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Chickpea leaf exudates: a green Brønsted acid type biosurfactant for bis(indole)methane and bis(pyrazolyl)methane synthesis†

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A clean and highly efficient protocol for green synthesis of bis(indole)methanes and bis(pyrazolyl)methanes has been successfully achieved by using a naturally sourced bio-surfactant, chickpea leaf exudates (CLE), as a Brønsted acid-type catalyst. The reaction proceeds smoothly with CLE in alcoholic medium at 60 °C in a very short reaction time, and therefore it is a green, environmentally sound alternative to the existing protocols. In comparison to the reported conventional methods, this synthetic pathway complies with several key requirements of green chemistry principles such as avoiding the use of any toxic/hazardous catalyst and additives/promoters, the use of a biodegradable catalyst obtained from renewable resources, auxiliary solvent conditions, and reusability of the catalyst. Thus, the reported protocol offers an attractive option because of its ecological safety, straightforward work-up procedure and excellent values of green chemistry metrics as compared with other reported methods.

1. Introduction

C–C bonding in organic transformations is an indispensable tool for synthesis of numerous structural moieties which are indeed building blocks of agrochemicals, natural products, medicinally important compounds, and so forth.[1,2] The simplest and of course the most imperative synthetic transformations are based on formation of carbon–carbon and carbon–nitrogen bonds. These transformations have been proved as a pioneer for synthesis of various biologically active compounds and construction of fine chemicals pharmaceutical agents, and smart engineering materials, including conducting polymers and molecular wires.[3–5]

Due to the environmental issues associated with many organic transformations, there is a huge challenge for researchers to develop chemical processes using more environmentally acceptable reagents, catalysts, solvents, and atom-efficient methods, and energy-efficient technologies eliminating waste production as well as employing renewable feedstocks are experiencing a profound challenge to meet sustainability criteria.[6] Furthermore, the environmental risks posed by volatile and toxic organic solvents have become a major concern, as organic reactions employ more consumption of solvents than reactants and the employed solvents are difficult to recycle;[7] to overcome this problem, the first task is to replace organic solvents with auxiliary ones.

Nowadays, an important aspect which is receiving growing attention is the use of alternative reaction media that avoid the problems associated with many of the traditional volatile organic solvents.[8] The use of hazardous solvents in the chemical industry is associated with a variety of indirect environmental impacts such as non-renewable resource reduction as a result of petrochemical solvent production, air emissions due to solvent incineration or high energy investment for solvent recycling processes.[9] Therefore, the ability to efficiently carry out organic reactions in more environmentally friendly solvents remains an important object of green chemistry research. It means that, wherever practicable, synthetic methods should be designed to use and generate substances that possess little or no toxicity to animal as well as human health and the environment.[10] Our interest is using easily available natural feedstocks to replace chemical catalysts and solvents.

Biosurfactants, being naturally sourced materials, have certain advantages over chemical surfactants, such as their biodegradable nature, their less toxic nature, and their ecological acceptability. One of the fundamental properties of surfactants is their self-association into organized molecular structures such as micelles,

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vesicles, microemulsions, bilayers, membranes and liquid crystals.[11] The simplest class of association colloids is the micelle. The micellisation characteristics of surfactants are determined by micellization parameters such as the critical micelle concentration, aggregation number, *etc.* Combined Brønsted acid surfactant catalysts have also been employed in several organic reactions.[12] Considering the significance of surfactants, in this work, chickpea leaf exudates (CLE) were chosen as catalytic media without using any external promoters, external acids, ligands, biphasic media and ionic liquids. The catalytic medium is directly collected from the chickpea leaf. From the literature record, the botanical name of chickpea is *Cicer arietinum*, locally known as chana (or harbhara) in India; commonly cultivated on a farm, it is an important source of protein for the local population. Chickpea is a grain legume adapted to dry and cool environments in Central and South America, southern Europe, western and southern Asia, and eastern and northern Africa. A solution containing surfactants shows appreciable changes in the physical and chemical properties at the critical micelle concentration (CMC). The CMC is the concentration of surfactants above which micelles form spontaneously. Efficient surfactants have very low CMC values, *i.e.* less surfactant is required to decrease the surface tension.[13,14]

Nowadays, the development of bis(indolyl)methanes has received significant attention because they are present in a variety of natural products and also play a vital role in plant growth, biomedicine, and agriculture.[15] In addition, these heterocyclic compounds and their analogues present various important biological and many pharmacological activities, such as antitumor,[16] antileishmanial,[17] antihyperlipidemic,[18] anticancer,[19] antifungal, anti-inflammatory, antibacterial, antibiotic, and analgesic properties.[20] Some applied methodologies with different catalysts such as microwave irradiation,[21] visible light,[22] the grinding technique,[23] ultrasound irradiation,[24] infrared,[25] the solvent free approach,[26] under aqueous conditions,[27] using an ionic liquid,[28] use of acids,[29] use of nano-materials,[30] use of natural materials,[31] in micellar media,[32] and eco-friendly reagents and catalysts[33] have been reported.

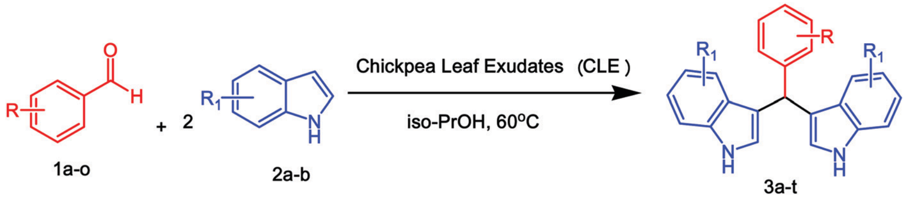
The 4,4′-(arylmethylene)bis(1*H*-pyrazol-5-ols) are another important class of bis-heterocyclic compounds. This is because the pyrazolone nucleus is one of the most important nitrogen heterocyclic moieties found in numerous bioactive molecules with predominant properties such as cytokine inhibitory,[34] COX-2 inhibitory,[35] and antitumor properties.[36] 2,4-Dihydro-3*H*-pyrazol-3-one derivatives including 4,4′-(arylmethylene) bis(1*H*-pyrazol-5-ols) also display a wide range of pharmacological activities for use as antibacterial,[37] antidepressant,[38] and antimalarial agents,[39] and a gastric secretion stimulatory drug.[40] They are also extensively applied as fungicides, pesticides, insecticides and dyestuffs.[41] Bis(pyrazolyl)methanes are usually synthesized by the reaction of aryl aldehydes with hydrazine hydrate and ethyl acetoacetate. For this purpose, a variety of methodologies with different catalysts including microwave irradiation,[42] electrolysis,[43] ultrasound irradiation,[44] the solvent free approach,[45] under aqueous conditions,[46] using ionic liquids,[47] use of acids,[48] use of nano-materials,[49] and in micellar media[50] have been reported. These reported methods have their own limitations such as low yield, lower product selectivity and an environmentally toxic catalyst. Considering these aspects, new methodologies in mild reaction conditions with a cheap and easily available catalyst will be beneficial as an interesting challenge. Although diverse approaches towards the synthesis of these derivatives have been developed, the use of a bio-surfactant is the most elegant strategy.

Therefore, the aim of the present work is to explore the synthetic utility of a naturally sourced acidic bio-surfactant in carbon–carbon and carbon–nitrogen bond formation. Considering the significance of a naturally sourced catalytic medium, we explore the catalytic activity of CLE for the synthesis of bis(indole)methanes (Scheme 1) starting from readily available substituted indole and aryl aldehydes and also synthesis of bis(pyrazolyl)methanes starting from aryl aldehyde, ethyl acetoacetate, and hydrazine hydrate in iso-propanol. To the best of our knowledge based on a literature survey, the pronounced catalytic effect of CLE as a Brønsted natural acid type biosurfactant is being described for the first time for organic synthesis and the CMC was determined by the conductivity method.

2. Experimental section

2.1 General information

Except chickpea leaf exudates all reactants and solvents were commercially obtained from Sigma-Aldrich and used without further purification. The FTIR spectra were recorded using the ATR technique on a Bruker ALPHA FT-IR spectrometer. Thermal gravimetric analysis (TGA) was performed using a TA SDT Q600 V20.9 Build 20 instrument in nitrogen at a linear heating rate of 10 °C min^{-1}. The ^{1}H NMR spectra (300 MHz and 400 MHz) and ^{13}C NMR spectra (75.5 MHz and 100 MHz) were measured with AVANCE-300 instruments, using TMS as an internal standard in DMSO-d_6 and CDCl$_3$ as a solvent. The pH of the catalyst and aqueous solutions of chemical surfactants was measured using a digital pH meter (model EQ-610). An HPLC-MS instrument (6200 series TOF/6500 series



Scheme 1 Synthesis of bis(indole)methane derivatives.

Q-TOF B.05.01 (B5125.3); Agilent Technologies, Santa Clara, CA, USA) was used for determination of the organic components in the CLE catalyst. Thin layer chromatography (TLC) analysis was performed on silica gel 60-F254 pre coated plates (250 μm layers). Optical microscopy measurements: a drop of turbid reaction mixture was subjected to light microscopy measurements using an ordinary light microscope under 50× and 100× magnification. The conductivity measurements for the CMC were performed with an Equiptronics (Model EQ-660B) digital auto ranging conductometer with a cell constant = 1 cm^{-1}.

2.2 Collection of chickpea leaf exudates

For quantitative collection of CLE as a catalytic medium we consider the growing period of newly cultivated chickpea crops. At first, for the purpose of exudate collection, cultivated crops on various lands were selected and then exudates were collected manually using a clean and soft cotton cloth by an absorption–wringing process. It was observed that a good quantity of exudates was obtained from chickpea crops of two months old (just before the flowering stage). It was also observed that the early morning (5.00 am to 6.00 am) period gave good collection of exudates (ESI†). The pH of the collected exudates was measured using a pH-meter before use and it was found to be 1.1. The collected catalyst was stored for several days at 5 °C.

2.3 General procedure for the synthesis of 3-((1*H*-indol-3-yl)(4-methoxyphenyl)methyl)-1*H*-indol

All the reactions were carried out under an air atmosphere in pre-dried glassware. A mixture of indoles (2.0 mmol), and aryl aldehydes (1.0 mmol) in a solution of CLE (5.0 mL) and iso-PrOH (3.0 mL) was stirred at 60 °C in a preheated oil bath till the completion of the reaction as indicated by TLC (petroleum ether : ethyl acetate). After completion of the reaction, 5.0 mL water was added to the reaction mixture. The solid products were separated by simple filtration followed by washing with 5.0 mL cold water. The pure products were obtained by recrystallization with 96% ethanol. All the products were confirmed by the spectroscopic method using NMR and FT-IR. The physical and spectroscopic data are consistent with the proposed structure and is in harmony with the literature values.

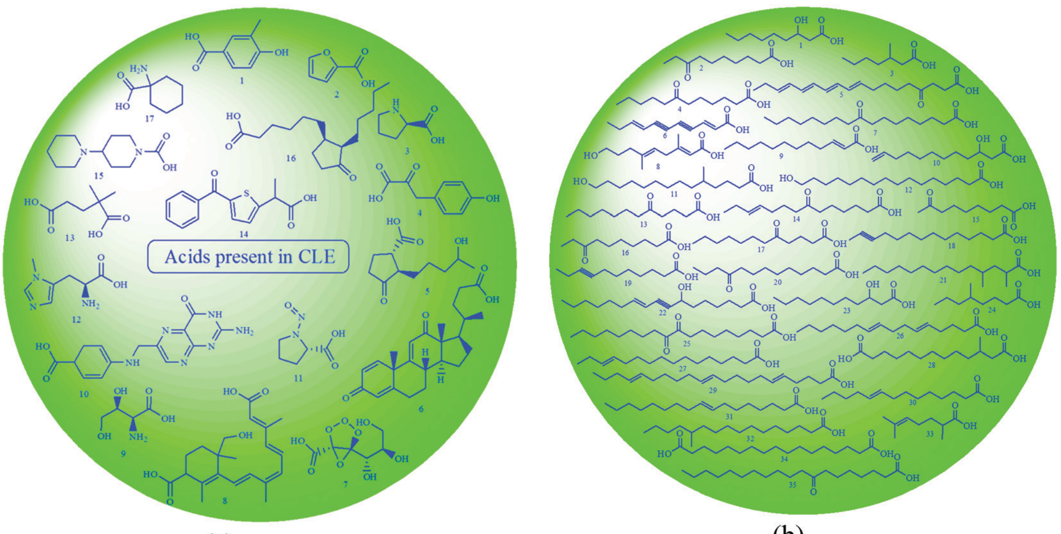
2.4 General procedure for the synthesis of 4-((5-hydroxy-3-methyl-1*H*-pyrazol-4-yl)(4-methoxyphenyl)methyl)-3-methyl-1*H*-pyrazol-5-ol

In a 25 mL round bottom flask aryl aldehyde (1.0 mmol), ethyl acetoacetate (2.0 mmol), and hydrazine hydrate (2.0 mmol) were placed in a solution of CLE (5.0 mL) in iso-PrOH (3.0 mL) and stirred at 60 °C in a preheated oil bath till the completion of the reaction as indicated by TLC (petroleum : ethyl acetate). After completion of the reaction, 5.0 mL water was added to the reaction mixture. The solid products were separated by simple filtration followed by washing with 5.0 mL cold water. The pure products were obtained by recrystallization with 96% ethanol. Representative compounds were confirmed by physical constants and characterized by spectral analysis.

3. Results and discussion

3.1 Characterization of the catalyst

3.1.1 HPLC-MS studies. High performance liquid chromatography-mass spectroscopy (HPLC-MS) is an analytical technique commonly used to identify the presence of organic components in biological samples. It has been reported that the leaf surfaces of the chickpea plant secrete several organic acids[51,52] such as malic, succinic, oxalic, quinic and citric acids which are responsible for the highly acidic nature (1.1 pH) and have been correlated with reduced pod damage.[53] Because of the acidic nature of CLE due to the presence of different organic acids reported in the literature,[54] we decided to



(a) (b)

Fig. 1 Structures of acids present in CLE.

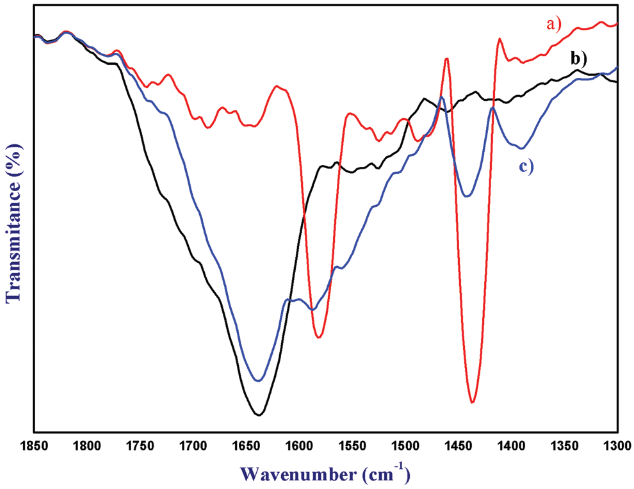


Fig. 2 FTIR spectra of (a) the CLE catalyst, (b) neat pyridine and (c) a mixture of pyridine with the CLE catalyst.

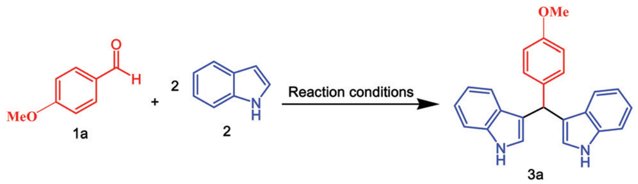
investigate the presence of these acids in the exudates. For this investigation we analyzed a fresh CLE sample by HPLC-MS and more than 50 acids along with other organic components were detected as shown in Fig. 1. The mass spectra of all acids are given in the ESI.†

In view of these data and in continuation of our ongoing research in the development of green synthetic protocols utilizing natural feedstocks,[55,56] we thought that this amazing medium may serve as a Brønsted acid type biosurfactant for this transformation.

3.1.2 FTIR analysis. The FTIR spectra of CLE were recorded in a frequency range 1850–1300 cm^{-1} using pyridine as a probe for Brønsted acidity measurement. The presence of a band near 1582 cm^{-1} is an indication of the formation of pyridinium ions resulting from the presence of Brønsted acid sites. In this work CLE (Fig. 2a), neat pyridine (Fig. 2b) and pyridine added to CLE (Fig. 2c) show well resolved spectra. The observation of an absorption band at 1587 cm^{-1} due to the formation of pyridinium ions suggests that Brønsted acids are also present (Fig. 2c). Also the band observed at 1637 cm^{-1} indicates the presence of –C=C– bonds and that at 1390 cm^{-1} indicates –OH bending vibrations present.

3.1.3. TGA analysis. As indicated in Fig. 3, the thermal stability of CLE was determined by thermogravimetric analysis. The TGA curves of CLE show three thermal decomposition peaks. The initial weight loss of 36.29% below 55.98 °C is due to the most volatile component present in CLE. The major weight loss of 51.30% up to 110 °C is attributed to dehydroxylation and decarboxylation of water soluble acids. The third weight loss of 2.664% corresponds to the decomposition of organic compounds. The DSC-TGA data confirm that the catalyst is stable to 120 °C.

Table 1 Optimization of the reaction conditions for the model reaction[a]



Entry	CLE (mL)	Co-surfactant (3 mL)	Temp. (°C)	Time (min)	Yield[b] (%)
1	0.5	—	Rt	180	Trace
2	1.0	—	Rt	180	Trace
3	1.5	—	Rt	180	Trace
4	2.0	—	Rt	180	12
5	2.5	—	Rt	180	15
6	3.0	—	Rt	180	32
7	4.0	—	Rt	180	32
8	5.0	—	Rt	180	32
9	3.0	—	60	60	69 (70, 69)[c]
10	3.0	MeOH	60	30	81
11	3.0	EtOH	60	30	88
12	3.0	iso-PrOH	60	60	94
13	3.0	*t*-BuOH	60	60	82
14	1.0	iso-PrOH	60	60	84
15	2.0	iso-PrOH	60	60	88
16	5.0	iso-PrOH	60	30	96
17	7.0	iso-PrOH	60	60	90
18	9.0	iso-PrOH	60	60	82
19	5.0	iso-PrOH	Rt	60	36
20	—	iso-PrOH	60	60	Nr

[a] Reaction conditions: 4-methoxybenzaldehyde (1.0 mmol), indole (2.0 mmol) and CLE (mL). [b] Isolated yield. [c] Temperature: 80 °C, 90 °C.

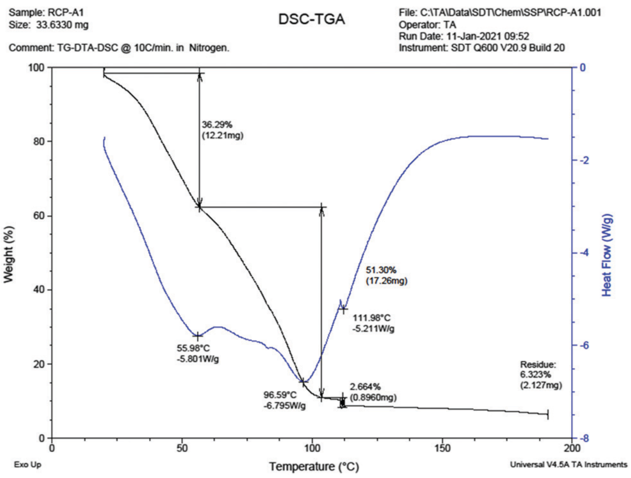


Fig. 3 DSC-TGA curves of CLE.

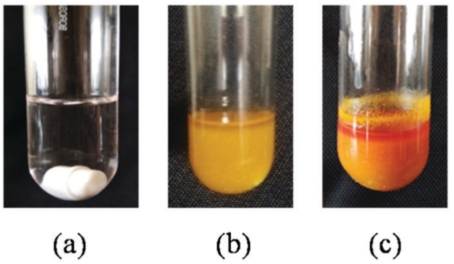

(a) (b) (c)

Fig. 4 The phenomenon of the reaction between 4-methoxybenzaldehyde and indole: (a) homogeneous phase of the reactants and catalyst at the beginning of the reaction, (b) the reaction mixture after 5 min, and (c) product formation after reaction completion.

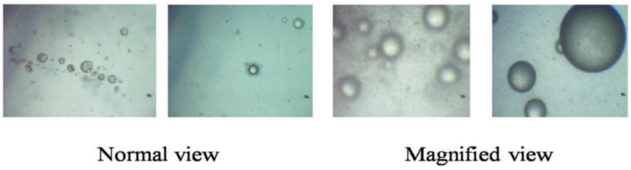


Fig. 5 Optical microscopic images of the model reaction mixture – normal view and magnified view.

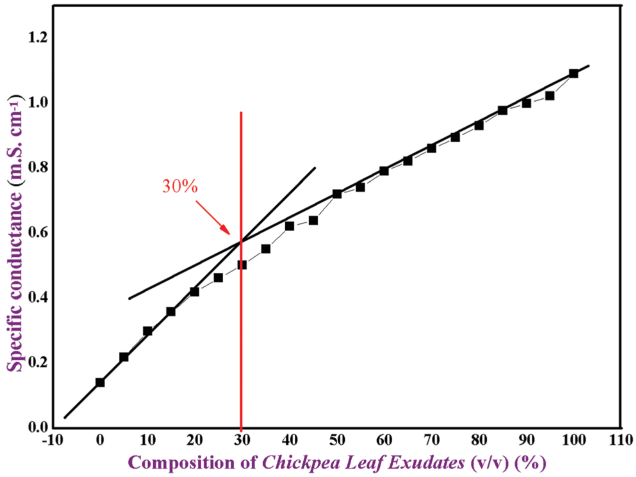


Fig. 6 Plot of specific conductance against percentage composition of CLE.

3.2 Application of CLE for bis(indole)methane and bis(pyrazolyl)methane synthesis

Our initial studies were focused on the development of an optimum set of reaction conditions for the synthesis of bis(indole)methane using chickpea leaf exudates as a bio-based catalyst by reacting aryl aldehyde and substituted indoles in alcoholic conditions.

3.2.1 Optimization of the reaction conditions. For optimization of the reaction conditions, a 25 mL round bottom flask was charged with 4-methoxybenzaldehyde (1.0 mmol), and indole (2.0 mmol) as a model substrate in the presence of CLE, and the reaction mixture was stirred at room temperature. After 3 h a low yield (32%) of corresponding product **3a** was observed in TLC (Table 1, entry 6). On increasing or decreasing the catalytic amount (0.5 to 5 mL), no significant improvement in the results was obtained after a prolonged reaction time (Table 1, entries 1 to 8). We continued our efforts for improvement of the results and when the model reactants were allowed to react under elevated temperature conditions in the presence of 3 mL CLE, surprisingly at a 60 °C temperature the product yields were doubled, while on a further increase in temperature nearly the same results were recorded (Table 1, entry 9) after 3 h. However, we were not satisfied with these moderate results, and, since solvents play a crucial role in organic synthesis, the effect of solvents as co-surfactants was studied for the model reaction (Table 1, entries 10–13). Among the tested co-surfactants, it was found that iso-propanol was found to be more efficient for the present transformation (Table 1, entry 12).

The amounts and nature of the organic solvent have produced a significant change in the properties of surfactants. Iso-propanol provides dual performance (co-surfactant and co-solvent) for organic transformation.[57] Iso-propanol as a co-surfactant increases the hydrophobicity of the micellar medium of the catalyst while as a co-solvent it increases the solubility of the reactants in the reaction mixture. Therefore, iso-propanol at a 60 °C temperature efficiently worked as a co-surfactant leading to effective synthesis of **3a** along with enhanced product yield. It was also noticed that the condensation using a co-surfactant proceeded rapidly and was superior to the reported procedures with respect to the reaction time and yields of the product.[58,59]

Furthermore, we also optimized the surfactant : co-surfactant ratio for the model reaction by changing the amount of CLE

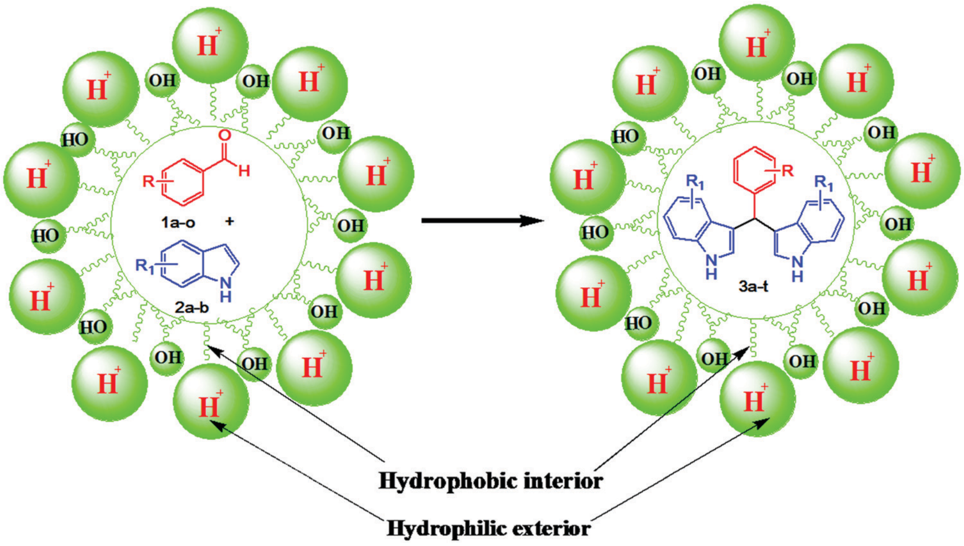
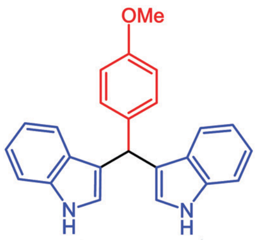
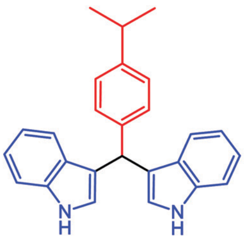


Fig. 7 Mechanistic picture of the role of micelles for bis(indole)methane formation.

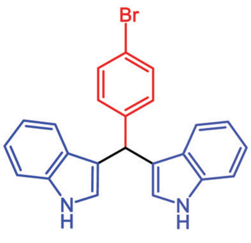
Table 2 CLE-catalyzed synthesis of bis(indole)methane derivatives (**3a–t**)[a]



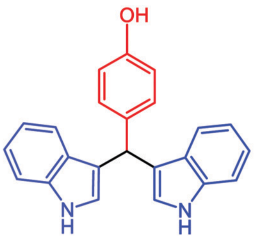
3a[b] (30[c], 96[d])



3b (25, 94)

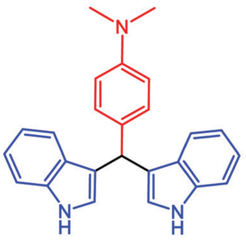


3c (40, 90)

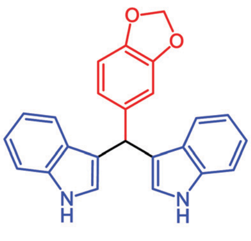


3d (15, 93)

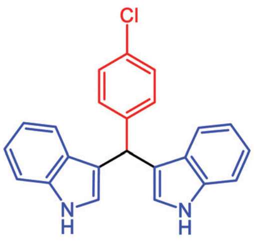
3e (15, 85)



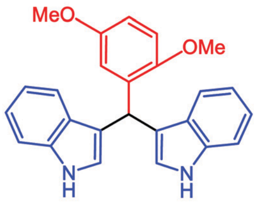
3f (15, 94)



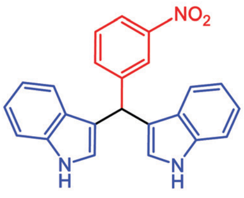
3g (30, 90)



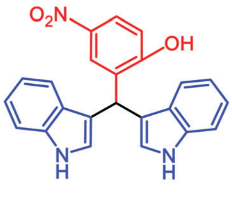
3h (40, 84)



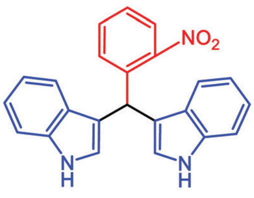
3i (15, 89)



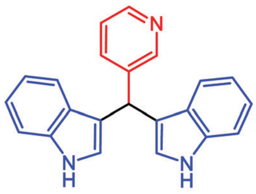
3j (10, 84)



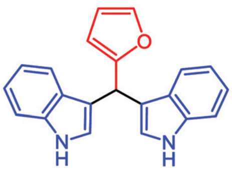
3k (15, 90)



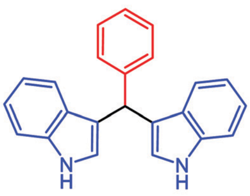
3l (20, 89)



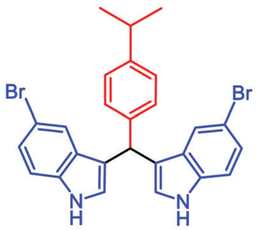
3m (20, 88)



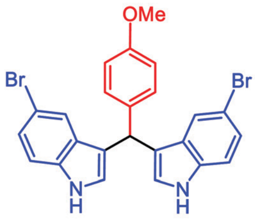
3n (20, 84)



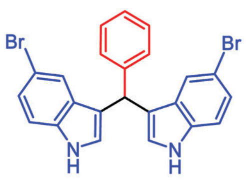
3o (35, 92)



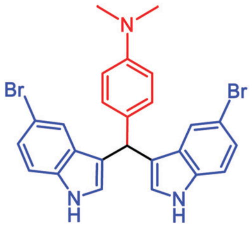
3p (40, 82)



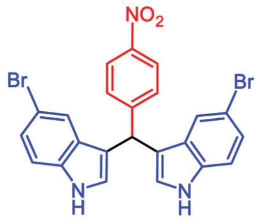
3q (30,85)



3r (40,85)



3s (35, 80)



3t (30, 88)

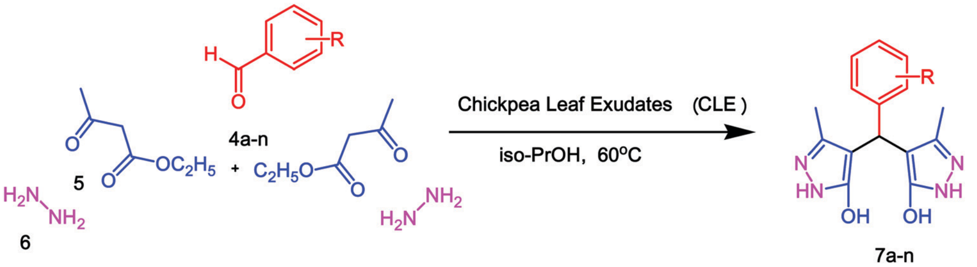
[a] Reaction conditions: aryl aldehydes (1.0 mmol), substituted indole (2.0 mmol), CLE (5.0 mL), and iso-PrOH (3mL) at 60 °C. [b] Entry. [c] Time in min. [d] Isolated yields in %.

(Table 1, entries 14–18). The results showed that a surfactant : co-surfactant ratio at just above the CMC (30%) is a suitable reaction medium for smooth conversion of the reactant to the product with respect to time and yield (Table 1, entry 16). From these results, it was also revealed that further decreasing or increasing the surfactant : co-surfactant proportion reduces the yield of the desired product. At ambient temperature with the same reaction conditions, a 36% yield of **3a** was obtained (Table 1, entry 19). Moreover, the catalyst-free condition was also examined (Table 1, entry 20); the result observed was a viscous reaction system with no product formation, which indicates that the role of the bio-surfactant is decisive for bis(indole)methane formation.

The HPLC-MS study of CLE showed the presence of several organic acids along with other organic components, which may

Table 3 Comparison of the efficiency of different chemical surfactants with the CLE bio-surfactant for synthesis of **3a**

Entry	Surfactants	Time	Yield (%)	Ref.
1	Sodium dodecyl sulfate (SDS)	5 h	80	60
2	Dodecylsulphonic acid (DSA)	18 min	94	61
3	Tetrabutylammonium tribromide (TBATB)	30 min	95	62
4	Tetrabutylammonium tribromide (TBAT)	3 h	65	63
5	Sodium 4-dodecylbenzenesulfonic acid (SDBS)	4.5 h	70	64
6	Cetyltrimethylammonium bromide (CTAB)	5 h	20	64
7	Ferric dodecyl sulfonate [$Fe(DS)_3$]	8 h	80	65
8	Ytterbium(III) triflate/sodium dodecyl sulfate ($Yb(OTf)_3$/SDS)	1.5 h	84	66
9	Chickpea leaf exudates (CLE)	30 min	96	Present work



Scheme 2 Synthesis of 4,4′-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ols).

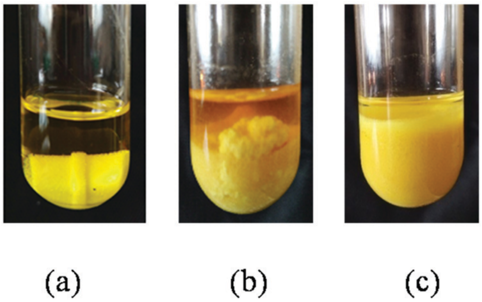


Fig. 8 The phenomenon of the reaction between 4-methoxybenzaldehydes (1.0 mmol), hydrazinehydrates (2.0 mmol), and ethyl acetoacetate (2.0 mmol): (a) the homogeneous phase of the reactants and catalyst at the beginning of the reaction, (b) the reaction mixture after 5 min, and (c) product formation after reaction completion.

collectively form micelles in the reaction mixture and support moving the reactions in the proper direction. We thought that this amazing medium may serve as an acidic bio-surfactant, a better alternative to chemical surfactants and also to harmful corrosive acids used for organic transformations.

At the beginning, the clear reaction mixture turned to a turbid emulsion (Fig. 4), which implies that there is the formation of micelles or micelle-like colloidal aggregates, which was visualized through an optical microscope (Fig. 5).

The aggregation of organic ingredients from CLE under the reaction conditions results in the semi-ordered structure of micelles protruding into the aqueous phase, whereas the hydrophobic parts are brought into close proximity in the core of the aggregate excluding water. When organic compounds are introduced in an alcoholic micellar solution, hydrophobic interactions will cause binding of these compounds to the micelles and they will get collected in the core of the micelle where the reaction occurs more easily. This further confirmed that the catalyst does not simply provide the acidic medium to activate the substrate molecules but also helps to aggregate all the reactants into micelles.

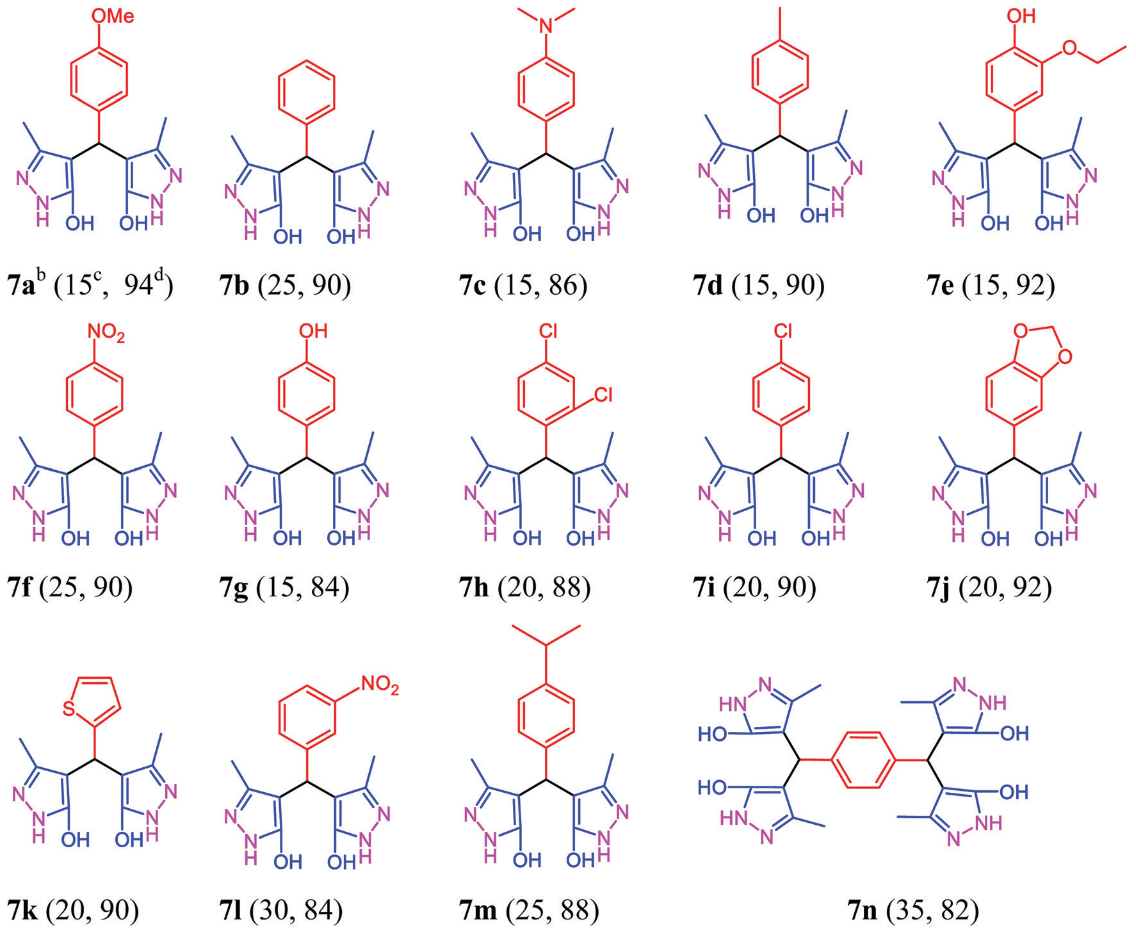
3.2.2 Determination of the CMC by the conductivity method. To maintain a proper CLE : iso-PrOH composition for this condensation reaction, we employed electrical conductivity measurement experiments to determine the CMC and it was found to be 30% v/v (Fig. 6).

During organic transformations micelle formation occurs above the CMC, at which the reactants undergo self-assembly to form aggregates in the solution, which causes conversion of the true solution to a colloidal system. The micellar solution is known as a colloidal dispersion of organized surfactant molecules. The micelle formed in the solution is in a spherical form in which the hydrophobic tails face toward the interior of the micelle structure while the hydrophilic head group is exposed to the solution. The role of micelles to catalyze the reaction in this condensation is schematically represented in Fig. 7.

After optimization of the reaction conditions, condensation reactions were carried out in CLE : iso-PrOH (5 : 3, v/v) at 60 °C using a series of structurally diverse aryl aldehydes with substituted indoles. Aldehydes with electron-withdrawing groups ($-NO_2$, $-Cl$, $-Br$) as well as electron-donating ($-OCH_3$, $-OH$, $-N(CH_3)_2$) and hetero aromatic functionalities reacted successfully and gave the expected products in the stipulated time period (Table 2).

Thus, the acidic nature of the exudates and the surfactant activity due to different organic acids offered a synergistic

Table 4 CLE-catalyzed synthesis of 4,4′-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) derivatives (**7a–n**)[a]



7a[b] (15[c], 94[d]) **7b** (25, 90) **7c** (15, 86) **7d** (15, 90) **7e** (15, 92)

7f (25, 90) **7g** (15, 84) **7h** (20, 88) **7i** (20, 90) **7j** (20, 92)

7k (20, 90) **7l** (30, 84) **7m** (25, 88) **7n** (35, 82)

[a] Reaction conditions: aryl aldehydes (1.0 mmol), hydrazinehydrates (2.0 mmol), ethyl acetoacetate (2.0 mmol), CLE (5.0 mL), and iso-PrOH (3.0 mL), 60 °C. [b] Entry. [c] Time in min. [d] Isolated yields in %.

Table 5 Comparison of the efficiency of different chemical surfactants with the CLE bio-surfactant for synthesis of **7a**

Entry	Surfactants	Time	Yield (%)	Ref.
1	Sodium dodecyl sulfate (SDS)	5 h	80	60
6	Sodium dodecyl benzene sulfonate (SDBS)	4.5 h	70	67
10	Chickpea leaf exudates (CLE)	15 min	94	Present work

effect, and the reaction proceeded rapidly in a short time. The comparison of efficiency of the different chemical surfactants with CLE bio-surfactant has been presented (Table 3, entries 1–8). The surfactant obtained from chickpea leaf was found to be excellent with respect to time as well as the yield of the product (Table 3, entry 9), suggesting that both the surfactant property and strong Brønsted acidity of CLE are essential to promote the reaction efficiency.

Inspired by these tempting results obtained for condensation of aldehydes with indoles to afford the desired bis(indole) methanes, we extended the optimized protocol for a one-pot pseudo five component synthesis of 4,4′-(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ols) (Scheme 2).

At the beginning, the yellow colour reaction mixture turned to a turbid emulsion (Fig. 8), which implies that there is the formation of micelles or micelle-like colloidal aggregates, and the obtained product was separated easily with the procedure described in the experimental procedure.

Condensation reactions were carried out in 5.0 mL CLE and iso-propanol at 60 °C using a series of structurally diverse aryl aldehydes with hydrazine hydrate and ethyl acetoacetate (Table 4). As the data in this table show, CLE were simple and highly efficient for the reaction; all aryl aldehydes (containing electron-donating substituents, electron-withdrawing substituents and halogens) afforded the desired products in high yields within short reaction times.

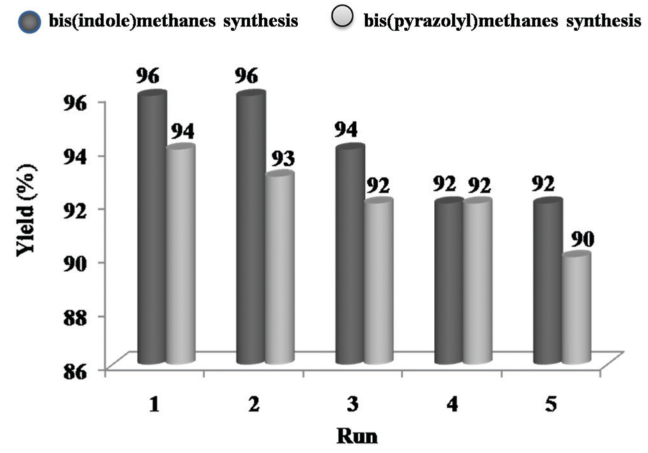


Fig. 9 Recyclability and reusability of the CLE catalyst.

To compare the catalytic activity of CLE with different chemical surfactants, we also carried out the reaction using various other chemical surfactants (Table 5, entries 1 and 2). Comparison of the results shows a better catalytic activity of CLE as a biosurfactant for synthesis of **7a** (Table 5, entry 3).

Recycling of the catalyst

In order to investigate the recyclability and reusability of the CLE catalyst, we synthesized compounds **3a** and **7a**. After completion of the reaction, H_2O (5.0 mL) was added to the reaction mixture and then it was filtered off. The whole filtrate containing CLE was concentrated under a vacuum and directly used for the next cycle with fresh reactants for synthesis of **3a** and **7a** in iso-PrOH at 60 °C. The recovered catalyst was employed for a further five successful cycles without significant loss of efficiency. However, the reaction times were found to be increased while reusing the recovered catalyst (Fig. 9).

4. Conclusion

In conclusion, we report a simple and new approach for synthesis of bis(indole)methanes and bis(pyrazolyl)methanes which represents a highly efficient and environmentally benign protocol. Apart from this, simplicity of product separation and effortless reusability of the catalyst are the significant advantages of this protocol. This new natural Brønsted acid bio-surfactant should thereby provide an attractive alternative to harmful corrosive catalysts. However in a true sense we think that a bio-surfactant doesn't offer only a synergistic effect of acidic nature and surfactant activity but there might be a combination of many other factors. Hence to have a good contribution in innovation of green chemistry, we will lengthen our research to have more exposure to natural surfactant catalyzed organic transformations.

Conflicts of interest

There are no conflicts to declare.

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