J Incl Phenom Macrocycl Chem (2009) 63:27–35
DOI 10.1007/s10847-008-9485-6

ORIGINAL ARTICLE

Azocalix[4]pyrroles: one-pot microwave and one drop water assisted synthesis, spectroscopic characterization and preliminary investigation of its complexation with copper (II)

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Received: 9 May 2008 / Accepted: 14 July 2008 / Published online: 15 August 2008

Abstract Modified and advanced approach has been developed for the synthesis of *meso*-tetra(methyl) *meso*-tetra(4-hydroxy phenyl) calix[4]pyrrole, *meso*-tetra(methyl) *meso*-tetra(3, 5-dihydroxy phenyl) calix[4]pyrrole and their azo dyes using microwave irradiation. Results obtained from conventional method and microwave assisted synthesis have been compared in terms of ease, yield and time. Detailed reaction mechanism has also been discussed. The structures of all compounds were characterized based on FT-IR, ^{1}H NMR and elemental analysis. A preliminary study on efficiency of these novel azocalix[4]pyrrole receptors towards copper (II) have been carried out by UV/Vis spectrophotometry at 25 °C which shows a distinct color change from yellow to red upon complexation.

Keywords Microwave-irradiation · Calix[4]pyrrole · Azo-dyes · Copper (II) · Optical response

Introduction

Calix[4]pyrroles [1] are cyclic tetramers belonging to a class of hetero-calixarenes and have exhibited significant importance owing to their anion and neutral substrate binding ability [2]. Calixpyrrole derivatives lend themselves well with numerous applications [1] such as optical sensors, anion transporting agents, electro-chemical signaling devices, oragno-catalytic reagent, colorimetric, fluorescence sensors, and new solid supports capable of separating anion mixtures. Recently, they have been used, as catalyst [3] in various reactions, for separation of medicines [4] and for selective separation and preconcentration of Ag^+ and Tl^+ [5].

The developments of chromogenic and fluorogenic ionophores have been a very active research area in supramolecular chemistry, since they can be used as efficient spectrophotometric analytical reagents [6], optical sensing functions [7] and important chemical sensor [8]. Azo dyes are an important class of organic colorants which consist of at least one conjugated chromophore azo (–N=N–) group and two or more aromatic rings. It has been known for many years that azo compounds are the most widely used class of dyes due to their versatile application in various fields [9] such as the dyeing of textile fiber and coloring of different materials, colored plastics, biological-medical studies, and advanced applications in organic synthesis. In recent years many diazo-coupling techniques have been designed for the synthesis of new azocalixarene dyes, which can also act as metal extractant [10] but the research in the area of azocalix[4]pyrrole dyes [11] is still in infancy. Therefore we became interested in synthesizing azocalix[4]pyrrole dyes bearing –N=N– group as well as –OH group to enable it to exhibit both coloring and binding properties.

Large amount of solvent, long reaction time and low yield are few limitations for the synthesis of parent calix[4]pyrroles [1, 2] by conventional methods. In fact in recent years, synthesis by microwave irradiation [12] have become popular among synthetic organic chemists to improve upon classical organic reactions in terms of improving yields, reaction time, clean reaction conditions and ease of manipulation as well as to promote new reactions.

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To the best of our knowledge only Sita Devi et al. [13] have reported the microwave-assisted synthesis of parent calix[4]pyrrole compounds using zeolite based molecular sieves. In our earlier publication [14] synthesis of parent *meso*-substituted calix[4]pyrroles by microwave irradiation technique have been reported. In this communication, we are reporting microwave-assisted synthesis of *meso*-tetra(-methyl) *meso*-tetra(4-hydroxy phenyl) calix[4]pyrrole (**4**) and *meso*-tetra(methyl) *meso*-tetra(3, 5-dihydroxy phenyl) calix[4]pyrrole (**5**) skeletons in less solvent, which is found to be better than their conventional method of synthesis [15]. Further eight novel tetra-functionalized azocalix[4]pyrrole chromogenic receptors **6a–d** and **7a–d** from **4** and **5** have been synthesized using potassium hydrogen sulfate ($KHSO_4$) and sodium nitrite ($NaNO_2$) in solvent free conditions using microwave irradiation technique and the results are compared with conventional method of synthesis.

We have also given preliminary account of complexation of these new chromogenic-receptors with copper (II) in ethanol by UV/Vis spectrophotometry.

Experimental section

Materials and instrumentation

All the reagents used were of AR grade, purchased from Sigma-Aldrich or Fluka and were used without further purification. All aqueous solutions were prepared with deionised double distilled water, which was further purified by a Millipore Milli-Q water purification system (Millipack 20, Pack name: Simpak 1, Synergy). Microwave synthesis work was carried out using a Kenstar OM-18 MSP domestic microwave oven. Melting points were taken in a single capillary tube using a VEEGO (Model No: VMP-DS, India) melting point apparatus and were uncorrected. Elemental analysis was carried out on Perkin Elmer, Series II, 2400 elemental analyzer. FT–IR spectra were recorded on Bruker tensor 27 Infrared spectrophotometer as KBr pellets and expressed in cm^{-1}. ^1H NMR and ^{13}C NMR spectra were recorded in DMSO on a Bruker-ARX 500 instrument. Mass spectra were obtained by the elctrospray technique (positive mode) on a MICROMASS QUATTRO II triple quadrupole mass spectrometer. The samples (dissolved in suitable solvents) were introduced into the ESI source through a syringe pump at the rate of 5 μL/min. The ESI capillary was set at 3.5 KV and the cone voltage was 60 V. The spectra were collected in 6 s scans and the print outs are averaged spectra of 6–8 scans. UV/Vis absorption studies were carried out on a JASCO 570 UV/VIS/NIR spectrophotometer using 10 mm quartz cells.

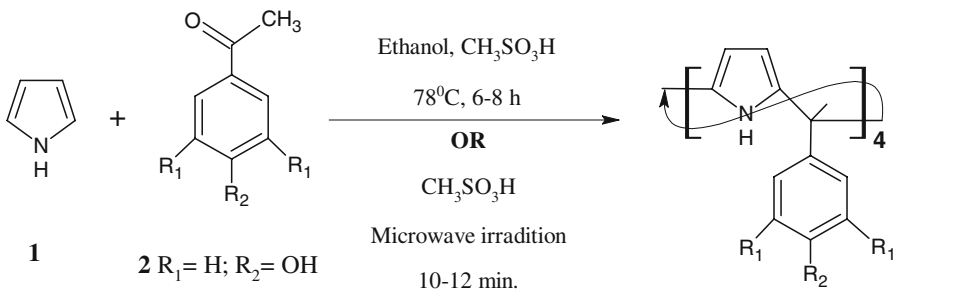
Synthesis

*Conventional and microwave assisted synthesis of parent meso-substituted calix[4]pyrrole skeletons (**4** and **5**) (Scheme 1)*

*Synthesis of meso-substituted calix[4]pyrroles **4** and **5** by Conventional Method [15]* Parent *meso*-substituted calix[4]pyrrole skeletons (**4** and **5**) were synthesized by the acid catalyzed condensation reaction of pyrrole (**1**) and aromatic ketones (**2** and **3**).

*Modified synthesis of meso-substituted calix[4]pyrroles **4** and **5** by microwave irradiation technique* Compound **4** [*meso*-tetra(methyl) *meso*-tetra(4-hydroxy phenyl) calix[4] pyrrole]

A mixture of pyrrole **1** (1.0 mL, 0.015 mol) and methanesulfonic acid (0.1 mL) in methanol (10 mL) were exposed to microwave irradiation for 2 min at 0% output. A solution of 4-hydroxy acetophenone **2** (2.0 g, 0.015 mol) in methanol (10 mL) was then added to the reaction mixture and was subjected to microwave irradiation for 8 min at 0% output with a slight pause after every 2 min. After



Scheme 1 Synthesis of parent calix[4]pyrroles by acid catalyzed cyclo-condensation of pyrrole and ketones by conventional and microwave irradiation technique

1

2 R_1= H; R_2= OH

3 R_1= OH; R_2= H

meso-substituted calix[4]pyrrole

4 R_1= H; R_2= OH

5 R_1= OH; R_2= H

completion of the reaction, a deep reddish brown reaction mixture was obtained which was poured into cold water (50 mL) to obtain orange colored precipitates. The residue was filtered off and collected, and then dissolved in diethyl-ether (25 mL × 2). The solution was again filtered gravitationally to get rid of the black tar. The solvent was evaporated to obtain orange colored mixture of four isomers with the yield 90%. The αααα isomer of the calix[4]pyrrole derivative was isolated by the method described by Angela et al. [16].

Compound **4**

Light pink, yield 65%, mp: 180 °C; IR (KBr) *v*: 3438 (pyrrole NH), 3319 (*β*-pyrrole C–H and –OH), 2886, 2829, 1740, 1356, 1396, 740; ^{1}H NMR *δ*: 8.75 (s, 4H, pyrrole NH), 5.96 (d, 8H, pyrrole-*β*H), 1.81 (12H, CH_3), 6.63–6.78 (Overlapping, 16H, ArH), 8.22 (s, 4H,–OH); ^{13}C NMR *δ*: 155.86, 140.42, 137.42, 127.86, 114.82, 104.16, 43.33, 31.54 ppm; ES–MS *m/z*, 741 $[M + H]^+$: elemental analysis calcd. (%) for $C_{48}H_{44}O_4N_4$: C 77.81, H 5.99, N 7.56; Found: C 76.98, H 5.60, N 7.20.

Compound **5** [*meso*-tetra(methyl) *meso*-tetra(3, 5-dihydroxy phenyl) calix[4]pyrrole]

An equimolar mixture of pyrrole **1** (1.0 mL, 0.015 mol), 3, 5-dihydroxy acetophenone (2.28 g, 0.015 mol) and methanesulfonic acid (0.2 mL) were placed in a conical flask with 20 mL of methanol. The reaction mixture was subjected to microwave irradiation for 12 min at 0% output with a slight pause after every 2 min. After completion of the reaction, a brown reaction mixture was quenched in 50 mL of cold water and 1 mL of tri-ethylamine (for acid neutralization). Pink colored precipitates were filtered and dissolved in diethyl ether (25 mL × 2), dried over $MgSO_4$, filtered and concentrated till light pink colored isomers (*ααββ* and αααα-isomers) were obtained with the yield 85%. The product was recrystallised in acetonitrile to get the enriched fraction of αααα **5**.

Compound **5**

White, yield 60%, mp: 220 °C; IR (KBr) *v*: 3453 (pyrrole NH), 3149 (*β*-pyrrole C-H and –OH), 2936, 2965, 1726, 1415, 1368, 759; ^{1}H NMR *δ*: 8.1–8.3 (br, s, 4H, pyrrole NH), 5.9–6.19 (d, 8H, pyrrole-*β*H), 1.82 (12H, CH_3), 6.2–7.0 (Overlaping, 12H, ArH); ^{13}C NMR *δ*: 152.9, 139.29, 137.20, 128.09, 113.98, 103.96, 44.30, 31.24 ppm; ES–MS *m/z*, 828 [M + Na]: elemental analysis calcd. (%) for $C_{48}H_{44}O_8N_4$: C 71.63, H 5.51, N 6.96; Found: C 71.23, H 5.29, N 6.89.

*Conventional and microwave assisted synthesis of azocalix[4]pyrrole dyes (**6a–d** & **7a–d**) (Scheme 2)*

*General procedure for the synthesis of azocalix[4]pyrrole dyes (**6a–d**, **7a–d**) by Conventional method (Scheme 2)* The synthesis of new azocalix[4]pyrrole dyes involved the following steps,

(i) The diazotization of aromatic primary amines (**a–d**)

A solution of aromatic primary amines (**a–d**) (0.01 mol) in 25 mL water and 0.8 mL of concentrated HCl (0.02 mol, 37%) were stirred until a clear solution was obtained. This solution was cooled to 0–5 °C and then 10 mL of sodium nitrite (0.01 mol) was added dropwise, maintaining the temperature below 2 °C. The resulting mixture was stirred for 45 min in an ice bath and excess nitrite was destroyed by urea.

(ii) Synthesis of azocalix[4]pyrrole dyes (**6a–d** & **7a–d**)

Compound **4/5** (0.0025 mol) and sodium hydroxide (0.6 g, 0.015 mol) was dissolved in 20 mL of water and cooled to 0–5 °C in an ice bath. This solution was then added gradually to diazonium chloride solution, maintaining the temperature between 0 and 5 °C. Resulting reaction mixture was stirred for an hour and allowed to keep at room temperature for 2 h. After adjusting its pH between 6.5 and 7.0 with Na_2CO_3, dark brown/red suspension (precipitate) was obtained. It was further stirred for a 1 h at 60 °C and the mixture was filtered and washed with water: methanol (9:1 v/v) to obtain brown/reddish solid.

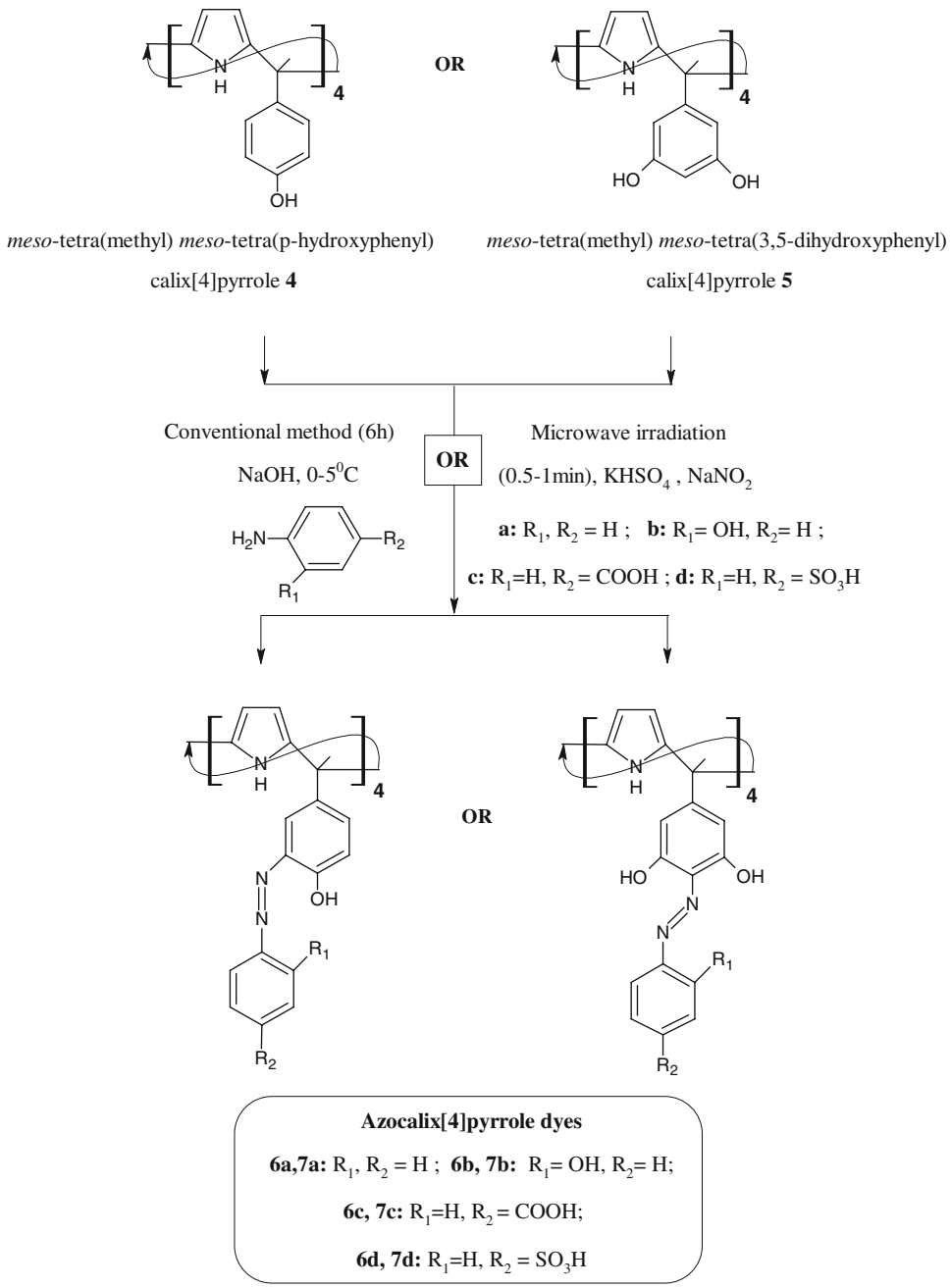
A sample for analysis was obtained by dissolving dark brown/red solid in 50 mL hot aqueous sodium hydrogen carbonate (2.0 g). Activated charcoal (1.0 g) was added to this solution, which was stirred gently, and charcoal was removed by simple filtration to obtain clear filtrate. The filtrate was cooled down to room temperature and acidified with dilute H_2SO_4. The solution was again warmed upto 60 °C for 30 min and cooled. The resulting brown/red precipitates were filtered off, washed with water, and dried in vacuum with the yield, 60–70%.

*Modified synthesis of azocalix[4]pyrrole dyes, **6a–d** and **7a–d** by Microwave- irradiation technique (General protocol) (Scheme 2)* In a typical experiment, a mixture of compound **4/5** (0.0025 mol), aromatic primary amines (**a–d**) (0.01 mol), sodium nitrite (0.69 g, 0.01 mol) and potassium hydrogen sulfate (2.04 g, 0.015 mol) was grinded to homogeneous fine powder and placed in a beaker in a domestic microwave oven and irradiated by microwave for 1 min at 0% output which was followed by addition of a drop of water and thorough agitation of reaction mixture outside the oven and again kept in oven under Microwave irradiation for 30 s. The color of the solid reaction mixture was turned to dark brown/red, which was washed with water:methanol (9:1 v/v). A sample for analysis was obtained as mentioned in (**2.2.2a–ii**).

Compound **6a**

Dark brown, yield 80%, mp: 201 °C; IR (KBr) *v*: 3223 (pyrrole NH), 3223 (Broad, *β*-pyrrole C–H and –OH), 3080, 3035, 2966, 1688, 1607, 789; ^{1}H NMR *δ*: 8.75 (s,

Scheme 2 Formation of azocalix[4]pyrrole dyes via conventional method and microwave irradiation technique



4H, pyrrole NH), 5.8–6.0 (d, 8H, pyrrole-βH), 1.96 (12H, CH_3), 6.8–7.88 (Overlaping, 32H, ArH), 8.20 (s, 4H,–OH); ^{13}C NMR δ: 165.78, 162.34, 149.22, 136.98, 134.46, 133.0 129.03, 127.76, 125.41, 123.57, 116.48, 103.89, 42.98, 26.70 ppm; ES–MS *m/z*, 1180 [M + Na]: elemental analysis calcd. (%) for $C_{72}H_{60}O_4N_{12}$: C 74.72, H 5.23, N 14.52; Found: C 74.40, H 5.03, N 14.16.

Compound **6b**

Dark brown, yield 85%, mp: 218 °C; IR (KBr) *v*: 3215 (pyrrole NH), 3215 (Broad, β-pyrrole C–H and –OH), 3079, 3018, 2928, 1643, 1589, 825; ^{1}H NMR δ: 8.76 (s, 4H, pyrrole NH), 5.8–6.0 (d, 8H, pyrrole-βH), 1.97 (12H, CH_3), 6.8–7.88 (Overlaping, 28H, ArH), 8.20 (br, s, 8H,–OH); ^{13}C NMR δ:166.71, 146.55, 142.25, 132.67, 131.07, 130.14, 129.52, 128.09, 126.81, 125.48, 121.72, 117.31, 114.07, 108.62, 43.01, 26.30 ppm; ES–MS *m/z*, 1244 [M + Na]: elemental analysis calcd. (%) for $C_{72}H_{60}O_8N_{12}$: C 70.76, H 4.95, N 13.76; Found: C 70.12, H 4.35, N 13.10.

Compound **6c**

Reddish brown, yield 82%, mp: 209 °C; IR (KBr) *v*: 3328 (pyrrole NH), 3328 (Broad, β-pyrrole C–H and –OH), 3071, 2998, 2960, 1703, 1625, 802; ^{1}H NMR δ: 8.75 (s, 4H, pyrrole NH), 5.8–6.0 (d, 8H, pyrrole-βH), 1.99

(12H, CH_3), 6.52–7.85 (Overlaping, 28H, ArH), 8.19 (br, s, 8H,–OH), 9.74 (s, 4H, –COOH); ^{13}C NMR δ: 176.80, 150.96, 145.67, 143.97, 141.89, 136.89, 132.40, 129.90, 127.40, 126.74, 123.96, 120.73, 108.20, 42.85, 25.98 ppm; ES–MS *m/z*, 1356 [M + Na]: elemental analysis calcd. (%) for $C_{76}H_{60}O_{12}N_{12}$: C 68.42, H 4.50, N 12.60; Found: C 68.17, H 4.29, N 12.48.

Compound **6d**

Brown, yield 84%, mp: 198 °C; IR (KBr) *v*: 3328 (pyrrole NH), 3328 (Broad, *β*-pyrrole C–H and –OH), 3071, 2998, 2960, 1703, 1625, 802; ^{1}H NMR δ: 8.75 (s, 4H, pyrrole NH), 5.8–6.0 (d, 8H, pyrrole-*β*H), 1.99 (12H, CH_3), 6.52–7.85 (Overlaping, 28H, ArH), 8.19 (br, s, 8H, –OH); ^{13}C NMR δ: 158.53, 150.47, 148.52, 145.88, 134.68, 129.70, 127.78, 121.9, 118.2, 114.33, 107.98, 41.96, 25.29 ppm; ES–MS *m/z*, 1500 [M + Na]: elemental analysis calcd. (%) for $C_{72}H_{60}O_{16}N_{12}S_4$: C 58.53, H 4.09, N 11.38, S 8.68; Found: C 58.25, H 3.99, N 11.02, S 8.58.

Compound **7a**

Red, yield 81%, mp: 245 °C; IR (KBr) *v*: 3297 (pyrrole NH), 3297 (Broad, *β*-pyrrole C–H and –OH), 3098, 3036, 2908, 1643, 1571, 789; ^{1}H NMR δ: 8.15–8.22 (br, s, 4H, pyrrole NH), 5.9–6.10 (d, 8H, pyrrole-*β*H), 1.97 (12H, CH_3), 6.5–7.8 (Overlaping, 28H, ArH), 8.81 (br, 8H,–OH); ^{13}C NMR δ: 155.97, 137.50, 130.74, 129.93, 127.83, 116.0, 115.21, 114.9, 104.2, 43.63, 26.31 ppm; ES–MS *m/z*, 1244 [M + Na]: elemental analysis calcd. (%) for $C_{72}H_{60}O_8N_{12}$: C 70.76, H 4.95, N 13.76; Found: C 70.56, H 4.49, N 13.68.

Compound **7b**

Dark Red, yield 84%, mp: 274 °C; IR (KBr) *v*: 3359 (pyrrole NH), 3359 (Broad, *β*-pyrrole C–H and –OH), 3071, 3018, 2918, 1661, 1589, 784; ^{1}H NMR δ: 8.14–8.25 (br, s, 4H, pyrrole NH), 5.7–6.10 (d, 8H, pyrrole-*β*H), 1.99 (12H, CH_3), 6.8–7.8 (Overlaping, 24H, ArH), 8.82 (br, 12H,–OH); ^{13}C NMR δ: 165.50, 160.11, 152.38, 137.60, 136.16, 132.70, 130.78, 128.6, 127.90, 123.88, 119.6, 103.92, 42.84, 25.30 ppm; ES–MS *m/z*, 1308 [M + Na]: elemental analysis calcd. (%) for $C_{72}H_{60}O_{12}N_{12}$: C 67.28, H 4.71, N 13.08; Found: C 67.19, H 4.62, N 12.89.

Compound **7c**

Red, yield 80%, mp: 250 °C; IR (KBr) *v*: 3257 (pyrrole NH), 3257 (Broad, *β*-pyrrole C–H and –OH), 3054, 2948, 1610, 1590, 854; ^{1}H NMR δ: 8.15–8.22 (br, s, 4H, pyrrole NH), 5.8–6.25 (d, 8H, pyrrole-*β*H), 1.85 (12H, CH_3), 6.8–7.8 (Overlaping, 24H, ArH), 8.68 (br, 8H,–OH), 9.83 (s, 4H, –COOH); ^{13}C NMR δ: 176.84, 145.67, 142.90, 141.68, 136.80, 129.98, 127.01, 126.4, 123.96, 120.73, 103.2, 42.62, 24.98 ppm; ES–MS *m/z*, 1420 [M + Na]: elemental analysis calcd. (%) for $C_{72}H_{60}O_{16}N_{12}$: C 63.32, H 4.33, N 12.03; Found: C 65.10, H 4.20, N 11.86.

Compound **7d**

Red, yield 83%, mp: 280 °C; IR (KBr) *v*: 3349 (pyrrole NH), 3349 (Broad, *β*-pyrrole C–H and –OH), 3012, 3086, 2945, 1670, 1610, 826; ^{1}H NMR δ: 8.12–8.29 (br, s, 4H, pyrrole NH), 5.8–6.25 (d, 8H, pyrrole-*β*H), 1.91 (12H, CH_3), 6.8–7.8 (Overlaping, 24H, ArH), 8.99 (br, 8H,–OH); ^{13}C NMR δ: 162.05, 156.66, 148.98, 134.18, 132.58, 129.25, 125.12, 123.28, 119.41, 110.48, 35.56, 29.80 ppm; ES–MS *m/z*, 1564 [M + Na]: elemental analysis calcd. (%) for $C_{72}H_{60}O_{20}N_{12}S_4$: C 56.10, H 3.92, N 10.90, S 8.31; Found: C 55.69, H 3.69, N 10.78, S 8.28.

Preliminary Complexation Studies by UV/Vis Spectrophotometry

For preliminary complexation studies, stock solutions of azocalix[4]pyrrole receptors (**6a–d** and **7a–d**) (0.1%, $\approx 10^{-4}$ M) were prepared in ethanol. Standard copper stock solution (0.1 M) was prepared by dissolving 0.413 g of copper nitrate [$Cu(NO_3)_2.3H_2O$] in 100 mL water and was standardized spectrophotometrically [17]. Working solution was subsequently prepared by appropriate dilution of the stock solution.

Preliminary complexation studies were carried out at 25 °C using a JASCO 570 UV/Vis spectrophotometer. Copper solution was directly injected by a precise Syringe (Hamilton, 10 μL) into the cuvette having the ethanolic solution of azocalix[4]pyrrole. The resulting solution was allowed to attain equilibrium for 1 min before recording the spectra. Usually, 0.05 M (10 μL) copper solution was added to 10^{-5} M solution (3 mL) of azocalix[4]pyrrole receptors **6a–d** and **7a–d**.

Result and discussion

Synthesis and characterizations

We have developed an economical, eco-friendly and very efficient microwave assisted protocol for the synthesis of *meso*-tetra(methyl) *meso*-tetra(4-hydroxy phenyl) calix[4] pyrrole (**4**) and *meso*-tetra(methyl) *meso*-tetra(3,5-dihydroxy phenyl) calix[4]- pyrrole (**5**) which can be a viable alternative to the conventional synthesis (Scheme 1). Conventional method being classical thermal reaction needs minimum 6–8 h [15], whereas proposed protocol by microwave irradiation takes only 10–12 min (results are compared in Table 1).

Parent *meso*-substituted calix[4]pyrrole macrocycles are spectroscopically silent towards complexation which can be observed only by NMR-titration [11c]. Therefore to improve upon its binding ability, the parent calix[4]pyrrole skeleton have been functionalized, especially in the *meso*-position or the *β*-position [18]. With this in view, we have functionalized calix[4]pyrrole at meso position bearing –N=N– group as well as –OH group to enable it to exhibit both coloring and binding properties. In this regard, we have described the

Table 1 Comparison of reaction time and yield of calix[4]pyrroles and its azo derivatives (**4**, **5**, **6a–d**, **7a–d**) under conventional and microwave irradiation conditions

Calix[4]pyrroles and its azo derivatives	Reaction time (h/min)		Yield (%)	
	Conventional method (h)	Microwave technique (min)	Classical method	Microwave technique
4	6–8	10	45	65
5	6–8	12	40	60
6a	4–5	0.5	60	80
6b	4–5	1	65	85
6c	4–5	1	62	82
6d	4–5	0.5	68	84
7a	4–5	0.5	58	81
7b	4–5	1	64	84
7c	4–5	1	70	80
7d	4–5	0.5	66	83

synthesis of eight novel azocalix[4]pyrrole dyes (**6a–d**, **7a–d**) which were obtained by coupling of diazonium salt of different aromatic amines (**a–d**) with macrocyclic phenols (**4** and **5**) by conventional as well as microwave irradiation method.

Azo dyes are generally synthesized in two steps: the diaotization of aromatic primary amines followed by the coupling reaction between diazonium salts and phenols. Synthesis of azocalix[4]pyrrole by conventional method involves diazotization of aromatic amine(**a–d**) in $NaNO_2$, conc. HCl at 0–5 °C and then its coupling with phenolic calix[4]pyrroles (**4** and **5**) in presence of NaOH to obtain the corresponding azo calix[4]pyrrole receptors (**6a–d**, **7a–d**) (Scheme 2).

In present investigation, we have reported a simple, one-pot microwave and one drop water assisted synthetic method for azocalix[4]pyrrole dyes which were carried out in one-pot in the absence of solvent by inducing microwave irradiation. Azocalix[4]pyrrole dyes were synthesised in the solid state without any mineral support and found that the reaction reaches to completion in a very short time with high yields. In a typical experiment, four moles of aromatic amines (**a–d**), sodium nitrite, potassium hydrogen sulfate and one mole of phenolic compound (**4** and **5**) were grinded to fine powder and irradiated with microwave for 1 min in a domestic microwave oven, followed by the addition of a drop of water and thorough agitation of mixture (Scheme 2). The addition of water is essential because the water acts as an activator or initiator and microwave activates the reactants and the reaction proceeds rapidly. It is important to note that reaction does not proceed in the absence of water. Excessive microwave power and longer reaction time should be avoided as the products gets carbonized or decomposed under such reaction conditions. The results are summarized in Table 1.

In contrast to the traditional two-step synthesis of azo dyes, the present protocol has number of advantages such as less reaction time, improved yields and simple experimental procedure. More significantly, this protocol is more environmental friendly and economical, neither requires solvent nor cooling (0–5 °C). The parent calix[4]pyrrole (**4** and **5**) and eight new azocalix[4]pyrrole dyes (**6a–d**, **7a–d**) were fully characterized by elemental analysis, FT–IR and ^{1}H NMR.

Characteristic FT–IR bands of the compounds (**4**, **5**, **6a–d**, **7a–d**); strong N–H stretching 3,400–3,450 cm^{-1}, a broad band in the range of 3,357–3,200 cm^{-1} corresponding to ν_{O-H} indicative of involvement of –OH group in intramolecular hydrogen bonding, a weak band or shoulder at 3,089–3,018 cm^{-1} assigned to aromatic CH. In addition, the FT–IR spectra of all azocalix[4]pyrrole dyes (**6a–d**, **7a–d**) showed intense azo (–N=N–) bands in the range of 1,625–1,500 cm^{-1} [9].

The ^{1}H NMR spectrum of all macrocyclic hosts (**4**, **5**, **6a–d** and **7a–d**), displayed two doublet 5.8–6.1 ppm and were assigned to the eight pyrrole ring β-protons. In addition, a singlet at 1.88 ppm was assigned for 12 methyl protons of *meso*-position. Compound **4** and **6a–d** displayed broad peak at 8.75 ppm, for pyrrolic NH, and one singlet at 8.22 ppm for –OH group. The compound **4** gave two doublets at 6.66–6.78 ppm for aromatic protons. While compound **5** gave one singlet at 8.1–8.3 ppm for pyrrolic NH protons, one singlet at 7.1 ppm for aromatic eight protons, and remaining aromatic four protons, respectively were observed between 5.8 and 6.3 ppm.

Compound **7a–d** showed one broad singlet in the range of 8.6–8.9 ppm for –OH group overlapping with pyrrolic NH protons. In addition, the eight pyrrolic β-protons were observed as doublets between 5.6 and 6.1 ppm. Compounds **6a–d** and **7a–d** gives many doublets and quartet (not resolvable) between 6.8 and 7.8 ppm for protons of eight aromatic rings attached at the meso-position.

The results of the elemental analysis for nitrogen confirms the formation of azocalix[4]pyrrole.

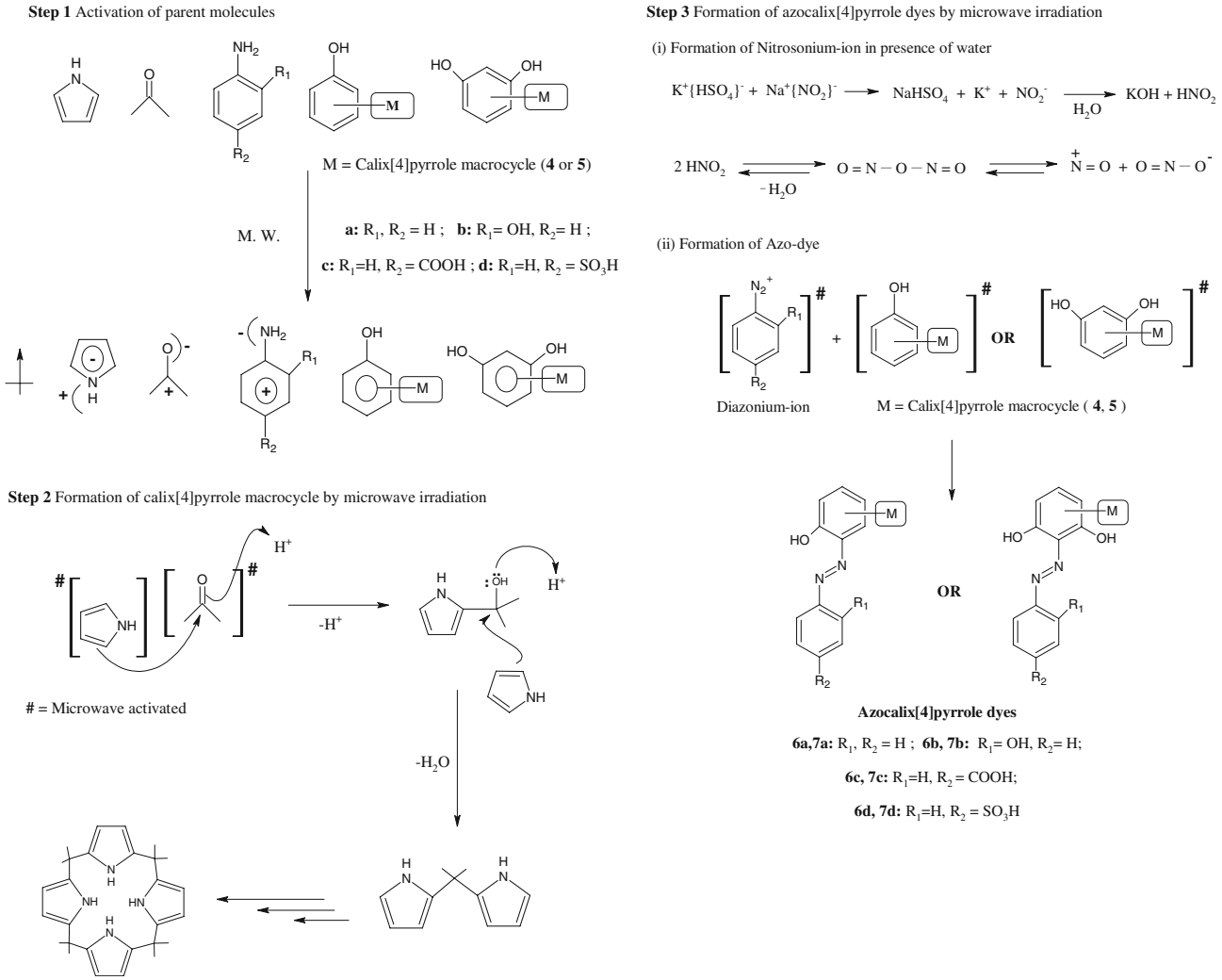
Proposed mechanism for synthesis by microwave irradiation technique

- When the parent molecules are subjected to microwave irradiation, the irradiation energy causes the molecules in vibration mode by increasing its dipole–dipole moment through increasing its charge separations which are shown in Scheme 3 (step 1).
- A non-conjugated macrocycle, calix[4]pyrrole is formed by electrophilic α-substitution of microwave activated molecules, pyrrole by ketone, acid catalyzed oligomerization, and spontaneous non-template cyclization wherein four pyrrole units are combined which is illustrated in Scheme 3 (step 2).
- The formation of nitrosonium-ion from the $KHSO_4$ and $NaNO_2$ salts in presence of water, yield nitrous acid (HNO_2) as an intermediate which provides a source of nitrosonium-ion [19] (Scheme 3, step 3-(i)), which electrophilicly replaces the hydrogen in the primary amine-group to form the diazonium-ion.
- The interaction between diazonium-ion and microwave activated phenol- macrocycles produces azo dye. Electrophilic substitution takes place at the ortho-position of phenol-macrocycles (Scheme 3, step 3-(ii)).

Complexation of Azocalix[4]pyrroles

In order to evaluate the ability of azocalix[4]pyrrole dyes to bind metal-ion, preliminary studies on complexation with copper (II) ion was carried out in ethanol by UV/Vis spectrophotometry.

In the UV/Vis spectra of the reagents (**6a–d**, **7a–d**), the only absorption band in the range 396–430 nm arise due to π–π* transition (–N=N–) but in the spectra of its copper-complex, new conspicuous absorption band appears in the range 460–505 nm (Table 2). The results obtained for optical response ($\Delta\lambda$) = [λ_{max}(complex) − λ_{max}(reagent)], are summarized in Table 2. Although all dyes show colour change from yellow to red upon complexation but two



Scheme 3 Proposed mechanism for synthesis by microwave irradiation technique

Table 2 Optical responses of azocalix[4]pyrrole dyes, **6a–d** and **7a–d** (10^{-4} M) with copper (10^{-3} M) in ethanol

Azo receptors	λ_{max} (reagent) nm	λ_{max} (complex) nm	$\Delta\lambda$[a]
6a	400	480	80
6b	405	505	100
6c	430	482	52
6d	398	438	40
7a	396	480	84
7b	390	505	115
7c	404	466	62
7d	402	447	45

[a] $\Delta\lambda = \lambda_{max}(\text{complex}) - \lambda_{max}(\text{reagent})$

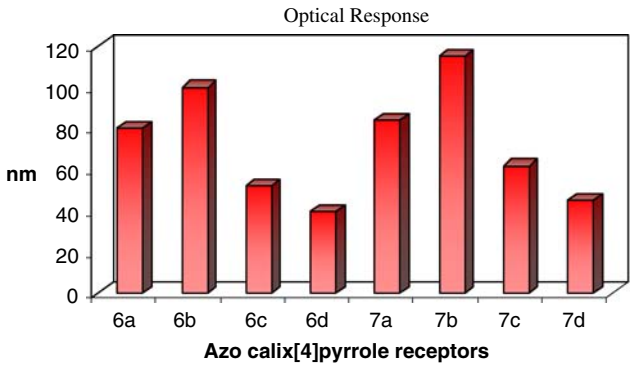


Fig. 1 Optical response ($\Delta\lambda$) of different azocalix[4]pyrrole receptors for copper

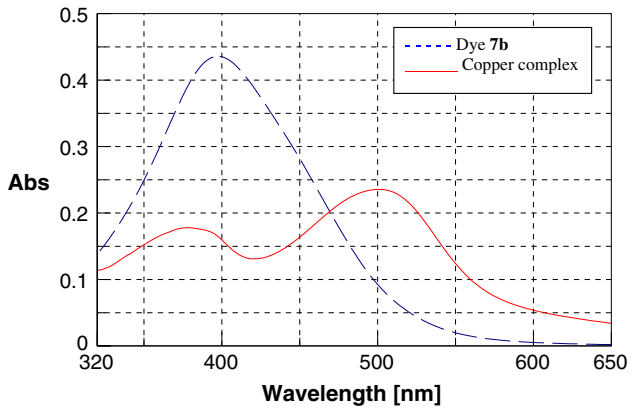


Fig. 2 Comparative spectra of dye **7b** and its copper (II) complex in ethanol

azocalix[4]pyrrole dyes, **6b** and **7b**, exhibits remarkable optical response ($\Delta\lambda$), Fig. 1. The absorption spectra of **7b** and its copper (II) complex under the neutral condition are shown in Fig. 2. These results indicates that azo groups which are circularly arranged on the *meso*-position of calix[4]pyrrole cavity, construct novel cyclic copper receptors.

Conclusion

We have developed an economical, using less solvent, very efficient microwave assisted method of synthesis of *meso*-tetra(methyl) *meso*-tetra(4-hydroxy phenyl) calix[4]pyrrole and *meso*-tetra(methyl) *meso*-tetra(3, 5-dihydroxy phenyl) calix[4]pyrrole. An environmentally benign one-pot microwave and one drop water assisted synthetic protocol for the rapid and direct azo-formation of aromatic amine to prepare azocalix[4]pyrrole dyes in a single step has also been developed. The reported microwave assisted methods can be viable alternative to the conventional method of synthesis. High optical response for copper ions exhibited by these dyes suggest that further fine tuning in the molecular design can be made to enable it to complex with various metal ions. The applications of the synthesized azocalix[4]pyrrole dyes for extraction of various bivalent and trivalent metal ions, screening of biological activity and their use as direct dyes on cotton, silk, wool, acrylic and nylon are under progress.

Acknowledgments The authors gratefully acknowledge the financial assistance provided by CSIR, New Delhi, India to carry out this work. The authors also acknowledge CDRI (Lucknow), SAIF (IIT, Mumbai) and CSMCRI (Bhavnagar) for providing instrumental facilities and INFLIBNET, Ahmedabad for providing online journals.

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