

the organism but are either the true components of starch or are closely related to such true com-

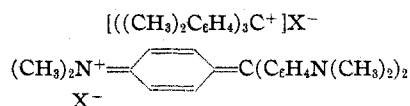
ponents. The research is being continued. WASHINGTON, D. C. RECEIVED SEPTEMBER 5, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 201]

Triarylcannabinols. VII.¹ 4'-Dimethylaminobiphenyldiphenylcarbinol and its Relation to the Theory of Color of Dyes

BY AVERY A. MORTON AND WILLIAM H. WOOD

This paper is concerned with the structure of triphenylmethane dyes, particularly with the effect of a dimethylamino group substituted in the 4'-position of a biphenyl nucleus. It will be recalled that Dilthey² and Wizinger³ have abandoned the conventional quinoid formula for dyes in favor of a carbenium, frequently called carbonium, structure in which the central carbon atom is given preference over nitrogen as the seat of basicity. Contrasting models for crystal violet are shown below.



The argument that the positions of nitrogen and carbon in the periodic table should favor a nitrogen base is met by claiming that the basic influence of the dimethylamino group is propagated through the benzene ring to a centrally located and basically enhanced carbon atom so that the latter becomes a superior base. In this scheme the coordinately unsaturated carbon atom is the chromophore which on conversion to the ionized state becomes colored. The dimethylamino group is the auxochrome.

We have applied this view to a system where the two competing, though vinylogously connected, points are separated by an additional phenyl nucleus in order to note, in a quantitative way, whether changes in basicity of the carbonium group are paralleled by changes in the properties of dyes. The sequence of reasoning underlying this work begins with the established fact that replacement of phenyl by a biphenyl nucleus enhances halochromism of triarylcannabinols and therefore by general opinion the basicity of the central carbon atom. This effect is well demonstrated with triphenyl- and triphenylcarbinol. While quantitative comparisons are difficult to make, the latter compound can be estimated qualitatively from colorimetric data of Ziegler and Boye⁴ to be over five times stronger than triphenylcarbinol. Moreover, triphenylcarbinol becomes colored in sulfuric acid-acetic acid solution which is about one hundredth the concentration needed to produce color with triphenylcarbinol.⁵ There is a definite shift in wave length from 414 to 542 m μ for the larger carbinol. As far as color can be used as the criterion of basicity there is no doubt but that substitution of phenyl by xenyl intensifies this property.

The second link in the chain of arguments is that substituents in the 4'-position of the biphenyl nucleus have their influence propagated through two phenyl nuclei, thus further enhancing the basicity of the central carbon atom. For example, trimethyltrixenyl- and trimethoxytrixenyl-carbinols previously⁵ have been observed to show color in acid which is approximately one-tenth and one-hundredth, respectively, the strength needed for triphenylcarbinol. There is also a shift in wave length from 542 for the unsubstituted compound to 575 and 638 m μ for the two substituted compounds, respectively. The evidence is conclusive that there is a definite transfer of influence of substituents over two phenyl bridges and that marked changes in basicity of the central carbon atom can be observed. Indeed, as shown in competitive titrations, the basicity of trimethoxytrixenylcarbinol is not far below that of a dimethylamino group present in a compound of the triarylmethane type.

It then appears reasonable that a dimethylamino substituent in the 4'-position of a carbinol

(1) Previous papers on triarylcannabinols are: Morton and Stevens, *THIS JOURNAL*, **53**, 2244, 4028 (1931); Morton and Peakes, Jr., *ibid.*, **56**, 2110 (1933); Clapp and Morton, *ibid.*, **59**, 2074 (1937); Morton and Emerson, *ibid.*, **59**, 1947 (1937); **60**, 284 (1938).

(2) Dilthey and Wizinger, *J. prakt. Chem.*, [2] **118**, 321 (1928).

(3) Wizinger, "Organische Farbstoffe," Ferd. Dümmlers Verlag, Bonn, 1933.

(4) Ziegler and Boye, *Ann.*, **458**, 229 (1927).

(5) Morton and Emerson, *THIS JOURNAL*, **60**, 284 (1938).

which is stronger than triphenylcarbinol might, in the same manner, have an influence transported to the central carbon atom. If Dilthey's view is applicable to this case, the compound should be a dye, possibly more pronounced than the corresponding compound in the triphenylmethane series, but at least with some tendency in that direction. It scarcely would be expected that dye-like properties would be snuffed out entirely. The compound first intended for these tests was *tris*-[4'-dimethylaminobiphenyl]-carbinol, the triphenyl analog of crystal violet. The customary synthesis by sodium condensation applied to preparation of this compound led to an amorphous material which probably contained the desired compound but resisted efforts to purify and crystallize. A pure crystalline compound, however, resulted from the reaction between benzophenone, sodium and 4'-dimethylaminobromodiphenyl. The product, $(\text{CH}_3)_2\text{NC}_6\text{H}_4\text{C}_6\text{H}_4\text{C}(\text{OH})(\text{C}_6\text{H}_5)_2$, 4'-dimethylaminobiphenyldiphenylcarbinol has one advantage, in that there is only one nitrogen competing against carbon for the anion. Its analog, dimethylaminotriphenylcarbinol, while not strictly a dye has many of the properties of dyes and is correctly considered the prototype of such substances. Unlike the simpler compound, however, the new product gave no color with dilute acids. Not only was it devoid of all properties remotely resembling a dye but the color of the carbinol was not realized until the basicity of the dimethylamino group had been neutralized completely. Moreover, the color of the carbonium salt was yellowish while that of the parent hydrocarbon was red, suggesting that the influence was that caused by a dimethylammonium salt in the 4'-position instead of the expected dimethylamino group. In this connection it is interesting to note that MacLean and Widdows⁶ some years ago prepared dimethylaminocinnamylidiphenylcarbinol and found that it gave no color in dilute acids. Furthermore, the *tris*-[4'-dimethylaminobiphenyl]-carbinol, though a crude product, showed in titration experiments that the basicities of the dimethylamino groups were neutralized before any color of a carbonium salt appeared. Apparently no gradual loss of dye-like properties can be observed.

As far as these tests are concerned, there is no tendency toward formation of colors in dilute solution when the distance between the nitrogen

atom and a central carbon atom is greater than one benzene ring. The principal seat of basicity in dimethylaminobiphenyldiphenylcarbinol is unquestionably on the nitrogen atom. This location is an eminently reasonable one, too, in all dimethylamino substituted triarylmethane compounds. In an energy transporting system of alternating single and double bonds such as are present in a phenyl nucleus, direction of movement of group influence can be either way. Enhanced basicity of a central carbon atom should accordingly increase the basicity also of the vinylogously connected nitrogen, so that maintenance of the vast natural superiority of nitrogen over carbon as a major sink for basicity of the molecule would thus be favored.

Approximate basicities of a number of amines and triphenylcarbinol have been made (see Table I). The method is not sensitive enough to catch fine differences but does reveal that the behavior of dimethylaminobiphenyldiphenylcarbinol toward perchloric acid is in accord with that expected of dimethylamino substituted compounds in general. The data also show that triphenylcarbinol is definitely stronger than such weak bases as acetamide or benzamide as contrasted with triphenylcarbinol which has been shown⁷ to be weaker.

Though the main interest of this research was to test the effect of separating positions of possible basicity, several other interesting observations have been made. Of the three nitroanilines, the meta isomer is by far the strongest base, for it is the only one which can be titrated appreciably with triphenylcarbinol as an indicator. Another interesting point was the five-fold increase in yield of dimethylaminobiphenyl in a sealed tube methylation of the amine as the size of the tube was decreased by half.

Experiments

4'-Dimethylaminobiphenyldiphenylcarbinol.—A solution of 4 g. of 4-bromo-4'-dimethylaminobiphenyl and 2.6 g. of benzophenone in 50 ml. of thiophene-free benzene was refluxed on a steam-bath while 0.7 g. of sodium chips was dropped through a condenser over a three-hour period. The mixture was refluxed for fifteen hours longer and then decomposed with 25 ml. of water. After separation and concentration, the benzene layer was cooled in ice and the yellow amorphous precipitate filtered and dried. Attempts at crystallization were unsuccessful but the material sublimed as a white solid at 200° (0.5 mm.). Recrystal-

(6) MacLean and Widdows, *J. Chem. Soc.*, **105**, 2174 (1914).

(7) Hall and Conant, *This Journal*, **49**, 3047 (1927); Hall, *ibid.*, **52**, 5115 (1930).

lization from alcohol gave fine needles melting at 177–178°; yield 2 g. or 36%; mol. wt. (Rast), 388, 415, 397 (calcd. 379); nitrogen analysis 3.63, 3.55%, calcd. 3.4%. The compound gave a strong red color in concentrated sulfuric acid and a yellow color in dilute solution of perchloric acid in glacial acetic acid. Observation of the light absorption in the Hardy Color Analyzer of the last solution showed the characteristic absorption of tertiary carbinols with a maximum value at 484 m μ .

Titration of the Carbinol.—Mallinckrodt 60% perchloric acid was treated with excess acetic anhydride and diluted with glacial acetic acid until the strength was 0.0421 *N*. The first drop of this solution added to a solution of 0.025 g. (0.000075 mole) of *p*-phenyltriphenylcarbinol⁸ caused the appearance of a red color. With 0.028 g. (0.000074 mole) of 4'-dimethylaminobiphenyldiphenylcarbinol 1.9 ml. (0.000080 mole) of the standard acid solution was required before a permanent red color appeared. With 0.014 g. (0.000037 mole) the amount of standard acid required was 0.95 ml. or 0.000040 ml. A mixture of 0.19 g. (0.000057 mole) of *p*-phenyltriphenylcarbinol and 0.0214 g. (0.000057 mole) of 4'-dimethylaminobiphenyldiphenylcarbinol required 1.45 ml. (0.000061 mole) of standard acid. A similar mixture of 0.0182 g. (0.0000373 mole) of trixenylcarbinol and 0.014 g. (0.0000369 mole) of the same dimethylamino compound was neutralized by 0.9 ml. (0.000038 mole) of acid. In all these cases it is apparent that in the presence of 4'-dimethylaminobiphenyldiphenylcarbinol, halochromism is not displayed until enough acid has been added to neutralize the basicity of the dimethylamino group; in absence of this dimethylamino compound it can be observed with the first drop of acid.

TABLE I

In addition to the compounds listed, 2,6-dichloro-4-nitroaniline, diphenyl urea, acetamide, butyramide, benzamide, thiobenzamide, acetanilide, *p*-nitroacetanilide, benzanilide all gave the carbinol color (trixenylcarbinol as an indicator) with the first drop of perchloric acid solution.

Base	Quantity, g.	Moles $\times 10^5$	Acid, ml.	Moles $\times 10^5$
Michler's ketone	0.253	9.44 ^a	4.35	18.35
4-Bromo-4'-dimethylaminobiphenyl	.029	11.7	2.75	11.6
Dimethylaniline	.050	41.4	10.4	43.8
<i>m</i> -Nitroaniline	.0566	41.0	9.05	38.1
2,6-Dichloroaniline	.0555	34.2	7.1	30.0
<i>p</i> -Aminobenzoic acid	.0725	52.8	11.8	49.7
<i>p</i> -Aminoacetophenone	.0332	24.6	5.4	22.8
Benzidine	.0410	22.4 ^a	10.1	42.6
Anthranilic acid	.0358	26.0	5.6	23.6
Glycine	.0344	45.8	10.2	43.0
<i>o</i> -Nitroaniline	.0543	39.3	No sharp end-point	
<i>p</i> -Nitroaniline	.0619	44.8	No sharp end-point	
<i>sym</i> -Tribromoaniline	.0600	18.2	0.1	...
Diphenylamine	.0565	33.4	3.9	16.4
Urea	.0607	101.1	5.0	21.0
Thiourea	.0525	69.2	12.0	50.1
Diphenylthiourea	.0520	22.8	0.9	3.8

^a The comparable value is twice this figure.

(8) Clapp and Morton, *THIS JOURNAL*, 59, 2074 (1937).

Titration of other Bases Using Trixenylcarbinol as an Indicator.—To ensure that results with the carbinol compound containing the dimethylamino group were not peculiar to this compound a number of bases were titrated in the same manner with 0.0421 perchloric acid in glacial acetic acid. The bases were Eastman Kodak Co. products used without any purification. Results are given in Table I. The series includes enough compounds to show the relative position of trixenylcarbinol as a base.

Titration of Dimethylaminobiphenyldiphenylcarbinol Using Trimethoxytrixenylcarbinol as an Indicator.—The dimethylamino compound 0.0188 g. (0.0000498 mole) in glacial acetic acid with 0.0181 g. (0.0000313 mole) of trimethoxytrixenylcarbinol required only 0.85 ml. (0.0000358 mole) of the standard perchloric acid solution before the blue color of the carbinol appeared. The result indicates that the trimethoxytrixenylcarbinol definitely competes with the dimethylamino compound for the acid and that transfer of group influence through two phenyl nuclei has been appreciable. Similar transfer of basic influence of the dimethylamino groups might therefore be expected.

Attempted Preparation of *tris*-(4'-Dimethylaminobiphenyl)-carbinol.—A solution of 8 g. of 4-bromo-4'-dimethylaminobiphenyl and 3.4 g. of diethyl carbonate in 50 ml. of thiophene-free benzene was refluxed while 2 g. of sodium chips was added over a period of forty-five minutes. After refluxing for sixteen hours longer the excess sodium was decomposed with alcohol and then with water. The mixture was filtered and the benzene layer treated with petroleum ether. A yellow amorphous solid was precipitated. Attempts to isolate a pure carbinol from this mass by crystallization, chromatographic adsorption on alumina, steam distillation to remove impurities, continuous extraction with petroleum ether and with ether, formation of salts with hydrochloric, sulfuric, and perchloric acids, and precipitation of the sodium carbinolate by either sodium or sodium alcoholate were all unsuccessful. The best material was obtained by dissolving the original yellow solid in concentrated sulfuric acid and diluting carefully with water until the sulfate of 4-bromo-4'-dimethylaminobiphenyl was precipitated. The filtrate was then neutralized with ammonia and a solid melting 160–183°, which could not be recrystallized from ether, alcohol or benzene, obtained. No color was observed in dilute acid solution. Titration of 0.0167 g. (equivalent to 0.000027 mole of the expected product) of this material with the standard perchloric acid solution showed that 1.6 ml. (0.000067 mole) could be added before a red carbonium salt color appeared. The product is obviously impure but it is apparent that the reaction produced no product which had any properties of a dye and that the carbinol color was not developed until after considerable neutralization of a stronger base had occurred.

Trixenylcarbinol.—Because so much difficulty was found in attempted syntheses of the above *tris* compound, a number of experiments were made to ensure that the best conditions for preparing the triarylcarbinols by the sodium condensation method were being applied. Best yields were secured when 19 g. of *p*-chlorobiphenyl and 5 g. of diethyl carbonate in 50 ml. of benzene were refluxed on a steam-bath while 5 g. of sodium (cut into chips 0.5 mm.

square and 2 mm. thick while kept under benzene in a beaker) were dropped through the condenser over a period of one-half hour. After twelve hours of refluxing the mixture was decomposed with water, the benzene layer was evaporated to 30 ml. and the carbinol precipitated with petroleum ether. The crude carbinol was then recrystallized either from xylene or alcohol after treatment with decolorizing carbon. Three experiments by this method gave 48, 48 and 47% yields, respectively, and a fourth, for some unexplained reason, gave 55%. Use of sodium sand instead of chips gave only 31%. Pieces of sodium 2-3 mm. in diameter and 2 cm. long produced only 39%. Activation of the chips with a little amyl alcohol before dropping through the condenser lowered the yield to 37%. Freshly distilled and excess diethyl carbonate did not improve the results.

4-Bromo-4'-dimethylbiphenyl.—Methylation of 4-amino-4'-bromobiphenyl (from reduction of the corresponding nitro compound by the method of García-Banús and Medrano⁹) was carried out in sealed tubes using 10 g. of the amino compound, 9 g. of methanol and 3 g. of concentrated hydrochloric acid. The tubes were heated to 140-150° for twelve hours and the products isolated in

(9) García-Banús and Medrano, *Añales soc. españ. fis. quím.*, **20**, 475 (1922); *C. A.*, **17**, 2574 (1923).

the conventional manner. The first two runs were made in Carius tubes about 66 cm. in length and gave yields of 0 and 9%. In the next three runs two of the tubes were only 43 cm., while a third was 66 cm. long. The batches were combined and gave an over-all yield of 28%. The final runs were therefore made in tubes only 36 cm. long and gave yields of 42, 44, 45, 42, and 45%. The length of the tube is limited by the volume of the reagent used. Seals of the short tubes must be well annealed in a luminous flame to prevent bursting at reaction temperatures.

Summary

4'-Dimethylaminobiphenyl has been prepared, its failure to have any properties resembling a dye noted, and the absence of any carbonium salt color until neutralization of the basic nitrogen atom observed. These results are not in accord with those predicted from the carbenium theory of triphenylmethane dyes.

Improved conditions for triarylcannabinol formation and for sealed tube methylation of an amine compound have been recorded.

CAMBRIDGE, MASS.

RECEIVED JULY 18, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 202]

Triarylcannabinols. VIII. Occurrence of Color with Trikenylcarbonium Salts

BY AVERY A. MORTON AND L. F. MCKENNEY

When trikenylcannabinol is dissolved in nearly dry acetic acid and the solution saturated with dry hydrogen chloride only a slight color is discernible. Upon adding a few drops of water a pronounced red color appears. By adding anhydrous calcium sulfate to the colored solution, the color gradually fades as would be expected if water were removed by the desiccant. It is apparent that water has played a definite part in production of color. Nor is the phenomenon limited to one reagent. Nitromethane, acetone, formamide, urea, methanol, benzamide and many other compounds intensify color in the same way. In all cases intensity of color goes through a maximum as the quantity of agent is increased.

Formation instead of destruction of color with water is remarkable. The action is suggestive of complex formation though efforts to crystallize a complex from the strongly colored solution yielded the carbinol only and the position of the maximum absorption band was not displaced in the case of agents with which the color was intense.

The very weak acid, acetic, will not form a color with the carbinol unless the solution is heated. Nitric acid in acetic acid will produce a color with a few drops of nitromethane but not with water. With still stronger acids, sulfuric and perchloric, colored crystalline salts were obtained. In particular trikenylcarbonium perchlorate, $(C_6H_5C_6H_4)_3CClO_4 \cdot HClO_4$, was a very stable compound, easily crystallized and purified. Upon electrolyzing a solution of this carbonium salt in nitromethane, nitrobenzene, or glacial acetic acid, the cathode rather than the anode portion became colorless. The same phenomenon was observed with an acetic acid solution of trikenylcannabinol to which a little sulfuric acid had been added, with a nitromethane solution of triphenylcarbonium perchlorate, $(C_6H_5)_3CClO_4$, and with nitromethane solutions of trikenylcarbonium sulfate, nitrate, and chloride. Furthermore, when a very dilute and colorless solution of trikenylcarbonium perchlorate in nitrobenzene was electrolyzed it was about the anode rather than the cathode that color reappeared.