346 mg. (80%) of a blue oil that slowly crystallized, m.p. 62–68°. A portion of this, 95 mg., was rechromatographed and recrystallized from hexane giving 67 mg. (70% recovery, 56% net yield) of blue crystals, m.p. 75–77.5°.

A cyclohexane solution of **12** showed maxima in mμ (log ε) in the ultraviolet at 246 (4.38), 288 (4.57), 304 (4.25), 351 (3.76), and 368 (3.73). There was a single broad maximum in the visible at 610 mμ (ε 490) with shoulders at 660 mμ (ε 403) and 731 mμ (ε 144). The infrared spectrum of a carbon tetrachloride solution showed carbonyl absorption at 6.00 μ.

Anal. Calcd. for $C_{18}H_{23}NO$: C, 80.25; H, 8.61; N, 5.20. Found: C, 80.31; H, 8.67; N, 5.22.

1,2,8-Trimethyl-6-isopropylcyclohepta[*d,e*]-1-pyrindine (10).—A dry flask containing 120 mg. (0.447 mmole) of 3-N-methylacetamidoguaiazulene was flushed with dry nitrogen, and 2.0 ml. of a 0.36 *N* sodium N-methylanilide–ether solution was injected with stirring. The blue reaction mixture immediately turned brown-green. After being refluxed and stirred for 4 hr., the mixture was treated with ammonium chloride solution and extracted with ether. The green ether phase was extracted with 5% hydrochloric acid giving a purple acid layer and a faint yellow-green ether layer. The combined acid extracts were washed well with ether (yellow ethereal extracts), and neutralized with solid sodium carbonate. Ether dissolved the precipitated green solid. The green ethereal extract was washed with water and dried over sodium sulfate. A rotary evaporator was used, first to remove the solvent at reduced pressure (water pump), and then all volatile material by heating the flask at a lower pressure (*ca.* 2 mm.) for several hours. The crystalline residue, after trituration with three 5-ml. portions of petroleum ether, yielded 68 mg. (61%) of red-brown needles, m.p. 179–180.5° (evacuated capillary). The analytical sample after recrystallization from ether melted at 180.5–182°. A cyclohexane solution of **10** showed maxima in mμ (log ε) in the ultraviolet at 238 (4.47), 253 (4.43), 270 (4.49), shoulder at 300 (3.84), 361 (4.12), 398 (3.69), 422 (3.62), 449 (3.43); the far wave length band had maxima μ (ε) at 763 (317), 862 (315), and 996 (166) with a shoulder at 690 (241). The infrared spectrum showed no absorption corresponding to NH or carbonyl groups.

Anal. Calcd. for $C_{18}H_{21}N$: C, 86.00; H, 8.42; N, 5.57. Found: C, 85.77; H, 8.51; N, 5.73.

1-Acetamidoazulene (13) was prepared from 1-nitroazulene by the method of Anderson, *et al.*[11] A cyclohexane solution exhibited the principal maximum in the visible at 637 mμ (5-cm. cells).

1-N-Methylacetamidoazulene (14).—About 5 ml. of dry tetrahydrofuran was distilled into a dry 10-ml. flask containing 37 mg. (0.20 mmole) of 1-acetamidoazulene and 12 mg. of a 51.5% sodium hydride–oil dispersion (6.2 mg., 0.26 mmole). The reaction mixture, which began to bubble and turn green, was stirred for 0.5 hr. Methyl iodide (1.0 ml., 16 mmoles) was added, and the mixture stirred for 45 min. Ether was added, and the blue ethereal solution was washed with water and dried. The blue oil left after removal of solvent was chromatographed over alumina. The single blue band was eluted with a 1:1 ether–dichloromethane mixture. Removal of solvent from the blue eluate left a blue oil that crystallized when triturated with petroleum ether giving 40 mg. (100%) of **14**, m.p. 71–73°. A cyclohexane solution exhibited maxima in the ultraviolet in mμ (log ε) at 237 (4.28), 277 (4.61), 282 (4.61), shoulder at 286 (4.51), 333 (3.51), shoulder at 342 (3.61), 344 (3.63), and 357 (3.40), and in the visible (ε) with a shoulder at 572 (291), 590 (341), 613 (319,) 642 (306), shoulders at 669 (177) and 710 (124). An infrared spectrum (carbon tetrachloride solution) showed carbonyl absorption at 6.0 μ.

Anal. Calcd. for $C_{13}H_{13}NO$: C, 78.36; H, 6.57; N, 7.03. Found: C, 77.93; H, 6.87; N, 6.94.

Acknowledgment.—The author is greatly indebted to Dr. A. G. Anderson, Jr., for providing a postdoctoral appointment, which enabled some of this work to be done, and for valuable discussions. Financial support by the National Science Foundation is gratefully acknowledged.

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

Benzopyrylium Salts. VIII. The Synthesis and Properties of 7-Dimethylaminoflavylium Salts[1]

BY WILLIAM C. BAIRD, JR.,[2,3] AND R. L. SHRINER

RECEIVED FEBRUARY 29, 1964

The synthesis of 7-dimethylaminoflavylium salts has been realized according to the reaction series: 4-dimethylaminosalicyaldehyde → 2-hydroxy-4-dimethylaminochalcone → 7-dimethylaminoflavylium salt. Flavylium salts have been prepared where the anion is represented by chloride, ferrichloride, and perchlorate ions. The ultraviolet and visible spectra of these compounds have been measured and compared to those of the parent compound, flavylium perchlorate. The effect of pH on 7-dimethylaminoflavylium chloride has been observed by noting the changes induced in the spectrum of this salt as the pH was varied.

The introduction of various auxochromes, notably hydroxy, methoxy, and amino groups, into the chromophoric flavylium cation has been the subject of several investigations designed to study the effects of structure and substitution on the spectra of flavylium salts.[4-9] The effect of a benzo-substituted dimethylamino group has not previously been observed; in fact only a single flavylium salt containing such an amino group, 2′,4′-dimethoxy-4-methyl-7-dimethylaminoflavylium perchlorate, has been reported.[8b] In this case the presence of the auxochromic methoxy groups in the 2-phenyl ring precludes a definite conclusion regarding the influence of the dimethylamino group on the spectrum of this salt.

The synthesis of 7-dimethylaminoflavylium salts has been achieved according to three general synthetic routes. These are summarized in Chart I, which illustrates the synthesis of 7-dimethylaminoflavylium perchlorate (I). The required intermediate, 4-dimethylaminosalicylaldehyde (II), was prepared by the reaction of *m*-dimethylaminophenol with dimethylformamide in the presence of phosphorus oxychloride. Subjecting this aminoaldehyde to an aldol condensation with acetophenone in the presence of ethanolic potassium hydroxide led to the formation of 2-hydroxy-4-dimethylaminochalcone (III). Cyclization of the chalcone with anhydrous hydrogen chloride gave 7-

(1) Preceding paper in this series: R. L. Shriner and R. Sutton, *J. Am. Chem. Soc.*, **85**, 3989 (1963).

(2) du Pont Predoctoral Fellow. Abstracted in part from a thesis submitted to the Graduate School of the State University of Iowa in partial fulfillment for the Ph.D. Degree.

(3) Central Basic Research Laboratory, Esso Research Center, Linden, N. J.

(4) E. H. Charlesworth and R. Robinson, *J. Chem. Soc.*, 1619 (1934).

(5) H. Healey and R. Robinson, *ibid.*, 1625 (1934).

(6) K. Hayashi, *Acta Phytochim.*, **7**, 117 (1933).

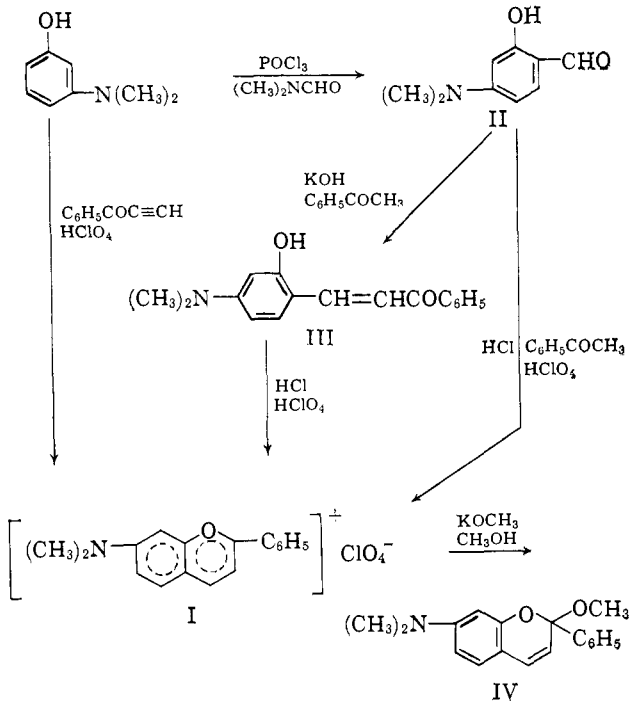
(7) A. M. Robinson and R. Robinson, *J. Chem. Soc.*, 1439 (1932); 25 (1933).

(8) (a) C. Michaelidis and R. Wizinger, *Helv. Chim. Acta*, **34**, 1761 (1951); (b) *ibid.*, **34**, 1770 (1951); (c) *ibid.*, **34**, 1776 (1951).

(9) R. Wizinger and A. Luthiger, *ibid.*, **36**, 526 (1953).

CHART I

SYNTHESES OF 7-DIMETHYLAMINOFLAVYLIUM PERCHLORATE



dimethylaminoflavylium chloride, which was subsequently converted to the perchlorate salt I by treatment with anhydrous perchloric acid.

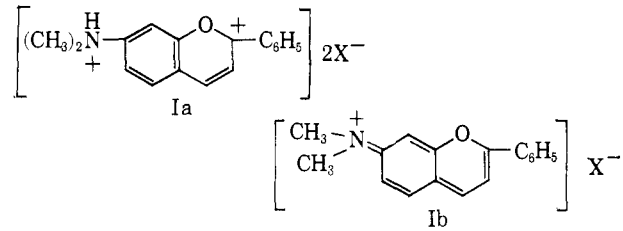
When an ethyl acetate solution of 4-dimethylaminosalicylaldehyde (II) and acetophenone was treated with anhydrous hydrogen chloride, 7-dimethylaminoflavylium chloride separated directly. If the same reaction were carried out in the presence of perchloric acid, the perchlorate I was isolated. Treatment of a solution of the flavylium chloride in glacial acetic acid with ferric chloride solution precipitated 7-dimethylaminoflavylium ferrichloride.

The third reaction applied to the synthesis of this aminoflavylium salt was that of *m*-dimethylaminophenol with phenyl ethynyl ketone. Both 7-dimethylaminoflavylium ferrichloride and perchlorate were prepared in this manner. The yields in these cases were poor in contrast to the above syntheses; this may conceivably be due to a 1,4-addition of the phenol to the acetylenic ketone.

The perchlorate I was converted to 2-methoxy-2-phenyl-7-dimethylamino-1,2-benzopyran (IV) by potassium methoxide in anhydrous methanol.[10]

The 7-dimethylaminoflavylium salts are lustrous, deep red, crystalline materials possessing relatively high melting points. The salts are stable to the atmosphere and do not exhibit any hygroscopic properties. The chloride is readily soluble in water, glacial acetic acid, acetonitrile, methanol, and ethylene chloride. The perchlorate is sparingly soluble in water and moderately soluble in the other solvents. The ferrichloride has solubility properties similar to those of the perchlorate.

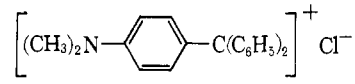
Even though an excess of hydrochloric acid, perchloric acid, or $HFeCl_4$ was used in the above reactions, no salt containing an extra mole of acid was ever obtained; *i.e.*, no salt of the structure Ia could be prepared even in the nonaqueous solvents used. This



$X^- = Cl^-, ClO_4^-, FeCl_4^-$

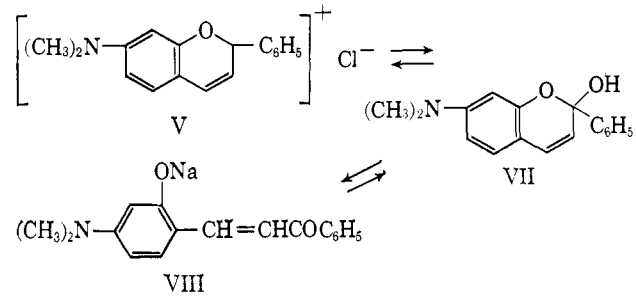
strongly suggests that the quinone-imine structure Ib is an important bond structure contributing to the resonance hybrid.[8,9]

The visible and ultraviolet spectra of flavylium perchlorate, 7-dimethylaminoflavylium perchlorate (I), and 7-dimethylaminoflavylium chloride (V) were measured, and the spectrophotometric data are presented in Table I. The introduction of the dimethylamino group into the 7-position of the flavylium nucleus produced a bathochromic shift of 130 mμ in the visible spectra of these salts when compared to the spectrum of the parent compound. This spectral shift is comparable in magnitude to that observed in other aminoflavylium salts.[8,9] The absorption maximum differs by only 10 mμ from that of 2′,4′-dimethoxy-4-methyl-7-dimethylaminoflavylium perchlorate (λ_{max} 530 mμ).[8b] The differences between the molar absorptivities of 7-dimethylaminoflavylium perchlorate and those of the chloride may be attributed to solvent effects and to the degree of dissociation of the salts. Flavylium perchlorates are nearly completely dissociated in acetonitrile[11] and 60–80% dissociated in nitrobenzene.[12] In the latter solvent flavylium chlorides are ionized to about 3–10%. The enhanced bathochromic nature of flavylium cations is reflected by a comparison of the absorption maxima of the salt V with those of *p*-dimethylaminotriphenylmethyl chloride (VI)[13] (Table I).



VI

The influence of pH on solutions of 7-dimethylaminoflavylium chloride (V) was studied by observing the changes induced in the spectrum of the salt as the pH was varied. The results of these studies indicated



(10) Flavylium salts have been previously demonstrated to yield 2-methoxy compounds: R. L. Shriner and R. B. Moffett, *J. Am. Chem. Soc.*, **63**, 1694 (1941).

(11) R. R. Otter and R. L. Shriner, *ibid.*, **73**, 887 (1951); R. L. Shriner in "Roger Adams Symposium," John Wiley and Sons, Inc., New York, N. Y., 1955.

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(13) H. Walba and G. E. K. Branch, *J. Am. Chem. Soc.*, **73**, 3341 (1951).

TABLE I
ABSORPTION SPECTRA OF FLAVYLIUM SALTS AND RELATED COMPOUNDS

Compound	λ_{max}, mμ	$\epsilon \times 10^4$
Flavylium perchlorate[a]	390	1.33
	260	1.27
	250	1.24
7-Dimethylaminoflavylium perchlorate (I)[a]	520	2.57
	335	1.47
	290	1.90
7-Dimethylaminoflavylium chloride (V)[b]		
pH 2	520	2.28
	335	1.06
	290	1.38
pH 4	445	1.49
	340	0.54
pH 7	440	2.38
	273	0.91
pH 9	455	2.12
	270	0.95
pH 11	485	2.68
	268	0.88
pH 13	485	2.64
	268	0.88
2-Hydroxy-4-dimethylaminochalcone sodium salt (VIII)[b]	485	2.65
	268	0.94
2-Methoxy-2-phenyl-7-dimethylamino-1,2-benzopyran (IV)[c]	430	1.37
	325	0.92
p-Dimethylaminotriphenylmethyl chloride (VI)[b]	463	1.52
	341	0.38
	263	0.52

[a] In acetonitrile. [b] In methanol–water (50:50). In methanol.

that as the pH was increased from 2 to 7, the salt was hydrolyzed to the corresponding carbinol VII. As the pH was further increased to 13, the carbinol was converted to the sodium salt of 2-hydroxy-4-dimethylaminochalcone (VIII).[14] The spectrum measured in the pH range 4–7 was assigned to the carbinol due to its similarity to that of the corresponding 2-methoxy compound. The spectra measured at pH 11 and 13 were identical with the spectrum of the sodium salt of the chalcone VIII.

Experimental[15]

4-Dimethylaminosalicylaldehyde (II).—A 500-ml. three-necked round-bottomed flask was equipped with a sealed stirrer, a dropping funnel, a reflux condenser topped with a calcium chloride tube, and a thermometer. Freshly distilled dimethylformamide (180 ml.) was added to the flask and cooled to 0°. Phosphorus oxychloride (57.5 ml.) was added dropwise with stirring at such a rate that the temperature remained near 5°. The dropping funnel was removed and replaced by a rubber sleeve connected to a flask containing 86 g. (0.63 mole) of *m*-dimethylaminophenol. The phenol was added in small portions so that the reaction temperature did not exceed 40°. The reaction was stirred and heated on the steam bath for 2 hr., and the reaction mixture was then poured over 600 g. of ice. The reaction flask was rinsed with 400 ml. of water, the rinsings were added to the ice mixture, and the slurry was stirred until the complex dissolved. Saturated sodium acetate solution was added dropwise with vigorous mechanical stirring until the pH was 6–8. The neutralized solution was chilled overnight in the refrigerator, filtered, and the solid material washed well with cold water. The crude product was recrystallized from 250 ml. of 95% ethyl alcohol to yield 42–45 g. (42–45%) of pure aldehyde, m.p. 78–79°. The literature reports[16] the melting point as 79–80°.

2-Hydroxy-4-dimethylaminochalcone (III).—A modification of the procedure described by Nagell and Tambor[17] was used to prepare this chalcone. Ten grams (0.06 mole) of 4-dimethylaminosalicylaldehyde and 6.9 ml. of freshly distilled acetophenone were dissolved in 40 ml. of 95% ethyl alcohol; 25 ml. of 50% potassium hydroxide solution was added, and the reaction was heated and stirred on the steam bath for 2 hr. The reaction mixture was poured into a chilled solution of 25.5 ml. of glacial acetic acid in 50 ml. of water. The precipitate was filtered, washed well with water, and recrystallized twice from 95% ethanol to give 8 g. (50%) of small red needles, m.p. 167–167.5°.

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.13; H, 6.54; N, 5.23.

7-Dimethylaminoflavylium Chloride (V).—According to the procedure described by LeFevre,[18] 4-dimethylaminosalicylaldehyde (4.4 g., 0.026 mole) and 3 ml. of acetophenone were dissolved in 75 ml. of ethyl acetate. The solution was stirred and treated with anhydrous hydrogen chloride at room temperature for 36 hr. The solid was removed by filtration, washed well with anhydrous ether, and dried to yield 4.4 g. (59%) of the flavylium chloride. Recrystallization from acetonitrile gave small, deep red needles, m.p. 179–182° dec.

Anal. Calcd. for $C_{17}H_{16}NOCl$: C, 71.46; H, 5.65; N, 4.90. Found: C, 71.64; H, 5.79; N, 4.93.

7-Dimethylaminoflavylium Perchlorate (I).—A solution of 1 g. (0.004 mole) of 2-hydroxy-4-dimethylaminosalicylaldehyde in 10 ml. of glacial acetic acid was treated with anhydrous hydrogen chloride for 2 hr. A solution of 1 ml. of 70% perchloric acid in 2.5 ml. of acetic anhydride was added, and the gas stream was continued for 22 hr. The red solid was removed by filtration, washed thoroughly with anhydrous ether, and dried to yield 1 g. (77%) of crude product. Recrystallization from acetonitrile gave lustrous, deep red needles, m.p. 287–288° dec.

Anal. Calcd. for $C_{17}H_{16}NClO_5$: C, 58.37; H, 4.61; ClO_4^-, 28.44. Found: C, 58.07; H, 4.66; ClO_4^-, 28.12.

According to the procedure of LeFevre,[18] a solution of 1.7 g. (0.01 mole) of 4-dimethylaminosalicylaldehyde, 1.5 ml. of acetophenone, and 3 ml. of 70% perchloric acid in 40 ml. of ether was treated with dry hydrogen chloride for 24 hr. at 0°. The reaction mixture was filtered, and the product washed with anhydrous ether to give 3 g. (66%) of the salt, m.p. 287–289° dec.

According to the method reported by Johnson and Melhuish,[19] 1 g. (0.07 mole) of *m*-dimethylaminophenol was added to a solution of 1 g. of phenyl ethynyl ketone[20] in 10 ml. of glacial acetic acid; 1 ml. of 70% perchloric acid was added, and the reaction was permitted to stand at room temperature for 3 days. The red, crystalline precipitate was removed by filtration and washed with anhydrous ether to yield 0.1 g. of the flavylium perchlorate. Mixture melting points with samples prepared by the above methods showed no depression.

7-Dimethylaminoflavylium Ferrichloride.—A solution of 0.5 g. of 7-dimethylaminoflavylium chloride in 1 ml. of glacial acetic acid was treated with 1 ml. of a ferric chloride solution prepared by dissolving 10 g. of anhydrous ferric chloride in 15 ml. of concentrated hydrochloric acid. The deep red precipitate was removed by filtration and washed well with anhydrous ether. The ferrichloride was recrystallized from glacial acetic acid to give lustrous, deep red needles, m.p. 212–214° dec.

Anal. Calcd. for $C_{17}H_{16}NOFeCl_4$: C, 45.57; H, 3.60; Fe, 12.47. Found: C, 45.48; H, 3.86; Fe, 12.59.

The ferrichloride salt was also prepared according to the method of Johnson and Melhuish[19] using 6 ml. of the ferric chloride solution as the reaction catalyst. A mixture melting point of the two reaction products was not depressed.

2-Methoxy-2-phenyl-7-dimethylamino-1,2-benzopyran (IV).—To 250 ml. of absolute methanol was added in small pieces 0.4 g. of clean potassium metal. 7-Dimethylaminoflavylium perchlorate (3 g., 0.008 mole) was added to the potassium methoxide solution, and the reaction was stirred at room temperature for 8 hr. The reaction mixture was filtered, and the methyl alcohol was removed by distillation under reduced pressure. The residue was extracted with ether, the ether was evaporated, and the residual brown oil was recrystallized from methyl alcohol to yield 1.2 g. (50%) of light tan crystals, m.p. 82°.

Anal. Calcd. for $C_{18}H_{19}NO_2$: C, 76.83; H, 6.80; N, 4.97. Found: C, 76.50; H, 6.86; N, 4.73.

(14) For a discussion of the hydrolysis reactions of flavylium salts see S. Wawzonek, "Heterocyclic Compounds," Vol. II, edited by R. Elderfield, John Wiley and Sons, Inc., New York, N. Y., 1951, pp. 316–328.

(15) All melting points and boiling points are uncorrected.

(16) Joh. Rud. Geigy and Co., German Patent 103,578; *Zentr.*, **71**, I, 238 (1900).

(17) H. Nagell and J. Tambor, *Helv. Chim. Acta*, **7**, 335 (1924).

(18) R. J. W. LeFevre, *J. Chem. Soc.*, 1532 (1933).

(19) A. W. Johnson and R. R. Melhuish, *ibid.*, 346 (1947).

(20) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weiden, *ibid.*, 39 (1946).

Spectrometric Measurements.—Ultraviolet and visible spectra were measured on a Cary Model 11 recording spectrophotometer using matched silica cells of path length 1.00 ± 0.01 cm. Pure solvent was used in the reference cell. Solutions of the perchlorate salts were prepared in anhydrous acetonitrile (refluxed and distilled from phosphorus pentoxide). Solutions of 7-dimethylaminoflavylium chloride were prepared using a solvent mixture of methanol–water (50:50). Beckman and Coleman buffer packages were employed to produce buffered solutions having the approximate pH values shown. The solutions were permitted to stand at room temperature for 24 hr. before their spectra were taken so that equilibrium might be established.

[CONTRIBUTION FROM THE DEPARTMENT OF BIOLOGY AND JOHN HARRISON LABORATORY OF CHEMISTRY, UNIVERSITY OF PENNSYLVANIA, AND CHEMISTRY DEPARTMENT, DREXEL INSTITUTE OF TECHNOLOGY, PHILADELPHIA, PENNA.]

Mechanistic Investigations of Porphyrin Syntheses. I. Preliminary Studies on *ms*-Tetraphenylporphin[1]

BY ALAN D. ADLER, FREDERICK R. LONGO, AND WILLIAM SHERGALIS

RECEIVED JANUARY 22, 1964

Investigations of the effect of various solvents, metallic cations, anions, temperature, time, and other conditions of reaction upon the homogeneous phase condensation of pyrrole and benzaldehyde to *ms*-tetraphenylporphin have offered considerable insight into the mechanism of this reaction. They also provide a basis for an extended thermodynamic and kinetic study, and also for a relatively rapid, readily purified, large yield reaction for the preparation of this material.

The biological importance of porphyrin-like materials such as hemin, chlorophyll, and vitamin B_{12}, coupled with their unusual and striking physical and chemical properties, make them both interesting and important objects of research. Many biochemical investigations have been devoted to studying the enzyme-catalyzed mechanism of biosynthesis of porphyrins.[2] An understanding of these biosynthetic reactions would be abetted by a further knowledge of the mechanism of some similar, simpler organosynthetic reactions. Such studies would be of interest in themselves and could also provide the improved routes of synthesis necessary to extended physical chemical and solid state investigations of these materials. With such objects in mind we have carried out preliminary researches on three parent compounds: porphin, tetraazaporphin, and *ms*-tetraphenylporphin (hereafter abbreviated as TPP). The preliminary TPP results are reported here.

TPP has previously been synthesized by the direct condensation of pyrrole and benzaldehyde in sealed tubes, the reaction taking place at 140 to 220° over 24 to 48 hr. and yielding 4 to 5% of TPP with variable amounts of tetraphenylchlorin (TPC) dependent upon temperature, concentration of reactants, etc.[3-6] Addition of zinc acetate to these sealed tube reaction mixtures increases the yield to 10 to 11% (based on pyrrole).[6] An increase of porphyrin yield in the presence of metallic cations has been noted in a variety of other porphyrin condensation reactions.[7-12] However, sealed tube TPP condensations are inconvenient for thermodynamic and kinetic investigations for a variety of obvious reasons. Therefore a preliminary study of possible simpler condensation conditions was undertaken.

Results

Rothemund and Menotti found that TPP was slowly formed by refluxing pyrrole, benzaldehyde, and pyridine in methanol for several days at atmospheric pressure.[4] They also obtained what is now recognized as TPC in admixture with the TPP from this reaction. Therefore, to initiate this present investigation, a number of solvents both with and without various metallic salts were refluxed with pyrrole and benzaldehyde and the time courses of the reactions followed spectrophotometrically using the extinction data of Dorough, *et al.*[13,14]

The usual procedure was to add 0.005 mole of redistilled pyrrole (approximately 0.35 ml.) and 0.005 mole of redistilled benzaldehyde (approximately 0.50 ml.) to 250 ml. of either the refluxing solvent or refluxing solvent containing 0.00125 mole of the metallic salt (reagent grade employed without further purification). Aliquots were then drawn at timed intervals and the spectra from 350 to 650 mμ were recorded, after appropriate dilutions, on either a Beckman DK-1 or a Bausch and Lomb Spectronic 505. Spectra in the Soret region were often rerun using a quartz spacer to diminish the usual 1.00-cm. path length to 0.100 cm. Although the yields (based on pyrrole) *vs.* time were routinely calculated from this spectrophotometric data, a few reactions were checked by chromatographic separation and weighing of the dried product. Such controls are necessitated by the frequent presence in the reaction mixtures of both highly scattering materials and by-products spectrally similar to the desired products. The yields obtained by the two methods always agreed to within the expected experimental errors (spectrophotometric yields were usually about 2–3% higher).

Porphyrins, metalloporphyrins, or mixtures of metallo derivatives and free bases or acid salts of porphyrins and chlorins were obtained with the following salt-

(1) This research has been supported by U. S. Army Signal Corps Research Grant DA-SIG-36-039-61-G9 and U. S. Army Research Office (Durham) Grant DA-31-124-ARO(D)-101.

(2) See part II, "Conference on Hemoglobin," Publication 557, National Academy of Sciences–National Research Council, Washington, D. C., 1958, pp. 66–140, for review and further sources. Also see "Porphyrin Biosynthesis and Metabolism," Ciba Foundation Symposium, Little, Brown, and Co., Boston, Mass., 1955.

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(6) R. N. Ball, G. D. Dorough, and M. Calvin, *J. Am. Chem. Soc.*, **68**, 2278 (1946).

(7) D. W. Thomas and A. E. Martell, *ibid.*, **78**, 1335 (1956).

(8) H. Corwin and V. L. Sydow, *ibid.*, **75**, 4484 (1953).

(9) A. W. Johnson and I. T. Kay, *J. Chem. Soc.*, 2418 (1961).

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(12) S. Krol, *J. Org. Chem.*, **24**, 2065 (1959).

(13) G. D. Dorough, J. R. Miller, and F. M. Huennekens, *J. Am. Chem. Soc.*, **73**, 4315 (1951).

(14) G. D. Dorough and F. M. Huennekens, *ibid.*, **74**, 3974 (1952).