Found: 10.12.

If, instead of using ethyl alcohol as a solvent, ethyl acetate was used, and 0.05 g. of catalyst for 14.4 g. of nitro compound, the reduction did not go readily to completion and a light red azo compound was found contaminating the amine. The former was removed by ethyl alcohol, in which it was insoluble. It melted at 203–205°.

Anal. Subs., 0.1295: 8.06 cc. of 0.0502 *N* $AgNO_3$. Calcd. for $C_{16}H_{14}ONBr$: 25.31. Found: 25.02.

3,5-Diaminobenzoylbromomesitylene.—This was reduced in a manner similar to the mono-amino compound and formed yellowish-brown crystals from alcohol, melting at 168–169°, which turned dark brown upon standing for a short time.

Anal. Subs., 0.1301: 7.92 cc. of 0.0502 *N* $AgNO_3$. Calcd. for $C_{16}H_{17}ON_2Br$: 24.02. Found: 24.44.

p-Aminobenzoylbromomesitylene d-Camphorsulfonate.—The *d*-camphorsulfonic acid used melted from 190–191° and gave α_D +21.08° in water. The salt was readily produced by dissolving 5 g. of the amino ketone in 30 cc. of ethyl acetate and adding this hot solution to a solution of 3.48 g. of *d*-camphorsulfonic acid in 30 cc. of ethyl acetate. After standing for half an hour, 7 g. of the possible 8.5 g. of salt crystallized in white, flat plates, melting at 175–200° with decomposition. The rotations were determined in a Schmidt-Haensch saccharimeter, using a 2-decimeter tube. The weighed sample was in each case dissolved in 20 cc. of the desired solvent at 20°. This salt gave a value α_D +13.7° (15 minutes) in chloroform, which, on standing for several hours, gradually became smaller and smaller until a constant value of +7.1° (38 to 40 hours) resulted. The fraction from the mother liquors gave essentially the same initial rotation and only a slightly higher final rotation. A rather large sample of this salt was fractionally crystallized. After three times the rotation was determined. The specific rotations on three fractions were, respectively, +12.7°, +12.8° and +11.4°, using acetone as a solvent. Two of these fractions in chloroform gave rotations of approximately +14° which, on standing, dropped to approximately +7°. Upon removing the chloroform from a solution which had given the low rotation, a product was obtained which, on redissolving in chloroform, gave a rotation of over 14°, which again gradually fell off upon standing.

Anal. Subs., 0.1938: 7.01 cc. of 0.0502 *N* $AgNO_3$. Calcd. for $C_{16}H_{16}ONBr\text{-}C_{10}H_{16}SO_4$: 14.54. Found: 14.53.

3,5-Diaminobenzoylbromomesitylene d-Camphorsulfonate.—This was prepared from equimolecular quantities of the acid and the amine in acetone solution. The

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[11] Adams, Shriner and Voorhees, "Organic Syntheses," John Wiley and Sons, Inc., New York, **8**, 92–99 (1928).

precipitated salt was in the form of fine, white needles, melting at 216–218°. It was fractionated five times and the rotations of the individual fractions were taken in methyl alcohol, using a 2-decimeter tube and making the solution up to 20 cc. at 20°. The rotation was +21.2° for the first fraction, +20.2° for the second, +16.4° for the third, +15.0° for the fourth and +18.2° for the fifth. Upon standing these solutions became colored and fluorescent and further readings were impossible. It was noticed, however, that the readings gradually fell off irregularly, somewhat as in the case of the monoamino compound. In this case decomposition of some sort obviously was taking place.

Anal. Subs., 0.1943: 4.75 cc. of 0.0502 *N* $AgNO_3$. Calcd. for $C_{16}H_{17}ON_2Br_2\cdot 2C_{10}H_{16}SO_4$: 10.03. Found: 9.82.

The carefully fractionated salts of the mono- and diaminobenzoylbromomesitylenes were decomposed with ammonia by adding concentrated ammonia water to a methyl alcoholic solution of the salt. Further dilution with water precipitated the free organic base. The free bases obtained from these salts with acid melted exactly as they had before forming the salt and showed no detectable rotation.

Brucine Salt of 2-Carbo-*iso*propoxy-3-nitrobenzoic Acid.—The free acid prepared by the method of Nicolet and Sacks[12] was converted to the brucine salt by mixing its ethyl acetate solution with a similar solution of brucine. The brucine used melted at 174–176°, and had an α_D −119.0°. The salt formed bright yellow needles melting indefinitely from 90–95° with decomposition. After five careful fractional crystallizations from acetone, the rotations of the fractions were taken in chloroform. A 2-decimeter tube was used and the solutions were made up to 20 cc. at 20°. The α_D of the five fractions were, respectively, −19.0°, −19.4°, −19.9°, −18.8° and −21.3°. No changes in rotations were observed on standing. Upon treating the chloroform solution of the crystallized salt with dry ammonia and then dissolving the precipitated ammonium salt in water and acidifying, the *iso*propylnitrophthalic acid was recovered and showed no signs of rotation.

Anal. Subs., 0.2217: CO_2, 0.5056; H_2O, 0.1264. Calcd. for $C_{34}H_{37}N_3O_{10}$: H, 5.71; C, 63.06. Found: H, 6.37; C, 62.20.

Brucine 2(2-Hydroxy-4-methylbenzoyl)3-nitrobenzoic Acid.—The acid was obtained by the method of Eder and Widmer[13] and the salt was formed in hot ethyl acetate. It forms yellow, needle-like crystals melting from 160–165° with decomposition. Upon fractionating four times from benzene, the rotations of the various fractions were determined. The α_D values were +18.3 for the salt initially, +18.39 for the first fraction and +16.3 for the fourth fraction. A 2-decimeter tube was used as in other cases. The samples were made up to 20 cc. at 20°, using acetone as a solvent. No rotation was observed in the free acid obtained by the precipitation of the ammonium salt and then acidification of the water solution.

Anal. Subs., 0.1169: CO_2, 0.2842; H_2O, 0.0546. Calcd. for $C_{38}H_{37}N_3O_{10}$: C, 65.60; H, 5.32. Found: C, 66.30; H, 5.26.

Aniline-*d*-camphorsulfonate.—The salt was prepared in the usual way and in chloroform gave the following rotations, using a 2-decimeter tube: 0.2079 g. subs. in 20 cc. of chloroform at 20° gave α_D +33.3° (ten minutes), +26.8° (five hours), +16.6° (seven hours), +6.6° (forty-eight hours).

Summary

1. *p*-Aminobenzoylbromomesitylene, 3,5-diaminobenzoylbromomesitylene, 2-carbo-*iso*propoxy-3-nitrobenzoic acid and 2-(2-hydroxy-4-methyl-

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[12] Nicolet and Sacks, This Journal, **47**, 2348 (1925).

[13] Eder and Widmer, *Helv. Chim. Acta*, **6**, 421 (1923).

benzoyl)-3-nitrobenzoic acid were prepared and attempts made to resolve them into optical components without success. A discussion of the relation of the compounds to optically active diphenyl compounds is included.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BARNARD COLLEGE]

ADDITION REACTIONS OF UNSATURATED ALPHA-KETONIC ACIDS. II

BY MARIE REIMER AND MARION HOWARD

RECEIVED JUNE 21, 1928 PUBLISHED SEPTEMBER 5, 1928

It has been previously shown[1] that the action of sunlight on the methyl ester of benzalpyruvic acid brings about addition of two molecules at the ethylenic linkage, cyclobutane derivatives being formed. The fact that *p*-methoxybenzalpyruvic acid and its methyl ester did not form such addition products, being entirely unaffected by sunlight, led to a comparative study of the addition reactions of the two ketonic acids and their esters with bromine[2] in which it was found that the ease with which both compounds combined with bromine was the same.

This study of unsaturated α-ketonic acids has now been continued with benzalpyruvic acid in which a substituting methoxyl group is in the *ortho* instead of the *para* position to the side chain. It has been found that the *o*-methoxybenzalpyruvic acid and its methyl ester also combine readily with bromine but that in almost all other respects the properties of the compound have been changed to a marked degree by this shift in the position of the methoxyl group. The color is deepened, that of *o*-methoxybenzalpyruvic acid being a brilliant orange, that of the *p*-methoxy acid a bright yellow.[3] The solubilities of the *o*-methoxy acid, its sodium salt and its methyl ester in the appropriate solvents are greater than those of the corresponding *p*-methoxy compounds; the acid and its esters do not combine with solvent of crystallization, a conspicuous characteristic of benzalpyruvic acid and its *p*-methoxy derivatives; the dibromo addition products are less stable than those of the other unsaturated α-ketonic acids studied, hydrogen bromide being lost with great ease. The most striking difference between the two methoxy derivatives is that *o*-methoxybenzalpyruvic acid and its methyl ester are sensitive to light; the aqueous solution of the acid is hydrolyzed rapidly in the sunlight; the acid, exposed in the dry condition, slowly loses its brilliant color; the methyl ester exposed to bright sunlight liquefies within a few minutes due to admixture with a light product.

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[1] Reimer, THIS JOURNAL, **46**, 783 (1924).

[2] Reimer, *ibid.*, **48**, 2454 (1926).

[3] Hodgson and Handley, *J. Chem. Soc.*, **1928**, p. 162.