Pergamon

Tetrahedron Letters, Vol. 38, No. 49, pp. 8443-8444, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10275-1

First Synthesis of an Expanded Calixpyrrole

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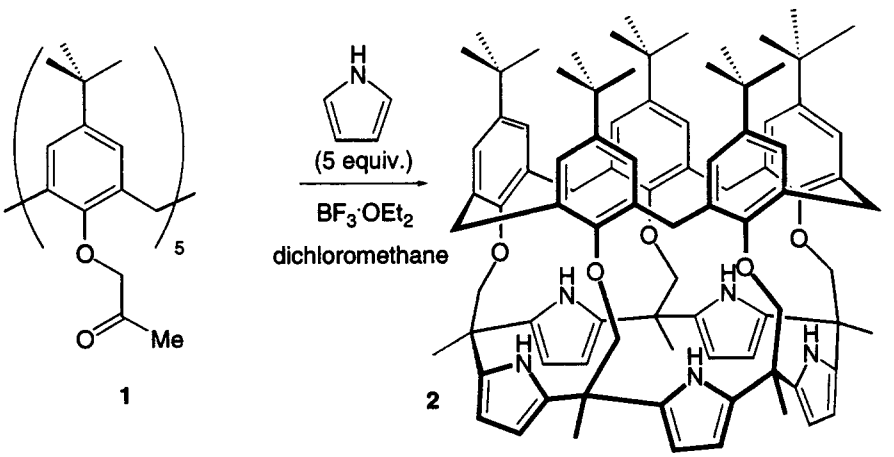
Abstract: The synthesis of the first expanded calixpyrrole: a calix[5]arene-capped calix[5]pyrrole **2** has been achieved using *p-tert*-butylcalix[5]arene pentamethyl ketone **1** as a template.

In a recent letter in this journal we reported the synthesis of a calix[4]pyrrole-calix[4]arene pseudo-dimer obtained *via* the templated reaction of a calix[4]arene tetraketone with pyrrole.[1] At that time, we speculated that a larger calixarene, such as a calix[5]arene pentaketone **1**, could also serve as a template around which an 'expanded' calixpyrrole might form. In contradistinction to what is true in the case of calixarenes,[2] such expanded calixpyrroles are currently unknown in the literature. Here we report that a template-mediated strategy may in fact be used to prepare expanded calixpyrroles; specifically, we describe the synthesis of the calix[5]pyrrole-calix[5]arene pseudo dimer **2**.

Our recent discovery that calix[4]pyrroles (*meso*-octaalkylporphyrinogens) are both selective and easy-to-make anion binding agents[3] led us to consider strategies for synthesizing expanded calixpyrrole analogues. As noted above, the template strategy was first investigated using a calix[4]arene.[1] Calix[5]arenes[2] are more challenging to synthesize than calixarenes containing even numbers of phenolic residues. However, with the relevant precursor, *p-tert*-butylcalix[5]arene pentamethylketone **1**,[4] now in hand, it was found that reaction with pyrrole in the presence of a Lewis acid did indeed afford the calix[5]pyrrole-calix[5]arene pseudo dimer **2**; to the best of our knowledge, this species constitutes the first example of an expanded calixpyrrole.



Scheme 1. Synthesis of compound **2**

SYNTHESIS

p-tert-Butylcalix[5]arene pentamethyl ketone **1** was synthesized according to literature procedures.[4] Reaction of compound **1** (200 mg, 0.153 mmol) with pyrrole (51 mg 0.765 mmol) in a dichloromethane mixture, in the presence of $BF_3{\cdot}OEt_2$, followed by column chromatography on silica gel (CH_2Cl_2, eluent) afforded the calix[5]pyrrole-calix[5]arene pseudo dimer **2** in 10% yield (20 mg) (Scheme 1). Compound **2** gave spectroscopic and analytical data in accord with the assigned structure.[5]

NMR STUDIES

The ^1H NMR spectrum of **2** in dichloromethane-d_2 is very similar to that of the calix[4]arene-calix[4]pyrrole pseudo-dimer reported previously.[1] However, the NH protons which resonated at 11.22 ppm in the tetramer, due to NH - O hydrogen bonds, resonate at 9.88 ppm in the pentamer, a finding that serves as a possible indication of weaker hydrogen bonding in the case of the larger species **2**. Addition of CD_3OD (50%) to the NMR solution causes the NH protons of **2** to shift downfield to 10.46 ppm. Such an effect is not observed in the case of the corresponding calix[4]arene-calix[4]pyrrole pseudo-dimer[1] and is consistent with the methanol serving to interfere with the hydrogen bonding array in **2**. Similarly, addition of five equivalents of tetrabutylammonium chloride to **2** causes a 0.28 ppm shift in the NH proton resonance. Chloride anion is known to bind to other calix[4]pyrroles[3] but not to the calix[4]arene-calix[4]pyrrole pseudo-dimer.[1] Thus, this result provides further support for the contention that the internal hydrogen bonding array in the calix[5]arene-calix[5]pyrrole pseudo-dimer is weaker than that in the corresponding tetrameric dimer.

CONCLUSIONS

The synthesis of a calix[5]pyrrole has been achieved successfully using a calix[5]arene pentaketone as a template. We are currently investigating the molecular recognition properties of this newest addition to the calix[n]pyrrole family.

ACKNOWLEDGMENTS

This work was supported by NSF and NIH grants (CHE 9122161 and AI 33577 to J.L.S.). P.A.G. wishes to thank the Fulbright Commission for a post-doctoral research fellowship.

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5. Analytical and spectroscopic data for compound **2**. High resolution positive ion FABMS: Calculated ($C_{90}H_{105}N_5O_5$) 1335.811; Found 1335.814 (Δ -1.9 ppm). ^1H NMR (CD_2Cl_2, 500 MHz) δ: 9.88 (s, 5H, NH), 7.44 (s, 10H, ArH), 5.82 (d, J = 2.5 Hz, 10H, CH), 4.57 (d, J = 13.0 Hz, 5H, $ArCH_2Ar$), 3.87 (s, 10H, OCH_2), 3.40 (d, J = 13.0 Hz, 5H, $ArCH_2Ar$), 1.58 (s, 15H, $pyCCH_3$), 1.20 (s, 45H, *tert*-Bu). ^{13}C NMR (CD_2Cl_2, 125 MHz) δ: 153.28, 146.07, 136.41, 133.00, 127.04, 104.56, 85.99, 39.89, 34.48, 31.64, 27.45, 26.15.

(*Received in USA* 15 *September* 1997; *accepted* 24 *September* 1997)