

New hydrogen bond assisted synthesis of calixarene quinone-hydrazones

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Dedicated to Prof. Sukh Dev on his 80th Birthday

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Abstract

The hydrogen bond assisted synthesis of calix[n]arene quinone-hydrazones(II) has been achieved through coupling octahydroxycalix[8]arenes with solutions of diazotized 2-amino benzoic acid and 4-nitrophenyl-2-aminobenzoate in pyridine.

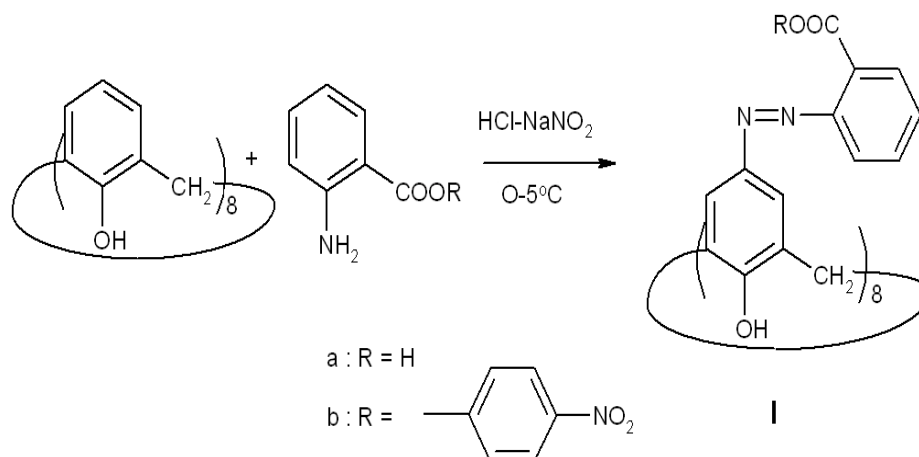
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Introduction

Quinone hydrazones represent a class of important chemical systems that are postulated as intermediates in various reactions.¹ Though rarely isolated as stable species due to rapid transformation to their azo-tautomers,² they have enormous potential for designing molecular receptors for ionic and molecular recognition.³ As a part of our programme on hydrogen bond assisted organic transformations,⁴ we have achieved the synthesis of stable calixarene quinone-hydrazones which are reported in this communication.

Results and Discussion

In a typical experiment, octahydroxycalix[8]arene (obtained from the reaction of *p*-tert-butyl(octahydroxy)calix[8]arene with AlCl₃)⁵ was coupled in THF-pyridine (1:5), with diazotized solutions of 2-aminobenzoic acid and 4-nitrophenyl-2-aminobenzoate (NaNO₂/HCl, 0-5°C), respectively, to yield red solids (**Ia,b**), which were purified by recrystallization from THF-petroleum ether (1: 1). The NMR, IR and UV of the resultant compounds were indicative of the assigned gross structures given in Scheme 1. For instance, **Ia** gave a signal at δ 8.2 (OH) that disappeared in D₂O, a multiplet at δ 6.8-7.78 (aromatic protons) and methylene protons of the calixarene moiety at δ 3.7-3.8 in its ¹H NMR. The carboxyl, azo, (-N=N-), and hydroxy linkages in **Ia** were observed at 1720, 1617 and 3370 cm⁻¹, respectively, in its IR spectrum.



Scheme 1

The inference that the synthesized dyes may be present in their quinone-hydrazone form (**II**) rather than their azo-form (**I**) was arrived at by the presence of a strong quinone carbonyl at 1640 cm^{-1} in its IR spectrum as well as through base (e.g., NaOH, buffer at pH 9.2) induced UV spectral studies. The isolated compound (**Ia**) showed two absorption maxima (500 nm and 288 nm) in neutral solutions (pH 7.09) and precipitated in acidic solutions at $\text{pH} < 5$. When a base was added to its neutral solutions (THF: distilled water; 1: 1), it changed its colour from pink to yellow with a concomitant change in λ_{max} . For example, a gradual increase in pH to 9.25 caused the colour to change from pink to orange-yellow with a gradual shifting of the peak at λ_{max} 500 nm to 480 nm while there was a gradual formation of new peak at λ_{max} 420 nm. At pH 9.37, the colour of solution turned dark yellow with a hypsochromic shift of 80 nm. Subsequently no change in absorption maxima was observed on further increase in pH. It was determined that at pH 9.37, the absorption maximum observed at 500-480 nm disappeared and a new intense peak at λ_{max} 420 nm ($\epsilon 2.4 \times 10^4 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) (**Figure 1** curve 5) appeared.

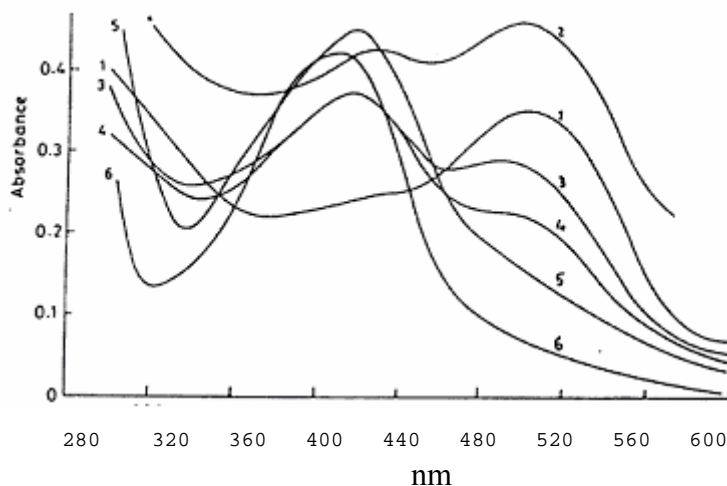
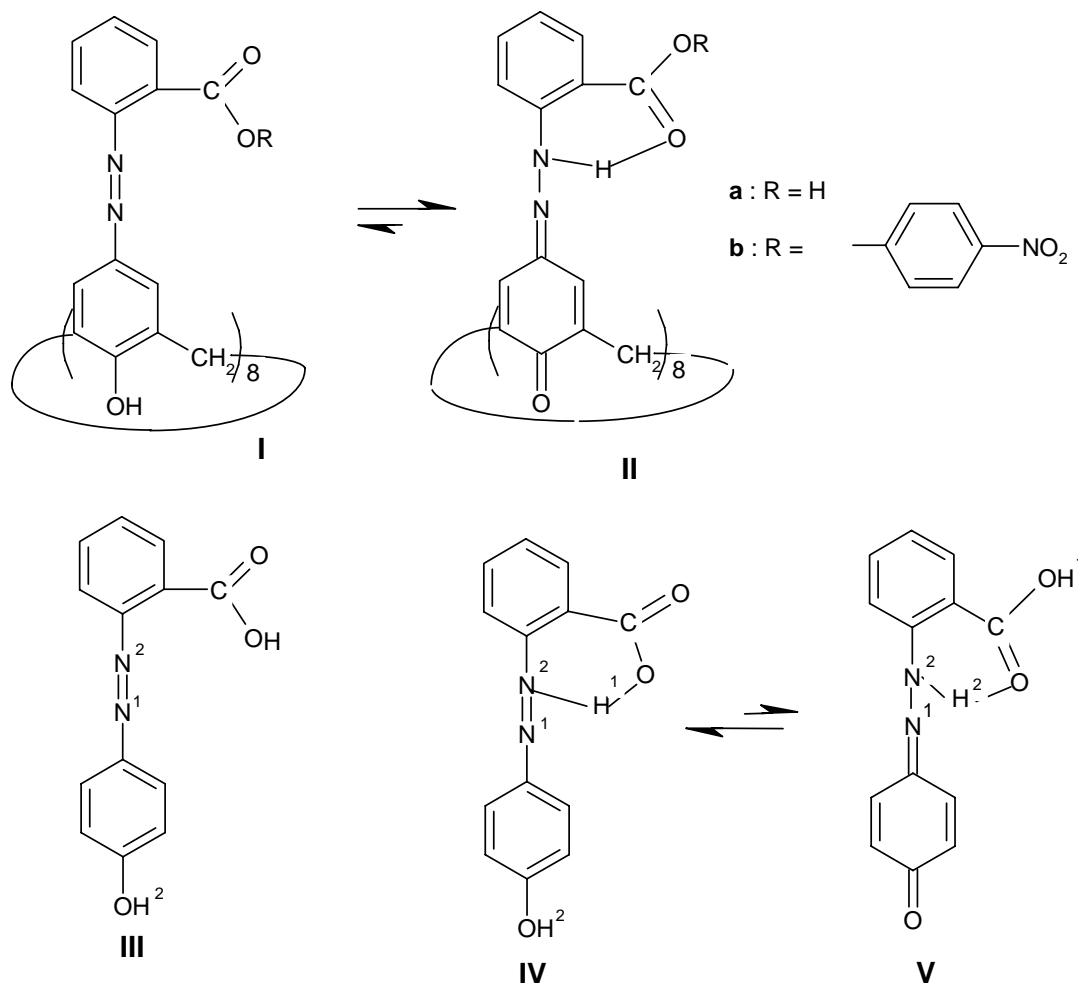


Figure 1. Spectral variation of **Ia** as a function of pH in 50% (v/v) THF-H₂O. The pH values are (1) 7.09 (2) 7.71 (3) 8.66 (4) 9.25 (5) 9.37 (6) 10.67.

The hypsochromic shift observed on addition of a base is characteristic of systems undergoing change from conjugated to a non-conjugated pattern. In order to ascertain the role of the calixarene structure for the observed hypsochromic shift, its open chain analog **III** was synthesized by coupling a diazotized solution of 2-aminobenzoic acid with phenol. When treated with base, (similar conditions as adopted in **I**), **III** gave a bathochromic shift of 54 nm (from 350 nm to 404 nm).

The hypsochromic shift on addition of base to **I** can be explained if we assume that the synthesized compounds are present in the calixarene quinone-hydrazone form (**II**), which is transformed to the azo calixarene tautomer (**I**) on addition of a base.



Since no hypsochromic shift was observed in **III** on similar addition of a base, the calixarene stereostructure must be vital for stabilization of the quinone-hydrazone form perhaps through hydrogen bonding as shown in **II**. This is confirmed by the fact that azo calixarenes lacking carboxyl groups in the ortho positions are usually present as their azo tautomers.⁶⁻⁹ In the present case, when ortho carboxyl group was esterified, the resultant compound was again observed to exhibit a hypsochromic shift on addition of a base.

These results suggest that both the ortho ester and the carboxyl groups can stabilize the quinone-hydrazone form in azo calixarenes but the same groups stabilize the azo hydroxy form in their open chain analogs. This can be explained by the assumption that the hydrazone form of **I** gets stabilized through a six-membered hydrogen bonded structure represented by **II**. The open chain analog **III** presumably exists mainly in its azo form (**IV**) probably because of an increase in electron density at ^2N , which gets protonated by the ortho carboxylic proton. Such protonation of ^2N in the calixarene series seems to be inhibited because of extensive flip-flop hydrogen bonding of lower rim hydroxyls which do not allow significant enhancement in basicity of ^2N .^{5,8,9} Such hydrogen bond assisted stabilization of calixarene quinone-hydrazone might also be dependent upon the size and shape of calixarene cavity and this is a subject for further investigation in our laboratories.

Experimental Section

Procedure for coupling octahydroxycalix[8]arene with diazotized 2-aminobenzoic acid. A solution of 2-aminobenzoic acid (0.719 g, 5.24 mmol), sodium nitrite (excess) and concentrated HCl (5 ml) in water (10 ml) was slowly added (over a period of about 15 minutes) into an ice cold solution of 49,50,51,52,53,54,55,56-octahydroxycalix[8]arene (0.214 g, 0.25 mmol) dissolved in tetrahydrofuran : pyridine (25 ml) (5 : 2) with constant stirring to give a red suspension which was stirred for 15 minutes at the same temperature and then gradually allowed to attain room temperature. The reaction mixture was kept for 10 minutes at room temperature and then poured into water (500 ml) and acidified with concentrated HCl to give a red precipitate, which was filtered and subsequently washed with water. The crude product was purified by recrystallization from tetrahydrofuran-hexane to give 5,11,17,23,29,35,41,47-octakis(2'-carboxyphenylazo)-49,50,51,52,53,54,55,56-octahydroxycalix[8]arene (**Ia**) (0.381 g, 75%) as a red solid; m.p. >230°C (calculated for $\text{C}_{112}\text{H}_{80}\text{O}_{24}\text{N}_{16}$: C, 66.14; H, 3.93; N, 11.02. Found: C, 66.26; H, 4.07; N, 10.96. Mol. mass (vapour pressure osmometry): 2050 (calcd. 2032). UV (λ_{max} , DMSO): 366 nm; IR (KBr, ν_{max} , cm^{-1}): 3249, 2955, 1657, 1592, 1468, 1447, 1383, 1258, 1211, 1094, 749. $^1\text{H-NMR}$ (DMSO- d_6 : δ , ppm): 8.2 (8H, bs, exchangeable with D_2O , OH): 7.78-6.8 (48H, m, Ar'H + ArH); 3.8-3.7 (16H, s, ArCH₂Ar). $^{13}\text{C NMR}$ (DMSO- d_6 : δ , ppm): 151.1, 149, 128.8, 127.7, 119.7, 30.72.

Coupling of octahydroxycalix[8]arene with diazotized 4'-nitrophenyl 2-aminobenzoate. A solution of 4-nitrophenyl 2-aminobenzoate (1.35 g, 5.24 mmol) sodium nitrite (excess) and conc. HCl (5 ml) in water (10 ml) was slowly added (over a period of about 15 minutes) to an ice cold solution of 49,50,51,52,53,54,55,56-octahydroxycalix[8]arene (0.213 g, 0.25 mmol) in tetrahydrofuran : pyridine (5 : 2, 25 ml) with constant stirring to give a red suspension. After stirring the suspension for 15 minutes, it was gradually allowed to attain room temperature. The reaction mixture was kept for 10 minutes at room temperature and the suspension was poured into 400 ml water and acidified with concentrated HCl to give a red precipitate that was filtered and subsequently washed with water. The crude product was purified by recrystallization from a mixture of tetrahydrofuran and hexane to give 5,11,17,23,29,35,41,47-octakis[2-(4-

nitrophenylcarbonyl)phenylazao]-49,50,51,52,53,54,55,56-octahydroxycalix[8]arene (**1b**) (0.525 g, 70%) as a red solid. m.p. >230°C (calculated for C₁₆₀H₁₀₄O₄₀N₂₄: C, 64.14; H, 3.46; N, 11.2. Found: C, 64.16; H, 3.39; N, 11.32. Mol. mass (vapour pressure osmometry): 3028 (calcd. 3000). UV (λ_{max} , DMSO): 370 nm; IR (KBr, ν_{max} , cm⁻¹): 3278, 2923, 1658, 1590, 1512, 1467, 1377, 1333, 1292, 1111, 753. ¹H-NMR (CDCl₃, δ , ppm): 9.49 (8H, bs, exchangeable with D₂O, OH), 8.34-8.18 (16H, m, Ar'H); 7.40-7.37 (16H, m, Ar'H) 7.12 (16H, d, Ar'H), 7.66-7.60 (8H, m, ArH), 6.9-6.89 (8H, m, ArH), 6.81-6.73 (16H, m, Ar'H), 3.74 (16H, s, ArCH₂Ar). ¹³C {H} NMR (DMSO-d₆, δ , ppm): 151.9, 131.9, 128.12, 126.2, 125.2, 123.5, 119.7, 116.7, 115.8, and 31.3.

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