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Synthesis of the First Azomethine Derivatives of Pd^{II} Coproporphyrins I and II

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Dedicated to the Corresponding member of Russian Academy of Sciences Prof. Oscar I. Koifman on the occasion of his 70th Anniversary

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The effective synthesis of Pd(II) monofunctional azomethine derivatives of coproporphyrin isomers I and II is reported. The proposed method is based on the interaction of a "phosphorus complex", generated in situ by Vilsmeier-Haack reaction, with various amines. The reaction with palladium complex of coproporphyrin II gave Schiff bases as a mixture of two structural isomers in 4:1 ratio. The structure of the obtained compounds was determined using ^{1}H, ^{13}C, ^{1}H-^{1}H NOESY and UV-vis spectroscopy and mass spectrometry data.

Keywords: Porphyrin, palladium, coproporphyrin, azomethine, Vilsmeier-Haack reaction.

Синтез первых азометиновых производных Pd^{II} копропорфиринов I и II

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Предложен эффективный метод синтеза Pd(II) монофункциональных азометиновых производных копропорфиринов I и II. Предлагаемый метод основан на взаимодействии так называемого "фосфорного комплекса", получаемого in situ путем реакции Вильсмейра-Хаака, с различными аминами. Реакция с палладиевым комплексом копропорфирина II приводит к образованию оснований Шиффа в виде смеси двух структурных изомеров в отношении 4:1. Строение полученных соединений установлено с привлечением методов ЯМР ^{1}H, ^{13}C, ^{1}H-^{1}H NOESY и УФ спектроскопии, а также данных масс-спектрометрии.

Ключевые слова: Порфирин, палладий, копропорфирин, азометин, реакция Вильсмейра-Хаака.

Introduction

Porphyrins and metalloporphyrins are widespread in nature; due to the aromatic bond system, porphyrins are very promising for use in various fields of science and technology. For instance, many achievements in supramolecular chemistry, including development of new materials, are related to porphyrin molecules linked by the intermolecular noncovalent bonds.[1-4] Due to the unique photophysical and photochemical properties, porphyrins and metalloporphyrins are used as sensors in bioassay,[5-7] active drug substances in cancer diagnostics and therapy.[8,9] Many fundamental studies in search of new sensors are presently carried out, which are aimed to find new multiparametric sensors, particularly covering such analytes as O_2, CO_2, *etc*.[10] The potential use of derivatives of mono-*meso*-substituted porphyrins and metalloporphyrins as multiparametric sensors for oxygen and H^+ is one of the main factors driving ever-growing interest in the synthesis of new porphyrin derivatives.[11] The porphyrins have attracted even more attention from researchers in various fields due to their phototherapeutic properties in past two decades.[12-14] Porphyrin derivatives and related systems have been used as photosensitizers in cancer phototherapy. Hematoporphyrin Derivative, such as Photofrin®, Photosan® and Photogem® have regulatory approval; however, they are complex mixtures of oligomers with the weak absorption at *ca*. 620 nm. At the same time, the high degree of skin photosensitivity is a major drawback in the use of such compounds.[15-17] For the effective application in photodynamic therapy (PDT) the porphyrin samples should be water-soluble and hydrophilic, possess high values of photophysical parameters, such as phosphorescence lifetime and quantum yield of phosphorescence and emit in the infrared region of the spectrum with a Stokes shift at *ca*. 100 nm.[18] Recently, the most part of synthetic studies in this field was focused mainly on the *meso*-tetraaryl porphyrins,[19-20] but these compounds have bulky benzene rings, which make them inherently hydrophobic and limits their further use in the biological systems. To overcome such limitation, it is necessary to use hydrophilic porphyrins with good solubility in organic solvents and water such as isomeric coproporphyrins having four carboxyl groups.[21-22] In this paper we have developed the effective method of producing mono-substituted azomethine derivatives of coproporphyrins I, II and their palladium(II) complexes that can be considered as phosphorescent labels and potential PDT candidates.

Experimental

Methylamine (38% aqueous solution), allylamine, propargylamine, $POCl_3$ were purchased from Sigma-Aldrich, Fluka, Merck and used without further purification. Solvents were purified by standard procedures: CH_2Cl_2 and 1,2-dichloroethane were distilled over CaH_2. Methanol (Merck, 99%) and *N,N*-dimethylformamide (Labscan, 99%) were used as received. Coproporphyrines I[21] and II[22] were prepared according to the described procedures. Palladium(II) complexes of coproporphyrins I (**1**) and II (**4**) were synthesized following the known procedures.[23]

UV-Vis electronic absorption spectra were registered using U-2900 (Hitachi) spectrophotometer and quartz rectangular cells of 1-10 mm path length. ^{1}H (600 MHz) NMR spectra were recorded at T = 298 K with a Bruker Avance III 600 spectrometer in $CDCl_3$. Chemical shifts δ are quoted in parts per million (ppm) downfield of tetramethylsilane. Coupling constants are given in Hz. ^{13}C (150 or 75 MHz) NMR spectra were recorded on a Bruker Avance III 600 or Bruker AVANCE I 300 in $CDCl_3$, respectively. The MALDI-TOF mass-spectra were obtained on a Ultraflex-II mass spectrometer (Bruker Daltonics) in a positive ion mode using reflection mode (20 mV target voltage) without matrix. High-resolution mass spectra were recorded on a Bruker ESI microTOF II mass spectrometer using electrospray ionization.

A typical procedure for synthesis of Pd(II) azomethine derivatives of coproporphyrin I and II. To a solution of Pd(II) coproporphyrin I tetraisopropyl ester (**1**) (47 mg, 0.05 mmol) in 25 mL of dry 1,2-dichloroethane the Vilsmeier reagent, in situ formed[24] from $POCl_3$ (0.25 ml, 2.75 mmol) and *N,N*-dimethylformamide (0.25 ml, 3.25 mmol), was added at 75 °C. The resulting mixture was stirred for 5 hours at the same temperature and the reaction was monitored by TLC (CH_2Cl_2/MeOH, 99:1 by volume). Then the solution was evaporated and the residue obtained was dissolved in CH_2Cl_2 (25 ml) and washed with H_2O (25 ml). The aqueous phase was extracted once with CH_2Cl_2 (25 mL). The combined organic phases were dried over Na_2SO_4, the salt was removed by filtration, and the solution was evaporated. Then the solid obtained was dissolved in a minimum amount of CH_2Cl_2 (5-10 ml) and an amine (0.25 mmol) was added. The reaction mixture was evaporated to afford the crude compound, which was purified by chromatography (silica gel). The traces of unreacted porphyrin were eluted first (CH_2Cl_2/MeOH, 99:1 by volume). Then the orange fraction of the azomethine derivative was collected (CH_2Cl_2/MeOH, 96:4).

*Palladium(II) azomethine derivative of coproporphyrin I with methylamine (**3a**).* Yield 78%. ^{1}H NMR: 10.55 (1H, s, C*H*N), 9.99 (1H, s, *meso-H*), 9.96 (1H, s, *meso-H*), 9.95 (1H, s, *meso-H*), 5.23 (1H, septet, *J* = 6.6, C*H*$(CH_3)_2$), 5.12 (1H, septet, *J* = 6.6, C*H*$(CH_3)_2$), 5.11 (1H, septet, *J* = 6.6, C*H*$(CH_3)_2$), 5.10 (1H, septet, *J* = 6.6, C*H*$(CH_3)_2$), 4.33 (2H, t, *J* = 7.2, $CH_2CH_2CO_2$), 4.31 (2H, t, *J* = 6.6, $CH_2CH_2CO_2$), 4.24 (2H, t, *J* = 7.8, $CH_2CH_2CO_2$), 4.00 (3H, s, NC*H*$_3$), 3.96-3.93 (2H, m, $CH_2CH_2CO_2$), 3.59 (3H, s, β-C*H*$_3$), 3.58 (3H, s, β-C*H*$_3$), 3.55 (3H, s, β-C*H*$_3$), 3.21 (4H, t, *J* = 7.8, $CH_2CH_2CO_2$), 3.11 (3H, s, β-C*H*$_3$), 3.10 (2H, t, *J* = 7.2, $CH_2CH_2CO_2$), 2.90-2.87 (2H, m, $CH_2CH_2CO_2$), 1.37 (6H, d, *J* = 6.6, CH(C*H*$_3$)$_2$), 1.20 (6H, d, *J* = 6.6, CH(C*H*$_3$)$_2$), 1.17 (6H, d, *J* = 6.6, CH(C*H*$_3$)$_2$), 1.15 (6H, d, *J* = 6.6, CH(C*H*$_3$)$_2$). MS (MALDI-TOF) *m/z*: 968.5. Calcd. for $[M]^+$ 968.5. UV-Vis ($CHCl_3$) λ_{max} nm (log ε·10^{-3}, M^{-1}cm^{-1}): 397 (252), 516 (11.2), 549 (46.5).

*Palladium(II) azomethine derivative of coproporphyrin I with allylamine (**3b**).* Yield 81%. ^{1}H NMR: 10.77 (1H, s, C*H*N), 10.03 (1H, s, *meso-H*), 10.00 (1H, s, *meso-H*), 9.99 (1H, s, *meso-H*), 6.39 (1H, ddt, , *J* = 16.8, *J* = 10.2, *J* ≈ 6.6, NCH_2CH), 5.55 (1H, dq, *J* = 16.8, *J* ≈ 1.8, NCH_2CHCH_2), 5.38 (1H, dq, *J* = 10.2, *J* ≈ 1.8, NCH_2CHCH_2), 5.20 (1H, septet, *J* = 6.6, C*H*$(CH_3)_2$), 5.14 (1H, septet, *J* = 6.6, C*H*$(CH_3)_2$), 5.11 (1H, septet, *J* = 6.6, C*H*$(CH_3)_2$), 5.10 (1H, septet, *J* = 6.6, C*H*$(CH_3)_2$), 4.85 (2H, dd, *J* = 6.0, *J* ≈ 1.2, NC*H*$_2$), 4.34 (2H, t, *J* = 7.2, $CH_2CH_2CO_2$), 4.32 (2H, t, *J* = 7.2, $CH_2CH_2CO_2$), 4.28 (2H, t, *J* = 7.8, $CH_2CH_2CO_2$), 4.03-4.00 (2H, m, $CH_2CH_2CO_2$), 3.60 (6H, s, β-C*H*$_3$), 3.58 (3H, s, β-C*H*$_3$), 3.22 (4H, t, *J* = 7.8, $CH_2CH_2CO_2$), 3.19 (3H, s, β-C*H*$_3$), 3.12 (2H, t, *J* = 7.8, $CH_2CH_2CO_2$), 2.94-2.91 (2H, m, $CH_2CH_2CO_2$), 1.34 (6H, d, *J* = 6.6, CH(C*H*$_3$)$_2$), 1.21 (6H, d, *J* = 6.6, CH(C*H*$_3$)$_2$), 1.16 (6H, d, *J* = 6.6, CH(C*H*$_3$)$_2$), 1.15 (6H, d, *J* = 6.6, CH(C*H*$_3$)$_2$). MS (MALDI-TOF) *m/z*: 994.4. Calcd. for $[M]^+$ 994.5. HRMS (ESI): calcd. for $C_{52}H_{66}N_5O_8Pd$ 994.3959; found 994.3944 $[M+H]^+$. HRMS (ESI): calcd. for $C_{52}H_{65}N_5NaO_8Pd$ 1016.3778; found 1016.3763 $[M+Na]^+$. UV-Vis ($CHCl_3$) λ_{max} nm (log ε·10^{-3}, M^{-1}cm^{-1}): 398 (251), 516 (11.4), 549 (46).

*Palladium(II) azomethine derivative of coproporphyrin I with propargylamine (**3c**).* Yield 80%. ^{1}H NMR: 10.82 (1H, s,

C*H*N), 10.03 (1H, s, *meso-H*), 9.98 (1H, s, *meso-H*), 9.95 (1H, s, *meso-H*), 5.35-5.33 (2H, m, CH_2CCH), 5.21 (1H, septet, J = 6.6, $CH(CH_3)_2$), 5.16 (3H, septet, J = 6.6, $CH(CH_3)_2$), 4.33-4.31 (4H, m, $CH_2CH_2CO_2$),), 4.28 (2H, t, J = 7.8, $CH_2CH_2CO_2$),), 4.05 (2H, t, J = 7.8, $CH_2CH_2CO_2$), 3.58 (6H, s, β-CH_3), 3.56 (3H, s, β-CH_3), 3.49 (1H, s, CH_2CCH), 3.25 (4H, t, J = 7.8, $CH_2CH_2CO_2$), 3.20 (3H, s, β-CH_3), 3.15 (2H, t, J = 7.8, $CH_2CH_2CO_2$), 2.94 (2H, t, J = 7.8, $CH_2CH_2CO_2$), 1.30 (6H, d, J = 6.6, $CH(CH_3)_2$), 1.27 (6H, d, J = 6.6, $CH(CH_3)_2$), 1.20 (6H, d, J = 6.6, $CH(CH_3)_2$), 1.16 (6H, d, J = 6.6, $CH(CH_3)_2$). MS (MALDI-TOF) *m/z*: 992.5. Calcd. for $[M]^+$ 992.5. UV-Vis ($CHCl_3$) λ_{max} nm (log ε·10^{-3}, M^{-1}cm^{-1}): 397(253), 514(11.3), 549(46.5).

*Palladium(II) azomethine derivative of coproporphyrin II with methylamine (major isomer) (**7a**).* Yield 70%. ^{1}H NMR: 10.47 (1H, s, C*H*N), 9.90 (2H, s, C_5H and $C_{15}H$), 9.87 (1H, s, $C_{20}H$), 4.28 (4H, t, J = 7.8, C_3CH_2 and $C_{17}CH_2$), 4.24 (4H, t, J = 7.8, C_7CH_2 and $C_{13}CH_2$), 4.18 (4H, q, J = 7.2, CH_2CH_3), 4.15 (4H, q, J = 7.2, CH_2CH_3), 4.06 (3H, s, NCH_3), 3.54 (6H, s, C_2CH_3 and $C_{18}CH_3$), 3.22 (4H, t, J = 7.8, $C_3CH_2CH_2$ and $C_{17}CH_2CH_2$), 3.14 (4H, t, J = 7.8, $C_7CH_2CH_2$ and $C_{13}CH_2CH_2$), 3.14 (6H, s, C_8CH_3 and $C_{12}CH_3$), 1.18 (6H, t, J = 7.2, CH_2CH_3), 1.14 (6H, t, J = 7.2, CH_2CH_3). ^{13}C{H} NMR (150.9 MHz): 173.12 and 173.10 (CO_2Et), 166.1 (*C*HN), 140.2 (C arom.), 139.0 (C arom.), 138.6 (C arom.), 138.5 (C arom.), 138.2 (C arom.), 137.9 (C arom.), 136.5 (C arom.), 136.2 (C arom.), 99.0 (C_5 and C_{15}), 98.8 (C_{20}), 60.54 and 60.50 (CH_2CH_3), 49.2 (NCH_3), 37.08 and 37.07 (CH_2CO_2Et), 21.8 and 21.7 ($CH_2CH_2CO_2$), 18.4 and 18.3 (C_2CH_3 and $C_{18}CH_3$), 14.15 and 14.11 (CH_2CH_3), 11.7 (C_8CH_3 and $C_{12}CH_3$). MS (MALDI-TOF) *m/z*: 912.2. Calcd. for $[M]^+$ 912.4. HRMS (ESI): calcd. for $C_{46}H_{56}N_5O_8Pd$ 912.3175; found 912.3170 $[M+H]^+$. UV-Vis ($CHCl_3$) λ_{max} nm (log ε·10^{-3}, M^{-1}cm^{-1}): 397(248), 514(10.8), 549(45.5).

*Palladium(II) azomethine derivative of coproporphyrin II with allylamine (major isomer) (**7b**).* Yield 69%. ^{1}H NMR: 10.49 (1H, s, C*H*N), 9.92 (2H, s, C_5H and $C_{15}H$), 9.88 (1H, s, $C_{20}H$), 6.39 (1H, ddt, J = 16.8, J = 10.2, $J \approx 6.6$, NCH_2CH), 5.55 (1H, dq, J = 16.8, $J \approx 1.8$, NCH_2CHCH_2), 5.39 (1H, dq (broad), J = 10.2, $J \approx 1.8$, NCH_2CHCH_2), 4.85 (2H, dd, J = 6.2, $J \approx 1.2$, NCH_2), 4.30 (4H, t, J = 7.8, C_3CH_2 and $C_{17}CH_2$), 4.25 (4H, t, J = 7.8, C_7CH_2 and $C_{13}CH_2$), 4.18 (4H, q, J = 7.2, CH_2CH_3), 4.15 (4H, q, J = 7.2, CH_2CH_3), 3.55 (6H, s, C_2CH_3 and $C_{18}CH_3$), 3.23 (4H, t, J = 7.8, $C_3CH_2CH_2$ and $C_{17}CH_2CH_2$), 3.14 (4H, t, J = 7.8, $C_7CH_2CH_2$ and $C_{13}CH_2CH_2$), 3.12 (6H, s, C_8CH_3 and $C_{12}CH_3$), 1.18 (6H, t, J = 7.2, CH_2CH_3), 1.13 (6H, t, J = 7.2, CH_2CH_3). ^{13}C{H} NMR (150.9 MHz): 173.14 and 173.13 (CO_2Et), 165.9 (CHN), 140.0 (C arom.), 138.8 (C arom.), 138.4 (C arom.), 138.3 (C arom.), 137.9 (C arom.), 136.4 (C arom.), 136.0 (C arom.), 134.6 (NCH_2CH), 117.5 (NCH_2CHCH_2), 98.8 (C_5 and C_{15}), 98.7 (C_{20}), 65.3 (NCH_2), 60.55 and 60.51 (CH_2CH_3), 37.0 (CH_2CO_2Et), 21.7 and 21.6 ($CH_2CH_2CO_2$), 18.3 (C_2CH_3 and $C_{18}CH_3$), 14.14 and 14.10 (CH_2CH_3), 11.7 (C_8CH_3 and $C_{12}CH_3$). MS (MALDI-TOF) *m/z*: 938.3. Calcd. for $[M]^+$ 938.4. HRMS (ESI): calcd. for $C_{48}H_{58}N_5O_8Pd$ 938.3332; found 938.3324 $[M+H]^+$. UV-Vis ($CHCl_3$) λ_{max} nm (log ε·10^{-3}, M^{-1}cm^{-1}): 397(249), 515 (10.5), 549(45.4).

*Palladium(II) azomethine derivative of coproporphyrin II with propargylamine (major isomer) (**7c**).* Yield 63%. ^{1}H NMR: 11.24 (1H, s, C*H*N), 9.92 (2H, s, C_5H and $C_{15}H$), 9.86 (1H, s, $C_{20}H$), 5.09 (2H, t, J = 2.4, CH_2CCH), 4.38 (4H, t, J = 7.8, C_3CH_2 and $C_{17}CH_2$), 4.36 (4H, t, J = 7.8, C_7CH_2 and $C_{13}CH_2$), 4.18 (4H, q, J = 7.2, CH_2CH_3), 4.15 (4H, q, J = 7.2, CH_2CH_3), 3.62 (6H, s, C_2CH_3 and $C_{18}CH_3$), 3.31 (6H, s, C_8CH_3 and $C_{12}CH_3$), 3.28 (4H, t, J = 7.8, $C_3CH_2CH_2$ and $C_{17}CH_2CH_2$), 3.21 (4H, t, J = 7.8, $C_7CH_2CH_2$ and $C_{13}CH_2CH_2$), 2.94 (1H, t, J = 2.4, CH_2CCH), 1.18 (6H, t, J = 7.2, CH_2CH_3), 1.13 (6H, t, J = 7.2, CH_2CH_3). ^{13}C{H} NMR (75.5 MHz): 173.1 (CO_2Et), 167.3 (CHN), 140.0 (C arom.), 139.9 (C arom.), 138.7 (C arom.), 138.3 (C arom.), 138.27 (C arom.), 137.7 (C arom.),136.3 (C arom.), 135.9 (C arom.), 98.8 (C_5 and C_{15}), 98.6 (C_{20}), 77.6 (NCH_2C), 77.2 (NCH_2CCH), 60.54 and 60.51(CH_2CH_3), 48.0 (NCH_2), 37.0 (CH_2CO_2Et), 21.7 and 21.63 ($CH_2CH_2CO_2$), 18.1 (C_2CH_3 and $C_{18}CH_3$), 14.14 and 14.11(CH_2CH_3), 11.7 (C_8CH_3 and $C_{12}CH_3$). MS (MALDI-TOF) *m/z*: 937.6. Calcd. for $[M+H]^+$ 937.4. HRMS (ESI): calcd. for $C_{48}H_{56}N_5O_8Pd$ 936.3175; found 936.3162 $[M+H]^+$. UV-Vis ($CHCl_3$) λ_{max} nm (log ε·10^{-3}, M^{-1}cm^{-1}): 397(253), 514 (11.3), 549(46.5).

*Palladium(II) azomethine derivative of coproporphyrin II with methylamine (minor isomer) (**8a**).* Yield 15%. ^{1}H NMR: 10.95 (1H, s, C*H*N), 10.08 (3H, s, *meso-H*), 4.37 (4H, t, J = 7.8, $CH_2CH_2CO_2$), 4.32 (4H, q, J = 7.2, CH_2CH_3), 4.18 (4H, q, J = 7.2, CH_2CH_3), 4.08-4.05 (4H, m, $CH_2CH_2CO_2$), 4.00 (3H, s (broad), NCH_3), 3.62 (6H, s, β-CH_3), 3.59 (6H, s, β-CH_3), 3.28 (4H, t, J = 7.8, $CH_2CH_2CO_2$), 2.99-2.96 (4H, m, $CH_2CH_2CO_2$), 1.30 (6H, t, J = 7.2, CH_2CH_3), 1.15 (6H, t, J = 7.2, CH_2CH_3). MS (MALDI-TOF) *m/z*: 912.2. Calcd. for $[M]^+$ 912.4. HRMS (ESI): calcd. for $C_{46}H_{56}N_5O_8Pd$ 912.3175; found 912.3167 $[M+H]^+$. UV-Vis ($CHCl_3$) λ_{max} nm (log ε·10^{-3}, M^{-1}cm^{-1}): 397(248), 515 (10.8), 549(45.5).

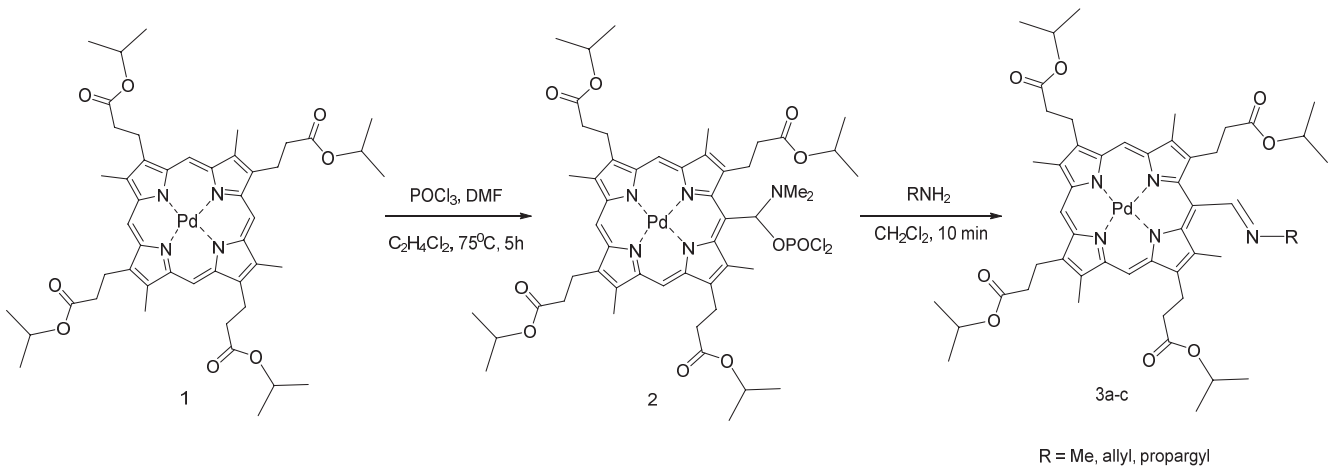
*Palladium(II) azomethine derivative of coproporphyrin II with allylamine (minor isomer) (**8b**).* Yield 14%. ^{1}H NMR: 10.89 (1H, s, C*H*N), 9.98 (2H, s, *meso-H*), 9.97 (1H, s, *meso-H*), 6.36 (1H, ddt, J = 16.8, J = 10.2, $J \approx 6.6$, NCH_2CH), 5.54 (1H, d (broad), J = 16.8, NCH_2CHCH_2), 5.35 (1H, d (broad), J = 10.2, NCH_2CHCH_2), 4.82 (2H, dd, J = 6.6, $J \approx 1.2$, NCH_2), 4.32-4.29 (4H, m, $CH_2CH_2CO_2$), 4.27 (4H, q, J = 7.2, CH_2CH_3), 4.17 (4H, q, J = 7.2, CH_2CH_3), 4.03-4.00 (4H, m, $CH_2CH_2CO_2$), 3.57 (6H, s, β-CH_3), 3.54 (6H, s, β-CH_3), 3.25 (4H, t, J = 7.8, $CH_2CH_2CO_2$), 2.97-2.94 (4H, m, $CH_2CH_2CO_2$), 1.32 (6H, t, J = 7.2, CH_2CH_3), 1.15 (6H, t, J = 7.2, CH_2CH_3). MS (MALDI-TOF) *m/z*: 938.1. Calcd. for $[M]^+$ 938.4. UV-Vis ($CHCl_3$) λ_{max} nm (log ε·10^{-3}, M^{-1}cm^{-1}): 398(249), 516 (10.5), 551(45.4).

*Palladium(II) azomethine derivative of coproporphyrin II with propargylamine (minor isomer) (**8c**).* Yield 11%. ^{1}H NMR: 11.44 (1H, s, C*H*N), 10.10 (2H, s, *meso-H*), 10.09 (1H, s, *meso-H*), 5.10 (2H, t (broad), $J \approx 2.4$, CH_2CCH), 4.38 (4H, t, J = 7.8, $CH_2CH_2CO_2$), 4.29 (4H, q, J = 7.2, CH_2CH_3), 4.17 (4H, q, J = 7.2, CH_2CH_3), 4.11-4.08 (4H, m, $CH_2CH_2CO_2$), 3.62 (6H, s, β-CH_3), 3.61 (6H, s, β-CH_3), 3.29 (4H, t, J = 7.8, $CH_2CH_2CO_2$), 3.00-2.97 (4H, m, $CH_2CH_2CO_2$), 2.90 (1H, t, $J \approx 2.4$, CH_2CCH), 1.34 (6H, t, J = 7.2, CH_2CH_3), 1.15 (6H, t, J = 7.2, CH_2CH_3). MS (MALDI-TOF) *m/z*: 937.1. Calcd. for $[M+H]^+$ 937.4. UV-Vis ($CHCl_3$) λ_{max} nm (log ε·10^{-3}, M^{-1}cm^{-1}): 397(249), 515 (10.5), 549.5(45.4).

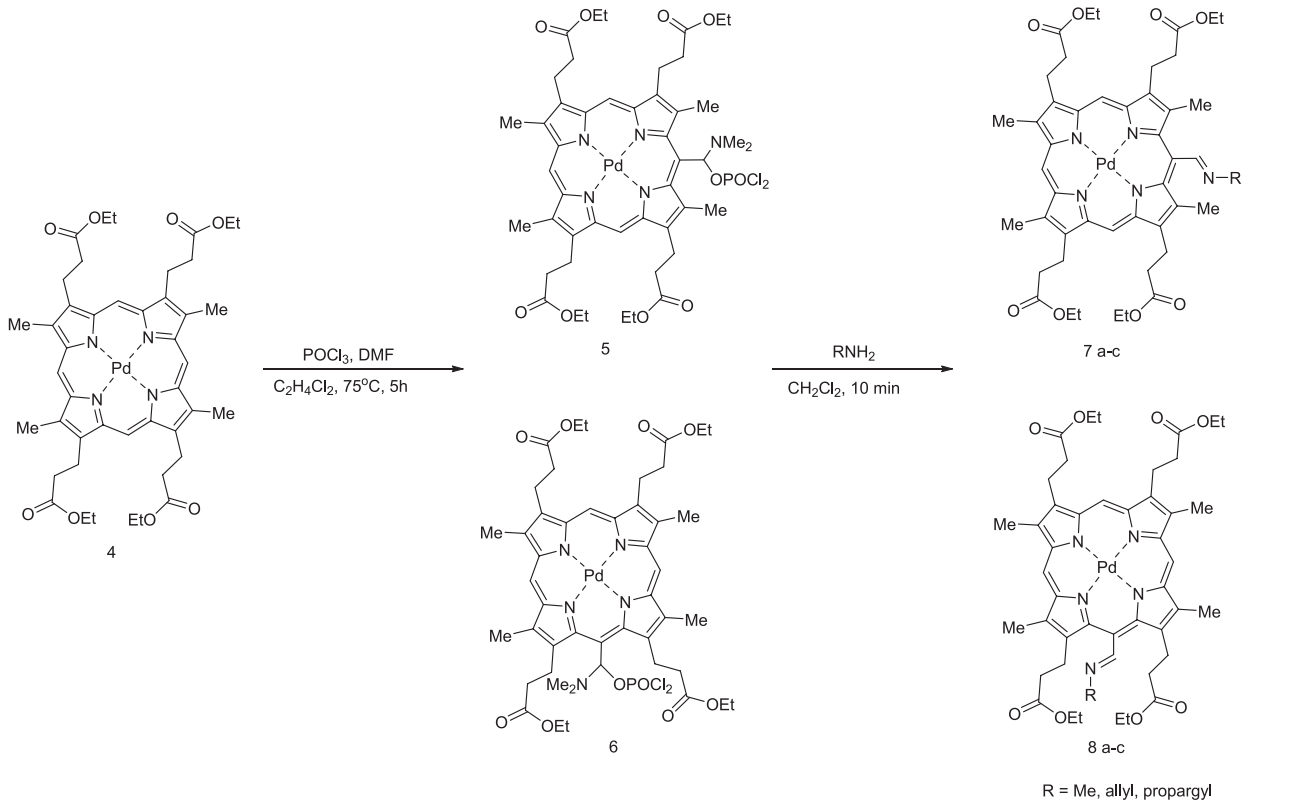
Results and Discussion

The corresponding palladium(II) complexes **1** and **4**[23] were selected as starting compounds for synthesis of azomethine derivatives of coproporphyrins (Schemes 1 and 2). For the synthesis of azomethine derivatives of coproporphyrin isomers I and II we have used method based on the reaction of imine salt, the so-called "phosphorus complex" generated *in situ* via the Vilsmeier-Haack reaction, with different amines. This method was successfully applied in the chemistry of porphyrins earlier.[25]

The Vilsmeier-Haack reaction of palladium complex of coproporphyrin II (**4**) gave the corresponding Schiff bases as two structural isomers in 4:1 ratio. We assume that the direction and the yield of this reaction strongly depends on substituents in adjacent pyrrole rings. Thus the formation of minor isomers **8a-c** with low yields could be explained by the sterically hindered propionic residues at adjacent β-positions that complicates the reaction at this center. The minor isomer was separated using 1% MeOH solution in dichloromethane, and then the major product was isolated using the CH_2Cl_2/MeOH (96:4) system. The new compounds were purified by column chromatography and characterized by a combination of mass spectrometry (MALDI-TOF and HR ESI) and ^{1}H,



Scheme 1. The synthesis of compounds **3a-c**.



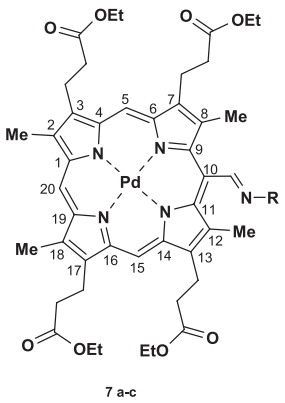
Scheme 2. The synthesis of compounds **7a-c** and **8a-c**.

^{13}C and ^{1}H-^{1}H NOESY NMR and UV-Vis spectroscopy (see Experimental Section for the data and Scheme 3).

First of all, to characterize the structure of the prepared azomethine derivatives, ^{1}H NMR spectroscopical investigations were carried out. For example, compound **7a** has resonances at 10.47, 9.90 (double intensity) and 9.87 ppm which correspond to the protons of CH=N-Me fragment and three free *meso*-positions.

The connectivity between the azomethine residue and the porphyrin core in complexes **7a-c** was determined from ^{1}H-^{1}H NOESY spectra. For instance, there is a correlation between a proton of the imine fragment (10.49 ppm) and the protons of β-Me group (3.12 ppm) in the NOESY spectrum of **7b** (Figure 1).

The imine CH=N- and the allyl CH_2 protons (4.85 ppm) have a correlation as well. Altogether, it means that the imine fragment is placed between the methyl groups of respective pyrroles and excludes any alternative structure of complex **7b**. It is also important to note, that the presence of cross peaks between protons of the azomethine fragment and the allyl, proves the (E)-configuration of the double C=N bond. These correlations confirmed the structure of the azomethine fragment, as well as a connectivity between the imine part and the porphyrin core.



Scheme 3. The numbering scheme for complexes **7a-c**.

Table 1. Absorption characteristics of azomethine derivatives in $CHCl_3$.

Compound	λ_{max} (nm)		
	Soret	Q_x	Q_y
1	392	512	546
3a	397	516	549
3b	398	516	549
3c	397	514	549
4	393	511	546
7a	397	514	549
7b	397	515	549
7c	397	514	549
8a	397	515	549
8b	398	516	551
8c	397	515	549

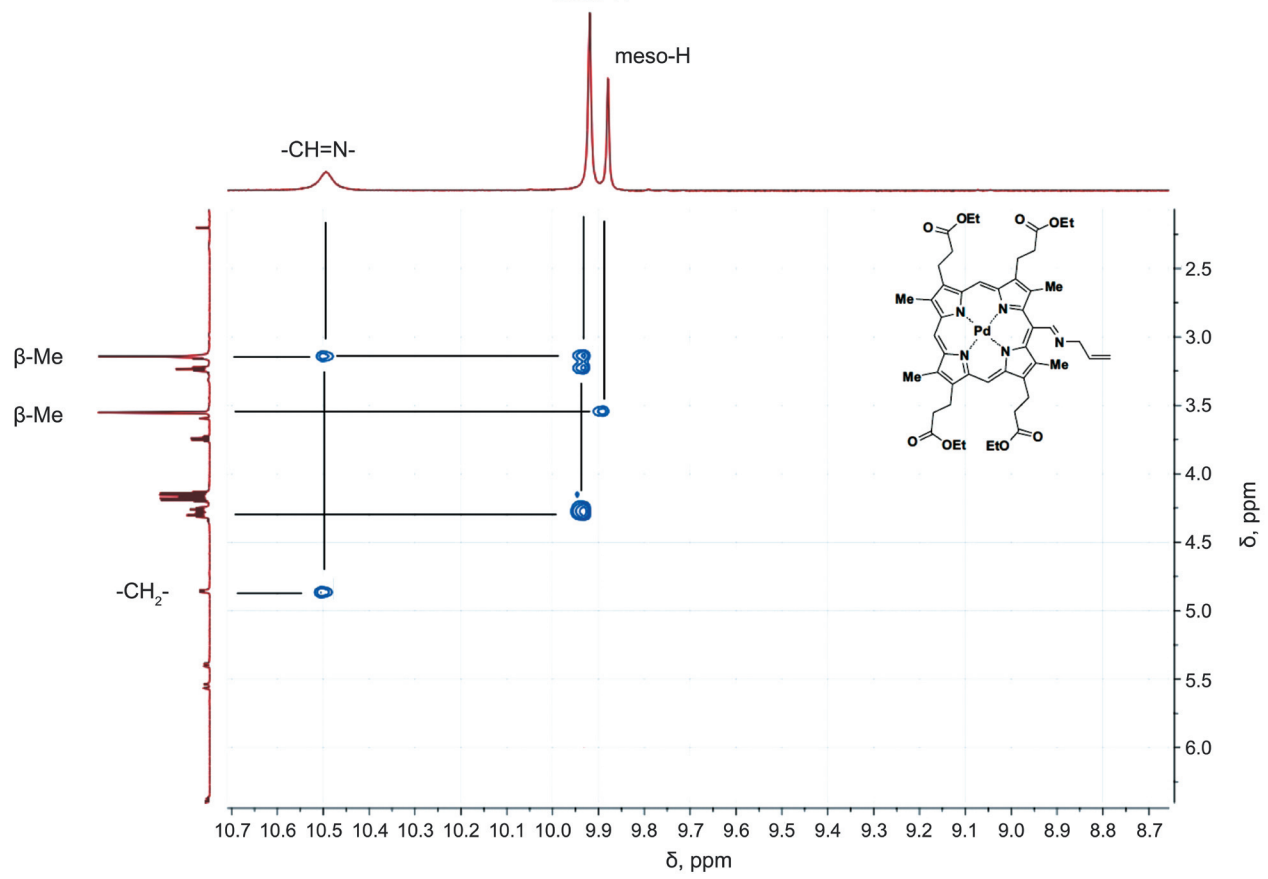


Figure 1. ^1H-^1H NOESY spectrum of compound **7b** in $CDCl_3$ at 298 K.

The electronic absorption spectral data of obtained complexes **3a-c**, **7a-c** and **8a-c** in comparison with the data for starting compounds **1** and **4** are given in Table 1. The pronounced bathochromic shifts (3-5 nm) of the Soret band and the Q-bands were observed in all cases.

The ^{13}C NMR spectroscopic data are also in good agreement with structures of complexes **7a-c** (see Experimental Part).

MALDI-TOF mass spectrometric examination of all synthesized compounds proved the mononuclear nature of the palladium complexes with the detection of molecular ions. HR ESI mass spectrometry additionally confirmed the elemental composition of compounds **3b**, **7a-c** and **8a**. Unfortunately, numerous attempts to grow single crystals of the new complexes suitable for an X-ray diffraction study have failed.

Conclusion

In summary, a new route for the preparation of Pd(II) coproporphyrin azomethine derivatives was suggested. This approach gives an access to the straightforward synthesis of unsymmetrical coproporphyrins bearing

different substituents at the nitrogen atom. Some detailed ^{1}H-^{1}H NOESY NMR studies of obtained complexes were performed as well. This information should be useful for the design and synthesis of new coproporphyrin azomethine derivatives. Further investigations concerned to the synthesis of related Pd(II) coproporphyrin complexes and their use in photochemical investigations are currently in progress.

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