The Study of Atropoisomers of *Meso*-Tetrakis[2.2]paracyclophanylporphyrin

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Theoretical considerations of atropoisomers of the title compound have revealed the existence of a large number of stable isomeric species. Syntheses, carried out according to two procedures at widely separated temperatures, resulted in the formation of mixtures of atropoisomers in good yield. Two isomeric fractions have been separated and characterized. Some analytical methods have been worked out and have proved useful in separational techniques.

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In the preliminary communication [1] we have described the formation of the porphyrin all-*meso*-substituted by [2.2]paracyclophane, the latter attached in 4 or 5 position. This *meso*-tetrakis[2.2]paracyclophanylporphyrin, **1** is not only unique because of its porphine and cyclophane components, but also because of the properties as a porphyrin derivative [2]. This stimulated the authors' interest in improving the conditions of synthesis, purification of the product and, in particular, in approaching the problem of atropoisomers formed, which for the reasons of molecular geometry of **1** seemed to be very complicated, see Figure 1 and 2.

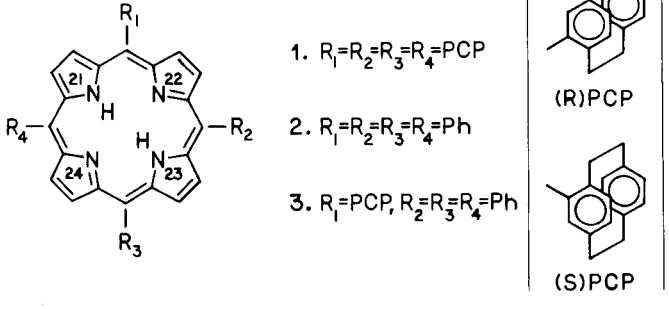


Figure 1. The derivatives of porphyrin under consideration: **1**, *meso*-tetrakis[2.2]paracyclophanylporphyrin; **2**, *meso*-tetraphenylporphyrin; **3**, *meso*-[2.2]paracyclophanyltriphenylporphyrin. The [2.2]paracyclophanyl substituent(s), PCP, in **1** and **3** are in the *R* or *S* configurations.

As stated in [1] we tried to obtain crystals of **1** for X-ray diffraction study. However, we attribute our lack of success in this regard to the fact that the compound was a racemic mixture of **1** since the paracyclophanyl (PCP) units originated from (*R*+*S*)[2.2]paracyclophane-4-carbaldehyde. Although the results presented in [1] referred to pure *meso*-tetrakis[2.2]paracyclophanylporphyrin, it was in fact a mixture of unidentified atropoisomers and the ^{1}H nmr spectra gave a complicated and blurred picture. Our present evidence shows that for isolated "narrow" fractions of atropoisomers it is possible to achieve microcrystalline forms. Their crystal growth however, is inhibited by the presence of a number of the elements of chirality and specific geometry of **1**.

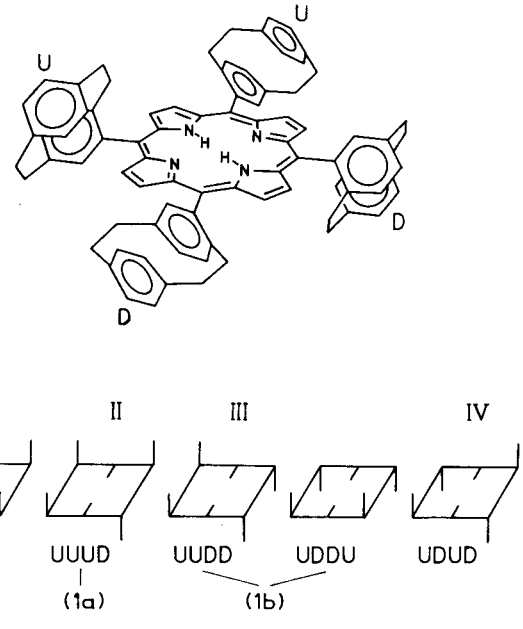


Figure 2. The structure of the **UDDU** atropoisomer of *meso*-tetrakis-[2.2]paracyclophanylporphyrin, **1**, based on the ORTEP drawing. Schematic drawings of the atropoisomeric groups I to IV.

The theoretical geometry optimization procedure [2] showed recently that the planes of porphyrin and PCP form the dihedral angle θ approximately in-between the perpendicular and co-planar, for each *R* or *S* chiral substituent represented by the PCP unit. This results in two alternate locations of the benzene ring not bonded directly to the porphyrin core: one location above ("up") the plane of the latter, *U*, another - below ("down") that plane, **D**. For each *R* and *S* configuration of the PCP substituent there exists a pair of **U**-location or **D**-location. Authors' considerations, resembling those presented for some derivatives of *meso*-tetraphenylporphyrin, **2** [3,4], suggest the existence of four groups of atropoisomers of **1**, shown

schematically in Figure 2, each containing numerous species, what greatly increases (to several dozens) the total number of atropoisomers [2]. Because of that, it is preferable to consider the problem in terms of the number of groups of atropoisomers rather than the number of individual isomers. Since atropoisomers of the same group are probably inseparable, we will denote the class of atropoisomers **UUUU** as belonging to group I, **UUUD** to group II, **UUDD** and **UDDU** to group III and **UDUD** to group IV. Note that the group I of atropoisomers (**UUUU**) contains the species of the **RRRR, RRRS, RRSS** and **RSRS** configurations. Similarly complex picture characterizes the groups II to IV, see Figure 2. According to statistics, the probability of the occurrence of these four groups should be 1:4:2:1. The overall picture is novel for the stereochemistry of porphyrins. It differs from what is well known for hindered biphenyl derivatives and those described for some *meso*-tetraarylporphyrins [3,4].

As the result of the described situation, **1** differs very much from the derivatives of **2**. For instance in the "picket fence" porphyrin of Collman [4], due to the perpendicular position of porphine and phenyl planes, the *ortho*-attached "pickets" resulted in much greater differentiation of molecular structures than in **1** as reflected in the dipole moments of atropoisomers, like $\alpha,\alpha,\alpha,\alpha;\alpha,\alpha,\beta,\beta$, *etc.* Among them, only the extreme atropoisomer $\alpha,\alpha,\alpha,\alpha$ formed crystals. In the case of **1**, the extreme atropoisomers differ in their dipole moments to a much smaller extent than the derivatives of **2**. Because the overall dipole moment matters so much in chromatographic separation, one would expect, that in spite of the large number of existing atropoisomers, the atropoisomer groups I to IV are separable. Atropoisomers of the groups III and IV have zero dipole moments, $\mu = 0$, while groups I and II have $\mu > 0$. The greatest dipole moment should appear for the group I. Our calculations [5] for **UUUU** gave a dipole moment $\mu = 0.447$ D, with the charge term mainly contributing to this value.

As discussed elsewhere [2], the geometry optimization procedure showed that all calculated atropoisomers are separated by energy barriers high enough to prevent atropoisomer interconversion. These barriers are much higher than the value of 24 kcal/mol calculated by Gottwald and Ullman [3] for *ortho* hydroxy substituted **2**. We did not find interconversion of atropoisomers of **1** under conditions in which both the partial isomerization of *meso*-tetra-(*o*-aminophenyl)porphyrin took place and a 5% isomerization of *o*-pivaloyl derivative of **2** was observed [4]. The calculated total energy of the atropoisomers of **1** is within 20 kcal/mol of each other [2]. The **UUUU** and **UUUD** atropoisomers are higher in energy than **UDUD** which represents the lowest energy form.

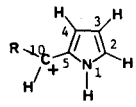
As described in the Experimental, under appropriate conditions a number of bands appear in the tlc corresponding to the groups of atropoisomers. Out of groups I, II, III and IV, the groups of atropoisomers II and III were separated. They were considered as "individuals" and denoted respectively, **1a** and **1b**, according to the correlation with the R_f values found, and theoretically calculated dipole moments. The yield of the atropoisomeric group I was extremely low and of insufficient purity. The strong adsorption on silica gel kept this fraction along with polymeric material immobilized. On the other hand, the atropoisomeric group IV, as seen on the tlc plates, formed very diffused band of low intensity and did not seem to be suitable for separation at this stage of investigation. The isolated atropoisomers **1a** (II) and **1b** (III), showed identical m/e values (ms) and gave well resolved, reproducible ^{1}H nmr spectra for which a reasonable qualitative interpretation could be given. The uv-vis spectra showed band patterns expected for **1** [1], compare also [6], with band positions differing for both atropoisomers by only 0-3 nm.

The generally accepted mechanism of porphyrinogen formation, *e.g.* in the synthesis of **2** [7], involves a number of successive steps, each requiring the electrophilic attack on an α-pyrrole center by the carbocation originating from benzaldehyde or benzhydryl type intermediate. This results in the successive formation of linear di-, tri- and tetrameric structures, the latter forming the cyclic structure (with a small yield because of the competition with linear polymer formation), which finally reaches stabilization by dehydrogenation into [18]-annulene-type macrocycle. The equilibria of all steps including the cyclic $\rightleftharpoons$ linear equilibrium are reversible as demonstrated by Lindsay *et al.* [8], until porphyrinogen loses six hydrogens to yield the substituted porphyrin. The difference in electronic structure between [2.2]paracyclophane-4-carbaldehyde [9] and benzaldehyde raised the question as to whether the electrophile generated from the former would be as effective as the electrophile generated from the latter. We calculated [5] the charge density at the cationic center and at the remaining centers for the respective models referring to the formation of dipyrrolemethane, see Table 1. The calculations showed that the one-electron defficiency formally localized in the conjugated model system at the C^+ center is distributed over the whole system. The changes of electrophilicity of the C^+ center are in the order of R: H < Ph < PCP because the respective π-electron density values on the 2pz atomic orbital are q^π: 0.689 > 0.610 > 0.599. This demonstrates that the electrophilic attack of the model structure containing the PCP unit is even more favorable than that of the structure containing phenyl. The optimization of geometry of the models listed in Table 1 shows that the orthogonal position of the planes of Ph or PCP and the C^+-pyrrole fragment represents the conformation of the lowest energy. This suggests in turn that at the stage of the formation of **1**, the geometry of double-layered PCP does not create any

obstacle to the progress of reaction. One can, therefore, expect that the mechanisms of formation of **1** and **2** should be very similar.

Table 1

The Distribution of Total Electron Density, q^t, *and* π-Electron Density, q^π in Three Pyrrole-α-C^+ Models Calculated by CNDO/2



Atoms		R = H	R = Ph (90°)	R = PCP (90°)
C 10	q^t	3.880	3.826	3.824
	q^π	0.689	0.610	0.599
C 2	q^t	3.772	3.806	3.810
	q^π	0.767	0.829	0.834
C 3	q^t	4.055	4.058	4.059
	q^π	1.089	1.097	1.099
C 4	q^t	3.875	3.899	3.943
	q^π	0.772	0.818	0.819

This prompted us to approach the problem of the different yields of **1** for the (i) room temperature and (ii) high temperature syntheses which has been previously found for **2** as 40% [8] and 20% [10] respectively. Because of the importance of reagent concentration with regard to the yield of **2** emphasized by Lindsay *et al.* [8], we carried out the comparison of (i) and (ii) under the concentration of reagents as similar as possible, expecting that for **1** the factor of concentration determines the cyclic *vs* linear oligomerization. We found that for the optimum concentration of [2.2]paracyclophane-4-carbaldehyde the yield of **1** in the high temperature synthesis can be greatly improved, from 7% [1] to *ca.* 24% and it approaches the yield achieved in the room temperature synthesis, *ca.* 28%. The high temperature process enables the formation of higher energy atropoisomers (for details see [2]), therefore the ratio of the latter should be greater in that process than in the room temperature synthesis. As pointed out in the Experimental we found, when the high temperature process was applied, a somewhat higher yield of the **UUUD (1a)** atropoisomer than of the **UUDD** and **UDDU (1b)** atropoisomers (**UUUD** represents higher energy than the others).

The difference between the separated atropoisomers of **1** were investigated by the uv-vis absorption spectroscopy and ^{1}H nmr spectroscopy. It appeared that the electronic spectra of the **1a** and **1b** atropoisomers were similar but not identical, in regards to the shapes, intensities and the positions of bands, see Figure 3. The differences in band positions, **1a-1b**, were as follows: band I, 1 nm; band II, 0 nm; band III, 3 nm; band IV, 3 nm; and Soret band, 1 nm. However, both atropoisomers show remarkable bathochromic shifts and differences in band intensities when compared to **2**, *e.g.*, for **1a** the Soret band is shifted bathochromically by 20 nm and the intensity decreases by $|\Delta\epsilon| = 100000$. For the band I the bathochromic shift is 21 nm and the intensity increases by $|\Delta\epsilon| = 2200$. Comparison of our results concerning **2**, **3** and **1** demonstrates a strictly linear dependence of bathochromic shifts on the number of PCP units present in a porphyrin system, respectively 0, 1 and 4, see Figure 4. As far as the changes of intensity are concerned, band II of mixed electron-vibronic nature (for the list of bands see Experimental) remains constant, the intensities of the Soret band and band IV linearly decrease, while that of band I and band III linearly increase. There is every reason to assume that when two and three phenyls in *meso*-tetraphenylporphyrin, **2**, are replaced by the PCP units the obtained paracyclophanylporphyrins would fit the presented correlations [11]. The protonation transforming **(1)**H_2 into **(1)**H_4^{2+} changes the uv-vis spectra, see Figure 3, due to the increase of the symmetry of the system. The intensity of the Soret band decreases, and the longest wavelength band increases. The latter band shows the significant bathochromic shift of 48 nm for **1a** and of 17 nm for **1b**. This demonstrates that in the symmetrical system of **(1)**H_4^{2+} with the 2+ charge delocalized over the porphin core, the influence of the geometry of molecule on the longest wavelength band is much greater than in the free base **(1)**H_2.

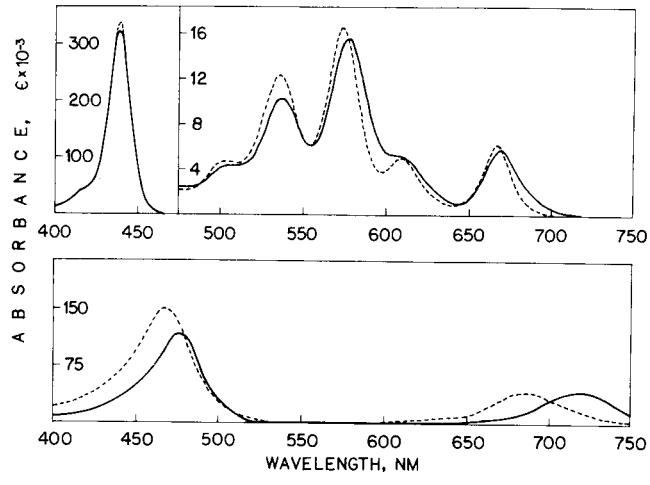


Figure 3. The electronic spectra of the **1a** (—) and **1b** (---) atropoisomers of *meso*-tetrakis[2.2]paracyclophanylporphyrin. Upper spectra (benzene) show the absorption of the free bases **(1)**H_2. Lower spectra (0.01 *M* trifluoroacetic acid in benzene) show the absorption of the protonated forms **(1)**H_4^{2+}. For the detailed values of λ max and log ε see the Experimental section.

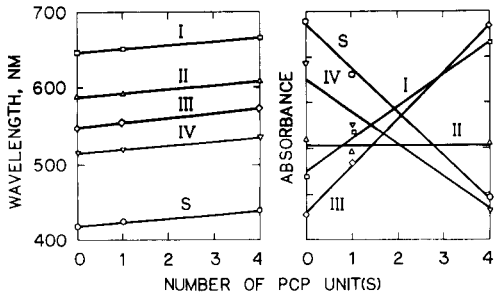


Figure 4. The changes in wavelength (left) and absorbance (right) of the bands (I, II, III, IV and (S)oret) *vs* the number of [2.2]paracyclophanyl substituents replacing the phenyl rings in *meso*-tetraphenylporphyrin.

The well resolved ^{1}H nmr (300 MHz) spectra of both atropoisomers showed similar trends of the down- and up-field shifts of the easily distinguishable groups of signals, these shifts exhibiting individual features. At the same time the spectra showed basic differences for porphine protons when compared to **2**. The differences between the atropoisomers consist of different degree of deshielding of some β-pyrrole protons. The shifts measured in deuteriochloroform are more down-field for **1b** than for **1a**, see Figure 5. In the first case, three Hs appear at δ 10.44 s, 9.86 d and 8.72 d ppm while for **1a** two pairs of Hs appear at δ 9.91 d and 8.79 d ppm, respectively. The skeleton of **1** gives rise to a complicated and characteristic interaction of (+) and (-) zones of magnetic anizotropy originating from porphine core and from four PCP units. Because no ring in PCP unit can be located perpendicular to the porphine plane, (in contrast to the location of phenyl rings in **2**) the magnetic anisotropy effects result in the substantial spread of the signals of the β-pyrrole protons (8 H) over the range 10.44 to 8.13 (9.92 to 8.13) ppm, the values in brackets referring to **1a** atropoisomer. The signals of aromatic PCP protons (28 H) range from 7.49 to 6.21 (7.50 to 6.34) ppm. The aliphatic protons (32 H) of PCP ethane bridges fall in the region 3.73 to 1.80 (3.70 to 1.79) ppm. All this remains in sharp contrast to β-pyrrole protons of **2** at 8.70 ppm (8 H, s) and of aromatic and aliphatic protons of the molecule of [2.2]paracyclophane at 6.34 (8 H, s) and 3.05 ppm (8 H, s), respectively. However, even the general consideration of the possible locations of the double-layered PCP units twisted relative to the plane of porphine by the θ angle points to the existence of different magnetic surroundings for most of the β-pyrrole protons, see Figure 2. On the other hand, the magnetic ring current in the porphyrin core enhances the deshielding of PCP protons (with the exception of two protons) and separates PCP aliphatic protons, highly sensitive to spatial position, into one group which is moderately deshielded and the other one which is much more shielded as compared to the molecule of [2.2]paracyclophane.

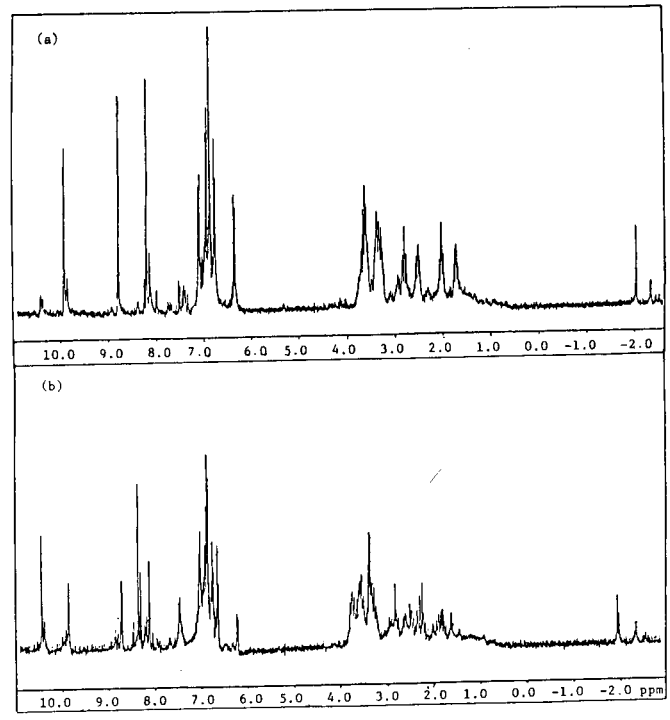


Figure 5. The ^{1}H nmr (300 MHz) spectra in deuteriochloroform of the **1a** and **1b** atropoisomers of *meso*-tetrakis[2.2]paracyclophanylporphyrin.

Particular attention must be paid to strongly shielded NH protons appearing at δ -2.04 and -1.94 ppm in the spectra of **1a** and **1b** respectively. These signals are located at substantially lower field than the NH protons of **2** (-2.74 ppm) and **3** (-2.63 ppm) [6]. One of the reasons is due to decrease in ring current caused by the PCP substituents, similar to the well known influence of phenyls on the ring current of the central porphyrin core in **2** [12]. In the latter case, the NH proton signals are shifted from δ *ca.* -4.0 ppm (porphine) [13] to the δ region of -3 ppm.

The redistribution of charge, calculated when **1** is compared with **2** and **3**, affects not only the *meso* positions but also the two N atom centers [5]. These centers show the π-electron densities q^{π}: 1.270 (N22,N24), 1.262 (N22,N24) and 1.282 (N24), the values practically the same for both atropoisomers of **1**. The location of the N centers is shown in Figure 1. At the same time, the alteration of the charge distribution takes place in the PCP unit, when the latter is compared to [2.2]paracyclophane. All this influences the ring current [14] and therefore is responsible, at least in part, for the shifts of porphyrin core NH protons. The tautomeric equilibrium of the NH and N: centers, so characteristic of **2** [15], as reflected by their appearance as the only singlet signal at room temperature, is known to be perturbed by the attachment of some substituents to the β-pyrrole positions, but not to the *meso* positions. Replacement of one phenyl in **2** by the PCP unit (resulting in the formation of **3**) still gives the spectrum with the singlet

signals of two NH protons (at -2.63 ppm) [6] at room temperature which is characteristic of the tautomeric equilibrium.

The study of atropoisomers described in this paper is necessary before any investigation of the phenomena of ligation, dioxygen binding and catalysis shown by the metallated derivatives of **1** could be reasonably undertaken. These properties deserve attention because of the unusual influence of the PCP substituent on the electronic structure of the paracyclophanylporphyrin which, among other things, decreases the first oxidation potential on the electrode to a level never found heretofore in any porphyrin system [6].

EXPERIMENTAL

A. Chemicals and Materials.

[2.2]Paracyclophane, dichloromethyl methyl ether, propionic acid puriss. p.a. and trifluoroacetic acid were used as obtained from Fluka. Titanium(IV) chloride, pyrrole, 1-bromobutane 99% (Aldrich) were used without further purification. Methylene chloride and chloroform (EM Science) were used for chromatography as received but for spectroscopic measurements were distilled from anhydrous potassium carbonate and kept on molecular sieves. Benzene OmniSolv, petroleum ether OmniSolv, ethyl acetate OmniSolv, pyridine OmniSolv and *N,N*-dimethylformamide OmniSolv were used as received from EM Science. Florisil (Applied Sciences) 60/200 mesh and Florisil (Aldrich) 100-200 mesh were used for column chromatography. DC-Fertigplatten Kieselgel 60 F_{254}, layer thickness 0.25 mm (Merck) were used for monitoring purposes in tlc. PSC-Fertigplatten Kieselgel 60 without fluorescent indicator layer thickness 2 mm (Merck) were used for preparative separations.

B. Solutions.

Pyrrole, 1.0 *M* solution: 7.0 ml of pyrrole was diluted with propionic acid to 100 ml. The solution was kept in refrigerator for a period not longer than one week if there was no precipitation of polymeric material or distinct coloration. Dichloromethyl methyl ether, 1.0 *M* solution: 8.9 ml of dichloromethyl methyl ether was diluted with methylene chloride to 100 ml. Titanium(IV) chloride, 2.5 *M* solution: 27:5 ml of titanium(IV) chloride was diluted in volumetric flask to 100 ml. Boron trifluoride 0.25 *M* solution: 3.1 ml of boron trifluoride etherate was diluted with chloroform to 100 ml.

C. Synthesis.

[2.2]Paracyclophane-4-carbaldehyde.

Although the procedure of Hopf and Raulfus was followed [16], it was necessary to introduce some modifications. The reason for that was due to a number of by-products which appeared on product's tlc when the excess of dichloromethyl methyl ether was applied as given in [16]. In a 1 ℓ three-necked, round-bottomed flask equipped with reflux condenser and an anhydrous calcium chloride moisture protecting tube, dropping funnel and thermometer, was placed 500 ml of methylene chloride and 5 g (24 mmoles) of finely ground [2.2]paracyclophane was added. The content of the flask was stirred by magnetic bar at room temperature until the solid was dissolved. The solution was cooled in an ice-bath with continued vigorous stirring until the temperature dropped to +8° and fine crystals were precipitated. The 2.5 *M* solution of titanium chloride (15 ml, 37 mmoles) was added dropwise causing a dark orange coloration and small increase of temperature. After 3 minutes of mixing when the temperature dropped again to 8°, 36 ml of 1.0 *M* solution of dichloromethyl methyl ether (36 mmoles) was introduced within 5 minutes. The ice bath was removed and the black solution was stirred for 1 hour at room temperature. The reaction mixture was poured onto 500 g crushed ice and mechanically stirred until the ice was completely melted. The lower layer was separated and washed twice with 5% hydrochloric acid and then several times with water, with 5% sodium hydrogen carbonate and once again with water. The organic layer was dried with anhydrous magnesium sulfate overnight. The removal of solvent left 5.2 g of crude product mp 133-140°. After recrystallization from glacial acetic acid (30 ml), 4.28 g of white needles mp 140-142° was obtained. The yield was 75%.

Meso-Tetrakis[2.2]paracyclophanylporphyrin (**1**).

(i) Condensation at 140° (in Boiling Propionic Acid).

[2.2]Paracyclophane-4-carbaldehyde (1.2 g, 5 mmoles) was dissolved in 500 ml of propionic acid in a 2 ℓ three-necked round-bottomed flask. The solution was heated to the boiling point and then 1.0 *M* solution of pyrrole (5 ml, 5 mmoles) was introduced within 5 minutes. Boiling and vigorous stirring was continued for six hours. Propionic acid was distilled off under reduced pressure from the water bath. The dark, sticky residue was dissolved in 150 ml of chloroform and washed with 5% sodium bicarbonate until neutral. The solution was dried with anhydrous potassium carbonate and the solvent removed by distillation. The crude product, an amorphous black solid, 1.39 g (98% of theoretical amount) was determined spectrophotometrically at the Soret band wavelength and by differential absorption method in benzene solution giving the porphyrin content 23.4% and 20.4%, respectively. The separation of the porphyrin product from the polymeric material was achieved according to the following procedure. The crude product (1.0 g) was dissolved in 200 ml of methylene chloride, then placed in 250 ml erlenmayer flask with ground glass stopper and weighed. An aliquot of 200 μl was taken, diluted with methylene chloride in volumetric flask to 100 ml, and its absorption measured at 438 nm. Silica gel (5 g) was added to the original solution and stirred with magnetic bar for 15 minutes. A second aliquot of 200 μl of the solution was taken, diluted to 100 ml and the concentration was again determined spectrophotometrically. The solution was decanted carefully and the silica gel was transferred to a sintered glass filter. A slight pressure was applied to the upper part of the funnel and the filtrate was combined with the previously decanted portion of the solution and placed in the erlenmayer flask. The flask was weighed and the difference in mass was determined. The silica gel on the sintered glass funnel was washed with a mixture of 100 ml of the solution used for photometric determination and 10 ml of ethyl acetate. The last few ml of the filtrate was photometered at 438 nm. If the absorption was below 1.0 the washing was ended, if not, the washing was continued with methylene chloride-ethyl acetate mixture 10:1 until the value of previously measured absorption was reached. The methylene chloride-ethyl acetate filtrate was evaporated to dryness and the residue was transferred to the erlenmayer flask using methylene chloride in quantity as calculated from losses connected with the filtration of silica gel. The next portion of 5 g of silica gel was added to the above described solution and stirred for 15 minutes. Aliquot of 200 μl was taken, diluted to 100 ml and photometered. The silica gel was filtered off and then washed with a mixture of 10 ml ethyl acetate and 100 ml of photometered solution. The above described operations of adsorption of polymeric material on silica gel with following desorption of porphyrins by means of methylene chloride-ethyl acetate (10:1) were repeatedly performed until the absorption quotient A_{574}/A_{474} measured in dimethylformamide (150 μl of the methylene chloride solution in 5 ml of DMF) was not less than 7. Florisil (30 g) was then added to the solution and the slurry was evaporated *in vacuo*. The dry material was put on the top of a chromatography column packed with 70 g of florisil. Washing with methylene chloride-petroleum ether (5:1) was performed (approximately 250 ml) until there was no residue after evaporation of 25 ml. The washing was continued with methylene chloride till the green band reached the bottom of the column. The washings were discharged. Then the elution with 1 ℓ of methylene chloride-ethyl acetate (10:1) was performed. After evaporation *in vacuo*, 0.199 g of purple microcrystalline material with metallic glistering was obtained. Tlc (1-bromobutane) yielded very broad, diffused, overlapping bands with R_f value 0.24-0.56; ms: (fab) m/e 1136 (M^+H^+); uv-vis and ^1H

nmr, see [1].

Anal. Calcd. for $C_{84}H_{70}N_4$: C, 88.85; H, 6.21; N, 4.93. Found: C, 88.5; H, 6.3; N, 5.2.

(ii) Condensation at Room Temperature (in Chloroform Solution).

To a solution of [2.2]paracyclophane-4-carbaldehyde (1.2 g, 5 mmoles) in chloroform (500 ml) a 1.0 *M* solution of pyrrole in chloroform (5 ml, 5 mmoles) was added. The solution was put into a 1 ℓ three-necked round-bottomed flask equipped with thermometer, gas inlet/outlet port, septum port and magnetic stirrer bar. A slow flow of argone was maintained for 5 minutes and then 0.25 *M* boron trifluoride solution (7 ml, 1.75 mmoles) was introduced by syringe. The stirred solution was kept at room temperature (25°) for 1 hour. To the dark purple solution, 2,3-dichloro-5,6-dicyanobenzoquinone (0.85 g, 3.8 mmoles) was added in one portion and the reaction mixture was stirred for 20 minutes at room temperature. Chloroform was removed in a rotary evaporator. The dry residue was put into a mortar, thoroughly ground with a few ml of methanol, then transferred on a Buchner funnel using several portions of methanol and filtered *in vacuo*. The black residue was washed with methanol until an almost colorless filtrate began to pass. After drying at room temperature, 1.04 g of crude product was obtained. Spectrophotometric determination of porphyrin (measured at Soret band) gave a content of 38.3%. The yield of reaction was 1.04 x 0.383 = 0.40 g (0.35 mmole), *i.e.* 28% of theoretical amount.

The purification was performed as follows. The crude material (1.0 g) was dissolved in 200 ml of methylene chloride and was repeatedly treated with 5 g portions of silica gel as in the procedure described previously for the product of condensation in boiling propionic acid. The final purification on the florisil column by washing with methylene chloride-petroleum ether mixture, pure methylene chloride and then elution with methylene chloride-ethyl acetate (10:1) was strictly the same as for the propionic acid condensation product. After removing the solvent in a rotary evaporator, 0.365 g of purple material with a metallic glare was obtained. Tlc (1-bromobutane) broad, overlapping, diffused bands within the range of 0.21-0.62 were found, uv-vis and ^{1}H nmr, see [1].

Anal. Calcd. for $C_{84}H_{70}N_4$: C, 88.85; H, 6.21; N, 4.93. Found: C, 88.5; H, 6.3; N, 5.2.

D. Separation of Atropoisomers.

General.

Florisil exhibits a great affinity to **1** as compared with silica-gel. The mobility of **1** in florisil chromatography column when using methylene chloride as developer is extremely slow. Nonetheless this very slow movement of the adsorbed porphyrin against the stationary phase was proved to be an advantageous feature for separation of atropoisomers. The prolonged washing with methylene chloride resulted in preliminary separation of the fractions on the florisil bed as could be seen in differentiated color intensities throughout the whole length of the column. This introductory preparation of the column, although a tedious and time-consuming procedure, was useful in its final result, giving full compensation for time and materials. The next washing with methylene chloride-ethyl acetate mixture of precisely balanced concentration resulted in obtaining well resolved fractions. We believe that two fractions of atropoisomers could be separated just in the middle of elutions with methylene chloride-ethyl acetate mixtures 200:1 and 50:1. This resulted in obtaining two fractions, a less polar and a more polar one. The recovery as calculated on purified atropoisomer was about 85%. However, the proportions between less polar and more polar fractions, although close for both products obtained according to (i) and (ii) syntheses, were different. Procedure. *Meso*-tetrakis[2.2]paracyclophanylporphyrin (**1**) (100 mg) from the high temperature synthesis (i), as obtained after purification by adsorption of polymeric material on silica gel and by column chromatography on florisil, was dissolved in 100 ml of methylene chloride, flurosil (10 g) was added to the solution and the slurry was dried in a rotary evaporator. The resulting green material was put on the top of the column packed with 90 g of florisil and developed with methylene chloride until the green band reached the bottom of the column. The washing with a mixture methylene chloride-ethyl acetate (200:1) and collection of twelve 50 ml fractions enabled to find two middle portions (sixth and seventh fraction) of remarkably concentrated solutions. After pronounced decrease of concentration in the twelfth fraction, as measured spectrophotometrically, the washing was continued using 50:1 mixture of methylene chloride and ethyl acetate. Collection of the fractions, 50 ml each, gave rise to separation of the next group of atropoisomers in the fractions from fourth to ninth. The evaporation of the above mentioned fractions (VI and VII from first elution, and IV-IX from the second elution) gave 37 mg of atropoisomeric concentrate **1b** of R_f = 0.59 (silica-gel, toluene) and 49 mg of atropoisomeric fraction **1a** of R_f = 0.20 (silica-gel, toluene), respectively. For spectral determination purposes **1a** and **1b** were put on tlc preparative plates and developed with 1-bromobutane. The R_f = 0.14-0.24 band (intense pure green) eluted with pyridine gave **1a**; ms: (fab) m/e 1136 (M^+H^+); uv-vis (benzene): λ max 668 nm (log ε 3.75), 608 sh (3.71), 577 (4.18), 538 (4.00), Soret band 439 (5.51), protonated $(\mathbf{1a})H_4^{2+}$ (0.01 *M* trifluoroacetic acid in benzene), 716 (4.75), Soret band 476 (5.07); ^{1}H nmr: (300-MHz), β-pyrrole protons, 9.91 (d, 2H), 8.79 (d, 2 H), 8.20 (m, 4 H), aromatic PCP protons, 7.50 (m, 2 H), 7.11-6.76 (m, 24 H), 6.39 (d, 2 H), aliphatic PCP protons, 3.63 (m, 8 H), 3.38 (m, 8 H), 2.80 (m, 4 H), 2.51 (m, 4 H), 2.02 (m, 4 H), 1.71 (m, 4 H), NH protons (2 H), -2.04(s), -2.34(weak s). The R_f = 0.32-0.36 stripe (brownish-green) was separated and eluted with chloroform giving rise to **1b**: ms: (fab) m/e 1136 (M^+H^+); uv-vis (benzene): λ max 667 nm (log ε 3.81), 608 (3.71), 574 (4.23), 535 (4.10), Soret band 438 (5.56), protonated $(\mathbf{1b})H_4^{2+}$ (0.01 *M* trifluoroacetic acid in benzene), 684 (4.62), Soret band 468 (5.18); ^{1}H nmr (300-MHz), β-pyrrole protons, 10.44 (s, 1 H), 9.86 (d, 1 H), 8.72 (d, 1 H), 8.37 (s, 2 H), 8.32 (s, 1 H), 8.13 (m, 2 H), aromatic PCP protons, 7.48 (d, 2 H), 7.05-6.63 (m, 26 H), 6.22 (d, 2 H), aliphatic PCP protons, 3.74-1.79 (a series of irreg m, 32 H), NH protons (2 H), -1.94 and -1.97 (d), -2.34 (weak s).

Anal. Calcd. for $C_{84}H_{70}N_4$: C, 88.85; H, 6.21; N, 4.93. Found for **1a**: C, 88.5; H, 6.2; N, 5.3. Found for **1b**: C, 88.8; H, 6.3; N, 4.9.

The separation of the purified product of the room temperature synthesis (ii) gave 40 mg of R_f = 0.20 fraction, **1a**, and 45 mg of R_f = 0.59 fraction, **1b**. For spectral determinations both fractions were purified by preparative tlc similarly as described above; ms: (fab) m/e 1136 (M^+H^+) for **1a** and **1b**; uv-vis and ^{1}H nmr (300-MHz) spectra of **1a** and **1b** correspond, respectively, to the spectra of **1a** and **1b** obtained in the high temperature synthesis (i), see above.

Anal. Calcd. for $C_{84}H_{70}N_4$: C, 88.85; H, 6.21; N, 4.93. Found for **1a**: C, 88.8; H, 6.45; N, 4.75. Found for **1b**: C, 88.6; H, 6.5; N, 4.5.

E. Analytical Procedures.

(a) Monitoring of the reaction rate in propionic acid. An aliquot of the reaction mixture was taken by a syringe and diluted with dimethylformamide using volumetric or gravimetric measure. The absorption of the resulting solution was read at 438 nm against dimethylformamide.

$$\text{Concentration} = 3.07 \times A_{438}\ \text{mg}/\ell$$

(b) Determination of the porphyrin in crude material. A sample was weighed and dissolved in benzene to obtain approximately 0.5-1.0 x 10^{-5} *M* solution as calculated on the expected content of porphyrin. The absorptions were measured at 574 nm and 608 nm against benzene.

$$\text{Concentration} = 98.7 \times (A_{574} - A_{608})\ \text{mg}/\ell$$

The solution 10^{-5} *M* used above was diluted 20 times and the absorption measured at 438 nm.

$$\text{Concentration} = 3.07 \times A_{438}\ \text{mg}/\ell$$

Both values are normally within the 5% error range.

(c) Determination of Porphyrin Concentration During the Purification Procedures.

The solutions in methylene chloride were diluted as described in the preparative part or were diluted, if necessary, to keep the absorption values between 0.3-0.7. The readings were then taken at 438 nm.

$$\text{Concentration} = 3.07 \times A_{438}\ \text{mg}/\ell$$

Warning: A possibility of severe error may occur when the solution

becomes acidic as a result of hydrolytic decomposition of the solvent. It is therefore strongly recommended to check the reading after putting one drop of triethylamine to the cuvette. The rise of the absorption value at 438 nm shows that there is present some fraction of the protonated species. The solution has to be made neutral by addition of a necessary amount of triethylamine and the reading taken once again.

(d) Monitoring of the Purification Process.

An aliquot of the methylene chloride solution taken during the successive steps of adsorption of polymeric material on silica gel was diluted with dimethylformamide. The absorptions at 574 nm and 474 nm were measured. The ratio $A_{574}/A_{474} \geq 7$ was accepted as necessary for the preliminary purification.

F. Spectroscopic Methods.

Electronic spectra were recorded on Perkin-Elmer Lambda 4c UV/VIS spectrophotometer C 688-0002 version. The ^1H nmr spectra were recorded on Bruker IBM AF 300 (300 MHz) Fourier transformed spectrometer; chemical shifts are reported in ppm *vs* tetramethylsilane. Mass spectrometry was performed by Fast Atom Bombardment on a VG Micromass 70/70 HS mass spectrometer with an 11/250 data system.

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