

# Phthalimide Reaction with 2-Methylquinoline as a Procedure for Synthesis of *meso*-Heteryl-substituted Tetrabenzoporphins

N.E. Galanin, N.A. Kolesnikov, E.V. Kudrik, and G.P. Shaposhnikov

Ivanovo State Chemico-technological University, Ivanovo, 153460 Russia

e-mail: ttos@isuct.ru

Received March 27, 2003

**Abstract**—A method was developed for preparation of *meso*-heteryl-substituted tetrabenzoporphins from phthalimide and 2-methylcholine in the presence of metal oxides. *meso*-Tetra(2-quinoly)tetrabenzoporphin and its zinc complex were prepared along this procedure.

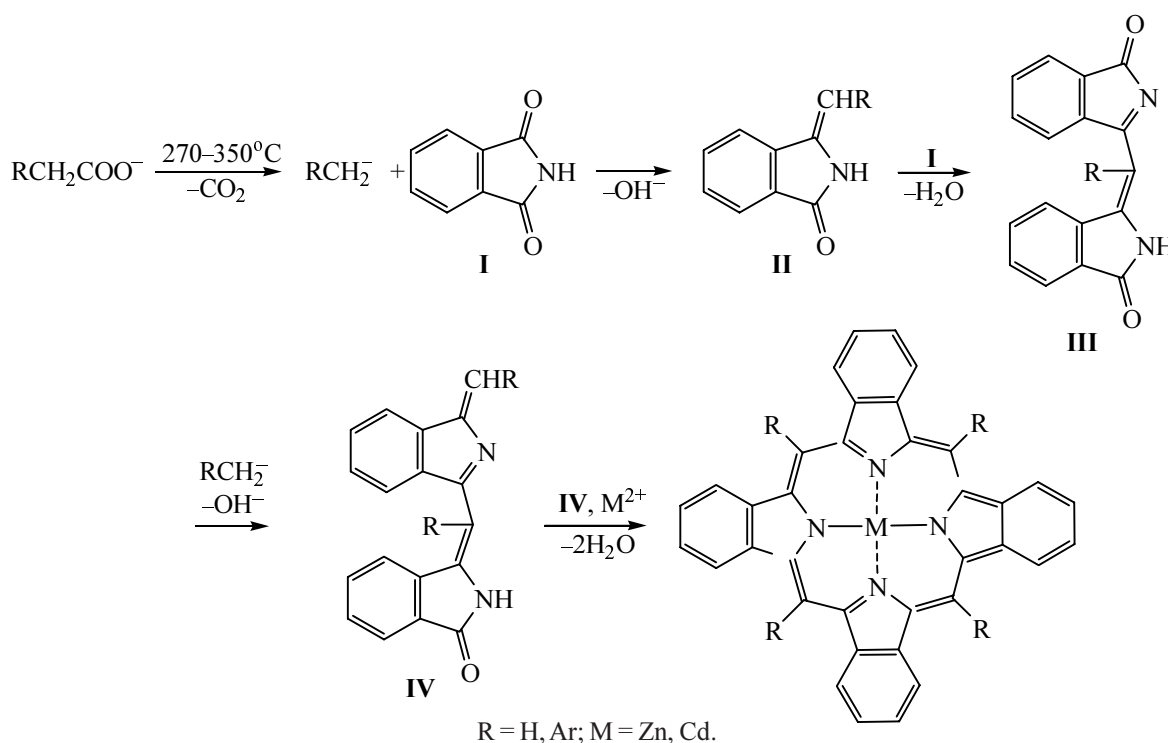
*meso*-Aryl-substituted tetrabenzoporphins belong to an important group of compounds that can find practical application as dyes [1], photochromic filters [2], photosensitizers for singlet oxygen generation in photodynamic therapy of cancer [3].

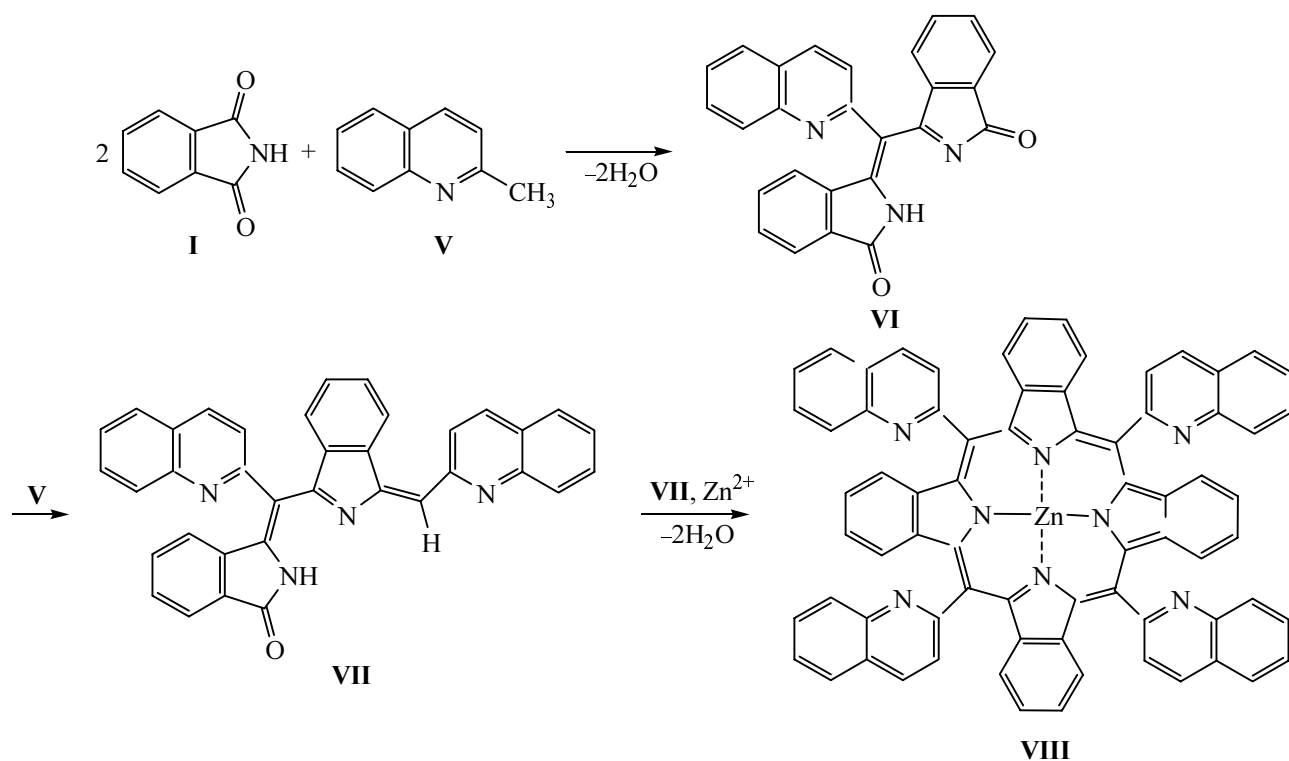
The tetrabenzoporphin and its structural analogs are prepared at high temperature from phthalimide **I** and zinc acetates or arylacetates; therewith the metal cations serve as template agents [4, 5].

The first stage of the reaction involves an addition of a nucleophile arising in the synthesis conditions to one of

the carbonyl groups of phthalimide molecule. This assumption is confirmed by the structure of intermediate products that are easily isolable from the reaction mixture when the process is carried out at various temperatures and for different periods. However the nature of the nucleophile involved into the reaction remains unknown. In this connection the goal of this study was investigation of the chemical nature of these interactions and also synthesis of *meso*-heteryltetrabenzoporphins.

Notice that the carbonyl group in phthalimide **I** possesses low reactivity in reactions of nucleophilic addition.





For instance, in contrast to aldehydes and ketones, compound **I** does not react under usual conditions even with nucleophiles like primary aliphatic and aromatic amines [6].

It is presumable that the thermal decarboxylation of an anion of a carboxylic acid results in formation of a reactive nucleophilic agent, a certain carbanion that reacts further with the phthalimide **I** molecule to give a 3-ylidenephthalimidine **II**. The latter reacts with the second molecule of **I** yielding on dehydration the dimer **III**. Compound **III** reacts with the carbanion to form compound **IV**, and two molecules of the latter coordinate to the metal cation and form a metal complex of the tetrabenzoporphin in keeping with the scheme on the previous page.

Compounds **II** and **III**, R = Ph were isolated from the reaction mixture by means of column chromatography.

The analysis of the assumed scheme suggests that the metal complexes of tetrabenzoporphins may form also when as a source of active anion would serve compounds containing a methyl group of a high CH-acidity. 2-Methylquinoline belongs to these compounds.

We carried out reaction of phthalimide with 2-methylquinoline **V** in the presence of zinc oxide. The heating of a mixture of phthalimide with zinc oxide in excess 2-methylquinoline at reflux (245–248°C) for 12 h afforded zinc *meso*-tetra(2-quinolyl)tetrabenzoporphinate **VIII**. We

isolated by column chromatography from the reaction mixture beside compound **VIII** also 3-[3-oxo-2,3-dihydro-1*H*-1-isoindolylidene(2-quinolyl)methyl]-1*H*-isoindolone **VI**.

Compound **VI** is a red substance soluble in polar and nonpolar organic solvents. Its structure was derived from the data of elemental analysis, <sup>1</sup>H NMR, and electronic spectra.

In the <sup>1</sup>H spectrum of a solution of compound **VI** in CDCl<sub>3</sub> appear the signals of aromatic protons as a multiplet in the 8.32–8.07 ppm region corresponding to three protons in positions 4, 6, and 8, and in the region 8.06–7.77 ppm is observed a multiplet belonging to the protons in positions 3, 5, 7 of the *meso*-substituent. The signals of 8 protons from isoindole fragments are located in the region 7.70–7.40 ppm. The singlet at 10.21 ppm corresponds to the resonance of the NH group proton.

Electronic spectrum of compound **VI** (Fig. 1) contains three absorption bands in the visible region at 427, 454, and 485 nm. The introduction of 2-quinolyl substituents into the molecule of 3-(3-oxo-2,3-dihydro-1*H*-1-isoindolylidene)methyl)-1*H*-isoindolone (**III**, R = H) [7] results in a blue shift of the absorption band by 65 nm due to both the effect of the electron-withdrawing substituents and deviation of the molecular structure of compound **VI** from planarity.

Zinc *meso*-tetra(2-quinolyl)tetrabenzoporphinate **VIII** was also isolated from the reaction mixture by column

chromatography. The treating of its chloroform solution with concn. HCl afforded *meso*-tetra(2-quinoly)tetra-benzoporphin **IX**.

Compounds **VIII** and **IX** are green substances well soluble in benzene, chloroform, acetone, and DMF. Their composition and structure was confirmed by elemental analysis, by vibrational, electronic, and  $^1\text{H}$  NMR spectroscopy, and also by mass spectrometry (method of field desorption).

In the IR spectra of porphirins **VIII** and **IX** a number of bands closely located is observed: at  $2974\text{--}2925\text{ cm}^{-1}$  (C–H bonds vibrations),  $1384\text{--}1371\text{ cm}^{-1}$  (C=N),  $1049\text{--}1042\text{ cm}^{-1}$  (C=C). In addition in the spectrum of compound **IX** in the region  $3300\text{--}3346\text{ cm}^{-1}$  appears a broadened band characterizing vibrations of N–H bonds.

In the  $^1\text{H}$  NMR spectrum of zinc complex **VIII** recorded in  $\text{DMSO-}d_6$  the signals of 12 protons from the *meso*-substituents in positions 4, 6, and 8 appear as singlets at 9.02, 8.85, and 8.72 ppm respectively. In the region 8.30–7.70 ppm the signals from 16 protons of isoindole fragments are observed, and the singlets at 7.53, 7.28, and 7.02 ppm belong to the resonances of 12 protons from the *meso*-substituents located respectively in positions 3, 5, and 7.

In the mass spectrum of compound **IX** (solution in  $\text{CHCl}_3$ ) the molecular ion peak is present,  $m/z$  1019, and also a peak with  $m/z$  2038  $[2M]^+$ .

Electron absorption spectrum of compound **VIII** (Fig. 2) contains a Q-band with a maximum at 631 nm and a stronger Soret band with a maximum at 435 nm.

In the spectrum of ligand **IX** (Fig. 2) a splitting of bands is observed, and like in the spectrum of the *meso*-tetraphenyltetra-benzoporphin the splitting of the Soret band is insignificant, and the intensity of the longwave component of the Q-band is low. This phenomenon is characteristic of the *meso*-tetraaryl-tetra-benzoporphins and is not characteristic of the tetra-benzoporphins with unsubstituted *meso*-positions [5, 9, 10].

In the spectrum of complex **VIII** as compared to that of zinc tetra-benzoporphinate a red shift of absorption bands maxima by 6 nm is observed. In the spectrum of compound **IX** a red shift of absorption bands compared to the spectrum of tetra-benzoporphin [8] was also observed, and it was the greatest for the short wave component of the Q-band (22 nm), whereas the red shift of the other bands was insignificant (2–3 nm). This spectral behavior was apparently caused by deviation of the molecular struc-

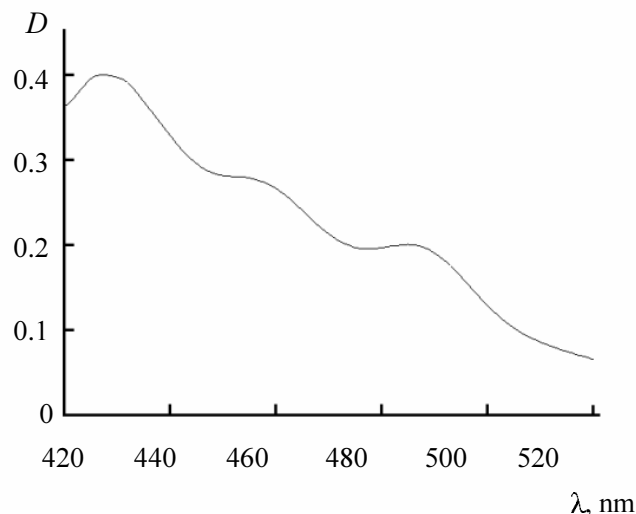


Fig. 1. Electron absorption spectrum of compound **VI** in chloroform.

ture from planarity. As resulted from the quantum-chemical calculations along the semiempirical AM1 procedure, the molecule of compound **IX** is actually strongly distorted (Fig. 3), and the *meso*-substituents are turned with respect to the rather tentative macrocycle plane through  $47\text{--}61^\circ$  and thus disengaged from the conjugation system.

## EXPERIMENTAL

Electron absorption spectra of compounds obtained were recorded on spectrophotometer Hitachi UV-2000, IR spectra on spectrophotometer Avatar 360 FT-IR in the region  $400\text{--}4000\text{ cm}^{-1}$  from samples pelletized with KBr.  $^1\text{H}$  NMR spectra were registered on spectrometer

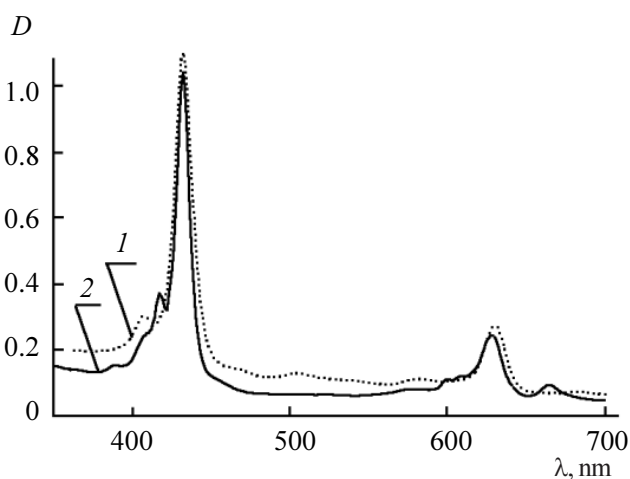


Fig. 2. Electron absorption spectra recorded in chloroform solutions. 1, zinc *meso*-tetra(2-quinoly)tetra-benzoporphinate **VIII**, 2, *meso*-tetra(2-quinoly)tetra-benzoporphin **IX**.

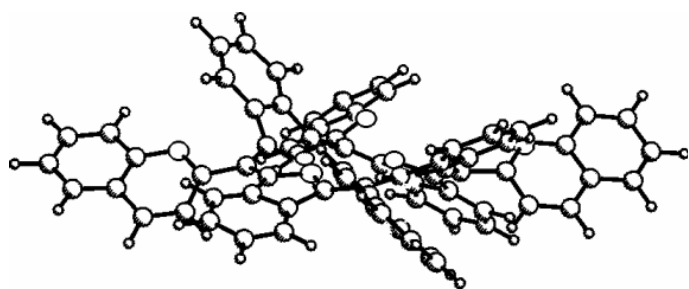


Fig. 3. Geometrical structure of the molecule of *meso*-tetra(2-quinoly)tetrabenzoporphin **IX** according to AM1 calculations.

Bruker AMD-300X (operating frequency 300 MHz, internal reference TMS), mass spectra (field desorption) were measured on JEOL JMS 700 instrument.

**3-[3-Oxo-2,3-dihydro-1H-1-isoindolylidene-(2-quinolyl)methyl]-1H-isoindolone (VI) and zinc *meso*-tetra(2-quinolyl)tetrabenzoporphinate (VIII).** A mixture of 1 g of phthalimide **I**, 0.3 g of zinc oxide, and 10 ml of 2-methylquinoline **V** was heated at reflux for 12 h. The mixture was cooled and subjected to chromatography on a column packed with aluminum oxide of **II** grade activity, eluent benzene-hexane, 1:10 (by volume). After elution of excess compound **V** the dark red zone was eluted with a mixture chloroform-hexane, 1:2 (by volume). On removing the solvent the red residue was boiled for 5 min in 50 ml of 5% hydrochloric acid, cooled, filtered off, and dried. Then it was dissolved in chloroform and subjected to chromatography on aluminum oxide of **II** grade activity (eluent chloroform). We obtained 0.02 g of compound **VI** as red powder well soluble in benzene, chloroform, acetone, DMF, insoluble in water. Electron absorption spectrum ( $\text{CHCl}_3$ ),  $\lambda_{\text{max}}$ , nm ( $D$ ): 485 (0.40), 454 (0.27), 427 (0.22).  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ ),  $\delta$ , ppm: 10.21 s (1H), 8.32–8.07 m (3H), 8.06–7.77 m (3H), 7.70–7.40 m (8H). Found, %: C 78.01; H 4.01; N 10.03.  $\text{C}_{26}\text{H}_{15}\text{N}_3\text{O}_2$ . Calculated, %: C 77.79; H 3.77; N 10.47.

Then the green zone was eluted with chloroform. After repeated chromatography on aluminum oxide of **II** grade activity (eluent chloroform-hexane, 1:1 by volume) and removing the solvent we obtained 0.27 g (14.7%) of compound **VIII** as green powder well soluble in benzene, chloroform, acetone, DMF, insoluble in water. Electron absorption spectrum ( $\text{CHCl}_3$ ),  $\lambda_{\text{max}}$ , nm (log  $e$ ): 631 (4.92), 585 (3.99), 435 (5.62), 410 (4.02). IR spectrum (KBr),  $\nu$ ,  $\text{cm}^{-1}$ : 2974 (C–H), 1384 (C=N), 1049

(C=C).  $^1\text{H}$  NMR spectrum ( $\text{DMSO}-d_6$ ),  $\delta$ , ppm: 9.02 s (4H), 8.85 s (4H), 8.72 s (4H), 8.30–7.70 m (16H), 7.53 s (4H), 7.28 s (4H), 7.02 s (4H). Found, %: C 79.89; H 3.72; N 10.35.  $\text{C}_{72}\text{H}_{40}\text{N}_8\text{Zn}$ . Calculated, %: C 80.03; H 3.98; N 10.01.

***meso*-Tetra(2-quinolyl)tetrabenzoporphin (IX).** To a solution of 0.1 g of compound **VIII** in 10 ml of chloroform was added 5 ml of concn. HCl, and the mixture was stirred for 1 h. Then 30 ml of 25% ammonia solution was added, the organic layer was separated, washed with water, and the solvent was evaporated. The residue was dissolved in chloroform and subjected to chromatography on aluminum oxide of **II** grade activity (eluent chloroform). The solvent was removed to obtain 0.07 g (76%) of compound **IX** as green powder well soluble in benzene, chloroform, acetone, DMF, insoluble in water. Electron absorption spectrum ( $\text{CHCl}_3$ ),  $\lambda_{\text{max}}$ , nm ( $D/D_{\text{max}}$ ): 664 (0.09), 628 (0.23), 608 (0.12), 432 (1.00), 417 (0.29). IR spectrum (KBr),  $\nu$ ,  $\text{cm}^{-1}$ : 3340 (N–H), 2925 (C–H), 1371 (C=N), 1042 (C=C). Mass spectrum,  $m/z$ : 1019 [ $M$ ] $^+$ , 2038 [ $2M$ ] $^+$ . Found, %: C 85.15; H 4.56; N 10.13.  $\text{C}_{72}\text{H}_{42}\text{N}_8$ . Calculated, %: C 84.85; H 4.15; N 10.99.

## REFERENCES

- Kopranenkov, V.N., Dashkevich, S.N., and Luk'yanets, E.A., USSR Inventor's Certificate 889675; *SSSR Byull. Izobr.*, 1981, p. 10.
- Maslyukov, A.P., Kopranenkov, V.N., Kopylova, E.M., and Goncharova, L.S., USSR Inventor's Certificate 765281; *SSSR Byull. Izobr.*, 1980, p. 147.
- Yasuike, M., Yamaoka, T., Ohno, O., Sakuragi, M., and Ichimura, K., *Inorg. Chim. Acta.*, 1991, vol. 184, p. 191.
- Luk'yanets, E.A., Kopranenkov, V.N., Makarova, E.A., Vazhnina, V.A., and Vorotnikov, A.M., USSR Inventor's Certificate 881101; *SSSR Byull. Izobr.*, 1981, p. 133.
- Luk'yanets, E.A., Dashkevich, S.N., and Kobayashi, Nagao., *Zh. Obshch. Khim.*, 1993, vol. 63, p. 1411.
- Sykes, P., *A Guidebook to Mechanism in Organic Chemistry*, 2nd edn., London: Longmans, 1966.
- Galanin, N.E., Kudrik, E.V., and Shaposhnikov, G.P., *Zh. Obshch. Khim.*, 2000, vol. 70, p. 1379.
- Elektronnyye spektry pogloshcheniya ftalotsianinov i rodstvennykh soedinenii* (Electronic Adsorption Spectra of Phthalocyanines and Relatives), Luk'yanets, E.A., Ed., Cherkassy: NIITEKHIM., 1989, p. 83.
- Kudrik, E.V., Islyaikin, M.K., and Frantseva, S.V., *Zh. Obshch. Khim.*, 1997, vol. 67, p. 1202.
- Galanin, N.E., Kudrik, E.V., and Shaposhnikov, G.P., *Zh. Obshch. Khim.*, 2002, vol. 72, p. 1198.