SHORT PAPER

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High-yield calix[4]pyrroles as αβαβ isomers and X-ray structure analysis[†]

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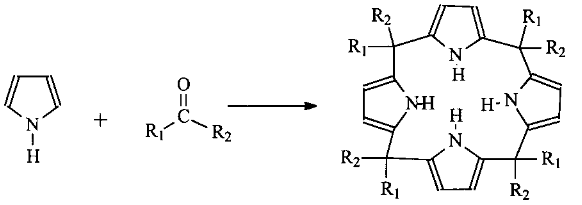
Two calix[4]pyrroles as aβaβ isomers were prepared by the reactions of pyrrole with asymmetry ketones in high yields. In addition, two single crystals of calix[4]pyrrole **2** and **2**·MeOH were solved by X-ray analysis, which further proved that either in free form or inclusion complex calix[4]pyrrole **2** is aβaβ isomer and adopts 1,3-alternate conformation.

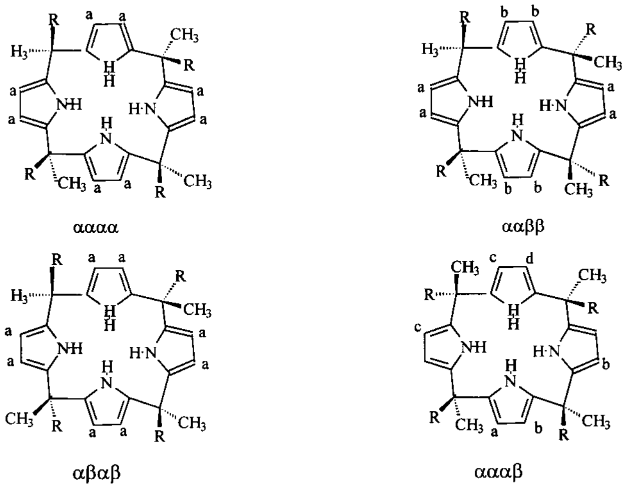
It is well documented that calixpyrroles derived from pyrrole and simple ketones are novel ligands[1] and good host molecules for anions and for neutral species such as simple alcohols, amines and amides.[2] Recent studies also showed that these calixpyrroles possess a remarkable selectivity for binding fluoride rather than other halides.[3] Furthermore, the guest selectivity would be modified when the calixpyrrole was C-rim substituted.[4] However, the reported calix[4]pyrroles are mostly derived from pyrrole and symmetrical ketones. In contrast, few have studied the reaction of pyrrole with asymmetric ketones.[5,6] Recently, Sessler's group studied the reaction of pyrrole with *p*-hydroxyacetophenone and the results showed that there were four isomers when pyrrole reacted with aromatic asymmetric ketones, in which αααα isomer dominated the others and the αβαβ isomer were obtained in low yield.[6] Floriani's group also reported similar results.[5c] Here, we decided to study the reactions of pyrrole with aliphatic asymmetric ketones like 2-butanone and 4-methyl-2-pentanone in order to explore what the main products are and to find out a simple way to obtain pure isomer in high yield. (Scheme 1)



1: R$_1$ = CH$_3$; R$_2$ = CH$_2$CH$_3$
2: R$_1$ = CH$_3$; R$_2$ = CH$_2$CH(CH$_3$)

Scheme 1 Synthesis of the meso-substituted calix[4]pyrroles.

A mixture of pyrrole with 2-butanone or 4-methyl-2-pentanone was stirred in methanol solution and the result was white-red solids were precipitated from the resulting solution. The white solid products which were isolated by filtration and washed by methanol, were pure enough to characterise. TLC indicates the new products are pure compounds and FAB ms showed that they were calix[4]pyrroles. Proton NMR spectroscopy was employed to confirm the configurational assignments. The symmetries of the various isomers were reflected directly in their ^{1}H NMR spectra, particularly in the number of pyrrole CH resonance; the αααα and αβαβ have one only type of CH group, while the ααββ has two types of pyrrolic CH group and the αααβ isomer possesses four different CH groups according to literature[6] (Fig. 1).



R = bulky group, **1** R = -CH$_2$CH$_3$, **2** R = -CH$_2$CH(CH$_3$)$_2$

Fig. 1 Conformations of calix[4]pyrroles (different types of protons are denoted as a, b, c, d. ref. 6).

There was only one signal (δ_H5.86 and 5.84, respectively) for the pyrrolic CH group in calix[2]pyrrole **1** and **2**, indicating only one type of CH in the pyrrolic ring, which is significantly different from the previous report.[5c] Since both αααα and αβαβ have one equivalent set of protons, it is difficult to assign the exact isomer solely from ^{1}H NMR spectra. Thus, single crystals of **2** and **2**·MeOH were obtained and analysed by X-ray. The crystal structure results proved that calix[4]pyrrole **2** adopts αβαβ isomer either in free form **2** or **2**·MeOH (Figs 2 and 3). Since **1** and **2** are similar in structure and have identical signals for pyrrolic CH group in the NMR spectrum, the isomer of **1** can be assigned as αβαβ.

It should be noted that raising the reaction temperature decreased the yield substantially. At refluxing condition, the resulting crude products were of dark brown solids containing a large amount of polymer. In addition, the purification required chromatography. Methanesulfonic acid was also applied as catalyst and gave similar results to hydrochloric acid.

The crystal **2**·MeOH was grown in the mixture of chloroform and methanol under slow evaporation. X-ray analysis indicated that **2**·methanol adduct complex (molar ratio 1:1) (Fig. 2), was different from Sessler's result[3] in which one calixpyrrole bound two methanols, and adopts a 1,3-alternate conformation. The methanol is along with C$_4$ axis, forming hydrogen bonds with N$_{\text{pyrrole}}$. The two symmetry-equivalent H-bonds (N$_{\text{pyrrole}}$ ··· O$_{\text{MeOH}}$) with the angle 151.07° are 3.161Å long, which are almost identical to that of N$_{\text{pyrrole}}$ ...O$_{\text{MeOH}}$[7]. The pure form crystal of **2** was obtained in the mixture of chloroform and acetonitrile (Fig. 3), in which the

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

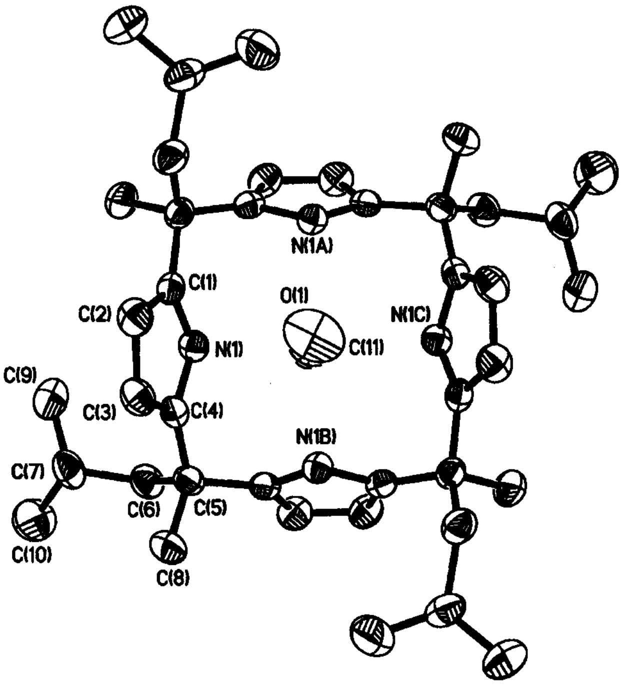

Fig. 2 View of the molecular structure of the methanol adduct of the αβαβ isomer of **2** in the 1,3-conformation. Thermal ellipsoids are scaled to the 30% probability level. Hydrogen atoms are omitted for clarity.

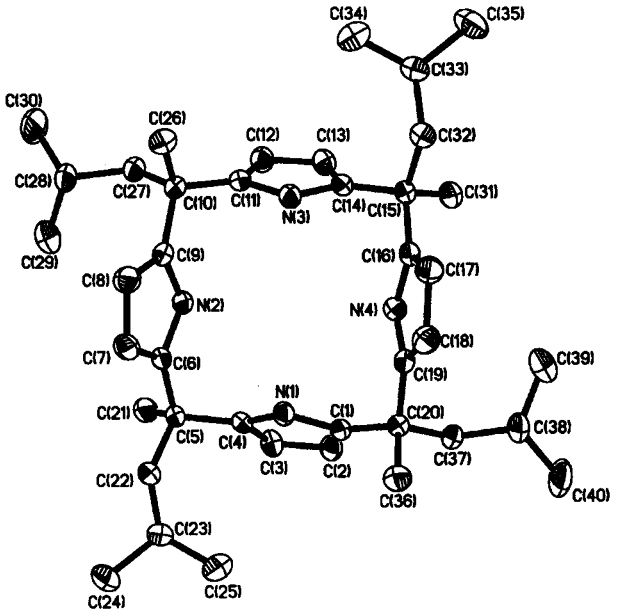

Fig. 3 View of the molecular structure of aβaβ isomer of **2**. Thermal ellipsoids are scaled to the 30% probability level. Hydrogen atoms are omitted for clarity.

pyrrolic rings also adopt a 1,3-alternate conformation with the four $N_{pyrrolle}$ nearly in one plane. In Fig. 3, there are no intramolecular hydrogen bonds and the N–H groups of the 1,3-pyrrole rings point towards the side of the meso-alkyl groups and are almost perpendicular to the macrocycle plane.

In conclusion, reactions of aliphatic asymmetric ketones with pyrrole give a high-yield of the αβαβ isomer, which was rarely found in that of aromatic ketones with pyrrole. The results were further confirmed by X-ray analysis. Moreover, this work may imply that: aliphatic and aromatic ketones could have different reaction mechanism in the formation of calixpyrroles when they react with pyrrole. The energy barriers of isomers in aliphatic calixpyrroles are so low that different isomers can be transformed from one to the other in solution at room temperature, while for aromatic compound, this is not the case.

Experimental

Typical experimental procedure for calix[4]pyrrole **1**, calix[4]pyrrole **2**: freshly distilled pyrrole (10 mmol) and asymmetry ketone (10 mmol) was dissolved in 40 ml of dry methanol in 100 ml round bottomed flask with stirring under an argon atmosphere. Hydrochloric acid (0.5 ml) in 10 ml of methanol was added to the solution dropwise within in 10 minutes at 0°C. The resulting reaction mixture was stirred at room temperature for 36 hours. The white-red solids of calix[4]pyrrole were precipitated. The precipitate obtained in this way were isolated by filtration and washed with methanol for three times.

Calixpyrrole[4] **1** (yield 62%): ^{1}HNMR (200MHz, $CDCl_3$): δ = 0.67 (s, 12H), 1.37 (s, 12H), 1.82(s, 8H), 5.86(s, 8H), 6.99 (m, 4H, NH). FAB MS: *m/z*: 484.9 (MH^+); elemental analysis: calculated for $C_{32}H_{44}N_4$: C 79.29, N 11.56, H 9.15; found: C: 78.86, N 11.39, H 8.85. IR (KBr diffuse reflectance): ν[cm^{-1}] = 3434, 2968, 2932, 2875, 1573, 1211, 1040, 762

Calixpyrrole[4] **2** (yield 76%): ^{1}HNMR (200MHz, $CDCl_3$): δ = 0.67 (s, 24H), 1.47 (s, 16H), 1.73(s, 8H), 5.84(s, 8H), 7.23 (s, 4H, NH). FAB MS: *m/z*: 597.1 (MH^+); elemental analysis: calculated for $C_{40}H_{60}N_4 \cdot CH_3OH \cdot H_2O$: C 76.11, N 8.86, H 10.28; found: C: 76.26, N 8.72, H 9.96. IR (KBr diffuse reflectance): ν[cm^{-1}] = 3448, 2952, 2867, 1575, 1202, 1045, 767.

Crystal data for **2**· MeOH: $C_{41}H_{64}N_4O$, M = 628.96, tetragonal, space group $P4_2/n$, a = 16.6543(13), b = 16.6543(13), c = 7.0739(8) Å, U = 1962.1 (3) Å^3, Z = 2, T = 298 (2) K, μ = 0.0.063 mm^{-1}. Goodness-of-fit on F^2 was 0.997. R1 [for $I > 2\sigma(I)$] = 0.0618, wR2 = 0.1734.The structure was solved by direct methods using SHELXTL-97.[8]

Crystal data for **2** : $C_{40}H_{60}N_4$, M = 596.92, triclinic, space group P-1, a = 12.1408(11), b = 13.1990(12), c = 13.2205(12) Å, U = 1841.7 (3) Å^3, Z = 2, T = 298 (2) K, μ = 0.0.063 mm^{-1}. Goodness-of-fit on F^2 was 1.053. R1 [for $I > 2\sigma(I)$] = 0.0532, wR2 = 0.1389.The structure was solved by direct methods using SHELXTL-97.[8]

Crystallographic data for the structures in this paper have been deposited as CCDC 147258 and 147257 [E-mail: deposit@ccdc.cam.ac.uk).

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