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Phthalocrowns: Isoindoline–Crown Ether Macrocycles

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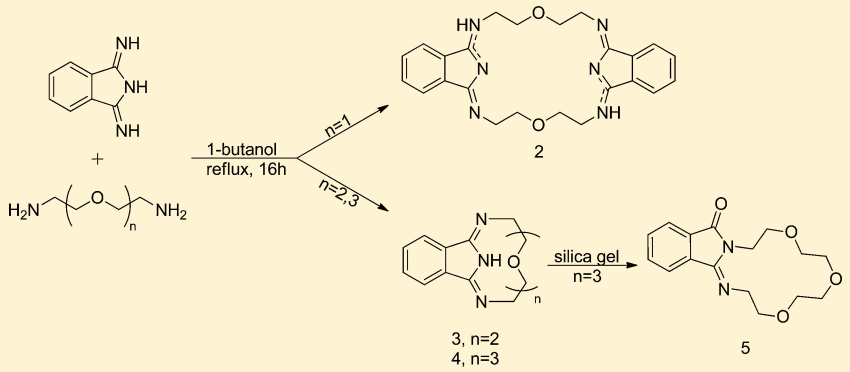
Supporting Information



ABSTRACT: The reaction of diiminoisoindoline with amine-terminated polyethers results in the formation of phthalocrown macrocycles. For n = 1 (where n is the number of ether units), a 2 + 2 condensation takes place, but for n = 2 and 3, a 1 + 1 macrocycle formation occurs. The n = 2 phthalocrown is particularly stable due to a strong intramolecular hydrogen bond, but the n = 3 ring hydrolyzes to form a 3-imino-1-oxoisoindoline derivatized crown ether species. For the n = 1 phthalocrown, we observed dynamic behavior in the ^{1}H NMR spectrum, and using VTNMR were able to measure a $\Delta G^{\ddagger}$ = 44.6 kJ/mol for proton exchange.

The binding and molecular recognition of cations is a significant field in coordination chemistry.[1,2] A variety of host molecules (ligands and macrocycles) have been synthesized, and the properties of these compounds to selectively bind cations continue to be studied. Two of the most studied metal-binding macrocycles are the synthetic dye phthalocyanine[3,4] and the cation-binding family of polyoxo macrocycles known as the crown ethers.[5−7] The crown ethers, first discovered in the 1960s by Pedersen, are known for their affinity to alkali metal ions and charged molecules such as ammonium (NH_4^+)[8] and play important roles as phase-transfer catalysts.[9] The phthalocyanines are also important metal binding macrocycles and are used heavily both as bulk colorants and as components of specialized materials.[10] Since 2006, we have been investigating the synthetic chemistry of phthalocyanine analogues known as the hemiporphyrazines, where rings other than isoindolines (such as benzene, pyridine, or cyclohexane) are introduced into the backbone of the phthalocyanine macrocyle.[11−14] In this paper, we present a family of phthalocyanine hybrid molecules using hemiporphyrazine synthetic methods. Specifically, herein we report the family of phthalocyanine/crown ether chimeras we call the phthalocrowns, fusions between these two macrocycles. Four different phthalocrowns were synthesized and characterized, including two which we were able to structurally elucidate. Depending on the number of ether units, either 2:2 or 1:1 macrocycles are formed. Additionally, between the dioxo and trioxo phthalocrowns, we observed significant differences in stability, with the trioxo macrocycle hydrolyzing to form an imino-oxo isoindoline derivative.

In the early 1950s, Linstead and co-workers reported the synthesis of 1,3-diiminoisoindoline (DII, **1**)[15] as a precursor to the synthesis of phthalocyanines, hemiporphyrazines, and related isoindoline-based chelates.[15−20] Compound **1**, shown in Scheme 1, is synthesized via the reaction of phthalonitrile with ammonia in a methanol solution in the presence of a small amount of sodium metal.[15] Diiminoisoindoline was found to be a precursor for the synthesis of a variety of chelating ligands and macrocycles. For example, compound **1** reacts with 2,6-diaminopyridine to produce hemiporphyrazine and with 2-aminopyridine to afford 1,3-bis(2-pyridylimino)isoindoline. Both hemiporphyrazine and 1,3-bis(2-pyridylimino)isoindoline coordinate to metal ions and exhibit rich transition element chemistry.[21−23] In addition to arylamines, compound **1** also reacts with aliphatic amines to afford the corresponding substituted diiminoisoindolines. Recently, we synthesized an aliphatic analogue of phthalocyanine, cyclohexylcyanine, by reacting 1,3 diaminocyclohexane with compound **1**.[14] We have surmised that we could extend this chemistry to the synthesis of new isoindoline based macrocycle types, and that we could generate phthalocyanine/crown ether chimera-type molecules via the reaction of amine terminated polyethers with **1**.

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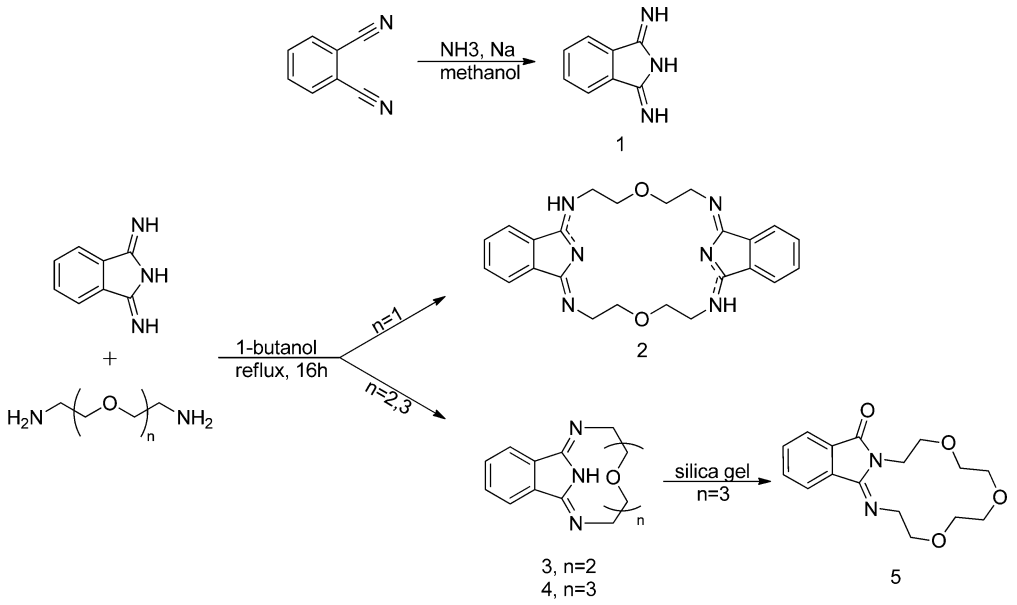
Scheme 1. General Synthesis of the Phthalocrowns



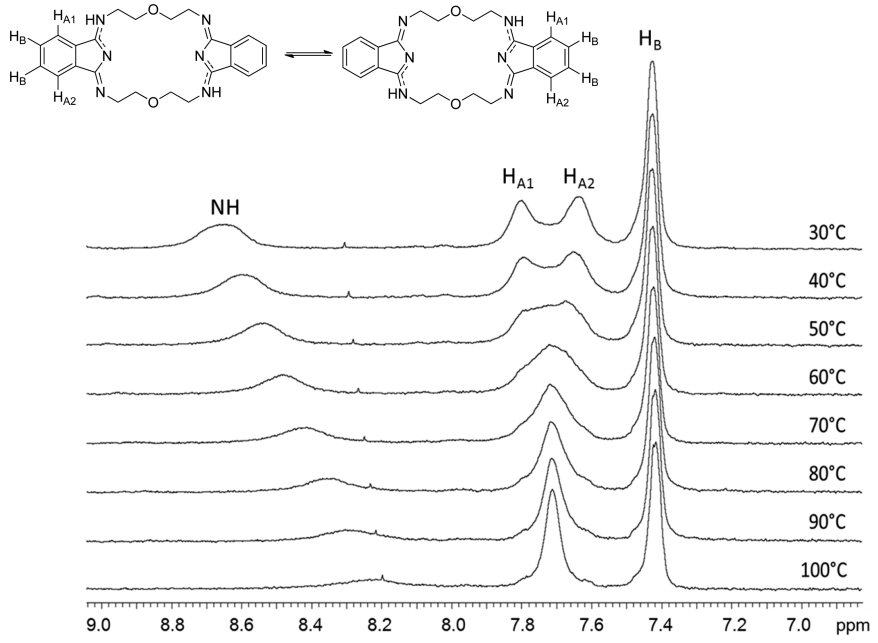


Figure 1. Variable-temperature ^{1}H NMR of **2** in DMSO showing dynamic proton exchange behavior.

We reacted diiminoisoindoline **1** with three amine terminated ethers, as shown in Scheme 1. The monooxo species 2,2′-oxybis(ethylamine) and the dioxo precursor 1,2-bis(2-aminoethoxy)ethane are commercially available, and the trioxo compound 1,11-diamino-3,6,9-trioxaundecane was synthesized from the corresponding chloride using the procedure described in a patent and by Thomas.[24,25] All three amino ethers were reacted with **1** in a slight excess in refluxing butanol for 16 h, and we observed two types of product formation depending on the size of the ether chain. In the case of 2,2′-oxybis(ethylamine), condensation with **1** produces a 2 + 2 product, shown in Scheme 1. The ratio of diamine and isoindoline in the macrocycle formation is most easily observed via mass spectrometry (and not very readily by NMR methods). The mass spectrum clearly shows the presence of a product peak from the reaction of **1** with 2,2′-oxybis(ethylamine) at 431.22 *m*/*z*, corresponding to the 2 + 2 product **2**. The 1,2-bis(2-aminoethoxy)ethane and 1,11-diamino-3,6,9-trioxaundecane precursors, however, form 1:1 ratio macrocycles **3** and **4**, exhibiting mass spectrometry peaks at 282.12 (M + Na) and 304.16 *m*/*z* values respectively. We surmise that the 2 + 2 product forms upon reaction of **1** with 2,2′-oxybis(ethylamine) due to the steric limitations of a 1 + 1 macrocycle. We also attempted to synthesize these compounds using a modified Siegl procedure[26] with alkali or alkali earth metal cations as templates but were unsuccessful in isolating any phthalocrowns.

Compound **2** shows limited solubility, as seen in the related hemiporphyrazines,[27] and dissolves in DMF, DMSO, high boiling alcohols, and a 1:9 solution of methanol/chloroform.

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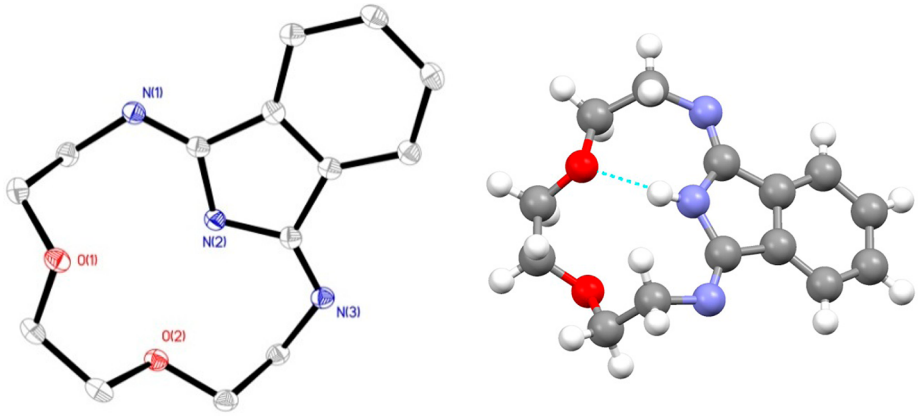

Figure 2. Structure of **3** with 35% thermal ellipsoids (left) and the structure of **3** showing the internal hydrogen bond (right). Hydrogen atoms on the thermal ellispoid plot have been omitted for clarity.

Compounds **3** and **4** exhibit increased solubility versus the hemiporphyrazines, dissolving in nearly all solvents with the exception the alkanes, ethers, benzene, and acetonitrile. The yields of all three compounds are inversely related to their solubility; compound **2** shows the highest product yield since it is the least soluble of the compounds. For compound **4**, we carried out the syntheses under a variety of dilution conditions, but did not observe many differences in yield. All three compounds do not exhibit UV−visible transitions in the visible region of the spectrum and as expected show UV transitions similar to those seen for diiminoisoindoline.

When we investigated the room-temperature ^{1}H NMR spectra of **2** in DMSO, we observed several broad resonances above 7.0 ppm that were indicative of both hydrogen bonding and dynamic behavior. In $CD_3OD/CDCl_3$, we did not observe this behavior due to H/D exchange with solvent. For the expected AA′BB′ spin system of the phenyl ring, the deshielded resonance is split into two broad peaks, and the more shielded resonance is also broad, indicative of a slow exchange process. We postulated that this might result from the presence of the ionizable proton on the external (i.e., Schiff base) nitrogen on the macrocycle rather than the central nitrogen of the isoindoline unit. To further investigate this possibility, we carried out a variable-temperature NMR experiment, shown in Figure 1. With increasing temperature, the split peak due to the phenyl hydrogen atom immediately adjacent to the imine coalesces and forms a single resonance, due to fast exchange of the ionizable hydrogen atom between external nitrogen atoms. We were able to calculate the $\Delta G^{\ddagger}$ for this ionizable hydrogen atom exchange process as 44.6 kJ/mol ($\Delta H^{\ddagger}$ = 41.8 kJ/mol and $\Delta S^{\ddagger}$ = −75 J/mol·K),[28] which is on the order of the energy of a hydrogen bonding type interaction. Also, the ionizable hydrogen resonance broadens and moves from ∼8.5 ppm to ∼8.2 ppm with increasing temperature. This shifting corresponds to the transfer of the proton, with more rapid exchange, from a more hydrogen bonded state to a less hydrogen bonded, and thus more shielded, state.

Compound **3** is stable to chromatographic purification on silica (chloroform/methanol 9:1). We were able to isolate single crystals and elucidate the structure of this compound from two different crystal forms.[29] The compositional difference between the monoclinic and orthorhombic crystal forms is the presence of a water molecule in the monoclinic form, which forms hydrogen bonds between Schiff base nitrogen positions in the solid state. The molecules of **3** in the monoclinic structure form linear arrays of hydrogen bound molecules (via these bridging water molecules) similar to that seen in alkyl-substituted diiminosisoindolines in the solid state.[30] The structure of **3** from the monoclinic form is shown in Figure 2, with nonionizable hydrogen atoms omitted for clarity. Unlike compound **2**, the ionizable proton in **3** is located inside the macrocycle on the central nitrogen of the isoindoline and is engaged in a strong hydrogen bond to one of the two ether oxygen atoms, also shown in Figure 2. The length of this hydrogen bond is nearly identical in both structures, with N···O distances of ∼2.72 and ∼2.71 Å for the monoclinic and orthorhombic forms of the macrocycle, respectively. This hydrogen-bonding interaction results in a nonplanar macrocycle, with planes defined by the two oxygen atoms and the central isoindoline nitrogen at angles of ∼52° and ∼45° for the monoclinic and orthorhombic forms respectively. For compound **3**, we did not observe any dynamic NMR behavior.

Compound **4** also is the product of a 1:1 condensation between the triether diamine precursor and **1**, but we observed significant differences between the dioxo macrocycle **3** and compound **4**. Whereas compound **3** is highly stable, **4** decomposes much more readily. When we attempted to purify **4** on a silica column, we observed the formation of a partially hydrolyzed product **5**, as shown in Scheme 1, formed by the addition of H_2O and loss of NH_3. Compound **5** is a 3-imino-1-oxoisoindoline substituted at the amide nitrogen and the Schiff base nitrogen positions. We were able to structurally characterize this compound by single crystal X-ray methods, as shown in Figure 3.[31] The C−O bond of the acyl group is clearly double in character (C−O: 1.2219(16) Å) and the C−N bond can be characterized as an imine (C−N: 1.2645(18) Å). As in compound **3**, the plane of the isoindoline deviates from that of the crown ether unit to a similar extent, ∼40°, as measured by the mean planes of the isoindole and the 11 atom crown fragment.

In conclusion, we present three crown ether type macrocycles composed of the phthalocyanine subunit molecule isoindoline and the diamines 2,2′-oxybis(ethylamine), 1,2-bis(2-aminoethoxy)ethane, and 1,11-diamino-3,6,9-trioxaundecane. These phthalocyanine/crown ether fusion molecules can either form as 2 + 2 condensations, as seen for the monooxo compound **2**, or as 1 + 1 products as in **3** and **4**. The ^{1}H NMR spectrum of 2 shows dynamic behavior due to proton exchange reactions at the external Schiff base nitrogen positions. Compound **3** is a highly stable macrocycle, due to the presence

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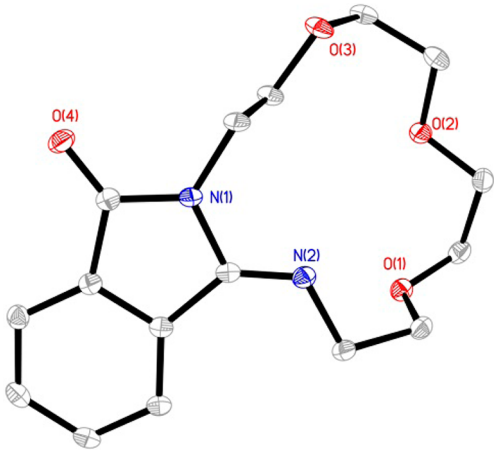

Figure 3. Structure of compound **5** with 35% thermal ellipsoids. Hydrogen atoms have been omitted for clarity.

of an internal hydrogen bond between the central isoindoline nitrogen atom and one of the two macrocycle oxygen atoms. In contrast, compound **4** undergoes hydrolysis to form compound **5**, a 3-imino-1-oxoisoindoline modified crown ether. Our work on these compounds, related macrocycles and their metal adducts is ongoing.

EXPERIMENTAL SECTION

All materials were obtained from commercial suppliers and were used without further purification. 1,3-Diiminoisoindoline (DII, **1**) was prepared according to Elvidge's modified procedure.[15] 1,11-Diamino-3,6,9-trioxaundecane was produced from the corresponding azide using the method reported in the patent by Nippon Shinyaku Co., Ltd.[25] The azide, 1,11-diazido-3,6,9-trioxaundecane, was synthesized using a procedure reported by Thomas et al.[24]

Proton (^{1}H) and carbon (^{13}C) spectra were performed on 300, 400, and 500 MHz spectrometers. High-resolution mass spectrometry experiments were performed on a mass spectrometer equipped with an orthogonal electrospray source (Z-spray) operated in positive ion mode. Sodium iodide was used for mass calibration for a calibration range of m/z 100−2000. Samples were prepared in a solution containing acidified methanol and infused into the electrospray source at a rate of 5−10 μL min^{-1}. Optimal ESI conditions were as follows: capillary voltage 3000 V, source temperature 110 °C, and a cone voltage of 55 V. The ESI gas was nitrogen. Data was acquired in continuum mode until acceptable averaged data was obtained.

X-ray intensity data for the monoclinic form of **3** and compound **5** were measured at 100 K on a CCD-based X-ray diffractometer system equipped with a Mo target X-ray tube (λ = 0.71073 Å) operated at 2000 W power. The data for the orthorhombic form of **3** (using Cu Kα radiation, λ = 1.54178 Å) were collected on a CCD-based diffractometer with dual Cu/Mo ImuS microfocus optics. The crystals were mounted on a cryoloop using Paratone oil and placed under a stream of nitrogen at 100 K. Data were corrected for absorption effects using the multiscan method. The structures were refined and solved using direct methods until the final anisotropic full-matrix, least-squares refinement of F^2 converged.

General Procedure for the Syntheses of Phthalocrowns 2−5. DII (**1**) and the corresponding diamine (2,2′-oxybis(ethylamine), 1,2-bis(2-aminoethoxy)ethane, or 1,11-diamino-3,6,9-trioxaundecane, 1.2 equiv) were dissolved in 1-butanol. The reaction mixture was refluxed for 16 h, cooled, and concentrated. The crude product were either recrystallized or purified by flash chromatography on silica.

5,20-Dioxa-2,8,17,23,31,32-hexaazapentacyclo-[22.6.1.1$^{\{9,16\}}$.0$^{\{10,15\}}$.0$^{\{25,30\}}$]dotriaconta-1,8,10,12,14,16,23,25,-27,29-decaene (2). 2,2′-Oxybis(ethylamine) (500 mg, 4.80 mmol) and DII (**1**) (634 mg, 4.36 mmol) were reacted in 1-butanol (100 mL). The solid was recrystallized in $CHCl_3/CH_3OH/Et_2O$ (49/1/50) to give **2** (657 mg, 1.53 mmol, 32% yield) as an off-white solid: mp 173−175 °C; ^{1}H NMR (500 MHz; $CDCl_3/CD_3OD$) δ 3.2 (bs, 2H), 3.77 (s, 8H), 3.94 (s, 8H), 7.39 (s, 4H), 7.84 (s, 4H) ^{13}C NMR (125 MHz, $CDCl_3/CD_3OD$) δ 46.8, 70.4, 121.0, 130.3, 137.5, 168.6; MS (ESI) calcd for $C_{24}H_{27}N_6O_2$ ([M + H]$^+$) 430.5, found 431.2; HR MS (ESI) calcd for $C_{24}H_{27}N_6O_2$ ([M + H]$^+$) 431.2195, found 431.2184, 2.6 ppm.

5,8-Dioxa-2,11,19-triazatricyclo[10.6.1.0$^{\{13,18\}}$]nonadeca-1,11,13,15,17-pentaene (3). 1,2-Bis(2-aminoethoxy)ethane (1.23 g, 8.3 mmol) and DII (**1**) (1.00 g, 6.89 mmol) were reacted in 1-butanol (150 mL). The crude product was purified by column chromatography on silica gel using 10% CH_3OH in $CHCl_3$ to give **3** (200 mg, 0.77 mmol, 11% yield) as a yellow solid. Single crystals of **2** were grown from a vapor diffusion of hexane into a chloroform solution: mp 138−140 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.65 (s, 4H), 3.78 (s, 8H), 7.54 and 7.83 (dd, J = 3.07, 5.71 Hz, 4H), 9.99 (b, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.11, 70.07, 71.38, 121.6, 130.9, 136.3, 155.9; MS (ESI) calcd for $C_{14}H_{17}N_3O_2$ ([M + H]$^+$) 260.3 found 260.2; HRMS (ESI) calcd for $NaC_{14}H_{17}N_3O_2$ ([M + Na]) 282.1218, found 282.1205, 4.6 ppm; IR (cm^{-1}) 3226, 2910, 2864, 1660.

5,8,11-Trioxa-2,14,22-triazatricyclo[13.6.1.0$^{\{16,21\}}$]docosa-1,14,16,18,20-pentaene (4). Reagents employed: 1,11-diamino-3,6,9-trioxaundecane (200 mg, 1.04 mmol), DII (**1**) (126 mg, 0.867 mmol), 1-butanol (50 mL). The crude product was purified by recrystallization in CH_2Cl_2/Et_2O to give **4** (65.1 mg, 0.215 mmol, 25% yield): mp 102−105 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.64 (s, 8H), 3.76 (s, 4H), 3.95 (s, 4H), 7.12 (bs, 2H), 7.72 (bs, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.7. 70.2, 70.5, 70.7, 120.8, 129.9, 137.6, 167.6; MS (ESI) calcd for $C_{16}H_{21}N_3O_3$ ([M$^+$]) 303.4 found 303.6; HRMS (ESI) calcd for $C_{16}H_{22}N_3O_3$ ([M + H]) 304.1661, found 304.1656, 1.6 ppm.

***(Z)*-5,6,8,9,11,12-Hexahydro-2*H*-[1,4,12,7,9]trioxadiazacyclo-tetradecino[8,7-*a*]isoindol-14(3*H*)-one (5).** Attempts to purify **4** on silica gel yields the hydrolyzed compound **5**. Single crystals of **5** were grown from a vapor diffusion of hexane into a chloroform solution (10 mg, 0.032 mmol, 9% yield): mp 165−169 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.53−4.05 (m, 16H), 7.53, 7.63, 7.78, and 7.88 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.5, 50.2, 67.9, 70.0, 70.1, 70.6, 70.7, 72.1, 123.2, 123.3, 125.7, 131.5, 132.7, 133.9, 151.2, 167.5; HRMS (ESI) calcd for $NaC_{16}H_{20}N_2O_4$ ([M + Na]) 327.1321, found 327.1318, 0.92 ppm.

ASSOCIATED CONTENT

Supporting Information

Spectra for compounds **2**−**5** and X-ray crystallographic tables for compounds **3** and **5** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Steed, J. W.; Atwood, J. L. *Supramolecular Chemistry*, 2nd ed.; John Wiley & Sons: New York, 2009.

(2) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1995**, *95*, 2529−2586.
(3) McKeown, N. B. *Phthalocyanine Materials: Synthesis, Structure, and Function*; Cambridge University Press: Cambridge, 1998.
(4) Leznoff, C. C.; Lever, A. B. P. *Phthalocyanines: Properties and Applications*; VCH: New York, 1989.
(5) Gokel, G. W. *Macrocyclic Polyether Syntheses (Reactivity & Structure)*; Springer-Verlag: New York, 1982.
(6) Gokel, G. W., Inoue, Y. *Cation Binding by Macrocycles: Complexation of Cationic Species by Crown Ethers*; Marcel Dekker: New York, 1990.
(7) Gokel, G. W.; Leevy, W. M.; Weber, M. E. *Chem. Rev.* **2004**, *104*, 2723−2750.
(8) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017−7036.
(9) Peters, J. C.; Odom, A. L.; Cummins, C. C. *Chem. Commun.* **1997**, 1995−1996.
(10) Erk, P.; Hengelsberg, H. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000; Vol. *19*, pp 106−149.
(11) Çetin, A.; Sripothongnak, S.; Kawa, M.; Durfee, W. S.; Ziegler, C. J. *Chem. Commun.* **2007**, 4289−4290.
(12) Barone, N.; Costa, R.; Sripothongnak, S.; Ziegler, C. J. *Eur. J. Inorg. Chem.* **2010**, 775−780.
(13) Costa, R.; Schick, A. J.; Paul, N. B.; Durfee, W. S.; Ziegler, C. J. *New J. Chem.* **2011**, *35*, 794−799.
(14) Costa, R.; Ziegler, C. J. *Chem. Commun.* **2011**, *47*, 982−984.
(15) Elvidge, J. A.; Linstead, R. P. *J. Chem. Soc.* **1952**, 5000−5007.
(16) Clark, P. F.; Elvidge, J. A.; Linstead, R. P. *J. Chem. Soc.* **1953**, 3593−3601.
(17) Elvidge, J. A.; Linstead, R. P. *J. Chem. Soc.* **1954**, 442−448.
(18) Linstead, R. P.; Whalley, M. *J. Chem. Soc.* **1954**, 3530−3536.
(19) Ficken, G. E.; Linstead, R. P. *J. Chem. Soc.* **1955**, 3525−3529.
(20) Elvidge, J. A.; Fitt, J. S.; Linstead, R. P. *J. Chem. Soc.* **1956**, 235−243.
(21) Gagne, R. R.; Marritt, W. A.; Marks, D. N.; Siegl, W. O. *Inorg. Chem.* **1981**, *20*, 3260−3267.
(22) Dietrich, B. L.; Egbert, J.; Morris, A. M; Wicholas, M. *Inorg. Chem.* **2005**, *44*, 6476−6481.
(23) Fernández-Lázaro, F.; Torres, T.; Hauschel, B.; Hanack, M. *Chem. Rev.* **1998**, *98*, 563−576.
(24) Thomas, J. R.; Liu, X.; Hergenrothe, P. J. *J. Am. Chem. Soc.* **2005**, *127*, 12434−12435.
(25) Nippon Shinyaku Co., Ltd. Galactose Derivative, Drug Carrier and Medicinal Composition. Patent EP1783137 A1, May 9, 2007.
(26) Siegl, W. O. *J. Org. Chem.* **1977**, *42*, 1872−1878.
(27) Ziegler, C. J. The Hemiporphyrazines and Related Systems. In *Handbook of Porphyrin Science*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; World Scientific Publishing: Singapore, 2012; Vol. *17*, pp 114−226.
(28) Gasparro, F. P.; Kolodny, N. H. *J. Chem. Educ.* **1977**, *54*, 258−261.
(29) Crystal data for **3**. Monoclinic form: $C_{28}H_{38}N_6O_6$, MW = 554.64, monoclinic, space group $P2(1)/n$, a = 10.461(5) Å, b = 8.172(4) Å, c = 16.100(7) Å, α = 90°, β = 95.244(8)°, γ = 90°, V = 1370.7(10) Å^3, Z = 2, ρ = 1.344 g·cm^{-3}, $R_{(int)}$ = 0.0343, R_1 = 0.0484, wR_2 = 0.1205 for 2873 independent reflections, $I_0 > 2\sigma(I_0)$, with a total of 9274 observed reflections. Orthorhombic form: $C_{14}H_{17}N_3O_2$, MW = 259.31, orthorhombic, space group $P2(1)2(1)2(1)$, a = 8.9063(3) Å, b = 10.3310(3) Å, c = 13.8954(4) Å, α = 90°, β = 90°, γ = 90°, V = 1278.53(7) Å^3, Z = 4, ρ = 1.347 g·cm^{-3}, $R_{(int)}$ = 0.0183, R_1 = 0.0257, wR_2 = 0.0734 for 2046 independent reflections, $I_0 > 2\sigma(I_0)$, with a total of 4825 observed reflections.
(30) Bochkarev, M. N.; Balashova, T. V.; Maleev, A. A.; Pestova, I. I.; Fukin, G. K.; Baranov, E. V.; Kurskii, Y. A. *Russ. Chem. Bull.* **2008**, *57*, 2162−2167.
(31) Crystal Data for **5**. $C_{16}H_{20}N_2O_4$, MW = 304.34, monoclinic, space group $P2(1)/n$, a = 8.719(2) Å, b = 15.485(4) Å, c = 11.213(3) Å, α = 90°, β = 97.564(3)°, γ = 90°, V = 1500.8(6) Å^3, Z = 4, ρ = 1.347 g·cm^{-3}, $R_{(int)}$ = 0.0392, R_1 = 0.0382, wR_2 = 0.1216 for 2663 independent reflections, $I_0 > 2\sigma(I_0)$, with a total of 10709 observed reflections.