1,3-Cycloaddition of the nickel *meso*-cyanooctaethylporphyrin *N*-oxide complex to olefins. Molecular and crystal structure of a double cycloaddition product to 2,5-norbornadiene

Yu. V. Morozova,[a] Z. A. Starikova,[b] B. I. Maksimov,[a] D. V. Yashunskii,[a] and G. V. Ponomarev[a]*

[a]V. N. Orechovich Institute of Biomedical Chemistry, Russian Academy of Medical Sciences, 10 ul. Pogodinskaya, 119121 Moscow, Russian Federation. Fax: +7 (095) 245 0857. E-mail: gelii.ponomarev@ibmc.msk.su

[b]A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. Fax: +7 (095) 135 5085. E-mail: star@xray.ineos.ac.ru

Starting from the nickel *meso*-formyloctaethylporphyrin oxime complex, the *meso*-cyanooctaethylporphyrin *N*-oxide complex was synthesized for the first time. The new complex enters into 1,3-cycloaddition to olefins. The double addition of the nitrile oxide to 2,5-norbornadiene affords a porphyrin dimer, whose structure was established by X-ray diffraction analysis.

Key words: porphyrin, norbornadiene, 1,3-cycloaddition, nitrile oxide, isoxazoline.

Recently, we have discovered a series of transformations, new in principle, of metal complexes with *meso*-formylporphyrin oximes giving rise to unique derivatives, such as hydroxy-1,2-oxazinochlorins, *exo*-alkylidene-1,2-oxazinochlorins, and tripyrrolylisoxazoles.[1—4] We have also developed a mild and efficient method for the transformation of aldoximes of the tetrapyrrole series into the corresponding nitriles.[5]

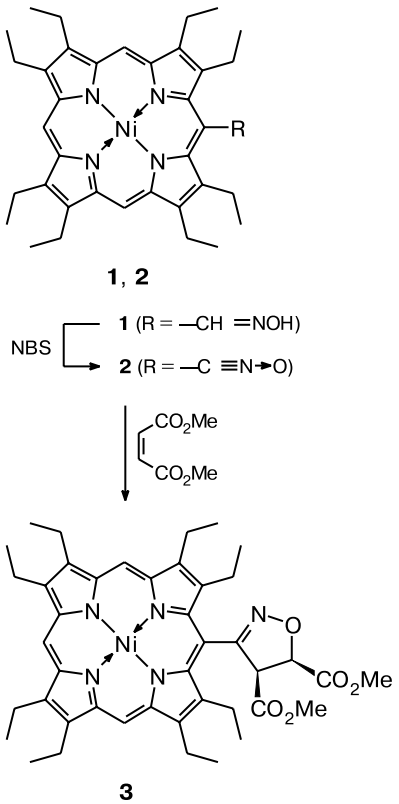
In the present study, we synthesized for the first time nitrile oxide based on a metal complex with *meso*-formylporphyrin oxime and studied its reactions with olefins.

Results and Discussion

The transformation of oxime **1** under the action of *N*-bromosuccinimide (NBS) in the presence of Et_3N afforded stable nickel *meso*-cyanoporphyrin *N*-oxide complex **2** in 92% yield. This compound was used in the classical 1,3-cycloaddition to olefins. For example, prolonged refluxing of nitrile oxide **2** with an excess of dimethyl maleate in dichloroethane gave adduct **3** in 91% yield (Scheme 1).

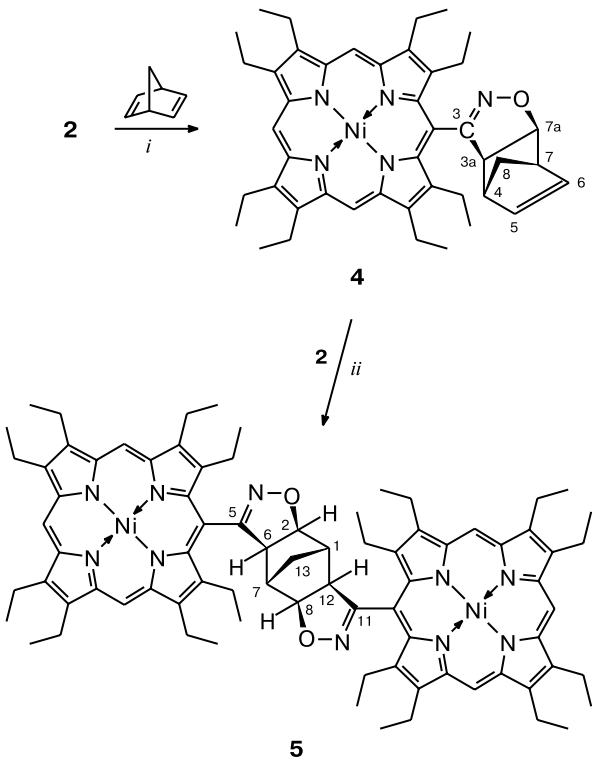
Heating of nitrile oxide **2** with an excess of 2,5-norbornadiene in dichloroethane for 2—3 h (or storage of the reaction solution at room temperature for 12 h) afforded stereoselectively one of two possible stereoisomers **4** in virtually quantitative yield (Scheme 2). The spatial prox-

Scheme 1



Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 10, pp. 2098—2101, October, 2004.

Scheme 2



i. 40 °C, 2—3 h, 97% yield; *ii*. 70 °C, 72 h, 92% yield.

imity of the C(8)H_a (doublet at δ 1.95) and C(7a)H (doublet at δ 2.80) atoms of the norbornadiene fragment to the methylene protons of two ethyl groups (δ 4.27, 3.73 and 3.65, 3.55) of the macrocycle (NOE data) suggests *exo* configuration of the addition product.

In turn, prolonged refluxing of the primary adduct **4** with an excess of *meso*-cyanoporphyrin *N*-oxide **2** in dichloroethane afforded stereoselectively bis-adduct **5** (see Scheme 2). Its structure was unambiguously established by X-ray diffraction analysis of a single crystal grown by crystallization from a mixture of dichloromethane and hexane. The molecule was demonstrated to have *exo*,*exo* configuration (Fig. 1), and the regioselectivity of the addition was proved.

The porphyrin macrocycles are nonplanar (the deviations of the atoms from the mean planes of the porphyrin core are 0.30 and 0.20 Å) and are coplanar. The distance between the macrocyclic cores is 8.29 Å. The mean plane of the 2,5-norbornadiene fragment (see Scheme 2) calculated without considering the C(13) atom (the maximum deviation of the atoms is 0.35 Å) is virtually orthogonal to the porphyrin macrocycles; the corresponding dihedral angles are 84.7 and 83.3°.

Cycloaddition of *meso*-cyanoporphyrin *N*-oxide to 2,5-norbornadiene occurs in accordance with the classical notions of such reactions based on benzonitrile oxides.[6]

Due to the ease of preparation and stability of metal complexes with *meso*-cyanoporphyrin *N*-oxides, on the one hand, and their high reactivity with respect to olefins, on the other hand, the new class of derivatives of tetrapyrrole macrocycles holds considerable promise for synthetic transformations.

Experimental

The ^{1}H NMR spectra were recorded on Bruker AC-200 (200 MHz) and Bruker DRX-500 (500 MHz) spectrometers in $CDCl_3$. The UV-Vis spectra were measured on Hitachi-320 and

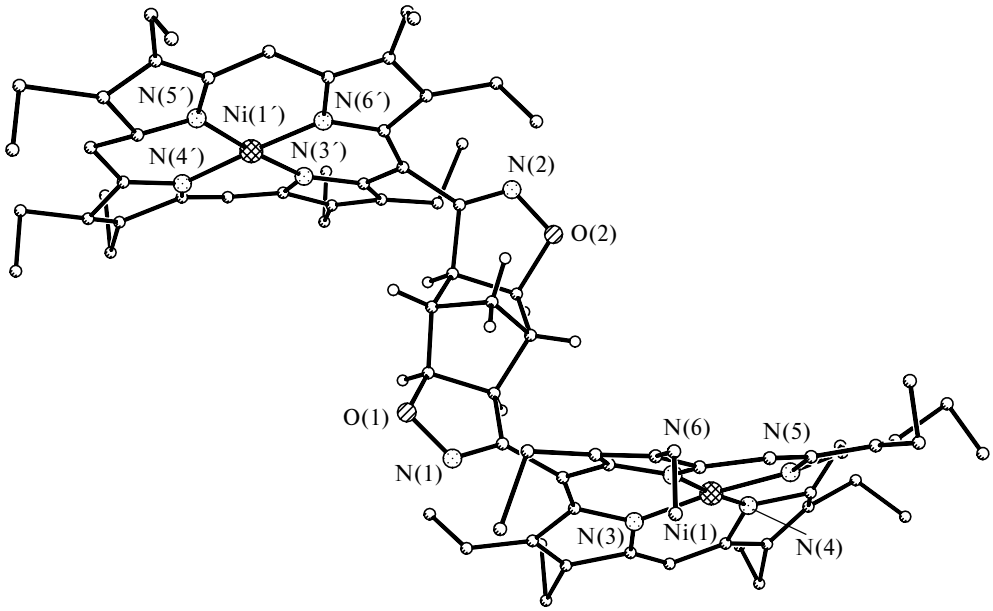


Fig. 1. Molecular structure of bis-adduct **5**.

Helios δ spectrophotometers in $CHCl_3$. The spectra were recorded without dilution of solutions at a concentration of ~1.2—1.7 of the optical density in the Soret band region; the relative intensities of the absorption maxima are given. The mass spectra were obtained on Bruker Reflex 3 and Finnigan MAT 311A instruments. The IR spectrum was recorded on a Nicolet Magna 750 Fourier-transform IR spectrometer in a KBr pellet. The purity of the reaction products and the course of the reactions were monitored by TLC on silica gel plates (Merck). The compounds were separated by column chromatography on silica gel Merck (G 60, 0.040—0.063 mm).

The starting nickel *meso*-formyloctaethylporphyrin oxime complex (**1**) was prepared in quantitative yield from the *meso*-(*N*,*N*-dimethyliminiomethyl)octaethylporphyrin iodide nickel complex according to a procedure described earlier.[7]

Nickel *meso*-cyanooctaethylporphyrin *N*-oxide complex (2). Oxime **1** (15 mg, 23.6 μmol) and NBS (9 mg, 59.6 μmol) were added to a solution of Et_3N (50 μL) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at ~20 °C for 5 min and washed with water. The organic phase was dried with anhydrous Na_2SO_4 and concentrated to dryness. A solution of the residue in CH_2Cl_2 was passed through a SiO_2 layer. The major fraction was precipitated with MeOH from a solution in CH_2Cl_2. The yield of nitrile oxide **2** was 13.8 mg (92%). Found (%): C, 70.08; H, 6.66; N, 11.12. $C_{37}H_{43}N_5NiO$. Calculated (%): C, 70.27; H, 6.85; N, 11.07. UV, λ_{max}/nm: 411 (15.0), 542 (1.0), 585 (1.6). IR, ν/cm^{-1}: 2305 (C≡N—O). ^{1}H NMR (200 MHz), δ: 1.65—1.90 (overlapping t, 24 H, 8 $CH_2C\underline{H}_3$); 3.70—4.10 (overlapping q, 16 H, 8 $C\underline{H}_2CH_3$); 9.50 (s, 3 H, H_{meso}). MS (EI, 70 eV), *m*/*z* (I_{rel} (%)): 632 $[M + H]^+$ (100), 615 $[M - O]^+$ (23).

Nickel 4,5-dimethoxycarbonyl-3-(octaethylporphyrinato-5-yl)-4,5-dihydroisoxazole complex (3). A solution of compound **2** (16 mg, 25.3 μmol) and dimethyl maleate (11 mg, 75.9 μmol, 3 equiv.) in 1,2-dichloroethane (3 mL) was refluxed with stirring for 5 h, cooled, diluted with dichloromethane, washed with water, dried by filtration through a layer of anhydrous sodium sulfate, and concentrated to dryness. The residue was purified by silica gel chromatography in dichloromethane. The yield of compound **3** was 18 mg (91%). Found (%): C, 66.31; H, 6.56; N, 8.93. $C_{43}H_{51}N_5NiO_5$. Calculated (%): C, 66.50; H, 6.62; N, 9.02. UV, λ_{max}/nm: 399 (13.3); 520 (1.0); 558 (1.9). ^{1}H NMR (200 MHz), δ: 1.60—1.90 (overlapping t, 24 H, 8 $CH_2C\underline{H}_3$); 3.20—4.00 (overlapping q and m, 16 H, 8 $C\underline{H}_2CH_3$); 3.93 (s, 6 H, 2 COOMe); 4.56 (d, 1 H, MeOOCC$\underline{H}$—CH—O, J = 9.9 Hz); 5.93 (d, 1 H, MeOOCCH—C$\underline{H}$—O, J = 9.9 Hz); 9.58 and 9.61 (both s, 1 H, 2 H, H_{meso}). MS (MALDI): 776.4 $[M + H]^+$.

Nickel 4,7-methano-3-(octaethylporphyrinato-5-yl)-3a,4,7,7a-tetrahydro-1,2-benzoisoxazole complex (4). Bicyclo[2.2.1]hepta-2,5-diene (0.1 mL, 85.4 mg, 0.93 mmol) was added to a solution of nitrile oxide **2** (6 mg, 9.51 μmol) in CH_2Cl_2 (1 mL). The reaction mixture was kept at ~20 °C for 12 h and concentrated *in vacuo* at 40—50 °C. The residue was chromatographed on a silica gel column in dichloromethane. The yield of compound **4** was 6.7 mg (97%). Found (%): C, 72.75; H, 7.08; N, 9.52. $C_{44}H_{51}N_5NiO$. Calculated (%): C, 72.93; H, 7.09; N, 9.66. UV, λ_{max}/nm: 408 (17.9), 536 (1.0), 575 (1.6). ^{1}H NMR (500 MHz), δ: 0.95 (br.s, 1 H, C(7)H); 1.24 (d, 1 H, C(8)H_b, J = 8.4 Hz); 1.71—1.88 (overlapping t, 24 H, 8 $CH_2C\underline{H}_3$); 1.95 (d, 1 H, C(8)H_a, J = 8.7 Hz); 2.80 (d, 1 H, C(7a)H, J = 8.2 Hz); 3.26 (br.s, 1 H, C(4)H); 3.55, 3.65, 3.80, 3.88, and 4.27 (all br.m, 16 H, 8 $C\underline{H}_2CH_3$); 4.98 (d, 1 H, C(3a)H, J = 8.7 Hz); 5.29 (dd, 1 H, C(6)H, J_1 = 3.4 Hz, J_2 = 5.3 Hz); 5.75 (dd, 1 H, C(5)H, J_1 = 3.5 Hz, J_2 = 5.1 Hz); 9.48 (s, 2 H, H_{meso}); 9.49 (s, 1 H, H_{meso}). The assignment of the signals was made based on the COSY and NOESY NMR spectra. MS (MALDI): 724.3 $[M + H]^+$.

Nickel 5,11-di(octaethylporphyrinato-5-yl)-3,9-dioxa-4,10-diazatetracyclo[5.5.1.0^{2,6}.0^{8,12}]trideca-4,10-diene complex (5). A solution of compound **4** (6.5 mg, 8.98 μmol) and nitrile oxide **2** (16 mg, 25.4 μmol) in 1,2-dichloroethane was refluxed for 72 h. Chromatography on silica gel in a 1 : 1 dichloromethane—hexane mixture yielded 11 mg (90%) of bis-adduct **5**. Found (%): C, 71.45; H, 7.03; N, 10.14. $C_{81}H_{94}N_{10}Ni_2O_2$. Calculated (%): C, 71.69; H, 6.98; N, 10.32. UV, λ_{max}/nm: 409 (17.6), 535 (1.0), 574 (10.6). ^{1}H NMR (500 MHz), δ: 0.75 (br.s, 2 H, C(1)H, C(7)H); 1.44 (br.s, 2 H, C(13)H_a, C(13)H_b); 1.51, 1.56, 1.64, 1.70, 1.74—1.87 (overlapping t, four t, 24 H, 6 H each, 16 $CH_2C\underline{H}_3$); 2.23 (d, 2 H, C(2)H, C(8)H, J = 7.12 Hz); 2.99—3.08, 3.38—3.51, 3.62—3.96, 4.31—4.39 (overlapping m, 32 H, 16 $C\underline{H}_2CH_3$); 3.67 (d, 2 H, C(12)H, C(6)H, J = 8.07); 9.44, 9.49, and 9.50 (all br.s, 2 H each, H_{meso}). The assignment of the signals was made based on the COSY and NOESY NMR spectra. MS (MALDI): 1356.3 $[M + H]^+$.

X-ray diffraction analysis of bis-adduct 5. Dark-red prismatic crystals were grown by crystallization from a solution in dichloromethane by adding hexane. The crystals of $C_{81}H_{88}N_{10}Ni_2O_2.C_6H_{14}$ (M = 1437.21) are triclinic, at 120 K a = 10.417(1) Å, b = 13.483(2) Å, c = 14.759(2) Å, α = 93.551(3)°, β = 101.569(3)°, γ = 111.625(2)°, V = 1866.9(4) Å^3, d_{calc} = 1.278, space group $P\bar{1}$, Z = 1.

The X-ray diffraction data (16712 reflections) were collected on a Bruker SMART CCD 1000 diffractometer at 120 K (λ(Mo-Kα) radiation, $2\theta_{max}$ = 58°) from a single crystal of dimensions 0.20×0.15×0.10 mm. After merging of equivalent reflections, the data set consisted of 15352 independent reflections (R_{int} = 0.0604), which were used for the structure solution and refinement. Absorption (μ = 0.561 mm^{-1}) was ignored (T_{max} and T_{min} are 0.862 and 0.717, respectively). The structure was solved by direct methods. All nonhydrogen atoms were revealed from difference electron density maps and refined anisotropically against F^2_{hkl}. All hydrogen atoms were placed in geometrically calculated positions and refined using the riding model with U(H) = 1.5U(C), where U(C) are the equivalent displacement parameters of their parent carbon atoms. The final reliability factors were R_1 = 0.0702 (based on F_{hkl} for 3988 reflections with $I > 2\sigma(I)$), wR_2 = 0.1522 (based on F^2_{hkl} for a total of 15352 reflections), GOOF = 0.771, 900 parameters were refined.

All calculations were carried out using the SHELXTL PLUS 5 program package. The atomic coordinates and complete data on the geometric parameters were deposited with the Cambridge Structural Database.

This study was financially supported by the Foundation of the President of the Russian Federation (Federal Program for the Support of Leading Scientific Schools, Grant NSh-1060.2003.3).

References

1. D. V. Yashunskii, Yu. V. Morozova, and G. V. Ponomarev, *Khim. Geterotsikl. Soedin.*, 2001, 405 [*Chem. Heterocycl. Compd.*, 2001, **37**, 380 (Engl. Transl.)].
2. D. V. Yashunskii, Yu. V. Morozova, and G. V. Ponomarev, *Khim. Geterotsikl. Soedin.*, 2000, 560 [*Chem. Heterocycl. Compd.*, 2000, **36** (Engl. Transl.)].
3. G. V. Ponomarev, Yu. V. Morozova, and D. V. Yashunskii, *Khim. Geterotsikl. Soedin.*, 2001, 277 [*Chem. Heterocycl. Compd.*, 2001, **37**, 253 (Engl. Transl.)].
4. Yu. V. Morozova, D. V. Yashunskii, B. I. Maksimov, and G. V. Ponomarev, *Khim. Geterotsikl. Soedin.*, 2003, 434 [*Chem. Heterocycl. Compd.*, 2003, **39**, 388 (Engl. Transl.)].
5. D. V. Yashunskii, Yu. V. Morozova, and G. V. Ponomarev, *Khim. Geterotsikl. Soedin.*, 2000, 558 [*Chem. Heterocycl. Compd.*, 2000, **36** (Engl. Transl.)].
6. *The Chemistry of Alkenes*, Ch. 7, Ed. S. Patai, Interscience Publishers, New York—London, 1964.
7. G. V. Ponomarev and G. B. Maravin, *Khim. Geterotsikl. Soedin.*, 1977, 85 [*Chem. Heterocycl. Compd.*, 1977, **13** (Engl. Transl.)].

Received April 27, 2004