SYNTHESIS OF TETRAPHENYLPORPHINS WITH REACTIVE GROUPS

IN THE BENZENE RINGS.

3.* USE OF DIAZOTIZATION FOR THE PREPARATION OF SUBSTITUTED

TETRAPHENYLPORPHINS

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Diazotization of tetra(aminophenyl)porphins has been employed to obtain halo- and hydroxy-tetraphenylporphins. Azo-coupling of tetra(diazophenyl)porphins has given isomeric tetra[(p-hydroxyphenylazo)phenyl]porphins.

There is currently much interest in metalloporphins, the catalytic properties of which are increasingly being utilized in a variety of important chemical processes. Of special significance are tetraphenylporphins, which are readily obtained by the single-step condensation of pyrrole with substituted benzaldehydes. The yields in this reaction, however, are highly dependent on the substituents in the benzene ring of the benzaldehyde, ranging from 1 to 35% [2, 3]. Since some benzaldehydes are difficult to obtain, difficulties were placed in the way of the wider study and use of substituted tetraphenylporphins.

These difficulties can be surmounted by varying functional groups in tetraphenylporphins which are obtained by condensation in high yields.

The aim of this investigation was to diazotize tetra(aminophenyl)porphins to give tetra-(diazophenyl)porphins, followed by conversion to the substituted tetraphenylporphins I-XIII (see below).



 $\begin{array}{c} I = -XIII \\ I = F; & II = F; & III = CI; & IV = CI; & VR^{1} = Br; & VI = R^{2} = Br; & VII = R^{1} = I; & VIII \\ R^{2} = I; & IX = R^{1} = OH; & XR^{2} = OH; & XI = P + HOC_{6}H_{4}N = N; & XII = R^{1} = n - HOC_{6}H_{4}N = N; & XIII \\ R^{2} = p + HOC_{6}H_{4}N = N; & nonspecified = R, R^{1}, R^{2} = H \end{array}$

The starting tetra(aminophenyl)porphins are fairly readily obtainable by reduction of the tetra(nitrophenyl)porphins [4, 5]. The latter were prepared in high yields by condensing pyrrole with the appropriate nitrobenzaldehydes [4, 5]. (see Formula, below table, following page.)

We have found that tetra(aminophenyl)porphins are readily diazotized with sodium nitrite in aqueous solutions of mineral acids. The resulting diazonium salt solutions are relatively stable, significant decomposition with evolution of nitrogen taking place only at temperatures above 25°C. The porphyrins were stable under the diazotization conditions, but on heat-

*For Communication 2, see [1].

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punoc	R ₁ *	Electronic absorption spec- trum, λ_{max} , nm (log)					Found, %			Empirical	Calculated, %			1 0%
Com		1	II	111	IV	Soret	с	н	N	tormul a	c	н	N	Yield
I	0,57 (A)	647	591	552	518	421	76,1	3,6	7,9	C ₄₄ H ₂₆ F ₄ N ₄	77.0	3,8	8,2	35
II		647 (3.62)	(5,00) 591 (3,85)	(5,32) 552 (3,94)	(4.37) 517 (4.30)	421	76.4	3,7	8,3	C44H26F4N4	77,0	3,8	8,2	(15) 40 (25)
111	0,35 (A)	648	592 (3.76)	550 (3.85)	515	421	70.4	3,5	7,3	C44H26Cl4N4	70,2	3,5	7,5	52
IV	0,59 (A)	651 (3,65)	593 (3,68)	551 (4,10)	517 (4,34)	422 (5,46)	69,8	3,8	7,6	$C_{44}H_{26}Cl_4N_4$	70.2	3,5	7,5	63
V	0,64 (A)	650 (3,76)	541 (3,95)	549 (4,24)	515 (4,39)	421 (5.74)	57,2	3,1	6,4	$C_{44}H_{26}Br_4N_4$	56,8	2,8	6,0	49,5
WI WI	0,70 (A)	652 (3,74)	595 (3,77)	553 (3,97)	517 (4,30)	422 (5,69)	56,9	2,6	6,4	C ₄₄ H ₂₆ Br ₄ N ₄	56,8	2,8	6,0	70
VIII	0.60 (B)	(3,72)	593 (3,81)	552 (3,96)	(4,33)	423 (5,66)	45,4	2,1	5,2	$C_{44}H_{26}I_4N_4$	47,3	2,3	5,0	56
IX	0.21 (C)	(3,82)	(3,84) 593	(4,07)	(4,35) 517	423 (5,70) 423	47,0 77.1	4 5	4,0 8.6	$C_{44}\Pi_{26}I_{4}N_{4}$	47,3	2,3	0,0 8 2	60
x	0,33 (D)	(3,57) 656	(3,72) 598	(3,87) 561	(4,26) 521	(5,65) 426	77.2	4.6	8.5	C44H 130IN4O4	77.9	4.5	8,3	72
xı	0.17; 0.26	(3,81) 656	(3,67) 599	(4,11) 561	(4,16) 526	(5,64) 436	74,9	4,1	15,0	C ₆₈ H ₄₆ N ₁₂ O ₄	74,6	4,2	15,3	74
	(E)T 0,45; 0,34	(3,84)	(3,95)	(4,06)	(4,38)	(5,36)								
хп	(E)); 0,06 (E);	647	590	553	517	428	75,2	3;9	15,8	$C_{68}H_{36}N_{12}O_4$	74,6	4,2	15,3	89
хш	0,45 (E)	(3,91) 650 (4,00)	(4,00) 595 (3,96)	(4,15) 559 (4,35)	(4,40) 521 (4,39)	(5,72) 435 (5,54)	75,0	4,0	15,3	C ₆₈ H ₄₆ N ₁₂ O ₄	74,6	4,2	15,3	98
		(1,00)	(0,00)	(4,00)	(2,00)	10,047								

TABLE 1. Properties of Substituted Tetraphenylporphins I-XIII

*The chromatographic systems are described in the experimental section.

[†]Yields in the thermal decomposition of the diazonium fluoroborates given in brackets.

*Separates into atropo-isomers.



ing diazotized tetra-(2-aminophenyl)porphin it undergoes oxidation to non-porphin compounds. Consequently, 2-substituted tetraphenylporphins are formed in low yields and with large amounts of difficultly-separable impurities. However, the azo-coupling of diazotized tetra-(2-aminophenyl)porphin with phenol has been accomplished successfully in the cold to give 74% of the azo-compound XIII. Diazotized tetra-(3- and 4-aminophenyl)porphins do not undergo oxidation, and on heating they give the hydroxy-tetraphenylporphins X and IX. The latter are obtained by condensing pyrrole with the appropriate benzaldehydes, in low yields [2]. Furthermore, tetra-(diazophenyl)porphins may readily be converted into the halo-tetraphenylporphins I-VIII in yields which are no lower, and in some instances higher, than when these are synthesized by condensation. Of interest are tetra[(p-hydroxyphenylazo)phenyl]-orphins, which are obtained readily by the azo-coupling of tetra(diazophenyl)porphins with phenol. In these compounds, two chromophoric systems are present, namely the porphin and the azo-dye. Compounds XI-XIII dissolve readily in alkalies to give orange-colored solutions. Reduction of XI-XIII with stannous chloride in hydrochloric acid gives the starting tetra(aminophenyl)porphins. The yields and some properties of the porphins obtained are shown in Table 1.



Fig. 1. Electronic absorption spectra of solutions of porphins XIII (----), XII (---), and XI (----) in pyridine.



Fig. 2. PMR spectra of porphins: α) XII, b) XIII, and c) XI in deuteroacetone.

Examination of the electronic absorption spectra of solutions of XI-XIII in pyridine shows that the absorption of the 2- and 4-isomers is broadened and shifted bathchromically as compared with that of the 3-isomer. This may be due to conjugation of the π -system of the azo-dye moiety with that of the porphyrin macrocycle. In the case of the 2-isomer this interaction appears to be steric in nature. This is confirmed by the PMR spectra in deuteroacetone. In the case of the 2-isomer, there is a considerable shift of the signals for the β -protons to high field (8.67 ppm) as compared with these signals for the 3- and 4-isomers (9.24 and 9.28 ppm). The broadening and splitting of the signals in the PMR spectrum of the 2-isomer is apparently due to the presence of a mixture of atropo-isomers.

EXPERIMENTAL

Electronic spectra were recorded on a Specord UV-VIS spectrophotometer in pyridine, and PMR spectra on a Tesla BS-497 in deuteroacetone, internal standard HMDS. The individuality and purity of the compounds were established by TLC on Silufol in the systems chloroform-hexane, 3:2 (A) and 2:1 (B), ether-benzene, 2:1 (C), acetone-hexane, 2:3 (E) and 1:1 (F).

Tetra-(3-fluorophenyl)porphin (I). To a solution of 0.5 g (0.74 mmole) of tetra-(3aminophenyl)porphin in 40 ml of 40% hydrofluoroboric acid was added with stirring and cooling at 5°C dropwise a solution of 0.2 g (2.9 mmoles) of sodium nitrite in 1 ml of water. To the resulting suspension of the diazonium fluoroborate was added with stirring a suspension of freshly-prepared copper (1 g) in 10 ml of water. The mixture was stirred on the boiling water bath until evolution of nitrogen ceased, and the solid was filtered off, washed with water, and dried in air at 100°C. The porphyrin was extracted from the solid by boiling with 200 ml of chloroform, and chromatographed on a column (4 × 40 cm) of trade III alumina with chloroform as eluent. The eluate was evaporated to 25 ml, and the porphyrin precipitated with 200 ml of methanol, filtered off, and dried in air at 100°C to give 0.18 g (35%) of product.

Tetra-(4-fluorophenyl)porphin (II) was obtained similarly from tetra-(4-aminophenyl)porphin, yield 0.2 g (40%).

<u>Tetra-(3-chlorophenyl)porphin (III)</u>. To a solution of 0.5 g (0.74 mole) of tetra-(3aminophenyl)porphin in a mixture of 5 ml of conc. HCl and 30 ml of water was added dropwise with stirring and cooling at 5°C a solution of 0.2 g (2.9 mmoles) of sodium nitrite in 1 ml of water. The resulting diazonium salt solution was added all at once to a solution of 0.5 g of cuprous chloride in 10 ml of conc. HCl. The mixture was heated on the boiling water bath until evolution of nitrogen ceased, and the solid was then filtered off, washed with 100 ml of 10% ammonia solution and water, and dried in air at 100°C. The resulting porphyrin was dissolved in 200 ml of chloroform at the boil, and chromatographed on a column (4 × 40 cm) of grade III alumina with chloroform as eluent. The eluent was concentrated to 25 ml, and the porphyrin precipitated with 200 ml of methanol, filtered off, and dried in air at 100°C to give 0.29 g (52%) of III.

Tetra-(4-chlorophenyl)porphin (IV) was obtained similarly, yield 0.35 g (63%).

<u>Tetra-(3-bromophenyl)porphin (V)</u>. To a solution of 0.5 g (0.74 mmole) of tetra-(3-aminophenyl)porphin in a mixture of 5 ml of 48% hydrofluoroboric acid and 30 ml of water was added dropwise with stirring and cooling at 5°C a solution of 0.2 g (2.9 mmoles) of sodium nitrite in 1 ml of water. The resulting diazonium salt solution was added all at once to a solution of 0.8 g of cuprous bromide in 10 ml of 48% hydrobromic acid. The mixture was heated on the boiling water bath until evolution of nitrogen ceased, and the solid was filtered off, washed with 100 ml of 10% ammonia and water, and dried in air at 100°C. The porphyrin was dissolved in 200 ml of chloroform at the boil, and chromatographed on a column (4 × 40 cm) of grade III alumina with chloroform as eluent. The eluate was concentrated to 25 ml, and the porphyrin precipitated with 200 ml of methanol, filtered off, and dried in air at 100°C to give 0.34 g (49.5%) of V.

Tetra-(4-bromophenyl)porphin (VI) was obtained similarly from tetra-(4aminophenyl)porphin, yield 0.48 g (70%).

<u>Tetra-(3-iodophenyl)porphin (VII)</u>. To a solution of 0.5 g (0.74 mmole) of tetra-(3-aminophenyl)porphin in a mixture of 5 ml of conc. H_2SO_4 and 30 ml of water was added dropwise with stirring and cooling at 5°C a solution of 0.2 g (2.9 mmoles) of sodium nitrite in 1 ml of water. The diazonium salt solution was added all at once to a solution of 1 g of potassium iodide in 10 ml of water. The mixture was heated on the boiling water bath until evolution of nitrogen ceased, and the solid was then filtered off, washed with 100 ml of 5% sodium hydroxide and water, and dried in air at 100°C. The resulting porphyrin was dissolved in 200 ml of chloroform at the boil, and chromatographed on a column (4 × 40 cm) of grade III alumina, eluent chloroform. The eluate was concentrated to 25 ml, and the porphyrin precipitated with 200 ml of methanol, filtered off, and dried in air at 100°C to give 0.42 g (56%) of VII.

Tetra-(4-iodophenyl)porphin (VIII) was obtained similarly from tetra-(4-aminophenyl)porphin, yield 0.56 g (68%).

<u>Tetra-(3-hydroxyphenyl)porphin (IX)</u>. To a solution of 0.5 g (0.74 mmole) of tetra-(3aminophenyl)porphin in a mixture of 10 ml of conc. sulfuric acid and 30 ml of water was added dropwise with stirring and cooling at 5°C a solution of 0.2 g (2.9 mmoles) of sodium nitrite in 1 ml of water. The resulting diazonium salt solution was heated on the boiling water bath until evolution of nitrogen ceased, and the solid was filtered off, dissolved in 200 ml of 5% sodium hydroxide, and filtered. The filtrate was neutralized with conc. HCl to pH 7, and the porphyrin filtered off, washed with 100 ml of 10% ammonia and water, and dried in the vacuum desiccator. For purification, the porphyrin was dissolved in 200 ml of boiling ether, and chromatographed on a column (5 \times 60 cm) of silica gel (L 100/250), eluent ether. The eluate was concentrated to 25 ml, the porphyrin (IX) precipitated with hexane, filtered off, and dried in air at room temperature to give 0.32 g (63%) of IX.

Tetra-(4-hydroxyphenyl)porphin (X) was obtained similarly from tetra-(4-aminophenyl)porphin, yield 0.36 g (72%).

<u>Tetra[2-(p-hydroxyphenylazo)phenyl]porphin (XI).</u> To a solution of 0.5 g (0.74 mmole) of tetra-(2-aminophenyl)porphin in a mixture of 0.5 ml of conc. sulfuric acid and 30 ml of water was added dropwise with stirring and cooling at 5°C a solution of 0.2 g (2.9 mmoles) of sodium nitrite in 1 ml of water. The resulting diazonium salt solution was added dropwise to a stirred solution of 0.3 g (3.2 mmole) of phenol and 1 g of KOH in 10 ml of water. The mixture was diluted to 150 ml with water, and filtered. The filtrate was neutralized with conc. HCl to pH 7, and the porphyrin filtered off, washed with 100 ml of 10% ammonia and water, and dried in the vacuum desiccator. The porphyrin was purified by dissolving it in 200 ml of boiling ether, and chromatography on a column (5 × 60 cm) of silica gel (L 100/250), eluent ether. The eluate was concentrated to 25 ml, the porphyrin precipitated with hexane, filtered off, and dried in air at room temperature to give 0.6 g (74%) of XI.

Tetra-[3-(p-Hydroxyphenylazo)phenyl]porphin (XII) was obtained similarly from tetra-(3aminophenyl)porphin, yield 0.72 g (89%), as was tetra-[4-(n-hydroxyphenylazo)phenyl)porphin (XIII) from tetra-(4-aminophenyl)porphin, yield 0.78 g (98%).

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ETHYL 1,4-DIHYDROPYRIDINECARBODITHIOATES AND THE ELECTRONIC EFFECTS

OF SULFUR-CONTAINING ESTER SUBSTITUENTS

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Methods have been developed for the synthesis of the ethyl esters of 2,6-dimethyll,4-dihydropyridine-3,5-bis(carbodithioic) and 4-aryl-2-methyl-5-oxo-4,5-dihydrolH-indeno[1,2-b]pyridine-3-carbodithioic acids. From the physicochemical properties (acid dissociation constants and electrochemical oxidation potentials of the 1,4dihydropyridines with sulfur-containing substituents in the β -positions, the electronic effects of these groups in the 1,4-dihydropyridine system have been determined. The inductive and resonance constants of these substituents in aromatic compounds have been found by ¹³C and ¹⁹F NMR spectroscopy.

Much attention has recently been devoted to 1,4-dihydropyridines (1,4-DHP) and hydrogenated nitrogenous heterocycles, with their unique chemical properties [1, 2] and manifold biological activity [3].

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