

## Synthesis of Calix[3]pyrrole and Its Strain-Induced Reaction

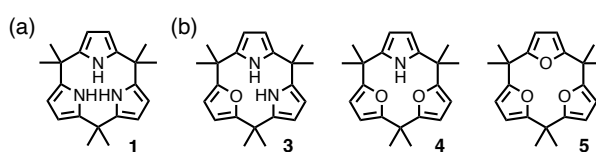
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**Keywords:** Calix[*n*]pyrrole; Ring Strain; Ring Expansion Reaction; Anion Binding; Carbonyl Compound

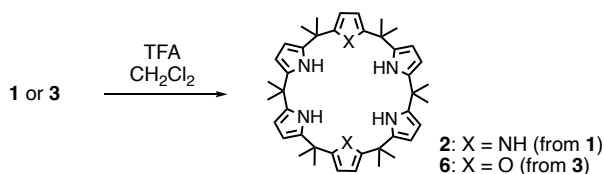
Tetrapyrrolic macrocycles such as porphyrins can be selectively obtained by condensation reaction of pyrrole and carbonyl compounds, whereas corresponding tripyrrolic macrocycles have been never observed except boron complex obtained by template synthesis. Calix[3]pyrrole, a tripyrrolic macrocycle bearing three *sp*<sup>3</sup> carbon linkage, might hold a key to explain the absence of macrocycle with three pyrrole subunits. In this work, we synthesized calix[3]pyrrole **1** and discovered its strain-induced ring expansion reaction.<sup>1</sup> Besides, core-modified analogues of **1** having different strain energies were prepared to investigate the substrate scope and reaction mechanism of the strain-induced ring expansion reaction.

Calix[3]pyrrole **1** (**Figure 1a**) was obtained from aliphatic hexaketone compound via cyclization and Paal-Knorr pyrrole formation reaction. Crystal structure of **1** have shown its strained structure, which was also indicated by computational analysis. This strain caused **1** a rapid ring expansion reaction under acidic conditions to give calix[6]pyrrole **2** within 30 seconds (**Scheme 1**). This result helps us to explain the absence of tripyrrolic macrocycles in classical acid-catalyzed condensation reactions.

To gain a better understanding about this ring expansion reaction, calix[*n*]furan[3–*n*]pyrrole **3–5** (*n* = 1–3, **Figure 1b**) were synthesized in a manner similar to **1**. Presumed from crystal structures and theoretical calculations, the ring strain increases as the number of inner NH sites increases. Under acidic conditions, calix[1]furan[2]pyrrole **3** caused regioselective ring expansion reaction to give macrocycle **6** over 5 minutes, while less-strained **4** and **5** were stable. Although **4** was inert, *N*-methylation of **4** impelled the ring expansion reaction and enabled the isolation of linear reaction intermediate which gives a clue to explain a reaction mechanism. This unique reactivity of calix[3]-type macrocycles could provide access to new larger pyrrolic macrocycles.



**Figure 1.** (a) Structure of **1** and (b) its analogues **3–5**.



**Scheme 1.** Ring expansion reaction of **1** and **3**.

1) Y. Inaba, Y. Nomata, Y. Ide, J. Pirillo, Y. Hijikata, T. Yoneda, A. Osuka, J. L. Sessler, Y. Inokuma, *J. Am. Chem. Soc.*, **2021**, *143*, 12355–12360.