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New corrinoid macrocycles from Schiff-base forming reactions

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Abstract

Contractive cyclization of the 1,14-bisformyl-16-oxa-tripyrromethane with 1,2-diamine gave new corinoid macrocycles depending on the nature of heteroatoms in the core. © 1999 Elsevier Science Ltd. All rights reserved.

The diverse chemistry performed by natural porphyrins has inspired work in the biological, synthetic, materials and medicinal chemistry fields. The development of porphyrin macrocycles that transcend biological examples has focused on synthetic tailoring of the parent macrocycles. We have chosen another approach, which focuses on the modification of the porphyrin core. The replacement of one or more pyrroles in the porphyrin with other heterocycles changes the core size, the electrochemical properties and the spectral characteristics. To date, the class of 'core-modified porphyrins' has included the incorporation of benzene, pyridine, furan, thiophene and cycloheptatriene. Most of the core-modified porphyrins prepared so far have been aromatic systems[1–4] in spite of the modification of the original π-systems. The syntheses of porphyrin isomers, which have various heteroaromatic structural units, are another major concern with regard to the aromaticity and possible applications. We recently reported the synthesis of pseudo-aromatic expanded porphyrin analogues by modification of Sessler's approach.[5] The expanded porphyrins are considered to be the [22]-π benzannulene systems. Modification of the basic framework of porphyrins while maintaining aromaticity, will change the energetics of the molecular orbitals and thus alter the spectroscopic properties. The systematic construction of a model system usually requires precise control of energetics and electronic state of molecules and such control could possibly be achieved by replacing nitrogen atoms with other heteroatoms. We were interested in the development of synthetic methods for preparing the core-modified porphyrins.[6,7] Because we were able to synthesize tripyrranes in two steps with high yields,[5] we began to investigate the synthesis of various core-modified expanded porphyrins using this method. We report the synthesis of new corrinoids macrocycles (**4**) via aldol-type condensation followed by cleavage of aliphatic 1,2-diamines. 5,10-Dimesityl-16-*oxa*-tripyrromethane (**1**) is easily synthesized by condensing 2,5-bis[(α-hydroxy-α-mesityl)methyl]furan with excess pyrrole in the presence of $BF_3 \cdot O(Et)_2$ at room temperature.[5] The key intermediate leading to the macrocycles (**4**) and (**6**), 1,14-diformyl-16-oxatripyrromethane (**1**),[5,8] was synthesized by the

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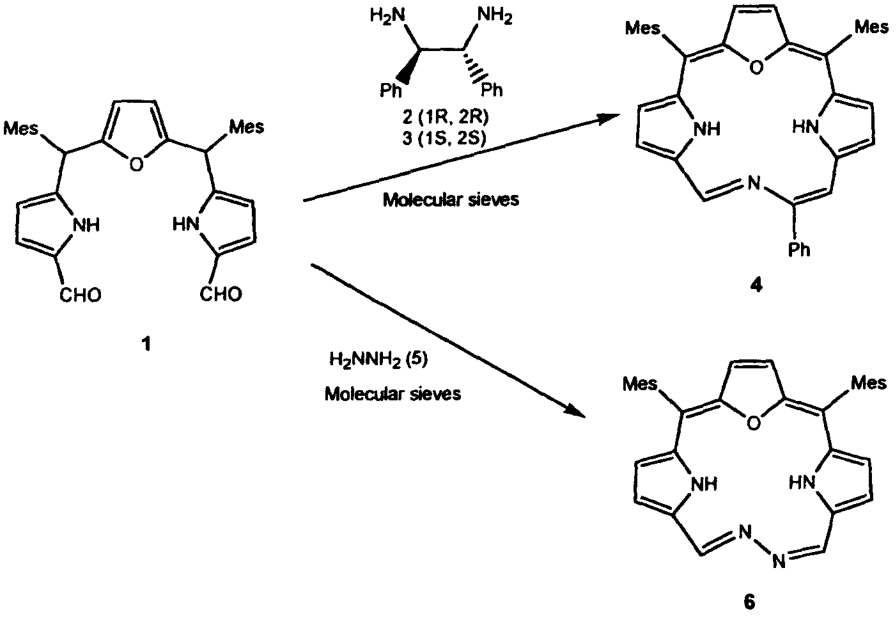
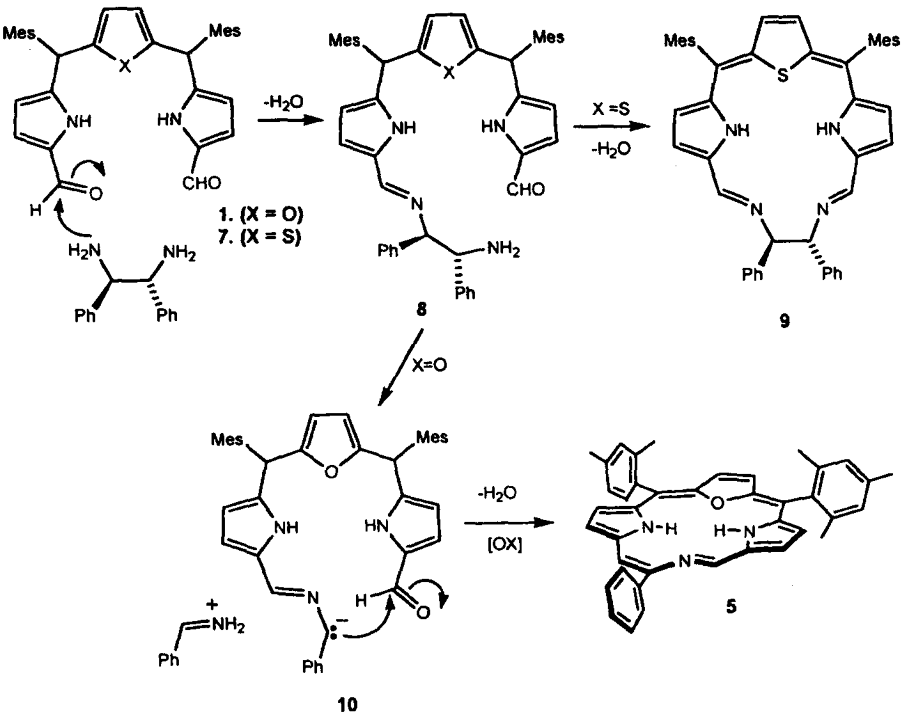
Vilsmeier formylation of the corresponding tripyrromethanes. The acid catalyzed addition–elimination reaction of (**1**) with 1,2-diamines is expected to afford a Schiff-base macrocycle as reported previously.[5] This reaction was found to be quite unreliable due to reversibility of the imine-forming reaction and in most reaction conditions surveyed, the starting material was recovered quantitatively. The use of $Ba(SO_4)_2$ or $CdCl_2$ did not lead to macrocycle formation either.[9] But in the presence of excess molecular sieves, we observed a clean reaction with the development of a bright red-purple reaction mixture (Scheme 1).

Refluxing (1*R*,2*R*)-1,2-diphenyl ethylenediamine (0.04 g, 0.19 mmol) with (**1**) (0.1 g, 0.19 mmol) in the presence of molecular sieves (type 4A, 5.0 g) in $CHCl_3$ afforded 32 mg (29%) of the new macrocyle (**4**). The condensation of (1*S*,2*S*)-1,2-diphenyl ethylenediamine with (**1**) also afforded (**4**) in 23%. The reaction of hydrazine (**5**) with (**1**) under similar conditions also afforded (**6**) in 43%. The exclusive formation of (**6**) indicated that macrocycles (**4**) and (**6**) are the 18-π aromatic system and stabilized macrocycles. The unusual rearrangements leading to (**4**) could be explained by assuming the formation of a stabilized carbanion type intermediate (**10**) with concomitant heterolytic cleavage of C–C bond of 1,2-diphenyl ethylenediamine (Scheme 2). The alternative mechanism involves oxidative disproportionation of the diamine via a cation radical intermediate (not shown).



Scheme 1.

On the other hand, when 1,14-diformyl-16-thiatripyrromethane (**7**) was condensed with (1*R*,2*R*)-1,2-diphenyl ethylenediamine, the only isolated product was (**9**) which was formed by a simple addition–elimination reaction of aldehyde and amine.[5] This result indicates that the size of the core-atoms is a critical factor in choosing the mechanistic pathway as shown in Scheme 2. All the reactions worked only when excess powdered molecular sieves were employed. The molecular sieve catalyst must have suitable acidity, dehydrating ability and templating effect. In macrocycle (**9**), the *meso*-position was oxidized during the reaction but the ethylene bridge remained intact. The forced oxidation of the ethylene bridge will result in the anti-aromatic [20]-π macrocycle, and indeed, various attempts at oxidation resulted in extensive decomposition of (**9**). The UV–vis spectrum of (**4**) shows a Soret-like band at 381 nm ($\varepsilon=1.8\times10^5$) and five less intense bands at 436 nm ($\varepsilon=5\times10^3$), 461 nm ($\varepsilon=1.0\times10^4$), 489 nm ($\varepsilon$=1.3×10^4), 554 nm ($\varepsilon$=1.8×10^3) and 603 nm ($\varepsilon$=3.7×10^3). The absorption spectrum of (**6**) also has a Soret-like band at 364 nm and the last bands overlap with (**4**).[18] The electronic spectrum is somewhat different from that of *meso*-5,10,15,20-tetraphenylporphyrin or texaphyrins[2]. But both (**4**) and (**6**) have somewhat similar absorption spectrum with corroles[9–12] indicating a corole-like macro-aromatic character of the macrocycles. The proton NMR spectrum of (**4**) showed clear evidence of macro-aromaticity; the inner two pyrrolic N–H protons showed two distinctive singlets at −1.38 and −0.84 ppm which completely disappeared upon addition of acidic deuterium oxide. The computer generated, energy minimized model of (**4**) and (**6**) also indicates that the core shape is similar to that of the corrole nucleus and is a stable 18-π aromatic system. The imine-double bond exist in transoid. The detection of benzaldehyde in the reaction mixture indicated the heterolytic cleavage of the ethylene C–C bond. These preliminary results suggest that the Schiff-base forming reaction between 1,14-bisaldehydes and 1,2-diamines would be a useful route for the synthesis of norcorrole-type aromatic macrocycles.[13]



Scheme 2.

The obvious advantages of the present syntheses are their wide applicability in synthesizing corrinoids having different ligands in the core arranged in a regiospecific manner. It has been well known that replacement of the nitrogen atoms in the core with other heteroatoms produces unique macrocycles with different cavity sizes and complexing abilities.[14–16] Our first demonstration of the synthesis of norcorrole-type macrocycles by contractive cyclization should be applicable in designing various model systems.[17,18] Currently, we are investigating the scope and limitation of the reaction using the same analogy with various diamines.

Acknowledgements

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17. Experimental procedures and spectroscopic data for compounds (**7**) and (**9**) have been reported in Refs. 5 and 7.
18. Compound (**1**): ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ 9.41 (s, 2H, aldehyde-H), 9.07 (s, 2H, N-H), 7.36–7.21 (m, 10H, phenyl-H), 6.90 (m, 2H, pyrrolic-H), 6.63 (m, 2H, thiophene-H), 6.09 (m, 2H, pyrrole-H), 5.58 (s, 2H, *meso*-H). HRMS calculated for $C_{34}H_{34}N_2O_3$: 518.2569; found: 518.2581 (M^+). Compound (**4**): ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ 10.94 (s, 1H, imine-H), 8.72 (s, 1H, *meso*-H), 8.46 (dd, 1H, *J*=4.1 Hz, pyrrole-H), 8.01 (dd, 1H, *J*=4.1 Hz, pyrrole-H), 8.52 (dd, 1H, *J*=2.1 Hz, pyrrole-H), 7.94 (dd, 1H, *J*=2.1 Hz, pyrrole-H), 8.28 and 8.22 (two doublets, 2H, *J*=5.1 Hz, furan-H), 7.38 (t, 1H, *J*=7.4 Hz, Ph(*p*)-H), 7.79 (t, 2H, *J*=7.4 Hz, Ph(*m*)-H), 8.09 (d, 2H, *J*=7.4 Hz, Ph(*o*)-H), 7.24 (s, 2H, Ar(*mesityl*)-H), 7.23 (s, 2H, Ar(*mesityl*)-H), 2.58 (s, 3H, Ar(*p*)-CH_3), 2.56 (s, 3H, Ar(*p*)-CH_3), 1.90 (s, 6H, Ar(*o*)-CH_3), 1.86 (s, 6H, Ar(*o*)-CH_3), –0.84 (s, 1H, N-H), –1.38 (s, 1H, N-H). UV–vis (CH_2Cl_2) $\lambda_{max}(\varepsilon\times10^4)$ 381 (18.17), 436 (0.53), 461 (0.99), 489 (1.30), 554 (0.18), 603 (0.37). HRMS calculated for $C_{41}H_{37}N_3O$: 587.2937; found: 587.2928 (M^+). Compound (**6**): ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ 11.03 (s, 1H, imine-CH), 9.85 (s, 1H, imine-CH), 8.33–8.31 (m, 2H, pyrrole-H), 7.96 and 7.93 (dd, 2H, *J*=5.4 Hz, furan-H), 7.63–7.62 (m, 1H, pyrrole-H), 7.58–7.56 (m, 1H, pyrrole-H), 7.19 (s, 4H, Ar-H), 2.53 (s, 3H, Ar(*o*)-methyl), 2.52 (s, 3H, Ar(*o*)-methyl), 1.94 (s, 6H, Ar(*o*)-methyl), 1.89 (s, 6H, Ar(*o*)-methyl), 0.55 (bs, 1H, N-H). IR (KBr, cm^{-1}) 3684.4 (w), 3021.4 (s), 2400.6 (m), 1522.3 (m), 1424.0 (m). UV–vis (CH_2Cl_2) λ_{max} ($\varepsilon\times10^4$) 364 (11.0), 436 (0.72), 442 (0.71), 487 (2.00), 514 (0.53). HRMS calculated for $C_{34}H_{32}N_4O$: 512.2576; found: 512.2558 (M^+).