Pergamon

Tetrahedron Letters 41 (2000) 697–701

TETRAHEDRON
LETTERS

Customized, core-modified corroles from [2+2] condensation of dipyrromethanes

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Received 12 October 1999; revised 4 November 1999; accepted 8 November 1999

Abstract

Corroles and core-modified corroles were synthesized by acid-catalyzed condensation under low-scrambling conditions. The synthesis utilized [2+2] condensation of two different dipyrromethanes. The condensation afforded different corroles bearing heteroatoms in a predesignated location depending on the starting dipyrromethanes. Selective α–α′ linkage was achieved by positioning a linking carbon unit at a different site of dipyrromethanes. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: corrole; dipyrromethanes; [2+2] condensation.

The corrin ring is more flexible than chlorins and allows easy change of the steric environment around the central metal ion. This steric versatility facilitates the catalysis of carbon–carbon bond formation in vitamin B_{12}.[1] Most of the corrole synthesis known so far includes biladiene cyclization,[2] *meso*-carbon or sulfur extrusion of *meso*-thiaporphyrin,[3] or direct synthesis from substituted pyrroles.[4] The primary target for the corrole research has been focused on the synthetic access to the ring structure of corrin and corroles. Although corroles have the bipyrrole ring junction, they usually exhibit the same dynamic range as found in porphyrins and chlorins. The first synthesis of corroles was reported in 1965 by photochemical cyclization of a,c-biladiene.[8] A synthesis of core modified corroles containing oxygen or sulfur has been reported by Broadhurst et al. However, McDonald type condensation of dipyrromethanes and 2,2′-bifuran or 2,2′-bithiophene at elevated temperature resulted in a complex mixture of products due to scrambling of starting material.[5] The synthesis of *meso*-aryl corroles from monopyrrole precursors has been reported.[6,10] The reaction proceeds only in the presence of cobalt(II) ion and these classical approaches have been extensively applied for various model systems and yields have been improved.[9a] Direct synthesis of corrole from pyrrole and aldehydes has been reported recently.[9b,c] The peripheral substitution usually induce electronic properties and is known to have reversed energy levels compared with porphyrin.[6] But little has been known for the synthetic method of corrole by direct

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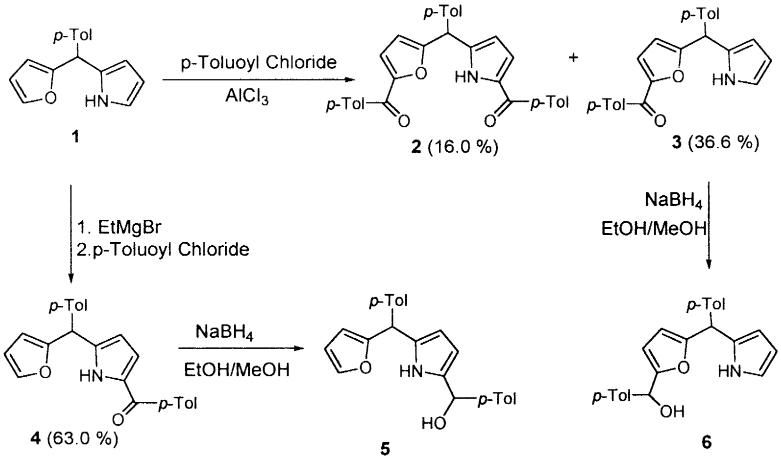
PII: S0040-4039(99)02142-5

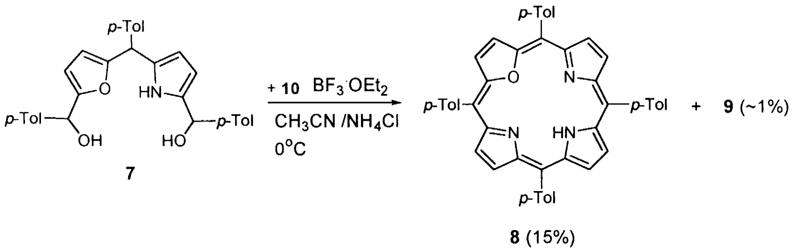
[2+2] condensation of dipyrromethanes. We here report the synthesis and characterization of new free base oxacorroles bearing an oxygen atom in a designated position in the core.

The synthesis of *p*-tolyl-(furan-2-yl)-(pyrrol-2-yl)methane (**1**) was achieved by acid catalyzed condensation of 2-[α-hydroxy-α-(*p*-tolyl)]methylfuran with pyrrole. As shown in Scheme 1, Lewis acid catalyzed acylation of **1** resulted in two products (**2** and **3**). The monoacylated **3** was obtained as the major product in 36.6% yield. 1,9-Bisacylated product **2** was also isolated in 16.0% yield. The dominant formation of **3** reflects higher reactivity of furan toward electrophilic species. Treatment of **1** with EtMgBr (5.0 equiv.) in THF followed by *p*-toluoyl chloride (2 equiv.) gave 63% yield of **4** as a single product. In our prior synthesis of core-modified porphyrin, the 1,9-bisacyldipyrromethanes were reduced to the corresponding diol using a large excess of reducing agents.[11] Treatment of **3** or **4** with $NaBH_4$ (100 molar equiv.) in MeOH:EtOH (2:1) gave clean reduction to the corresponding alcohols **5** and **6**, respectively. The use of a large excess amount of reducing agent is crucial in order to complete the reduction. The TLC analysis showed single spot and the disappearance of carbonyl stretching associated with the appearance of –O–H stretching was clearly observed in IR. The reduced compounds were unstable in air and extensive decomposition was observed in 24 h even if it was stored in a freezer. Thus, the crude alcohols were not purified further and directly used in the next step.



Scheme 1.

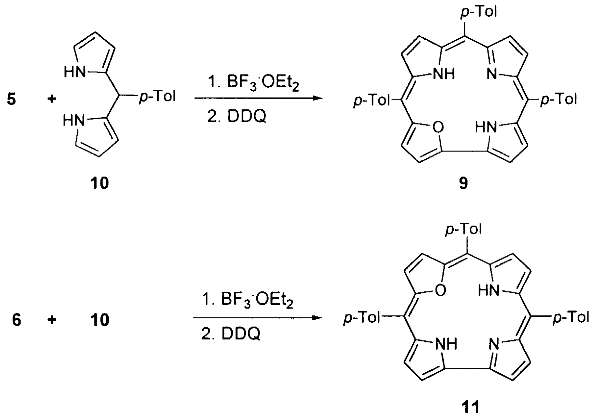
We applied the previously identified low-scrambling and acid-catalyzed conditions in synthesizing core-modified porphyrins by [2+2] condensation.[12] As shown in Scheme 2, during the preparation of 5,10,15,20-tetra-(*p*-tolyl)-21-oxaporphyrin (**8**)[7b] by [2+2] condensation of diol (**7**) with *meso*-(*p*-tolyl)dipyrromethane (**10**), we were able to isolate a trace amount of corrole (**9**).



Scheme 2.

The formation of corrole (**9**) from the condensation of **10**[13] with **7** must arise via cleavage of the furan-C2 and 2α–C bond of **7**. The site of cleavage was verified by independent synthesis of authentic corrole

(**9**) (Scheme 3). Acid-catalyzed condensation of **5** with dipyrromethane (**10**) exclusively afforded corrole (**9**) in 9% yield. The spectroscopic data of corrole (**9**) obtained from the reaction shown in Scheme 2 were identical with the corrole isolated from the condensation of **10** with **5**. Scheme 3 shows two different types of [2+2] condensation. Different α–α linkage could be achieved depending on the position of 2α-hydroxy group. Although the exact mechanism leading to the corrole is not certain yet, all the experimental evidence indicates that the presence of BF_3 is important in the formation of α–α linkage. Only a small amount of corrole was isolated when the same condensation was carried out in the presence of TFA. The major product was self-condensed, ONON type porphyrin.

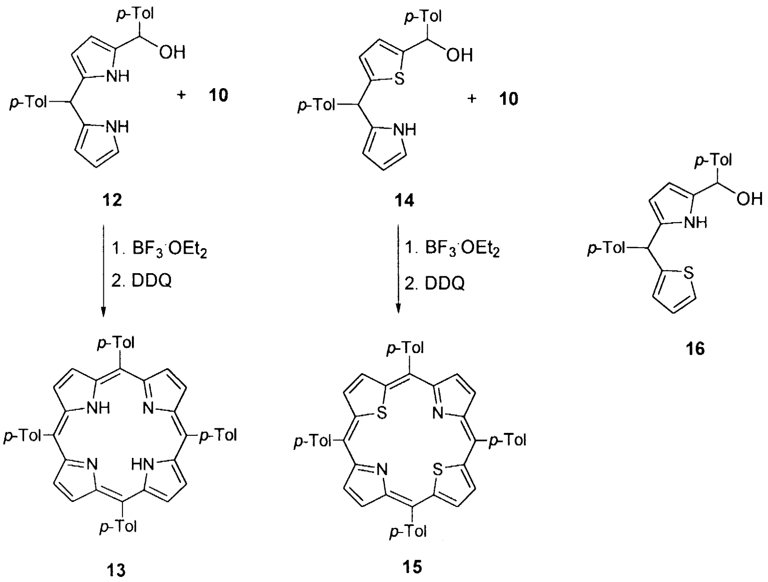


Scheme 3.

The Soret band was observed in 402 nm in **9** and 412 nm in **11**.[14] These values are somewhat red-shifted compared with those which do not have *meso*-substituents. The blue-shifted Soret band of **9** indicates that **9** must be less flexible and more stable than **11**. These facts indicate that the α–α connection of pyrrole–furan is more stable than the pyrrole–pyrrole connection. The other possible tautomeric form of **11** must be a less stable isomer. The spectroscopic evidence also support those observations; the β-pyrrolic resonances of **9** are shifted further down than those of **11**. The inner N–H resonances in **9** was shown at –3.00 ppm while **11** was shown at –1.85 ppm as broad singlet. Only one N–H resonance was observed in both cases. This is the first example of core-modified corroles obtained from the direct condensation of two different dipyrromethanes.

Attempted condensation of 5-(*p*-tolyl)-1-[α-hydroxy-α-(*p*-tolyl)]methyldipyrromethane (**12**) with dipyrromethane (**10**) in the presence of $BF_3 \cdot OEt_2$ did not give any corrole component, but self-condensed **13** was isolated in 11% yield (Scheme 4). However, condensation performed in the presence of *p*-toluenesulfonic acid afforded a mixture of 5,10,15-tri(*p*-tolyl)corrole in trace amounts ($\ll\sim 1\%$) and porphyrin **13** in 10% yield. The condensation of **14** with **10** under the same conditions ($BF_3 \cdot OEt_2$, 1 mM) also afforded porphyrin **15**[15] in 12% as a single product. On the other hand, the condensation of **16** with **10** did not result in any porphyrinoid components. Exceptional interaction of furan with BF_3 seems important in the intramolecular cyclization. BF_3 seems to make a strong complex with tetrapyrrolic intermediate and consequently the intermediate becomes more electrophilic so that intramolecular coupling is possible.

In conclusion, customized corrole could be synthesized by acid-catalyzed ($BF_3 \cdot OEt_2$) condensation of two different dipyrromethanes. The extension of this reaction will give a variety of corroles bearing different *meso*-substituents. The scope and limitation of the reaction will be reported in due course.



Scheme 4.

Acknowledgements

Support from the Korea Science and Engineering Foundation (grant no. 985-0300-001-2) is gratefully acknowledged. The author thanks Professor J. S. Lindsey at North Carolina State University for helpful discussions.

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13. *meso*-(*p*-Tolyl)dipyrromethane (**10**) was synthesized from the condensation of *p*-tolualdehyde and pyrrole as reported.[7]
14. Corrole (**9**): ^{1}H NMR (CDCl$_3$): δ 9.52 (d, 1H, J=4.2 Hz), 9.22 (d, 1H, J=4.4 Hz), 9.04 (d, 1H, J=4.2 Hz), 8.89–8.84 (m, 3H), 8.74–8.73 (m, 1H), 8.63 (d, 1H, J=4.5 Hz), 8.21–8.17 (m, 4H), 8.06 (d, 2H, J=7.8 Hz), 7.63–7.60 (m, 4H), 7.54 (d, 2H, J=7.8 Hz), 2.69 (s, 3H, Ar–CH$_3$), 2.68 (s, 6H, Ar–CH$_3$), −3.00 (bs, 1H, N–H). ^{13}C NMR (CDCl$_3$): δ 152.32, 150.15, 147.27, 139.44, 139.34, 137.65, 137.52, 137.01, 136.70, 135.99, 134.78, 134.49, 134.24, 134.08, 133.63, 131.66, 130.32,

128.91, 128.45, 127.63, 126.20, 125.27, 123.28, 123.26, 120.19, 117.11, 115.02, 113.35, 112.32, 106.97, 21.48, 21.43. UV–vis (CH_2Cl_2:EtOH, 3:1) λ_{max} ($\varepsilon \times 10^{-3}$) 402 (93), 418 (49), 488 (3.2), 524 (7.2), 551 (19), 604 (7.4). FAB-MS calcd for $C_{40}H_{31}N_3O$ 569.25, found 570.07 (M^++H). (**11**): Yield 35.09 mg (15.1%); ^{1}H NMR ($CDCl_3$): δ 9.07 (d, 1H, *J*=5.1 Hz), 9.02–9.01 (m, 1H), 9.00 (d, 1H, *J*=4.0 Hz), 8.81 (d, 1H, *J*=4.3 Hz), 8.78 (d, 1H, *J*=4.8 Hz), 8.76 (d, 1H, *J*=5.1 Hz), 8.55–8.54 (m, 1H), 8.34 (d, 1H, *J*=4.5 Hz), 8.19–8.15 (m, 4H), 7.99 (d, 2H, *J*=7.8 Hz), 7.61–7.59 (m, 4H), 7.54 (d, 2H, *J*=7.7 Hz), 2.68 (s, 3H, Ar–CH_3), 2.67 (s, 6H, Ar–CH_3), −1.85 (br s, 1H, N–H). ^{13}C NMR ($CDCl_3$): δ 150.44, 149.84, 145.44, 142.75, 138.50, 137.78, 137.63, 137.29, 137.05, 135.78, 134.70, 134.00, 133.88, 133.74, 132.23, 129.20, 129.00, 128.56, 128.27, 124.75, 123.71, 123.19, 123.17, 122.76, 121.21, 120.09, 120.02, 114.75, 108.79, 108.73, 105.29, 21.54, 21.48, 21.44. UV–vis (CH_2Cl_2:EtOH, 3:1) λ_{max} ($\varepsilon \times 10^{-3}$) 412 (211), 498 (13), 529 (13), 583 (6.2), 634 (20). FAB-MS calcd for $C_{40}H_{31}N_3O$ 569.25, found 570.48 (M^++H).

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