Synthesis of calixpyrroles and porphyrins over molecular sieve catalysts☆

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Abstract

The macrocyclization reaction of calix(4)pyrroles and porphyrins prepared by zeolite catalyzed synthesis in liquid phase under microwave irradiation conditions was subsequently optimized for quantitative yields. The reactions are carried out with different zeolite catalysts such as HZSM-5, HY and mesoporous Al-MCM-41 molecular sieves and the reactions are monitored by HPTLC for performance evaluation of the catalysts. The present method to synthesize macrocycles, using molecular sieves, such as solid acid catalysts in heterogeneous system, was selective and quantitative. Al-MCM-41 (pore diameter more than 20 Å) performs better as to facilitate good selectivity towards quantitative yield and demonstrated excellent conversions when compared to other catalysts.
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Keywords: Macrocyclization; Al-MCM-41; Zeolite; Calix(4)pyrroles

1. Introduction

Calix(4)pyrroles [1,2] and Porphyrins [3–6] represent a subset of a class of macrocycles, where calix(4)pyrroles are non-conjugated colourless macrocyclic species, composed of four pyrrole rings linked in the α-position via sp^3 hybridized carbon atoms. Such systems have attracted a lot of attention, primarily because they may be oxidized to form porphyrins, where pyrrole units are linked with sp^2 hybridization [7,8]. These macrocycles are found to be very important moieties in host guest chemistry as drug transporting agents and enzyme mimics, since calix(4)pyrroles bind anions and neutral species and porphyrins bind cations in both solution as well as solid state in an efficient way [9,10]. Thus, the selective synthesis of these macrocycles is of topical interest as envirofriendly technologies are normally accomplished by zeolites. Selective synthesis of these macrocycles [11,12] has great significance because of their commercially viable end use. The yield of these macromolecules is generally enhanced by using certain catalysts, sometimes by microwave conditions as well.

Zeolites are the potential candidates as catalysts for the synthesis of complex molecules and have emerged as an exciting area of supramolecular chemistry. Zeolites are uniform porous crystalline aluminosilicates and their lattice is composed by TO_4 tetrahedra (T=Al and Si) linked by sharing the apical oxygen atoms. However, the smaller pore size of zeolite molecular sieves restricted their wide range applications, especially in the synthesis of macrocycles. Nevertheless, this has been overcome by the use of mesoporous molecular sieves. These mesoporous molecular sieves (MCM-41) opened a new era in the zeolite catalysis and many reports are available on their use as catalysts for the oxidation, alkylation, cyclization and also in photo catalysis [13–15]. As it has been found that reactions under microwave conditions offer highly efficient, rapid conversions [16] for the selective synthesis of compounds of industrial application, we therefore utilized this information in our present studies and attempted the liquid-phase macrocyclization reactions using these catalysts to prepare calix(4)pyrroles and porphyrins under

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microwave irradiation. Herein, we report the potential utility of this method along with the quantitative conversions accomplished.

2. Experimental

2.1. Materials and methods

Calix(4)pyrroles were prepared in the laboratory, purified by column chromatography and used as standard reference materials throughout this study. The standard porphyrins are from Sigma–Aldrich. The reactants such as pyrrole, cyclopentanone, cyclohexanone, cycloheptanone, cyclooctanone, methylethylketone, 3-pentanone, acetone, benzaldehyde, anisaldehyde and tolualdehyde are all from Sigma–Aldrich. For the present work, ZSM-5 catalyst with Si/Al ratio 15, Hβ obtained from M/s. Conteka (Sweden) and HY obtained form M/s. PQ Corporation (USA) were used. Al-MCM-41 was synthesized in our laboratory according to the procedure reported in the literature [17].

3. Instrumentation

3.1. Chromatography

An HPTLC system consisted of Linomat-IV sample application device equipped with 100 μl syringe and a scanner 3 (CAMAG, Switzerland) was used. The scanned data were programmed through CAMAG-CATS software resident in personal computer (VINTRON-586). All the solvents used were of chromatographic grade (Merck, India). The TLC plates (10 cm × 10 cm and 20 cm × 10 cm, Merck) were used. Known solutions of reactants, viz., pyrrole, ketones and aldehydes, along with the standard calix(4)pyrroles and porphyrins, were prepared in DCM solvent, where each 1 μl of solvent contained 2.5 μg of sample and 5 μl of each sample was applied on prewashed TLC plates. The mobile phase was hexane, containing 15% ethyl acetate (8.5:1.5, v/v) for calix(4)pyrroles and chloroform containing 5% methanol (9.5:0.5, v/v) for porphyrins.

4. Spectrometric analysis

In a separate analysis, the reaction mixtures of calixpyrrole and porphyrin, were quantitatively (23 mg) applied on the TLC plate along with the standard reference materials. The band corresponding to macrocycles and their corresponding dimers were marked under UV light and separately scrapped out, eluted with DCM in a small elution column. The solvent was evaporated to dryness and the solid material obtained was further analyzed by mass spectrometry, NMR and CHNS.

4.1. ^1H NMR

NMR spectra were recorded on a VARIAN GEMINI 200 MHz spectrometer.

4.2. Mass spectrometry

Low-resolution and high-resolution electron impact mass spectra were recorded on AUTOSPEC mass spectrometer (Micromass, Manchester, UK).

5. Preparation of samples

5.1. Condensation reaction

5.1.1. Calix(4)pyrroles

Calix(4)pyrroles were prepared as described earlier [11]. In short, pyrrole (7.2 m mol) and ketone, taken in an equimolar ratio, were dissolved in 20 ml of dichloromethane (DCM), 0.5 g of calcined dried catalyst was added to it and allowed to reflux, depending on the ketone. When the reaction completed, the catalyst was separated by filtration and washed thoroughly with DCM. The solvent was removed under reduced pressure and products were separated by column chromatography using silica gel (100–200 mesh size) with *n*-hexane: ethyl acetate (8.5:1.5) as an eluent.

5.1.2. Porphyrins

Here the strategy of microwave-assisted synthesis in dry media onto solid inorganic support systems was mostly adapted. The reaction was carried out in a pyrex bottle, in which equimolar ratio of pyrrole (0.25 ml) and aldehyde (0.26 ml) was mixed with 0.5 g of zeolite molecular sieve in an appropriate solvent which is then evaporated. The bottle is closed with cotton/glass wool. The mixture was subsequently subjected to microwave irradiation for 12 min with intervals (BPL domestic microwave oven, with microwave frequency 2450 MHz, 1.2 kW). Upon completion of the reaction, the catalyst was separated by filtration and washed thoroughly with 100 ml of chloroform (20 ml × 5 times). Further, the solvent was removed under reduced pressure to give a viscous residue. Products were separated by column chromatography using silica gel (100–200 mesh size) with *n*-hexane as eluent. Porphyrin thus prepared was characterized by UV, NMR and mass spectrometry.

6. Results and discussion

The results as presented here, depict that the selective synthesis of porphyrins and calix(4)pyrroles fundamentally depend on the nature of the catalysts.

6.1. Calix(4)pyrroles

The reactions over zeolite molecular sieves, with various reactants, have been carried out and the results are compared with respect to individual performance of catalysts (Table 1). As evident from the data, mesoporous Al-MCM-41 [14] proved to be the most efficient catalyst among the various

Table 1
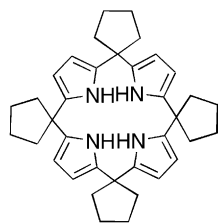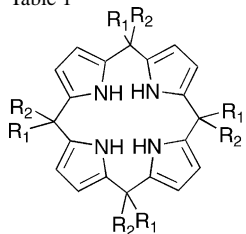
1: R$_1$ = R$_2$ = CH$_3$
2: R$_1$ = CH$_3$; R$_2$ = CH$_2$ CH$_3$
3: R$_1$ = R$_2$ = CH$_2$ CH$_3$

Synthesis of calix(4) pyrrole

Entry	Pyrrole+	Conversion of pyrrole (%)	% Yield of the product		
			Calix(4)pyrrole	Dimer	Others[a]
1	Acetone[a]	92.4	67.5 (**1**)	3.1	21.8
2	Acetone[b]	72.5	–	58.5	14.0
3	Acetone[c]	81.4	40.0 (**1**)	11.6	29.8
4	Methylethyl ketone[a]	48.0	34.8 (**2**)	8.7	4.5
5	3-Pentanone[a]	84.0	10.1 (**3**)	62.1	4.8
6	Cyclopentanone[a]	74.3	62.7 (**4**)	4.3	7.3

[a] Others include linear trimer and tetramer; pyrrole:ketone (1:1 molar), solvent: DCM; catalyst is (a) Al-MCM-41, (b) HY, (c) HZSM-5(30).
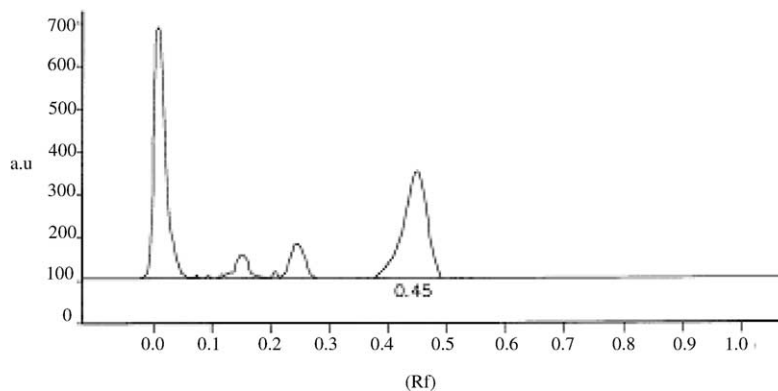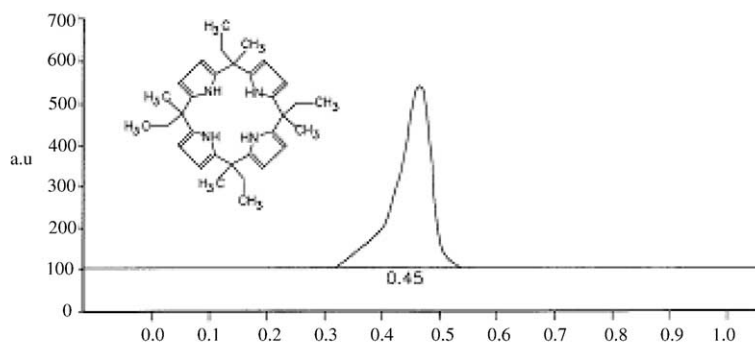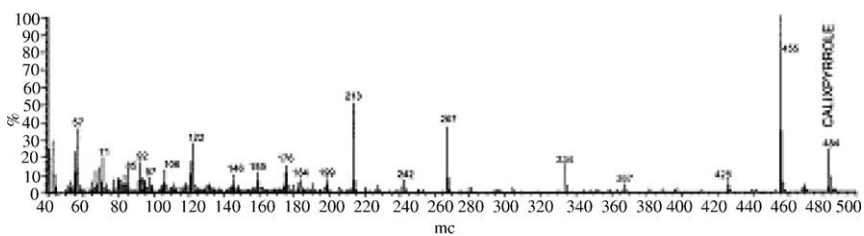

Fig. 1. Typical densitograms of (below) reaction mixture of calix(4)pyrrole and (above) authentic sample of meso tetramethyl tetraethyl calix(4)pyrrole.

other zeolites studied. A typical densitogram of reaction products, dimer and the cyclic tetramer, i.e. meso-octamethyl calix(4)pyrrole **2** as obtained are shown in Fig. 1.

Compound **1**, which was obtained as maximum product over Al-MCM-41, emerged at Rf 0.67 (67.5% yield) when both R_1 and R_2 are CH_3 groups and is perfectly comparable with the standard reference materials. However, dimer at Rf 0.45 obtained as a byproduct is always present in minor amounts (3.1%) with this catalyst along with small amounts of linear trimer and linear tetramer. However, when R_1 and R_2 are CH_3 and $-CH_2-CH_3$ the Rf of the main product has been observed at 0.45 (Fig. 1).

A rather different picture is obtained when HY is used as catalyst. Dimer is the major product and no cyclic tetramer is obtained, which may be attributed to the smaller pore size of the catalyst (7.2 Å pore dia). Thus, the data led us to conclude that HY catalyst is not a suitable proposition for the quantitative preparation of **1**. Surprisingly, HZSM-5, with smaller pore size, is found to promote both dimer and cyclic tetramer. The formation of cyclic tetramer is attributed to external surface reaction as confirmed by the formation of dimer alone when catalysts surface is poisoned. Since the molecular size of calix(4)pyrrole (∼13.1 Å) is lower than that of the super cages of Y-zeolite, its formation in the super cages (∼13.4 Å) of HY zeolite is expected. After the reaction, the catalyst HY without washing has been subjected to solid-state NMR studies (^1H and ^{13}C NMR) and compared the generated data with that of calix(4)pyrrole from liquid state NMR. These studies confirmed that cyclic tetramer is not formed in supercages and supported our observation that the surface is poisoned and the formation of calix(4)pyrrole occurred only inside the pores, because, a thorough characterization of the catalysts

was carried out wherein XRD, IR and sorption studies were undertaken [18].

Upon identification of the optimum reaction parameters, the synthesis of these calix(4)pyrroles were also performed with other ketones, viz., methylethylketone, 3-pentanone and cyclopentanone, respectively, and the results are depicted in Table 1. It is evident that increasing the carbon number of the ketone reduces the yields of the corresponding calix(4)pyrroles.

6.2. Porphyrins

In case of porphyrins unlike calix(4)pyrroles, because of the characteristic spectral pattern, the identification of porphyrins is not hampered by other byproducts and the novel advantage of an online, in situ UV spectrum facilitates the identification in a single step. Pyrrole when reacted with benzaldehyde to yield 23.5% of the meso-tetraphenyl porphyrin over mesoporous Al-MCM-41 as catalyst, the peak corresponding to product shows the soret band at 417 nm and Q bands at 515 nm confirming the porphyrin formation as shown in Fig. 2. Similarly, when anisaldehyde was used (Table 2), 16.0% of corresponding porphyrin was obtained, which was also confirmed by online UV spectrum and mass spectrometry (m/z at 735) as shown in Fig. 2.

The results show that HZSM-5 and Al-MCM-41 promote best yields with good selectivity. Eventhough the former is endowed with low pore size (5.6 Å), the higher yield of porphyrin is due to the surface reaction and the high acidic nature of the catalyst. When the surface of the catalyst is poisoned by tetraethoxy silane (TEOSi), porphyrin yields were dropped to negligible level, confirming the role of
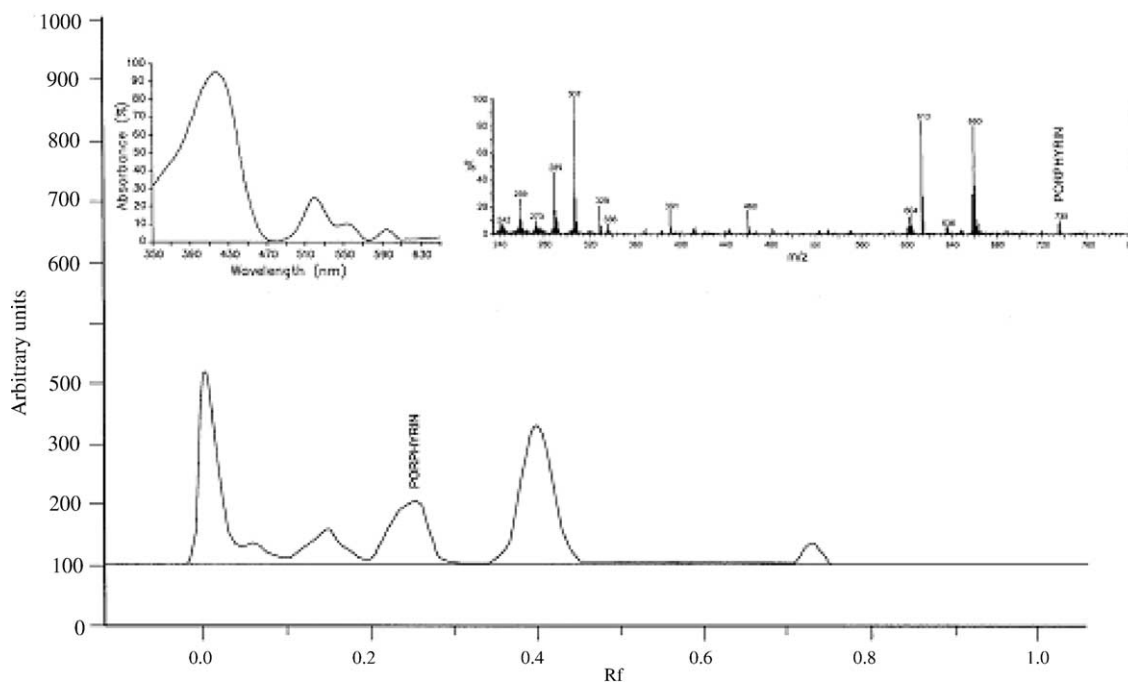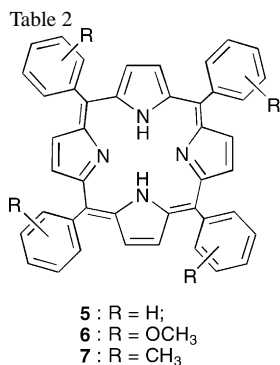

Fig. 2. HPTLC profile of the reaction mixture of meso tetra phenyl porphyrin. Inset shows the online UV spectrum (419 nm) and mass spectrum (m/z at 735).

Table 2

5 : R = H;
6 : R = OCH$_3$
7 : R = CH$_3$

Synthesis of porphyrins

S No.	Pyrrole+	Product R=	Yield %	Soret band	Q bands
1	Benzaldehyde[a]	H (**5**)	23.5	419	515, 548, 597, 645
2	Anisaldehyde[a]	Para-OCH$_3$ (**6**)	16.0	420	519, 598, 642
3	Tolaldehyde[a]	Para-CH$_3$ (**7**)	40.1	419	535, 592
4	Benzaldehyde[b]	H (**5**)	28.0	419	512, 545, 592, 640

Catalyst is (a) Al-MCM-41, (b) HZSM-5(30) (0.5 gm); microwave power = H1, time =12 min; molar ratio of pyrrole: aldehyde = 1:1; yield and selectivities were based on pyrrole.

surface reaction. HY being a medium pore (7.6 Å) zeolite as compared to HZSM-5 (5.6 Å), the tetra phenyl porphyrins formation is more likely inside the void space of supercages. On the other hand, Al-MCM-41 with its mesoporous structure and acidic nature, facilitated the synthesis of tetra phenyl porphyrin in high yields. The porphyrin formation has also been tested in liquid phase, under the influence of microwave irradiation with and without solvent. It has been observed that solvent free synthesis facilitated the selective formation of porphyrin with high yields. It is characterized by UV–VIS spectroscopy where characteristic soret band of porphyrin at 417 nm and Q bands at 515, 547, 598, 647 nm were observed. The UV–VIS spectra of tetra phenyl porphyrin as obtained in the presence of various catalysts is shown as inset in Fig. 2.

The results of our present study suggest that the reactions were quantitative with the catalyst used in this study. However, Al-MCM-41 is the most potential candidate with a conversion of 92.4% pyrrole to give a yield of 67.5% of calix(4)pyrrole. On the other hand, porphyrins yielded 23.5, 16.0 and 40.1% with benzaldehyde, anisaldehyde and tolualdehyde, respectively. The yield was comparatively higher than the earlier reports. HPTLC offered a good choice for a process development with good selectivity for the end product separation and quantitation.

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