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# Synthesis of Pyridylazo-substituted Chromogenic Calix[4]arenes

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**Abstract:** This letter reports a novel method for preparing chromogenic calix[4]arenes, in which the 4-aminopyridine was diazotized with *iso*amyl nitrite in EtONa/EtOH, and mono(azo)-, bis(azo)- and tetra(azo)-substituted calix[4]arenes were obtained as main product respectively by diazo-coupling in different molar ratio to calix[4]arene in non-aqueous solution at 0-5°C.

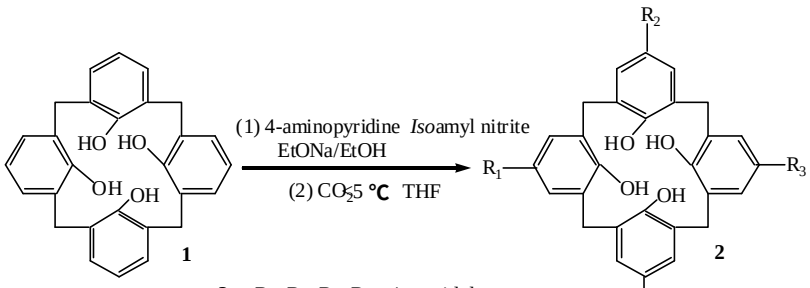
**Keywords:** Chromogenic calix[4]arene, diazo-coupling, *iso*amyl nitrite, aminopyridine.

Calixarenes are a versatile class of macrocyclic compounds which have attracted extensive interest due to their ability to form host-guest complexes and act as enzyme mimic, especially when appropriately functionalized[1]. Introduction of azo group to calixarenes can make the later to be easily detected in the process of molecular recognition, azo groups have been introduced into calixarenes by the diazo-coupling reaction of calix[4]arene with $BF_4^-$ or chloride salt of substituted benzene diazonium to give the so-called "chromogenic calixarenes[2-3]". However, the above methods only suit for the preparation of tetra(arylazo)-substituted calix[4]arenes. Here we report a novel convenient method (**Scheme 1**) for preparing chromogenic calix[4]arenes, in which the 4-aminopyridine **3** as aromatic amine was diazotized with *iso*amyl nitrite as a source of nitrous acid in EtONa/EtOH under refluxing condition. Mono(azo)-, bis(azo)- and tetra(azo)-substituted calix[4]arenes were obtained as main product by diazo-coupling in different molar ratio to calix[4]arene **1** (**Table 1**). The reactions took place in non-aqueous solution under pH 7-9 adjusted by passing carbon dioxide at 0-5°C. The purification of the products was carried out by column chromatography ($CHCl_3/CH_3OH$ or $EtOAc/CH_3COCH_3$). All pyridylazo-substituted calix[4]arenes are red-brown solids, mp >300°C (dec). Compared with the literatures, this method has the following advantages: (1) the mono-, bis-, or tetra(azo)-substituted calix[4]arenes as a main product, which can be prepared under different conditions. (2) the reaction can be carried out in a non-aqueous solution.

The structures of chromogenic calix[4]arenes are confirmed by $^1H$ NMR, $^{13}C$ NMR, MS, IR and elemental analysis. In the $^1H$ NMR spectra at low-temperature (–20°C), the chemical shift values and splitting pattern of the methylene protons of $ArCH_2Ar$ (**2a**: 5.14, 3.93 ppm, one pair of doublets; **2b**: 5.19, 5.02, 3.88, 3.72 ppm, two pair of doublets; **2c**: 5.21, 5.12, 4.78, 3.78, 3.66, 3.58 ppm, three pair of doublets; **2d**: 5.28,

4.83, 3.59, 3.56 ppm, two pair of doublets; All coupling constants are about 12.6 Hz) indicate that all chromogenic calixarenes have a cone conformation[4] and compounds **2c** is *proximal* isomers rather than *distal* products[3].

**Scheme 1** Synthesis of chromogenic calix[4]arenas




**2a** $R_1=R_2=R_3=R_4=$ 4 - pyridylazo
**2b** $R_4$ = H ; $R_1=R_2=R_3=$ 4 - pyridylazo
**2c** $R_3=R_4$ = H ; $R_1=R_2=$ 4 - pyridylazo
**2d** $R_2=R_3=R_4$= H ; $R_1$ = 4 - pyridylazo

**Table 1** Reaction conditions and product distributions for diazo-coupling of calix[4]arene **1** with diazonium solution of 4-aminopyridine **3**

| Molar ratio (**3**/**1**) | Distribution of products (mmol % ) | | | |
|---|---|---|---|---|
| | **2a** | **2b** | **2c** | **2d** |
| 1:1 | 0 | 0 | 13.2 | 59.1 |
| 2:1 | 17.6 | 16.8 | 37.1 | 12.3 |
| 3:1 | 32.8 | 18.6 | 13.7 | .0 |
| 4:1 | 57.1 | 14.2 | .0 | .0 |

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