A novel zeolite based stationary phases for in situ synthesis and evaluation of porphyrins and calix (4) pyrroles

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Abstract

The application of zeolite based molecular sieves as catalysts and sorbents in thin layer chromatography (TLC) has been investigated for a single step evaluation of porphyrins and calix (4) pyrroles by in situ synthesis from pyrrole with aromatic aldehydes and ketones under microwave irradiation. The molecular sieves used were microporous zeolites such as HZSM-5, HY, Hβ and mesoporous MCM-41 material and the results are compared. Among the various sorbents studied, MCM-41 proves to be the potential candidate and offered quantitative conversions. This glass-backed zeolite coated TLC plate presumably acted as a reactor and facilitated simultaneous chromatographic separation of the macrocycles as well. The process is simple, economically viable, rapid, selective, solvent free and finds a novel application in high through put parallel synthesis and chromatographic screening in a single step.
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1. Introduction

Zeolites and related molecular sieves have emerged as an exciting area of supramolecular chemistry and the mesoporous molecular sieves such as MCM-41 opened a new area in the zeolite catalysis [1–3]. Recently attempts are being made to utilize these zeolite types of catalysts in organic synthesis and speciality chemicals in particular at low temperatures or under microwave conditions to enhance the yield of the principal product significantly [4]. However, only simple molecules have been prepared using this technique. Further, the first use of silica, alumina, titanica, zirconia and novel mesoporous silicas and alumino silicates as stationary phases in normal phase high performance liquid chromatography was reported by Grun et al. [5]. The potential performance of these versatile compounds due to their organized pore structure [6] with large surface area and finds immense application in different fields such as catalysts, adsorption and chromatography. Thus, great attention is being presently focused on the synthesis of different macrocycles as well [7,8] and essentially, the methods adopted vary with respect to cata-

lysts and stationary phases [9]. Williams [10] has utilized TLC for reaction optimization in microwave assisted synthesis of n-substituted arylpiperizines. Again, the method evolved out of a simple silica gel TLC and limited only to the simple molecules.

Combinatorial chemistry has emerged out as an exciting area of synthetic methodologies and reports are available as to how this approach has been accomplished the yield oriented synthesis in different areas [11]. Supramolecular chemistry is fascinating and fast growing area with many aspects related to various structures, properties and their applications [12]. Thus, combinatorial chemistry gained importance as a one step methodology for the synthesis of compounds of commercial nature, where mesoporous silicas [11] and alumino silicates are being used as stationary phases. However, there are no available reports as to any time zeolites being used in synthesis as thin layers involving a simultaneous separations though there is one report available [13] on using zeolites as stationary phases in TLC. Thin layer chromatography is a versatile technique that facilitates a very convenient isolations or qualitative identification, sometimes of very complex organic compounds such as porphyrins as reported earlier in a very short time without resorting to any sophisticated equipment or technology [14]. Thus, a research programme has been launched to utilize zeolites and mesoporous MCM-41 molecular sieves as stationary phases in TLC for a

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rapid, in situ synthesis, identification and quantification of calix (4) pyrroles and porphyrins under microwave conditions.

Earlier, we synthesized these compounds using conventional methodology, where in, stirring, supported under liquid phase conditions [15] by heating yielded only 10–65% of the final product particularly in case of porphyrins. However, the unreacted materials, polymerized in due course, completely entrapped the zeolite and recovery was rather clumpsy. Not only the product conversion was poor, again in case of porphyrins, but also the final product was highly coloured. This prompted us to look for a solvent free synthetic methodology of these macromolecules. Nevertheless, this objective could be accomplished by employing molecular sieves as TLC sorbents.

Hence, here in, we describe a simple procedure for simultaneous synthesis and screening over solid acid catalysts as stationary phases on inert glass-backed TLC support in microwave assisted synthesis of macrocycles, i.e., calix (4) pyrroles and porphyrins and the potential utility of the method is described. However, our initial studies are limited to using pyrrole, the common reactant in both the cases, and acetone in case of calix (4) pyrroles and benzaldehyde in case of porphyrins.

2. Experimental

2.1. Materials

The authentic samples of porphyrins are from Sigma–Aldrich. Calix (4) pyrroles were prepared in the laboratory, purified by column chromatography and used as standard reference materials through out this study. The reactants pyrrole, acetone and benzaldehyde and anisaldehyde are from Sigma–Aldrich.

For the present study, Al-MCM-41 has been synthesized and characterized in our laboratory according to the procedure reported in literature [16,17]. ZSM-5 catalyst with Si/Al ratio 15, Hβ obtained from M/s Conteka (Sweden) and HY obtained from M/s PQ Corporation (USA) were used. All the solvents were of chromatographic grade.

2.2. Preparation of stationary phases

Sorbents, as employed in the present study were microporous zeolites and mesoporous MCM-41 molecular sieves. The micropores range from 5 to 15 Å and mesopores range from 20 to 50 Å. Using glass plates as the inert solid support, the molecular sieves were layered as a matrix with the help of calcium sulphate as a binder. For this, 200 mg of the binder ($CaSO_4 \cdot 2H_2O$) is taken in 45 ml of boiling water and maintained at boiling condition for 10 min. Ten grams of each of the zeolite (HZSM-5, Hβ, HY) or mesoporous molecular sieve (MCM-41) were added to the boiling solution of the binder and mixed vigorously for 1 min. The viscous adsorbent was applied in hot condition uniformly on to the glass plates (10 cm × 10 cm) as thin layers. Upon drying at 110 °C for 45 min, the plates were cooled to room temperature and stored in a desiccator until further use. The reactants were applied on to the plate with the help of a micro syringe. The reactants were dissolved in suitable solvents such as chloroform

in the case of porphyrins and dichloromethane for calix pyrrole prior to application.

3. Methods

3.1. In situ synthesis and evaluation of meso-octamethyl calix (4) pyrrole (**1a**)

The equimolar ratio of reactants, pyrrole (0.1 ml) and acetone (0.1 ml) were dissolved in 5 ml of dichloromethane and applied on HZSM-5/Hβ/HY/MCM-41 coated TLC plates. On each plate, 30 μl of reactant mixture is applied as first track and irradiated in domestic microwave oven at a power of 2450 MHz (BPL) for 3 min. The irradiation time varied from 3 to 5 min and subsequently 5 μl of authentic **1a** sample was applied as a second track. The sample was subsequently developed using chloroform and methanol (9.5:0.5) as mobile phase. Quantification was carried out using HPTLC (CAMAG, Switzerland) and compared with isolated yields. For further confirmation, from the TLC plate, the corresponding band of **1a** was scrapped out and extracted with DCM solvent in a small elution column using column silica gel. The solvent was evaporated, the sample was then subjected to EI-MS and corresponding *m/z* 428 was observed confirming the formation of **1a**.

3.2. In situ synthesis and evaluation of meso-tetraphenyl porphyrins (1b)

Pyrrole (0.1 ml) and benzaldehyde (0.15 ml) are dissolved in 5 ml of chloroform and applied on the HZSM-5/Hβ/HY/MCM-41 coated TLC plates (2.5 cm × 7.5 cm). On each plate, 30 μl of reactant mixture is applied on the first track and irradiated in a microwave oven for 12 min with 2 min interval of time. After irradiation, 5 μl of authentic **1b** was applied on second track and the plate was subsequently developed in twin trough chamber using chloroform and methanol (9.5:0.5) as mobile phase. Quantification was done by densitometry, along with online UV–visible scanning between 350 and 650 nm. The soret band supported the formation of porphyrins at 417 nm along with the Q-band at 515, 598 and 647 nm. Matrix effect on UV range is always noticed with a bathochromic shift. For FAB MS analysis, the solid material under the porphyrin peak on TLC plate was scrapped, extracted with chloroform and the solvent evaporated. The crystals obtained upon evaporation, were subjected to FAB-MS. The mass at *m/z* 735 confirmed the presence of **1b**.

3.3. General experimental procedures

Different volumes of the samples and standard solutions were applied to the plates by means of a Linomat IV sample applicator (CAMAG, Muttenz, Switzerland). The plates were then developed in respective solvent systems to a distance of 6.5 cm in a 10 cm × 10 cm twin trough TLC chamber (CAMAG). The development time was ca. 12 min. The spots were identified under UV-visualization chamber and identification has been accomplished by comparison with the R_f values of the standard reference materials. The plates were further scanned by means
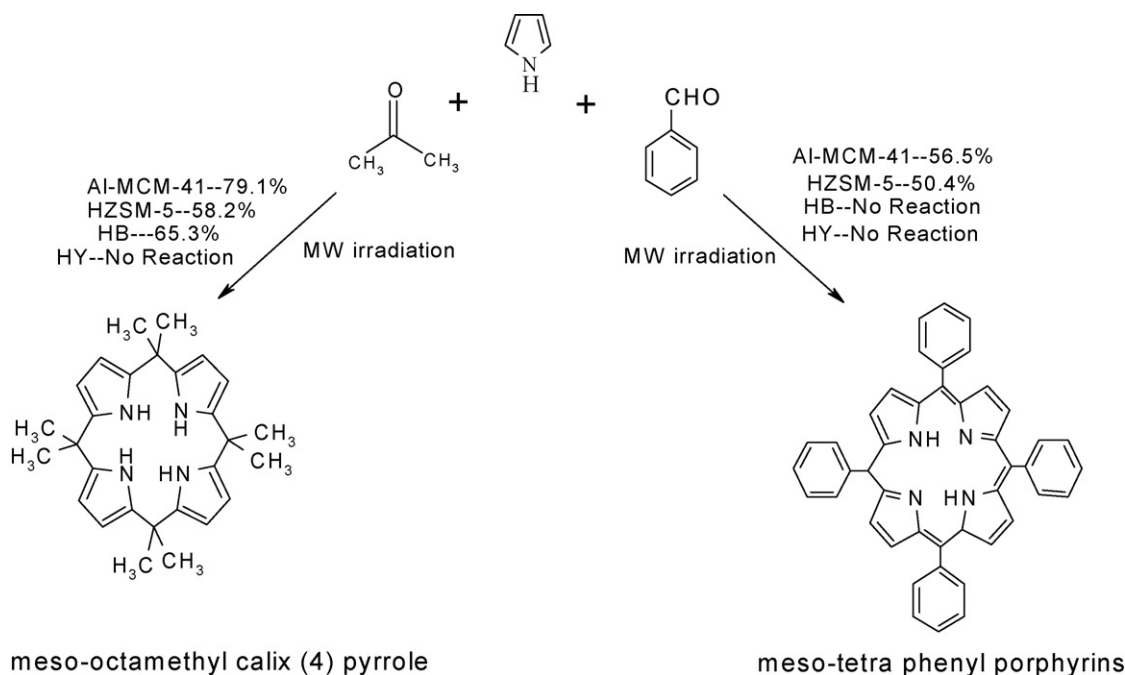
Fig. 1. Reaction scheme.

of a TLC Scanner-3 (CAMAG) in absorbance/reflection mode with a slit width of 6 mm × 0.45 mm. The scanned data were processed by means of CAMAG-CATS software, resident in a Vintron-586 personal computer.

UV spectra (dichloromethane) were recorded on a Shimadzu UV-160 spectrophotometer. FAB-MS (LSIMS) on a VG-Autospec mass spectrometer (Manchester).

4. Results and discussion

4.1. An overview of the developed method

The present studies are aimed at investigating the performance of zeolites on thin layers as catalysts for a single step synthesis and evaluation of porphyrins and calix (4) pyrroles. Although, silica gel is considered the best stationary phase in TLC, it remained only as a separation tool in chromatography and alternative materials for silica gel with similar separation selectivity are hardly available. The other stationary phases such as cellulose, ion exchange resins, impregnated and modified layers are intended for very selective studies and meant again only for separations.

On the other hand, if a layer performs a simultaneous selective synthesis and separation with an online comprehensive scanning to study the separation capability of the layer in terms of resolution with a reasonable range of retention times, there is an ample scope to minimize the reaction time drastically, with an obvious advantage of reducing the operational hassles and number of measurements that are involved in liquid phase synthesis. Though the maximum amount that could be collected was 150–200 mg in the present studies because the plates used were small (10 × 10), this work facilitated to logically understand whether a reaction is possible or not and enables to formulate

library synthesis programmes. Therefore, the evident conclusion is, compared to liquid phase synthesis, the present method offered good yields of the final compound whereby a qualitative analytical profile could be accomplished for identification of the desired product and the online UV and other spectral studies supported the formation of porphyrins and calix (4) pyrroles.

The reaction programme of the present work has been schematically represented in the text (Fig. 1). The reactants are applied on the plates in solution with varied stoichiometry and the results are compared with those of standard reference materials. Preliminary studies indicated that direct conversion to expected product was absolutely selective, especially in case of calix (4) pyrroles, though surprisingly the yields were double fold in case of porphyrins.

4.2. Calix (4) pyrroles

Though the product was the main component (79.1%), minor amounts of dimer and tetramer were noticed and identified with the help of respective authentic samples. It is rather interesting observation that while calix (4) pyrroles in liquid phase formed to a large extent (92.4% conversion of pyrrole), they are not as high as expected under solvent free microwave assisted synthesis and totally selective with the stationary phases presently employed, i.e., HZSM-5, Hβ, HY and MCM-41 (Table 1). As observed, mesoporous AL-MCM-41 [18,19], proved to be the most efficient sorbent, compared to the other catalysts studied.

Compound (1) which has been obtained as the main product and emerged at R_f 0.69 (Fig. 2) when AL-MCM-41 was used (79.1%) where R_1 and R_2 are CH_3 groups, with traces of linear trimer and tetramer. However, dimer (2.7%) has always been present. Whereas, in case of Hβ, as it has smaller pore

Table 1
Formation of meso-octamethyl calyx (4) pyrroles (**1a**) on different stationary phases with pyrrole and acetone as reactants

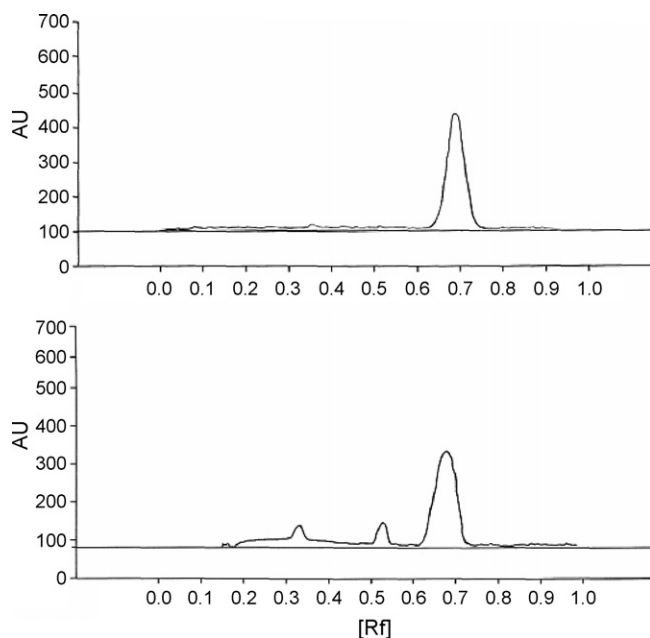| S. No.	Stationary phase	% Yield
1	Al-MCM-41	79.1
2	HZSM-5	58.2
3	Hβ	65.3
4	HY	–

Fig. 2. Densitograms of (above) standard reference material—meso-octamethyl calix (4) pyrrole and (below) the reaction products as separated on the zeolite coated TLC plate (AL-MCM-41) obtained up on densitometric scanning of the plate.

size (7.2 Å pore diameter), dimer (R_f 0.38) is the major product (65.3%), while HZSM (5.6 Å) facilitated totally a surface reaction that resulted in the formation of both dimer and cyclic tetramer (58.2%). We noticed the same trend in our earlier studies as well [18]. However, HY did not facilitate any reaction at all, in the present procedure, may be perhaps, due to low pore size of the sodalite cage.

4.3. Porphyrins

It is well known that the reaction is never to completion, in case of porphyrins. Fortuitously, the yields (56.5%) (Table 2; Fig. 3) were very encouraging with porphyrins compared to

Table 2
Formation of meso-tetraphenyl porphyrin (**1b**) on different stationary phases with pyrrole and benzaldehyde as reactants

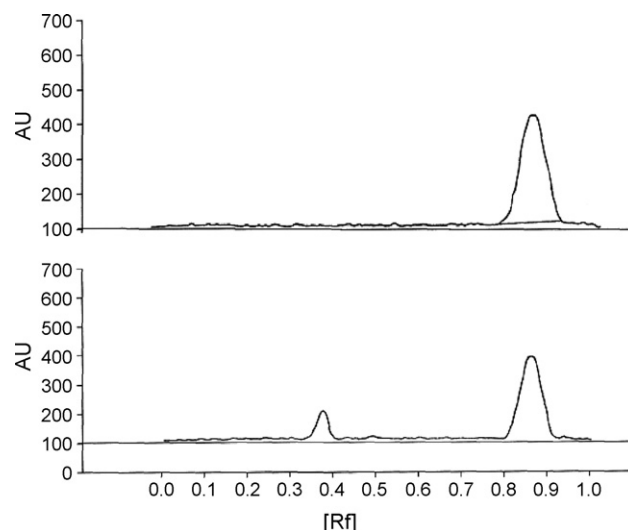| S. No.	Stationary phase	% Yield
1	Al-MCM-41	56.5
2	HZSM-5	50.4
3	Hβ	–
4	HY	–

Fig. 3. The typical densitograms of (above) authentic sample of meso-tetraphenyl porphyrins and (below) the reaction products as separated on AL-MCM-41 TLC stationary phase obtained up on densitometric scanning.

liquid phase synthesis (23.5%). This finding also suggests that solvent free, open bed stationary phases did not, in any manner hamper the reaction efficiency neither has it reduced the quality of the product which has been evident from the online in situ UV spectrum (Fig. 4) that is absolutely characteristic of porphyrins. Thus, it is very encouraging to note a soret band at 419 nm along with Q-band at 575, 598 and 647 nm, which is in agreement with m/z 735 obtained by FAB-MS confirming the authenticity of the analysis. However, matrix effect on UV range is always noticed with a bathochromic shift. Simultaneously, the percentage composition has been obtained from the densitograms complimented by the characteristic UV spectra.

One potential concern with porphyrins is their instability, which makes it difficult to understand the true quality as well as the nature of products formed just after the reaction. Nevertheless, this could be accomplished by the online UV spectroscopy resident in the system. This further reduced the analytical cycle times drastically and confirmed the formation of porphyrins,
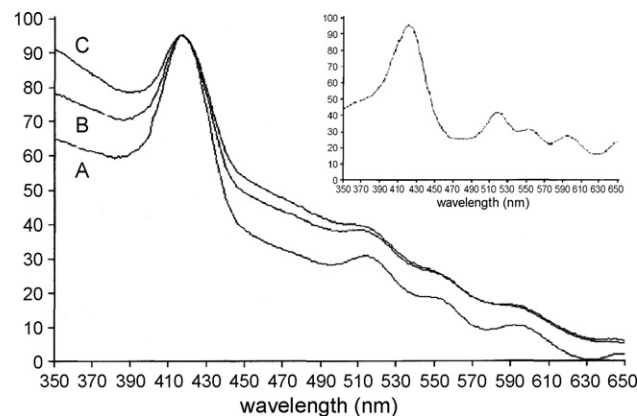

Fig. 4. Online absorption spectra of (A) meso-tetraphenyl porphyrin standard reference material (B and C) obtained from in situ synthesis using Al-MCM-41 as stationary phase. Inset shows the absorption spectrum of standard reference material obtained from conventional UV spectroscopy.

which underlines the efficient performance of the stationary phases.

Because of the simplicity and robustness of the analytical procedure, a few other zeolites when analyzed as stationary phases, has resulted in a different reaction conversions as has been noticed even in case of calix (4) pyrroles. Here again, AL-MCM-41 offered maximum conversion (56.5%), which is rather unusual with porphyrins. However, when HZSM-5 coated plate was used, the formation of porphyrins was noticed (50.4 ± 10% deviation) but selectivity was less because of its high acidic nature. Also, it may also be due to the low poracity (5.6 Å) of the zeolite, whereby only a surface reaction has been facilitated.

Interestingly, when Hβ was used as catalyst, a low sensitivity of the cyclized product has been observed with low conversion of pyrrole. This could be attributed to very high acidic nature of Hβ [17], while HY coated TLC did not facilitate the reaction at all as indicated by the densitogram, may be again due to low pore size of sodalite cage.

5. Conclusions

The present study, using a novel concept of reaction cum separation on a single plate for efficient evaluation of porphyrins and calix (4) pyrroles by in situ synthesis from pyrrole with aromatic aldehydes and ketones respectively over zeolite based molecular sieve catalysts as sorbents in thin layer chromatography (TLC) was accomplished in one step with microwave heating. The design and methodology of this glass-backed zeolite coated TLC, which acted as a micro reactor as well as separator for the in situ synthesis and chromatographic separation of macrocycles is described. Thus, this method has an inherent advantage of performing the synthesis and evaluation in one step and the specificity of the methodology has a unique role to offer a product oriented synthesis. However, the general observation in the present studies is, pore size, acidity and surface area of all the zeolite molecular sieve catalysts played a major role in these reactions and MCM-41 offered the best results as the pore size and the surface area available provided an ideal conversion conditions. The process is simple, economical, rapid, selective and

finds a possible application in high throughput parallel synthesis and screening on a single micro plate employing microwave irradiation in combinatorial chemistry. Further studies are underway, aimed at using metal incorporated zeolites for the synthesis and evaluation of industrially important organic moieties using the present approach along with possible effect of varied stoichiometry and environmental conditions.

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