

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE STATE UNIVERSITY OF IOWA]

Benzopyrylium Salts. VI. Reaction of Flavylium Perchlorate with DimethylanilineBY R. L. SHRINER AND JAMES A. SHOTTON¹

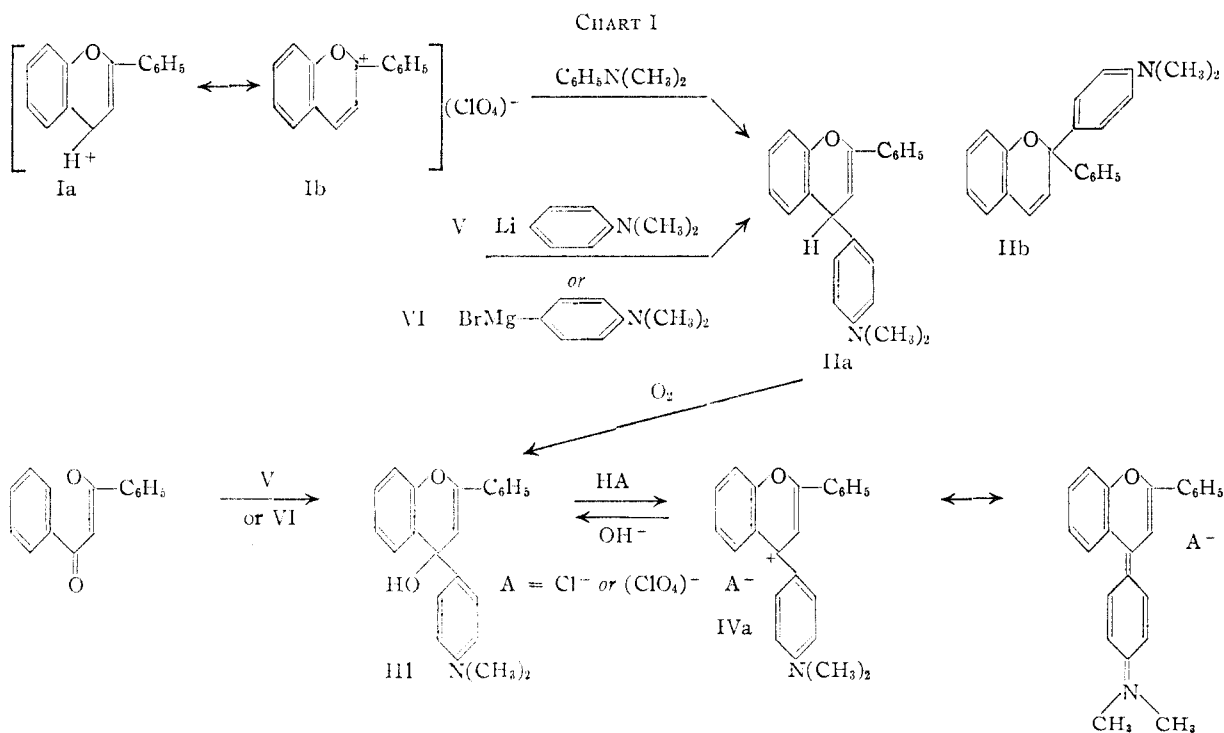
RECEIVED FEBRUARY 25, 1952

Flavylium perchlorate reacts with dimethylaniline to produce 2-phenyl-4-(*p*-dimethylaminophenyl)-1,4-benzopyran which is easily oxidized to the substituted 4-benzopyranol. Acids convert the latter to a blue dye, 2-phenyl-4-(*p*-dimethylaminophenyl)-1,4-benzopyrylium salt. The structures were established by independent syntheses of the intermediates.

As part of the study of the reactions of benzopyrylium salts² it has been found that addition of yellow flavylium perchlorate (Ia↔Ib) to an ether solution of dimethylaniline produced the colorless compound, 2-phenyl-4-(*p*-dimethylaminophenyl)-1,4-benzopyran (II) and the salt of dimethylaniline with perchloric acid. The compound II was easily oxidized by air to the carbinol (III) which reacted with strong acids, perchloric or hydrochloric, to produce a beautiful blue dye (IVa↔IVb). In fact when the reaction is carried out in the presence of air, a mixture of these compounds results. The structures of these compounds and the reactions used to verify them are summarized in Chart I.

steric hindrance involved in the reaction with the cationic resonance form, Ia, than with Ib, and this also is in favor of structure IIa for the leuco compound.

Since Löwenbein³ found that phenylmagnesium bromide coupled with flavylium perchlorate to introduce a phenyl group in the 4-position leading to 2,4-diphenyl-1,4-benzopyran, a similar coupling reaction was tried using *p*-dimethylaminophenylmagnesium bromide (VI) and *p*-dimethylaminophenyllithium (V). In both cases the compound IIa was formed which readily oxidized to the carbinol (III) and yielded the blue dye (IVa↔IVb) on treatment with acid.



The flavylium salt could have reacted with dimethylaniline in two ways leading to either structure IIa or IIb. These structures are vinylogs of a triphenylmethane system but structure IIb has no tertiary easily oxidizable hydrogen atom whereas the hydrogen on carbon 4 of structure IIa is similar to the methine hydrogen of the leucobase of a triphenylmethane dye and hence easily oxidized to the carbinol (III). Moreover, there would be less

The next step was to synthesize the carbinol (III) utilizing the well established fact⁴ that Grignard reagents react initially with flavone and chromones by 1,2-addition to the carbonyl group to produce carbinols. A low yield of the carbinol was obtained when *p*-dimethylaminophenylmagnesium bromide reacted with flavone. When *p*-dimethylaminophenyllithium (V) was used in the

(3) A. Löwenbein, *Ber.*, **59**, 1865 (1926).

(1) From a thesis submitted to the Graduate School of the State University of Iowa in partial fulfillment of the requirements for the Ph. D. degree.

(2) Preceding paper in this series, R. J. Shriner and R. K. Oltter, *This Journal*, **73**, 887 (1951).(4) E. R. Watson, K. B. Sen and V. R. Medlin, *J. Chem. Soc.*, **107**, 1477 (1915); I. M. Heilbron and A. Zaki, *ibid.*, 1902 (1926); K. Ziegler, F. A. Pries and F. Salzer, *Ann.*, **443**, 249 (1926); I. M. Heilbron, D. H. Hey and A. Lowe, *J. Chem. Soc.*, 1380 (1936); I. M. Heilbron, R. N. Heslop and F. Irving, *ibid.*, 430 (1933).

reaction with flavone, the yield of the carbinol (III) was 66%. Both samples of the carbinol prepared by these reactions gave the perchlorate of the dye (IVa \leftrightarrow IVb) upon treatment with perchloric acid.

The new blue dye, for which formulas IVa \leftrightarrow IVb represent only two of the possible resonating cationic structures, was isolated both as the perchlorate and chloride. Aqueous solutions of the dye possessed typical indicator properties, the blue color developing at pH 6.9–7.1. It is pale yellow in alkaline solutions. In strongly acid solutions (pH 0.15) it became a pale greenish-yellow. This behavior parallels that of other basic triphenylmethane dyes: such as crystal violet which becomes green in strongly acid solutions and malachite green which turns yellow in strongly acid solutions. Adams and Rosenstein⁵ ascribe the change in color to salt formation with the basic nitrogen atom with shift in the absorption spectrum. The dye IVa \leftrightarrow IVb has high tinctorial properties; 0.05 mg./l. being sufficient to impart a distinct blue color.

Experimental

Flavylium Perchlorate and Dimethylaniline.—To a solution of 12.1 g. (0.1 mole) of dimethylaniline in 200 ml. of ether was added 15.3 g. (0.05 mole) of flavylium perchlorate⁶ in portions with vigorous shaking. After about 3 hours the dark colored precipitate was collected on a filter and the ethereal filtrate evaporated to give a compound which, after crystallization from petroleum ether, yielded colorless crystals of 2-phenyl-4-(*p*-dimethylaminophenyl)-1,4-benzopyran (IIa) melting at 121–122°.

Anal. Calcd. for C₂₃H₂₁ON: C, 83.4; H, 6.43; N, 4.28. Found: C, 83.1; H, 6.47; N, 4.30.

The above mentioned dark precipitate was mixed with 200 ml. of ether and 100 ml. of 5% sodium carbonate solution. Filtration of this solution gave a dark blue precipitate which was purified by solution in hot glacial acetic acid, filtration and cooling of the filtrate. Dark blue metallic-like plates of the dye (IV) were obtained which melted at 246° dec. Since perchlorates decomposed rather vigorously during attempted combustion, this product was analyzed for perchlorate anion by treatment of a hot absolute methanol solution with tetraphenylarsonium chloride hydrochloride.⁷ The tetraphenylarsonium perchlorate was collected, dried at 105° and weighed.

Anal. Calcd. for (C₂₃H₂₀ON)⁺(ClO₄)⁻: ClO₄, 23.38. Found: ClO₄, 23.47.

Separation of the ether layer from the filtrate from the above separation of the blue dye and evaporation of the ether gave crude 2-phenyl-4-(*p*-dimethylaminophenyl)-1,4-benzopyranol-4 (III) which was purified by recrystallization from petroleum ether (60–70°) to a constant melting point of 89–91°.

Anal. Calcd. for C₂₃H₂₁O₂N: C, 80.4; H, 6.13; N, 4.08. Found: C, 80.15; H, 6.25; N, 4.24.

Treatment of an ether solution of this carbinol (III) with perchloric acid in acetic acid gave a precipitate of the blue dye (IV) melting at 246° dec.

Flavylium Perchlorate and *p*-Dimethylaminophenyl Lithium.—To 25 ml. of absolute ether was added 0.76 g. of

sliced lithium metal and one-third of a solution of 10 g. of *p*-bromodimethylaniline in 25 ml. of absolute ether. The mixture was refluxed until the reaction started and then the balance of the solution of *p*-bromodimethylaniline added at such a rate as to keep the mixture refluxing. After the addition was completed, an additional half-hour's heating was necessary to complete the reaction with the lithium. To this solution was added 15.3 g. of flavylium perchlorate in small portions. This was accomplished by placing the flavylium perchlorate in a 125-ml. conical flask and attaching this to one of the side necks of the 200-ml. 3-neck flask by means of a piece of Gooch tubing. This prevented air oxidation as the perchlorate was added without opening the flask. A white precipitate of lithium perchlorate was formed which was separated from the ether solution by filtration. The ether solution was evaporated to dryness and the residue was recrystallized from 60–70° petroleum ether. The yield of 2-phenyl-4-(*p*-dimethylaminophenyl)-1,4-benzopyran (IIa) was 9.5 g. or 58.2% of theory. The melting point was 120–121° and a mixed melting-point with the sample prepared from dimethylaniline and flavylium perchlorate gave no depression.

In a similar manner, *p*-dimethylaminophenylmagnesium bromide was prepared and treated with flavylium perchlorate. A low yield (about 10%) of the substituted pyran (IIa) was obtained.

This pyran was easily oxidized by air, hydrogen peroxide or ferric chloride solution. Addition of perchloric acid or hydrogen chloride to an oxidized solution of IIa gave the perchlorate or chloride of the blue benzopyrylium dye (IV).

Flavone and *p*-Dimethylaminophenyl Lithium.—A solution of *p*-dimethylaminophenyl lithium was prepared as described above using 0.485 g. of lithium and 6.35 of *p*-bromodimethylaniline. To this solution was added 7.0 g. of flavone (prepared as described by Ruhemann⁸) suspended in 50 ml. of dry ether. After the addition of the flavone, the mixture was refluxed for half an hour and the addition compound decomposed by 50 ml. of cold water. The ether layer was removed, treated with 1.0 g. of Norite, filtered, and dried over anhydrous potassium carbonate. The ether was evaporated and 7.0 g. or 66% of theory, of the crude carbinol remained. The crude product was recrystallized from petroleum ether (60–70°) and came out as a pale yellow solid melting at 89–91°. A mixed melting point with the substituted pyranol (III) obtained from the reaction of dimethylaniline with flavylium perchlorate showed no depression.

A 9% yield of this pyranol (III) was obtained using a similar procedure for the reaction of flavone with *p*-dimethylaminophenylmagnesium bromide.

The 2-Phenyl-4-(*p*-dimethylaminophenyl)-1,4-benzopyrylium Chloride (IV).—Dry hydrogen chloride was passed into an absolute ether solution of the above pyranol (III) until it was saturated. Dark blue crystals of the dye (IV) precipitated. After drying in a vacuum desiccator over potassium hydroxide they melted at 125–126° dec.

Anal. Calcd. for C₂₃H₂₀ONCl: ionic Cl, 9.89. Found: Cl, 9.98.

Conversion of the Salt (IV) to the Pyranol (III).—To 100 ml. of ether and 50 ml. of concentrated ammonium hydroxide in a separatory funnel was added 8.2 g. of the perchlorate of the dye (IV) in portions with vigorous shaking. After the blue color had disappeared, the ether layer was separated, dried over anhydrous potassium carbonate and the ether removed. After recrystallization from petroleum ether, 6.2 g. (96%) of pale yellow crystals of the pyranol (III), melting at 89–91° was obtained. This compound did not depress the melting point of the above described samples of the pyranol.

The chloride of IV was also converted to the pyranol (III) by the same procedure.

IOWA CITY, IOWA

(5) S. Ruhemann, *Ber.*, **37**, 2634 (1904); M. T. Bogert and J. K. Marcus, *THIS JOURNAL*, **41**, 87 (1919).

(5) E. Q. Adams and L. Rosenstein, *THIS JOURNAL*, **36**, 1452 (1914).

(6) R. J. W. Le Fèvre, *J. Chem. Soc.*, 2771 (1929).

(7) R. L. Shriner and C. N. Wolf, *Org. Syntheses*, **30**, 95 (1950); R. L. Shriner, H. W. Johnston and C. E. Kaslow, *J. Org. Chem.*, **14**, 208 (1949).