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COMMUNICATION

Asymmetrically substituted calix[4]pyrrole with chiral substituents†

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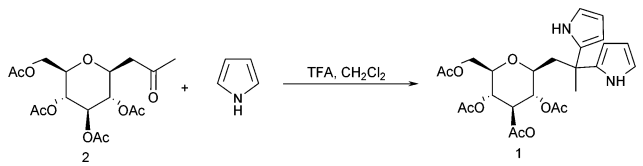
We have prepared first calix[4]pyrrole containing unprotected carbohydrate moiety directly linked to *meso*-position of oligopyrrole by stable "C-glycosidic" bond. Basic examination of its superassembly capability is presented.

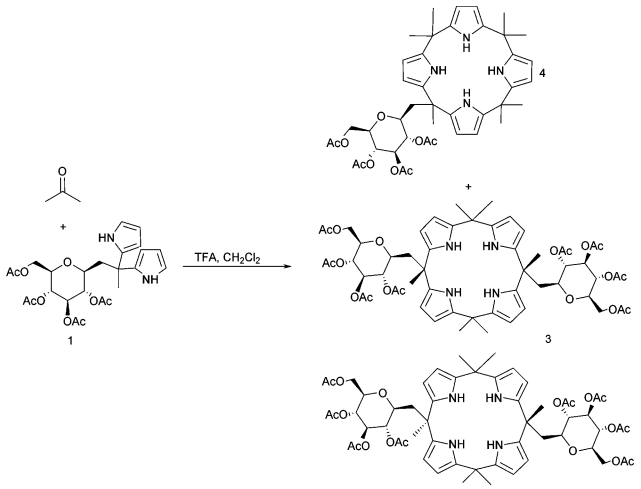
Synthesis of cyclic oligopyrroles represent challenging field with many fruitful expectations. Among them, calix[4]pyrroles are described as anion[1] and neutral binders,[2] chromatic, fluorescent, and electrochemical or optical sensors.[3] Also, they are used as anion sensors and selectors,[4] ionophores[5] and drug sensors.[6] Within this group, with the experience with chiral moiety modified ones,[7] we aimed our attention to the direct carbohydrate functionalisation of the molecule. Even when we enlarge the scope, cyclic oligopyrroles with sugar substitution on the *meso*-like and β-pyrrolic carbons are rather rare.[8] We can see in this context some attempts to study sugar[9] and nucleoside derivatives.[10] In this communication we wish to present broadening of our work on oligopyrrole macrocycles with dominant chiral substitution.[11,12] Our goal is the utilisation of self assembled solvated chiral systems as scaffoldings or chiral inductors. For preparation of symmetric calix[4]pyrrole containing chiral moiety we employed classical synthetic two-step procedure: Acid catalysed condensation of pyrrole with ketone derivative which results in formation of respective dipyrryl derivative and subsequent acid catalysed MacDonald (2+2) reaction with ketone which results to calix[4]pyrrole.

We started the synthesis with preparation of dipyrrylnonitol **1** by reaction of pyrrole and acetylated carbohydrate ketone **2** (ref. 13) in aprotic solvent by trifluoroacetic acid (TFA) catalysis. The product was purified by chromatography to give 60% of the dipyrrylnonitol **1** (Scheme 1).



Scheme 1

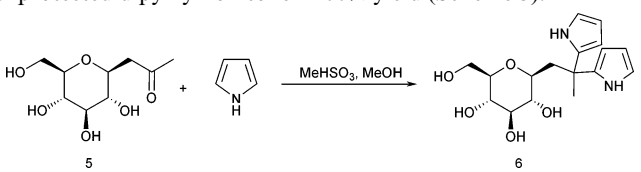
Dipyrrylnonitol **1** was subsequently reacted in dichloromethane with acetone under catalysis of TFA. We isolated not only expected mixture of diastereoisomers 5,10-*cis* and 5,10-*trans* calix[4]pyrrol-5,10-diyl-bis-D-*glycero*-D-*gulo*-heptitols (**3**), that we were not able to separate, but also in 16% yield the monosubstituted calix[4]pyrrole **4** (Scheme 2).



Scheme 2

In order to improve the result of cyclisation we decided to test this strategy on similar unprotected carbohydrate derivative **5**.

Seeing that there was not the risk of hydrolysis of ester protective groups at sugar moiety we chose methane sulfonic acid as catalyst. Ketone **5** was reacted with pyrrole in dry methanol using catalysis by methanesulfonic acid. We obtained expected unprotected dipyrrylnonitol **6** in 60% yield (Scheme 3).



Scheme 3

For condensation reaction of nonprotected dipyrrylnonitol **6** with acetone (Reaction A) methanesulfonic acid was used as catalyst following Eichen *et al.*[14] in order to eliminate formation of undesirable side-products. Interestingly, after chromatographic purification we obtained 11% of the monosubstituted calix[4]pyrrole **7**. Neither any sign of expected disubstituted derivative was observed in the reaction mixture or after careful chromatographic separation (LC-MS).

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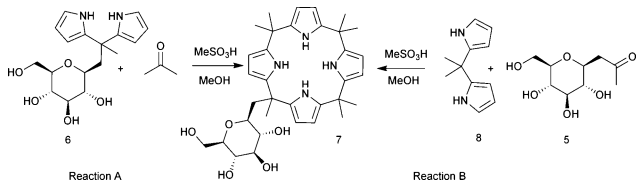
We have therefore investigated possible impact of nature of dipyrryl derivative. When we performed the same reaction with ketone **5** and dipyrrylmethane **8** (ref. 15) in 10% yield we also obtained monosubstituted derivative **7** (Reaction B) (Scheme 4). The yields of *ca.* 10% are considerably "high" for this field of chemistry.



Scheme 4

Whereas pyrrole itself was found to have ability to make clusters,[16,17] we tried to investigate the possible self-assembling. This phenomenon can be observed by characteristic changes of absorbance in UV spectrum.[18] Compounds **7** (Fig. 1), **1**, **4**, **3** were dissolved first in ethanol and the UV spectra of their solutions with increasing percentage of water (from 0 to 100%) were measured. UV spectra showed only moderate changes with time or with concentration changes.

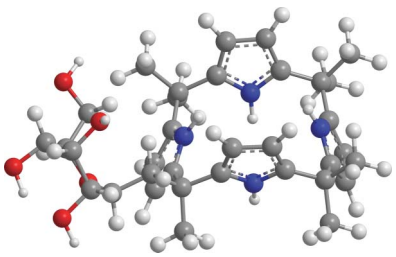


Fig. 1 3-D representation of monosubstituted derivative **7** after MMFF94 minimization at ChemBio3D Ultra ver. 12.0.

The best response to the polarity changes of solvent system was in compound **1**, that is shown on the Fig. 2.

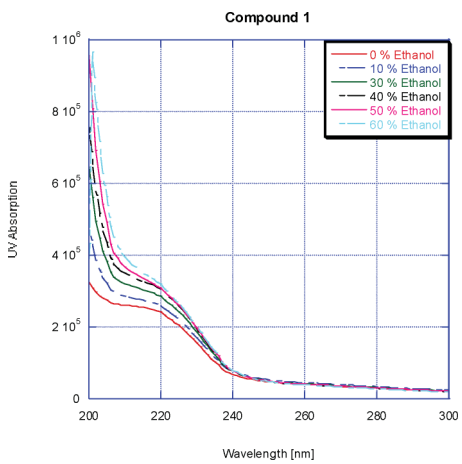


Fig. 2 Spectral dependence of UV absorption of compound **1** with increasing percentage of water in ethanol (from 0%; see insert).

In conclusion, we have prepared first calix[4]pyrrole containing unprotected carbohydrate moiety directly linked to *meso*-position of oligopyrrole by stable "C-glycosidic" bond.

Although dipyrrylmethane derivatives are commonly used for preparation of symmetric disubstituted oligopyrroles in opposite position on the calix (type 2+2) we were not able to find any precedence of our result in literature so far on calix[4]pyrrole containing spiro-steroid moiety.[11] This type of calix[4]pyrrole (3+1) is currently prepared only by mixed condensation of acetone and two different dipyrrylderivatives.[19,20] The study of impact of different carbohydrate synthons, solvents and catalysts on selectivity of four-member cycle formation is currently under investigation. In chiral substituted calix[4]pyrroles could be anticipated possible associations with other synthons,[7] so the new types of monosubstituted calix[4]pyrrole as **7** and **4** will be further studied as synthon for build-up of supramolecular devices, sensors and ionophores.

The supramolecular assembly behaviour of the compounds, as investigated by matrix assisted assembly in solution, proved that there is, mainly with the oligopyrrole macrocycles, unfavorable steric hindrance that is stronger that possible non covalent interactions.

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Notes and references

1 J. L. Sessler, D. An, W. S. Cho, V. Lynch, D. W. Yoon, S. J. Hong and C. H. Lee, *J. Org. Chem.*, 2005, **70**, 1511.
2 L. Bonomo, E. Solari, G. Toraman, R. Scopelliti, C. Floriani and M. Latronico, *Chem. Commun.*, 1999, **23**, 2413.
3 (*a*) H. Miyaji, W. Sato, D. An and J. L. Sessler, *Collect. Czech. Chem. Commun.*, 2004, **69**, 1027; (*b*) S. Lozovanu, L. Silaghi-Dumitrescu and I. A. Silberg, *Chemia*, 2004, **49**, 125.
4 (*a*) A. F. Danil de Namor, M. Shehab, I. Abbas, M. V. Withams and J. Zvietcovich-Guerra, *J. Phys. Chem. B*, 2006, **110**, 12653; (*b*) K. A. Nielsen, J. O. Jeppesen, E. Levillain and J. Becher, *Angew. Chem. Int. Ed. Engl.*, 2003, **42**, 187; (*c*) S. H. Kim, S. J. Hong, J. Yoo, S. K. Kim, J. L. Sessler and C. H. Lee, *Org. Lett.*, 2009, **11**, 3626; (*d*) C. J. Woods, J. W. Essex and M. A. King, *J. Phys. Chem. B*, 2003, **107**, 13711.
5 K. S. Park, S. O. Jung, I. Yoon, K. M. Park, J. Kim, S. S. Lee and J. S. Kim, *J. Inclusion Phenom.*, 2001, **39**, 295.
6 R. Nishiyabu and P. Jr. Anzenbacher, *J. Am. Chem. Soc.*, 2005, **127**, 8270.
7 M. Dukh, P. Drasar, I. Cerny, V. Pouzar, J. A. Shriver, V. Kral and J. L. Sessler, *Supramol. Chem.*, 2002, **14**, 237.
8 (*a*) O. Rusin, V. Král, J. O. Escobedo and R. M. Strogin, *Org. Lett.*, 2004, **6**, 1373; (*b*) K. Zelenka, T. Trnka, I. Tišlerová, V. Král, M. Dukh and P. Drašar, *Collect. Czech. Chemm. Commun.*, 2004, **69**, 1149.
9 (*a*) M. Cornia, G. Casiraghi, S. Binacchi, F. Zanardi and G. Rassu, *J. Org. Chem.*, 1994, **59**, 1226; (*b*) P. Maillard, C. Huel and M. Momenteau, *Tetrahedron Lett*, 1992, **33**, 8081.
10 M. Cornia, S. Binacchi, T. Del Soldato, F. Zanardi and G. Casiraghi, *J. Org. Chem.*, 1995, **60**, 4964.
11 P. Štěpánek, M. Dukh, D. Šaman, J. Moravcová, L. Kniežo, D. Monti, M. Venanzi, G. Mancini and P. Drašar, *Org. Biomol. Chem.*, 2007, **5**, 960.
12 N. T. T. Huong, P. Klímková, A. Sorrenti, G. Mancini and P. Drašar, *Steroids*, 2009, **74**, 715.
13 F. Rodrigues, Y. Canac and A. Lubineau, *Chem. Commun.*, 2000, 2049.
14 B. Turner, A. Shtereberg, M. Kapon, K. Suwinska and Y. Eichen, *Chem. Commun.*, 2002, 404.
15 B. J. Littler, M. A. Miller, C. H. Hung, R. W. Wagner, D. F. ÓShea, P. D. Boyle and J. S. Linsdey, *J. Org. Chem.*, 1999, **64**, 1391.
16 V. Poterya, O. Tkac, J. Fedor, M. Farnik, P. Slavicek and U. Buck, *Int. J. Mass Spectrom.*, 2010, **290**, 85.
17 Y. Matsumoto and K. Honma, *J. Chem. Phys.*, 2007, **18**, 184310.
18 D. Monti, M. De Rosii, A. Sorrenti, G. Laguzzi, E. Gatto, M. Stefanelli, M. Venanzi, L. Luvidi, G. Mancini and R. Paolesse, *Chem. Eur. J.*, 2010, **16**, 860.
19 C. N. Warriner, P. A. Gale, P. E. Light and M. B. Hurshouse, *Chem. Commun.*, 2003, 1810.
20 A. Aydogan, J. L. Sessler, A. Akar and V. Lynch, *Supramol. Chem.*, 2008, **20**, 11.