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Tetrahedron Letters
Tetrahedron Letters 47 (2006) 6205–6207

One-pot synthesis of *meso*-tris-aryl-substituted *N*-21-methyl- and *N*-21-benzyl-corroles

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Received 18 May 2006; revised 21 June 2006; accepted 29 June 2006

Abstract—A simple and versatile synthesis of *meso*-substituted *N*-21-alkylcorroles was achieved directly from aldehydes, pyrrole and *N*-alkylpyrroles via mix-condensation. Compounds inaccessible via previous routes have been obtained in acceptable yields. It was proved that *meso*-substituted *N*-21-alkylcorroles differ from N-unsubstituted corroles in absorption spectra, stability and solubility.

Corroles, analogues of porphyrins bearing a direct pyrrole–pyrrole link, emerged a few years ago as an independent area of research.[1] Their coordination chemistry, photophysics, synthesis, chemical transformations and other properties have recently been studied in great detail.[2] On the other hand, *N*-alkylcorroles were discovered in 1965 by Kay and Johnson[3] and subsequently 'rediscovered' by Gross and co-workers a few years ago.[4] Gross noted that these molecules are chiral and could be separated into enantiomers.[4] *N*-alkylcorroles were transformed into their complexes with Rh, Zn and Cu.[5,6] It can be envisioned that these interesting compounds, due to their chirality, can form the basis of ligands for enantioselective catalysis. Analogous N-substituted porphyrins are powerful inhibitors of the enzyme ferrochelatase.[7]

As a part of our ongoing photophysical project, we required access to a broad range of N-alkylated corroles. Typically, N-substituted corroles are prepared as a mixture of *N*-21 and *N*-22 regioisomers, via alkylation of β- or *meso*-substituted corroles with alkyl bromides in the presence of K_2CO_3. We have attempted to employ these conditions for the alkylation of 5,10,15-tris(4-methylphenyl)corrole. However, the use of both MeI and benzyl bromide in this reaction did not afford the expected products (only starting material and decomposition were noted). Difficulties with this procedure forced us to consider an alternative route to *N*-alkylcorroles via the direct mix-condensation of pyrrole, *N*-alkylpyrrole and an aldehyde. The obvious potential advantage of this route is the fact that it is a one-pot process. We thought that this method could be of particular value for corroles, which possess functional groups that can be alkylated or decomposed under basic conditions. Last but not the least, we were intrigued in the output of such a condensation from a mechanistic point of view. To the best of our knowledge, such a mix-condensation was never successfully performed for *N*-alkylporphyrin synthesis. However, the stepwise process has been carried out, which involved the condensation of N-methylated dipyrromethane and a diformyldipyrromethane followed by oxidation.[8]

We started our investigation with the reaction of 3,5-bis(trifluoromethyl)benzaldehyde (**1**) with a mixture of pyrrole and *N*-methylpyrrole (**2**) in a suitable ratio (i.e., 3:1). One has to bear in mind that the one-pot synthesis of *meso*-substituted A_3-corroles from aldehydes and pyrrole consists of two independent steps. The first step is an acid-mediated electrophilic substitution to yield a mixture of various aldehyde–pyrrole oligocondensates including bilane (tetrapyrrane), which is a direct precursor of corrole. The second step is the oxidative ring closure. While *N*-methylpyrrole (**2**) is more reactive towards electrophilic substitution and will undoubtedly build into the structure of oligocondensates (dipyrromethanes, tripyrranes, tetrapyrranes, etc.), it is rather difficult to predict if tetrapyrranes possessing one, two or three such units will undergo ring closure due to the intrinsic steric hindrance.

Keywords: Corroles; Porphyrins; Pyrrole; Macrocyclization.
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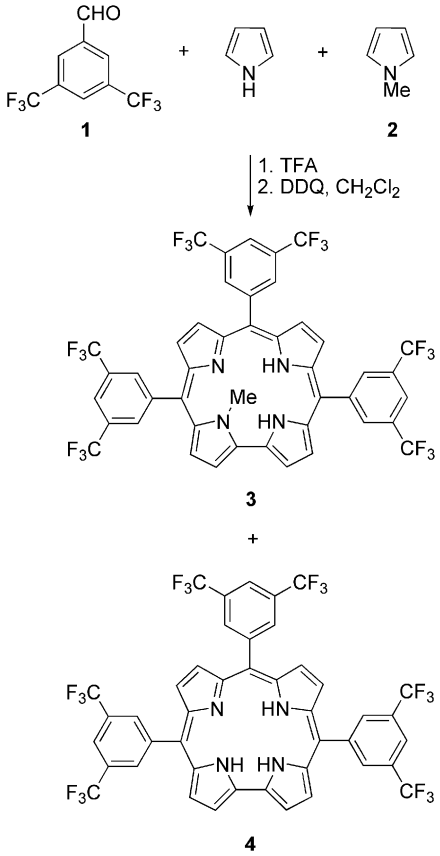
0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.06.171

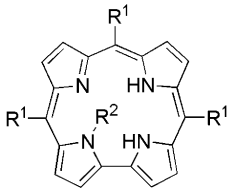
Aldehyde **1** was chosen due to the fact that the respective A_3-corrole **4** is particularly stable and that no porphyrin is formed during its synthesis,[9] which simplifies purification. The reaction was performed under conditions previously optimized for the synthesis of *meso*-substituted corroles from highly reactive aldehydes (TFA-catalyzed neat condensation and DDQ as an oxidizing agent) (Scheme 1).[9]

After addition of DDQ, we found two fluorescent corrole-like products. One of them was identified as the respective A_3-corrole **4** and the second one formed a less polar spot on TLC. We separated both compounds by column chromatography. The yield of *N*-methylcorrole **3** was 3.9%, while the yield of A_3-corrole **4** was 5.5%. During this first experiment, we immediately noticed a few interesting phenomena. Firstly, *N*-methylcorrole **3** is significantly more stable than corrole **4**. This can be easily observed via the decreasing intensity of the fluorescence of both solutions in the presence of air. Secondly, corrole **3** is, by far, more soluble in all organic solvents than **4**. Last but not the least, *N*-methylcorrole **3** is distinctly more blue than **4**.

Encouraged by this initial result, we decided to carry out analogous condensations with other aldehydes and *N*-methylpyrrole as well as with *N*-benzylpyrrole. We performed reactions with 4-trifluoromethylbenzaldehyde and 4-methylbenzaldehyde, as well as with pentafluorobenzaldehyde (Fig. 1). Altogether, we obtained four additional N-alkylated *meso*-substituted corroles **5**–**8** in



Scheme 1.



5 R^1 = 4-$CF_3C_6H_4$ R^2 = Me 2.9%
6 R^1 = 4-$CH_3C_6H_4$ R^2 = Me 5.8%
7 R^1 = 4-$CH_3C_6H_4$ R^2 = Bn 2.5%
8 R^1 = C_6F_5 R^2 = Bn 1.3%

Figure 1.

yields ranging from 1.3% to 5.8% (experimental details are given in the Supplementary data).[10] Interestingly, we found that in all cases only one of the regioisomers (*N*-21 and *N*-22 are possible) was formed. Comparison of the ^{1}H NMR spectrum of corrole **8** (formed in the reaction of *N*-benzylpyrrole, pyrrole and pentafluorobenzaldehyde) with literature data[4a] clearly showed that we had obtained the *N*-21 regioisomer. Apparently, if the *N*-alkylpyrrole moiety is located in the middle of a linear tetrapyrrane, the resulting steric hindrance hampers ring closure into the corrole. Reactions involving 4-methylbenzaldehyde were performed under H_2O/MeOH/HCl conditions.[11] These conditions were chosen because they afford A_3-corroles in yields of up to 30% for benzaldehyde derived analogues. We obtained the desired corroles **6** and **7** in 5.8% and 2.5% yields, respectively. No corroles with multiple N-substituents were detected using ESIMS. It is important to emphasize that no porphyrin formation was noticed in any of these reactions and that many of the *N*-alkylcorroles were easily purified via single column chromatography and crystallization. All attempts to replace *N*-alkylpyrroles with *N*-phenylpyrrole failed to yield any *N*-phenylcorroles.

The final confirmation of the structure of new corroles and the positioning of the *N*-alkyl substituent were achieved via X-ray crystallographic analysis. We were able to obtain crystals of corrole **7** suitable for single-crystal X-ray diffraction analysis (Fig. 2). The X-ray

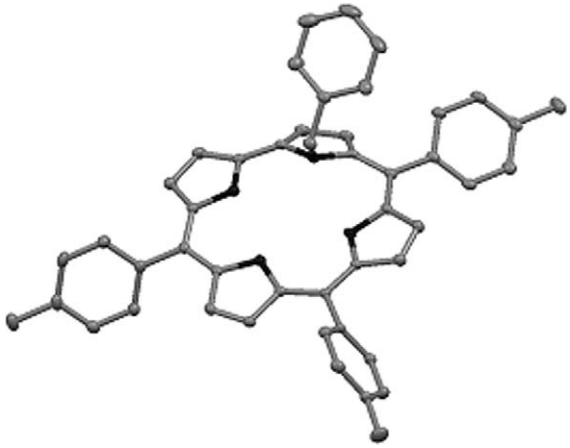


Figure 2. X-ray structure of corrole **7** in ball and sticks representation (solvent molecules are omitted for clarity).

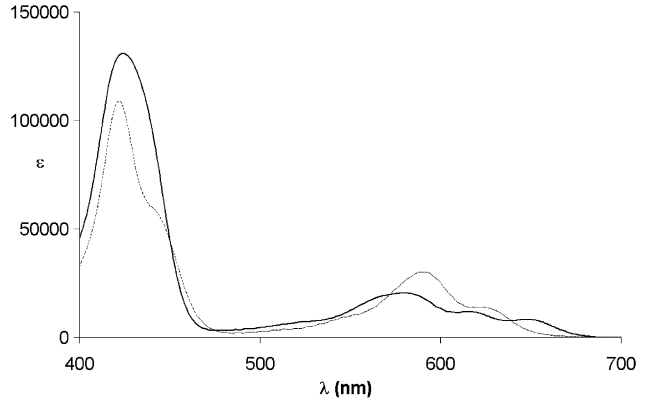


Figure 3. UV–vis absorption spectra (toluene) of corroles **3** (thin dotted line) and **4** (solid line).

structure confirmed that the benzyl group was situated on *N*-21. In analogue with previous structures obtained by Gross and co-workers, corrole **7** was severely distorted from planarity.[4]

It was proved (via separation into enantiomers using a chiral column) that *N*-methylcorroles **3**, **5** and **6** are chiral, in analogue to the previous findings of Gross for *N*-benzylcorroles.[4a]

A comparison of the UV–vis spectra of corroles **3** and **4** is presented in Figure 3. The absorption spectra of *N*-21-alkylcorroles have distinctly more intense Q-bands than in N-unsubstituted corroles, which is responsible for their bluish colour. In analogue to N-substituted porphyrins,[7] the Q-bands of N-substituted corroles are generally red-shifted in the order of 10 nm from the bands of the corresponding N-unsubstituted corroles.

In summary, we have proved that a variety of *N*-21-alkylcorroles can be obtained via simple one-pot procedures from commercially available materials. Although the yields are in the range 1.3–5.8%,[10] the procedure works well for cases where a traditional route via *N*-alkylation of corroles failed. Moreover, we noticed that only one regioisomer is formed, which could be an important observation from the point of view of the mechanism of ring closure.

Acknowledgements

This work was supported by the Ministry of Science and Education (Grant T09A 15728) and Volkswagen Foundation. We thank Michał Gałęzowski for logistic support. The X-ray measurements were undertaken in the Crystallographic Unit of the Physical Chemistry Lab at the Chemistry Department of the University of Warsaw.

Supplementary data

Crystallographic data (excluding structure factors) for the structure in this letter have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 607844. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0)1223336033 or e-mail: deposit@ccdc.cam.ac.uk]. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.06.171.

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10. These yields are comparable to the combined yields obtained by Gross and co-workers:[4] 12% (for the synthesis of a corrole from C_6F_5CHO and pyrrole) × 33% (for alkylation) = 4%.
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