NITRATION OF TETRABENZOPORPHINS

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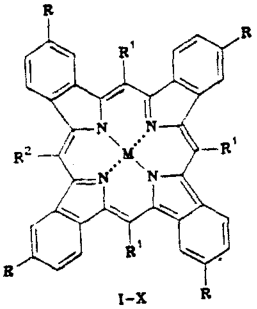
Zinc meso-trinitrotetrabenzoporphin and zinc meso-tetranitrotetrabenzoporphin were obtained by nitration of zinc tetrabenzoporphin and its tert-butyl-substituted analog with a mixture of nitric and acetic acids. A demetallated compound is formed in 88% yield when zinc meso-tetranitrotetrabenzoporphin is treated with HCl in acetic acid, and reduction of the nitro groups to amino groups occurs when it is treated with tin in acetic acid.

Electrophilic substitution reactions in the macrocycle are some of the possible methods for the synthesis of substituted tetrabenzoporphins (TBP) [1-4]. In our opinion, nitration is of greatest interest, since nitro compounds make it possible to proceed to TBP derivatives with various functional substituents. Information on the nitration of TBP is limited to nitration of its cadmium complex with a nitrating mixture at 0°C. Under the conditions of this reaction, the complex undergoes demetallation to give a monosubstitution product, presumably 3-nitro-TBP, in 23% yield [4], in which, however, the position of the nitro group was not rigorously proved. It, therefore, seemed of interest to find conditions for the nitration of TBP with retention of the central metal atom, to increase the degree of nitration, and to establish the site at which the nitro groups are incorporated.

We selected the zinc complex (I) of TBP and its tetra-4-tert-butyl-substituted analog (II) [5] as the subjects of our investigation. A mixture of nitro compounds is formed in 33% yield when I is treated with nitric acid in trifluoroacetic and acetic acids at 25°C. By preparative separation of this mixture on Silufol plates we were able to isolate two fractions, the first of which was the zinc complex (III) of meso-tetranitro-TBP.



I–X

I, III R=H, II, IV–X R=*t*-Bu; I, II, VI $R^1=R^2=H$, III, IV, VII $R^1=R^2=NO_2$, V $R^1=NO_2$, $R^2=H$, VIII $R^1=R^2=NH_2$, IX $R^1=R^2=AcNH$, X $R^1=R^2=C_{17}H_{35}CONH$; I–V, VIII–X *M*=Zn, VI, VII *M*=2H

Two signals of benzene ring protons with δ 9.33 (3-H and 6-H) and 8.09 ppm (4-H and 5-H), which are shifted 0.60 and 0.25 ppm, respectively, to stronger field as compared with I [6], are observed in the PMR spectrum* of this compound (Fig. 1) in the weak-field region. Each of the signals is a quartet with spin-spin coupling constants (SSCC) J_o = 6 Hz and J_m = 3 Hz. Signals of protons of methine bridges are absent in the spectrum of III. Three signals of protons of methine bridges with δ 11.39, 11.41, and 11.49 ppm with an integral intensity ratio of 4:3:1, respectively, and four signals of benzene ring protons with δ 8.15, 9.33, 9.43, and 9.85 ppm, the first of which coincides with the signal of I, and the last of which coincides with the signal of III, are observed in the PMR spectrum of the second fraction.

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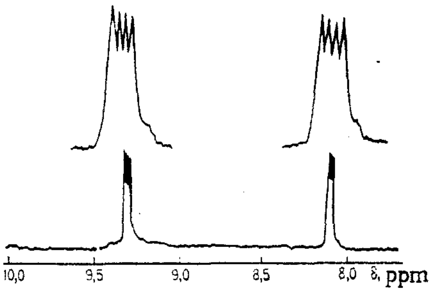

Fig. 1

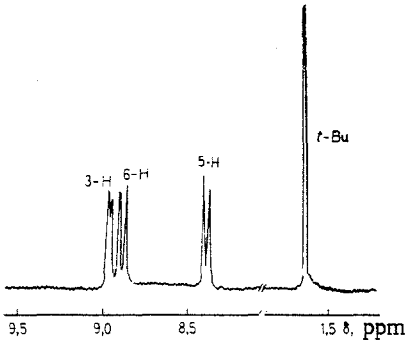

Fig. 2

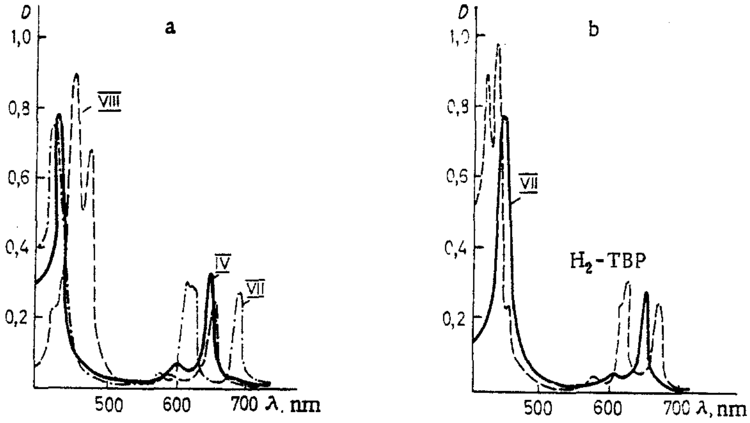

Fig. 3

Fig. 1. PMR spectrum (250 MHz) of III in C_5D_5N.

Fig. 2. PMR spectrum (360 MHz) of IV in C_5D_5N.

Fig. 3. Electronic absorption spectra: a) IV, VII, and VIII (in chloroform); b) VII and H_2-TBP (in DMSO).

The integral intensity ratio of the protons of the methine bridges and the benzene rings is 1:14. The PMR spectral data and the results of elementary analysis make it possible to assume that the second fraction is a mixture of mono-, di-, and tri-meso-nitro-substituted zinc complexes of TBP.

Products with a higher degree of substitution are not formed, probably as a consequence of the deactivating effect of the nitro groups already incorporated with respect to electrophilic substitution. An increase in the nitric acid concentration or the reaction time leads to a decrease in the yields of nitration products because of destruction of the macrocycle.

The increased solubility of zinc complex II in acetic acid made it possible to avoid the addition to the reaction mixture of trifluoroacetic acid, in the presence of which protonation and oxidation of the macrocycle are observed. A mixture of the zinc meso-tetranitrotetrakis(4-tert-butylbenzo)porphin (IV) (60% yield) and zinc meso-trinitrotetrakis(4-tert-butylbenzo)porphin (V) (6% yield) was formed in the nitration of II with nitric acid in acetic acid for 1 h at 25°C. After chromatographic purification and separation on aluminum oxide, we isolated IV and V in the form of monosolvates with pyridine. Bands of stretching vibrations of a nitro group at 1363 (sym) and 1522 cm^{-1} (asym) are present in the IR spectrum of a KBr pellet of IV. Four resonance regions with centers at δ 1.66, 8.18, 9.28, and 9.43 ppm, which are related to the protons of tert-butyl groups and benzene rings in the 5, 6, and 3 positions, respectively, are observed in the PMR spectrum of this compound (Fig. 2), and signals of protons of methine bridges are absent.

As in the case of I, an increase in the nitric acid concentration or the reaction time does not lead to products with a greater degree of substitution.

TABLE 1. Electronic Absorption Spectra of III-V and VII-X in Chloroform

Compound	λ_{max}, nm (log ε) [relative intensity]				
III	640 [1,0]	585 [0,13]		432 [2,61]	410 sh [1,02]
IV	646 (5,08)	596 (4,17)		436 (5,41)	412 sh (4,80)
V	644 (5,08)	590 (4,18)		434 (5,40)	410 sh (4,81)
VII	688 (4.75); 632 (4,803; 624 (4.82); 618 (4,83)	582 (4,24)		428 (5,22)	400 sh (4,89)
VIII	652 [1,0]	600 [0,28]	476 [2,84]; 456 [3,74]	430 [0,88]	
IX	648 (5,17)	594 (4,22)		436 (5,65)	410 (4,95)
X	650 (5,18)	596 (4,33)		422 (5,61)	414 (4,88)

Nitro compound IV is formed in the nitration of II with nitronium tetrafluoroborate in sulfolane; however, its yield is only ~2% as a consequence of pronounced destruction of the macrocycle. It should be noted that only monosubstitution products are formed in high yields in the nitration of metal complexes of phthalocyanine under similar conditions [7].

Attempts to nitrate demetallated VI with nitric acid in acetic acid were unsuccessful, since protonation, which deactivates electrophilic substitution in the macrocycle, occurs under these conditions. meso-Tetranitrotetrakis(4-tert-butylbenzo)porphin (VII) was obtained only by demetallation of zinc complex IV by passing a stream of hydrogen chloride through a solution of the complex in acetic acid.

Attempts to reduce zinc complex IV by refluxing with stannous chloride in concentrated hydrochloric acid with and without ether, sodium borohydride, and sodium hydrosulfite in aqueous alkaline solution, as well as by hydrogenation in the presence of Pd/C in alcohol, were unsuccessful. Only by reduction of IV with tin metal in refluxing acetic acid were we able to obtain zinc meso-tetraaminotetrakis(4-tert-butylbenzo)porphin (VIII), which we could not isolate in analytically pure form in sufficient amounts because of its lability during chromatographic purification. Compound VIII was characterized in the form of zinc meso-tetra-N-acetamido- (IX) and zinc meso-tetra-N-stearylaminotetrakis(4-tert-butylbenzo)porphin (X), which were obtained by refluxing amino compound VIII for 1 h in acetyl chloride or a benzene solution of stearyl chloride; the yields were 78 and 40%, respectively, based on nitro compound IV.

The electronic absorption spectra of solutions of the synthesized III-V and VII-X at 220-800 nm were recorded (Table 1). As in the case of the unsubstituted compounds, the presence of two groups of bands, viz., Q and B [8], is noted in their electronic absorption spectra, i.e., the character of the spectrum does not change substantially in the case of nitro and amino substitution. However, in contrast to phthalocyanines and porphyrazines [9, 10], for which nitro substitution has virtually no effect on the positions of the absorption bands, in the case of TBP we noted a bathochromic shift (up to ~25 nm) simultaneously of the Q and B bands both for zinc complexes III-V and for demetallated compound VII. An even greater bathochromic shift of the corresponding bands is observed in the case of amino (VIII) and N-acyl (IX, X) derivatives.

A characteristic property of nitro-substituted TBP is their increased, as compared with other known TBP, resistance to oxidizing agents in solutions and particularly on sorbents (aluminum oxide, silica gel). One should note the increased acidity of the N–H protons of VII, which readily forms a dianion even when it is dissolved in DMSO, whereas the addition of an alkali is required for the formation of a dianion in the same solvent in the case of II.

EXPERIMENTAL

The electronic absorption spectra of chloroform solutions (10^{-5}-10^{-4} m) were measured with a Hitachi-356 spectrophotometer. The IR spectra (KBr pellets) were recorded with a UR-20 spectrometer. The PMR spectra were obtained with Bruker WM-250 (250 HMz) and Bruker WM-360 (360 MHz) spectrometers in deuteropyridine with tetramethylsilane (TMS) as the internal standard. Activity II aluminum oxide was used for the chromatographic purification and monitoring of the individuality of the synthesized compounds. Compound III was isolated preparatively on Silufol UV-254 plates.

Zinc meso-Tetranitrotetrabenzoporphin (III). A 10-ml sample of a 5% solution of nitric acid in acetic acid was added with stirring to a solution of 0.06 g (0.14 mmole) of I in a mixture of 20 ml of trifluoroacetic acid and 30 ml of acetic acid, after which the mixture was maintained at 25°C for 1 h and then poured into 250 ml of water. The resulting precipitate was removed by filtration, washed successively on the filter with 100 ml of water, 50 ml of 5% sodium hydroxide solution, and 100 ml of water, and dried at 25°C for 12 h. The residue was dissolved in 5 ml of pyridine, and the solution was transferred to a chromatographic column (3 × 40 cm) packed with aluminum oxide and eluted with chloroform–pyridine (4:1). Repeated chromatography [chloroform–benzene (2:1)] and evaporation of the solvent gave 0.03 g (33%) of a mixture of nitro products containing an average of three nitro groups. Found, %: C 61.9, H 3.2, N 14.3. $C_{36}H_{17}N_7O_6 \cdot C_5H_5N$. Calculated, %: C 62.5, H 2.8, N 14.2. Preparative separation of the mixture on 10 Silufol UV-254 plates (20 × 20 cm) with elution by benzene gave 15 mg (17%) of III with R_f 0.65 (Silufol, benzene).

Zinc meso-Tetranitro- and meso-Trinitrotetrakis(4-tert-butylbenzo)porphin (IV, V). A 50-ml sample of a 5% solution of nitric acid in acetic acid was added in portions in the course of 5 min with stirring to a solution of 0.25 g (0.31 mmole) of II [5] in 300 ml of acetic acid, after which the mixture was maintained at 20°C for 1 h and then poured into 500 ml of water. The resulting precipitate was removed by filtration, washed on the filter with 200 ml of water, and dried. The residue was dissolved in 10 ml of pyridine–benzene (1:50), and the solution was transferred to a chromatographic column packed with aluminum oxide and eluted with the same mixture. The green fraction was collected to give 0.25 g of a substance which, according to the results of thin-layer chromatography (TLC) [ethyl acetate–hexane (1:2)], was a mixture of two compounds. The first fraction [0.20 g (60%)] was IV with R_f 0.70 [Al_2O_3, ethyl acetate–hexane (1:2)]. Found, %: C 65.1, H 5.1, N 12.0. $C_{52}H_{48}N_8O_8 \cdot C_5H_5N$. Calculated, %: C 64.7, H 5.1, N 11.9. The second fraction [0.02 g (6%)] was V with R_f 0.5. Found, %: C 67.8, H 6.2, N 10.9. $C_{52}H_{49}N_7O_6 \cdot C_5H_5N$. Calculated, %: C 67.6, H 5.4, N 11.0.

meso-Tetranitrotetrakis(4-tert-butylbenzo)porphin (VII). A stream of hydrogen chloride was passed through a solution of 0.3 g (0.31 mmole) of IV in 300 ml of glacial acetic acid for 30 min at 25°C, after which the mixture was diluted with 500 ml of water, and the resulting precipitate was removed by filtration, washed on the filter with 250 ml of water, and air dried. It was then dissolved in 10 ml of benzene, and the solution was transferred to a chromatographic column packed with aluminum oxide and eluted with benzene–hexane (1:1) to give 0.23 g (88%) of VII with R_f 0.41. Found, %: C 68.6, H 5.7, N 12.2. $C_{52}H_{52}N_8O_8$. Calculated, %: C 68.3, H 5.5, N 12.3.

Zinc meso-Tetra-N-acetamidotetrakis(4-tert-butylbenzo)porphin (IX). A 2-g (16.9 mmole) sample of granulated tin was added to a solution of 0.07 g (0.72 mmole) of IV in 50 ml of glacial acetic acid, and the reaction mixture was then cooled and filtered. The filtrate was diluted with 100 ml of water, and the resulting precipitate was separated by filtration and air dried to give 56 mg of crude VIII, which was dissolved in 15 ml of acetyl chloride. The mixture was refluxed for 1 h, the excess acetyl chloride was removed by distillation, and the residue was dissolved in 5 ml of chloroform. The solution was transferred to a chromatographic column (3 × 30 cm) packed with aluminum oxide and eluted with chloroform. The solvent was removed to give 53 mg (78%) of IX with R_f 0.19 (Al_2O_3, chloroform). IR spectrum (KBr): 1690 (NHCO), 2870-2960 (C–H), and 3400 cm^{-1} (N–H). Found, %: C 70.5, H 6.4. $C_{60}H_{64}N_8O_4$. Calculated, %: C 70.2, H 6.3.

Zinc meso-Tetra-N-stearylaminotetrakis(4-tert-butylbenzo)porphin (X). A 6-g (20 mmole) sample of stearyl chloride was added to a solution of 0.20 g of amino compound VIII, obtained from 0.25 g (0.26 mmole) of nitro compound IV, in 50 ml of benzene, and the mixture was refluxed for 1 h. The benzene was removed by distillation, and the residue was purified by preparative TLC on a loose layer of aluminum oxide on six plates (15 × 20 cm) with collection of the fraction with R_f 0.21 (chloroform) to give 0.18 g (40%) of X. IR spectrum (KBr): 1670 (NHCO), 2855-2960 (C–H), and 3395 cm^{-1} (N–H). Found, %: N 5.1. $C_{124}H_{129}N_8O_8$. Calculated, %: N 5.8.

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