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Bronsted acid-type biosurfactant for heterocyclization: a green protocol for benzopyran synthesis†

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A natural biosurfactant, a biobased green acidic catalyst for cyclo-condensation of salicylaldehyde (or 2-hydroxy naphthaldehyde) and cyclic 1,3-diketones for benzopyran synthesis in water has been reported for the first time. The structures of the final compounds were confirmed with the aid of IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. Lemon extract as a natural biosurfactant provides a micellar media for effective organic transformation. The CMC of lemon extract was determined by the conductivity method. In comparison to the conventional methods, this synthetic pathway complies with several key requirements of green chemistry principles such as the utilization of renewable feedstock, auxiliary aqueous conditions, waste prevention, and atom economy along with the use of biodegradable catalyst. Thus, the reported protocol offers an attractive option because of its ecological safety, environmental acceptance, sustainability, and low-cost straightforward work-up procedure.

Introduction

While considering the increasing environmental pollution and its intensive impact on living systems, the development of chemical processes using more environmentally acceptable chemicals, catalysts, solvents, atom-efficient methods, and energy-efficient technologies eliminating waste production as well as employing renewable raw materials is experiencing a profound challenge to meet sustainability criteria.[1] In addition, the environmental risks posed by the toxic and volatile organic solvents have become a major concern. The reason is that the organic transformations employ higher consumption of solvents than the reagents and the employed solvents are difficult to recycle;[2] for the process to be in line with the green chemistry principles, the first task is to replace the organic solvents with green ones.

Performing organic reactions in water have attracted much attention over the past decades due to its numerous advantages such as being considerably safe, nontoxic, environmental-friendly, and cheap.[3–6] Nowadays, biosynthetic processes involving bio-based solvents or catalysts have received much attention as a viable alternative for the development of green protocols for organic transformations.[7]

In this regard, natural biosurfactants as part of the chemical process offer an excellent alternatives to volatile organic solvents in being more environmental-friendly technologies due to their ease of biodegradability, ability to act as catalysts, low toxicity, and non-flammable properties as compared to chemical surfactants.[8] Again, due to the high natural abundance, their production is potentially less expensive.

The term 'biosurfactant' can be applied to a surfactant that is obtained directly from a natural source (from plant, animal or microbial cells) by some kind of separation procedure such as extraction, precipitation or distillation. They form a part of an emergent tool with a great potential for industrial applications including the use in enhanced oil recovery, crude oil drilling, lubricants, health care and food processing industry.[9] In addition to this, full evaluations of the potential of these natural dispersants in cosmetic and soap formulations, foods and dermal or transdermal drug delivery systems are developing at an incredible rate.[10] It is notable that, despite their diverse applications in industry and environmental biotechnology, their potential in accelerating the organic transformations has not been evolved till this date.

Therefore, the aim of the present work is to explore the synthetic utility of natural biosurfactant in organic transformations. The catalytic medium is sourced from the direct extraction of citrus fruit. From literature records it is well-known that the citrus fruit locally known as Limbu (or Nimbu) in India; it is a plant species commonly cultivated in a home garden or on a farm and traditionally used for antioxidant activity.[11] The power of phytochemical, in a lemon which initiates varieties of chemical transformations within biological systems is well-known.[12,13] Polyphenolic flavonoids in lemon, of which epigallocatechin

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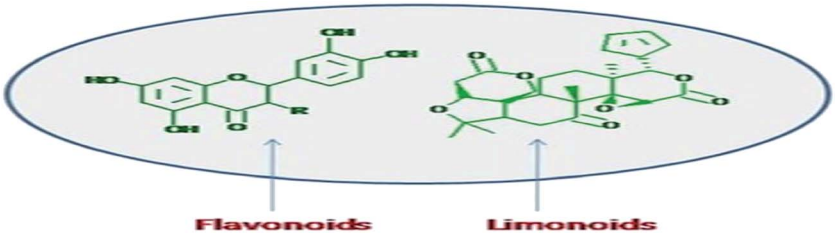


Fig. 1 Structure of flavonoids and limonoids.

gallate (EGCG) is the major constituent, has anti-carcinogenic activity.[14,15] Phytochemical study showed the presence of limonoids and flavonoids[16] (Fig. 1) which may collectively form micelles and help to forward the reactions in proper direction. In addition to this lemon fruit extract exhibits acidic pH (2.3). In view of this data and in continuation of our ongoing research in the development of green synthetic methodologies,[17] we thought that, this amazing medium may serve as Bronsted acid-type biosurfactant, a better alternative to chemical surfactants and also to harmful corrosive acids for organic transformations. Combined Bronsted acid surfactant catalysts in water have been employed in a number of organic reactions.[18,19]

Results and discussion

At the beginning, we focused our attention on selection of citrus fruit from different citrus species based on acidic pH. For this purpose different fresh fruits were cut by using a knife and then pieces were pressed manually using domestic presser to obtain turbid extracts. The turbid extracts were then filtered through cotton/muslin cloth and then through filter paper to remove solid material to get clear extract. The pH of extracts were measured using pH meter (ProLab 3000 laboratory pH meter) and pH of *Citrus limonium* extract was found to be 2.3, which is the lowest among all species, and therefore, it was used as acid catalyst for this protocol.

The next task was to optimize different reaction parameters for benzopyran synthesis. Benzopyran derivatives act as potassium channel opener,[20] PPAR α/γ agonists,[21] selective thrombin (THR) inhibitors,[22] anti-*Helicobacter pylori* agents.[23] Benzopyrans also exhibit insulin-sensitizing activities,[24] antimicrobial activities,[25] and antibacterial activities.[26]

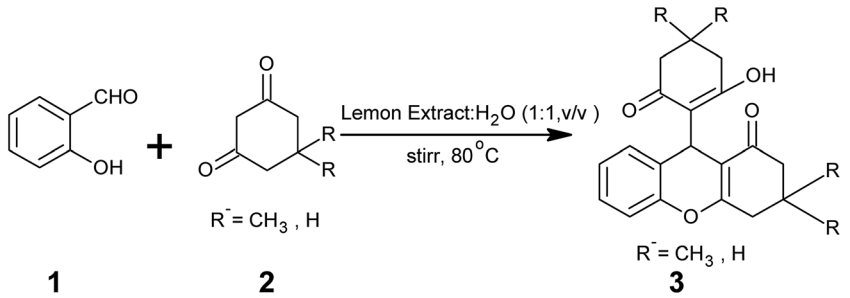
Recently some benzopyran derivatives have been synthesized by the reaction of substituted salicylaldehydes with dimedone using different catalysts such as KF/Al_2O_3,[27] triethylbenzylammonium chloride,[28] 2,4,6-trichloro-1,3,5-triazine,[29] *p*-TSA[30] and ionic liquid.[31] These reported methods have their own limitations such as low yield, less product selectivity and an environmentally toxic catalyst. Considering these aspects, new methodologies in mild reaction condition 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, use of biosurfactant is the most elegant strategy.

To optimize the reaction conditions, 25 mL round bottom flask was charged with salicylaldehyde **1** (1.1 mmol), 1,3-dimedone **2** (2.2 mmol), lemon extract (3 mL) and the reaction mixture was stirred at room temperature as a model reaction. After 3 h low yield (30%) of corresponding product was observed on TLC (Table 1, entry 5). On increasing or decreasing catalytic amount (1 to 5 mL), no significant improvement in the result was obtained after prolonged reaction time (Table 1, entries 1 to 7). We continued our efforts for improvement in the result when model reactants were allowed to react at elevated temperature (80 °C), in presence of 3 mL lemon extract, after 40 min, surprisingly the product was obtained in 81% yield (Table 1, entry 8). In order to check and verify further the effect of the solvent on the yield of the product, the model reaction was performed in methanol, ethanol, iso-propanol, *t*-butanol (Table 1, entry 9) which afforded product in moderate yields. To our outmost expectations, the reaction to perform in aqueous media, the reaction proceeded very well, and 96% yield was obtained when equi-volume quantity of lemon extract and water (3 mL each) employed under identical conditions (Table 1, entry 10) (Scheme 1). We also optimized the catalyst-solvent proportion

Table 1 Effect of catalytic amount of biosurfactant and temperature on time and yield of the model reaction[a]

Entry	Amount of Catalyst (mL)	Solvent	Temp (°C)	Time (min)	Yield[b] (%)
1	1.0	—	RT	180	Trace
2	1.5	—	RT	180	Trace
3	2.0	—	RT	180	10
4	2.5	—	RT	180	10
5	3.0	—	RT	180	30
6	4.0	—	RT	180	30
7	5.0	—	RT	180	30
8	3.0	—	80	40	81
9	3.0	MeOH	80	60	84, (87, 78, 72)[c]
10	3.0	Water	80	40	96
11	3.0	Water[d]	80	40	95, 88
12	4.0	Water	80	40	93
13	5.0	Water	80	40	90
14	—	Water	80	180	Trace

[a] Reaction conditions: salicylaldehyde **1** (1.1 mmol) and 1,3-dimedone **2** (2.2 mmol), solvent (3 mL). [b] Isolated yield based on salicylaldehyde. [c] Ethanol, iso-propanol, *t*-butanol. [d] Water 4 and 5 mL.



Scheme 1 Standard model reaction of salicylaldehyde and 1,3-dimedone.

for model reaction by changing catalyst-solvent ratio. The result showed that 3 : 3 and 3 : 4 catalyst : solvent proportion which is above the CMC composition (40% v/v) is a suitable medium for smooth conversion of reactant to the product with respect to time and yield (entry 10 and 11). From these results, it was also revealed that on further decreasing or increasing the catalyst : solvent proportion reduces the yield of desired product (entry 11–13). Moreover, the catalyst-free condition was also examined; the result observed was viscous reaction system and low yield which indicates that the role of biosurfactant is decisive for benzopyran **3** formation (Table 1, entry 14).

On the completion of the reaction as monitored by TLC, the product was separated out by simple filtration, successively washed with cold water, and recrystallized from 96% ethanol which afforded the corresponding product of high purity. Pure products obtained by recrystallization from ethanol were characterized by their physical constants and spectral techniques. In ^{1}H NMR spectrum (Fig. 4a) of the product of the model reaction (Table 3, entry 1), observation of sharp singlet at δ 10.50 due to enolic proton, and at δ 4.65 corresponding to tertiary C–H proton as well as incorporation of 23 signals in ^{13}C NMR spectrum (Fig. 4b) supports its formation. Further, in FT-IR spectrum (Fig. 4c), observation of broad band due to enolic –OH at 3207 cm^{-1} and at 1628 cm^{-1} corresponding to α,β-unsaturated cyclic carbonyl group supports its formation.

Thus, the acidic nature of fruit extracts as well as surface activity due to flavanoids and limonoids offered synergistic effect, and reaction proceeded rapidly within short time. To compare the catalytic activity of different natural surfactant obtained from other fruit species, we also carried out the model reaction using various other natural biosurfactants (Table 2, entries 2–6). Surfactant obtained from *Citrus limonium* was found to be excellent with respect to time as well as yield of the product (Table 2, entry 1) suggesting that both the surfactant property and strong Bronsted acidity of lemon extract are essential to promote the reaction efficiency.

After optimization of reaction condition, the condensation reactions were carried out in lemon extract : water (1 : 1, v/v) at 80 °C in a preheated oil-bath using a series of structurally diverse salicylaldehydes with 1,3-ketones (Table 3). On the completion of reactions as monitored by TLC, the reaction mixtures were filtered to isolate products and purified by recrystallization from 96% ethanol. The reactions of salicylaldehydes, bearing electron-donating as well as electron-withdrawing groups, underwent successfully.

Table 2 Comparison of efficiency of different biosurfactants for benzopyran synthesis[a]

Entry	Biosurfactant	pH	Time (min)	Yield[b] (%)
1	Lemon extract	2.30	40	96
2	Lime extract	2.40	90	92
3	Pineapple extract	3.71	90	73
4	Grapefruit extract	3.38	100	79
5	Orange extract	3.51	90	65
6	Tangerine extract	3.90	60	60

[a] Reaction conditions: salicylaldehyde **1** (1.1 mmol) and 1,3-dimedone **2** (2.2 mmol), biosurfactant : water (1 : 1 v/v), 80 °C temperature. [b] Isolated yield based on salicylaldehyde.

Inspired by these tempting results obtained for cyclocondensation of benzopyran, we extended a same protocol for treating various 1,3-diketones **2** with 2-hydroxy naphthaldehyde **4** (Scheme 2) and we found that these substrates also worked very efficiently under this catalytic system (Table 4).

As discussed before, in the absence of the catalyst, the reaction proceeded sluggishly which explains the role of catalytic activity of biosurfactant in product formation. Under ambient conditions, surfactant molecules can aggregate in an aqueous phase to form micelles with hydrophobic core and hydrophilic corona. The use of micellar surfactants as a catalyst is widespread and has been investigated in detail for various reactions in aqueous solutions.[32] The role of micelle to catalyze the reaction is schematically represented in Fig. 2a.

As the impact of micellar solution, hydrophobic reactants *i.e.* salicylaldehyde and 1,3-diketones get pushed away from water molecules towards the hydrophobic core of micelle leading to the effective collisions and water formed by condensations is repelled out to give corresponding Knoevenagel product **6**, which was further reacted with another molecule of 1,3-diketones with shifting of equilibrium towards formation of desired product **3** (Scheme 3) with excellent yield.

During the progress of the reaction, the reaction mixture turned turbid due to the formation of colloidal aggregates which was confirmed on the basis of optical microscopy (Fig. 2b). At the critical micelle concentration (CMC) of

Table 3 Biosurfactant catalysed synthesis of benzopyran[a]

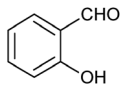
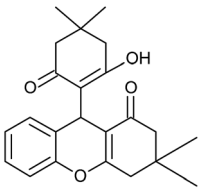
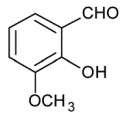
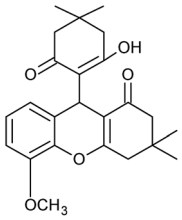
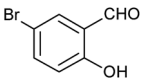
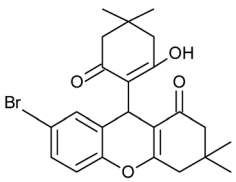
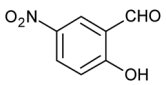
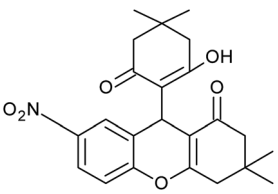
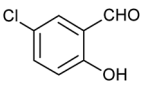
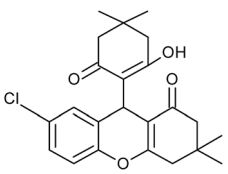
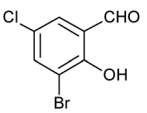
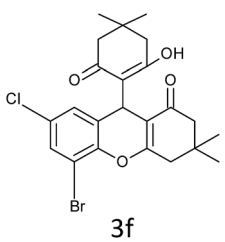
Entry	Carbonyl compounds	Products	Time (min)	Yield[b] (%)
1		 3a	40	96
2		 3b	45	80
3		 3c	45	92
4		 3d	30	91
5		 3e	30	91
6		 3f	30	90

Table 3 (*Contd.*)

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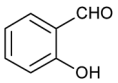
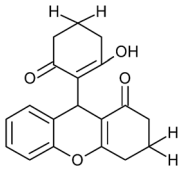
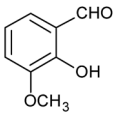
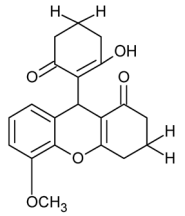
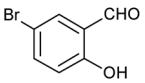
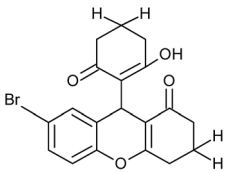
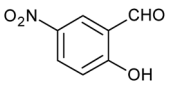
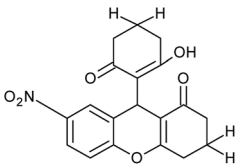
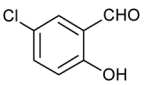
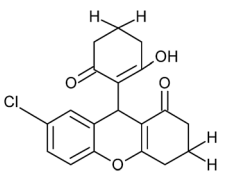
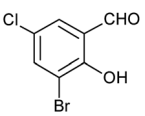
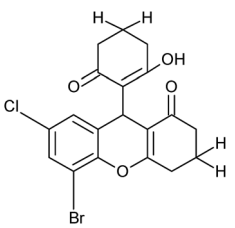
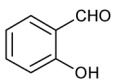
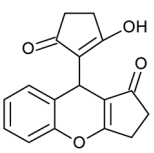
7		 3g	60	87
8		 3h	55	84
9		 3i	45	88
10		 3j	40	93
11		 3k	45	94
12		 3l	50	91
13		 3m	60	87

Table 3 (*Contd.*)

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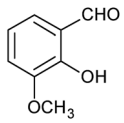
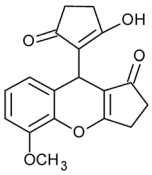
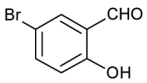
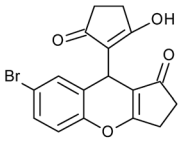
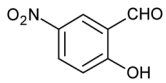
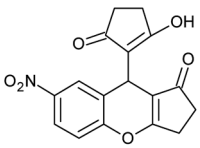
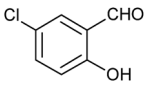
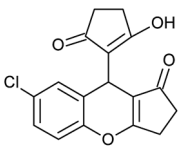
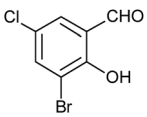
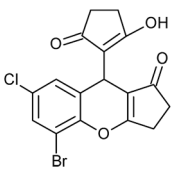
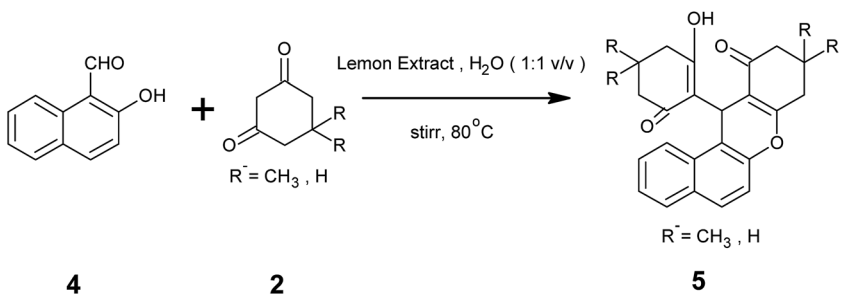
14		 3n	60	84
15		 3o	50	86
16		 3p	40	89
17		 3q	50	90
18		 3r	40	91

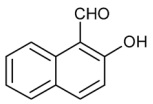
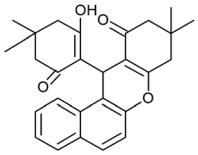
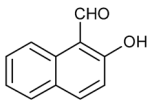
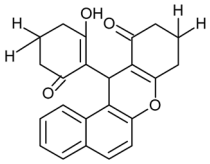
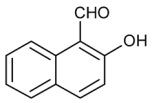
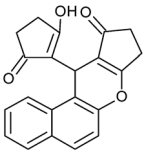
[a] Reaction conditions: salicylaldehydes **1** (1.1 mmol) and 1,3-diketones **2** (2.2 mmol), biosurfactant (3 mL), water (3 mL), 80 °C temperature. [b] Isolated yield based on salicylaldehyde.



4 **2** **5**

Scheme 2 Reaction of 2-hydroxy naphthaldehyde and cyclic 1,3-diketones under optimized conditions.

Table 4 Biosurfactant catalysed cyclocondensation of 2-hydroxy naphthaldehyde and cyclic 1,3-diketones[a]

Entry	Carbonyl compounds	Products	Time (min)	Yield[b] (%)
1		 5a	60	95
2		 5b	60	91
3		 5c	60	94

[a] Reaction conditions: 2-hydroxy naphthaldehyde **4** (1.1 mmol) and cyclic 1,3-diketone **2** (2.2 mmol), biosurfactant (3 mL), water (3 mL), 80 °C temperature. [b] Isolated yield based on 2-hydroxy naphthaldehyde **5**.

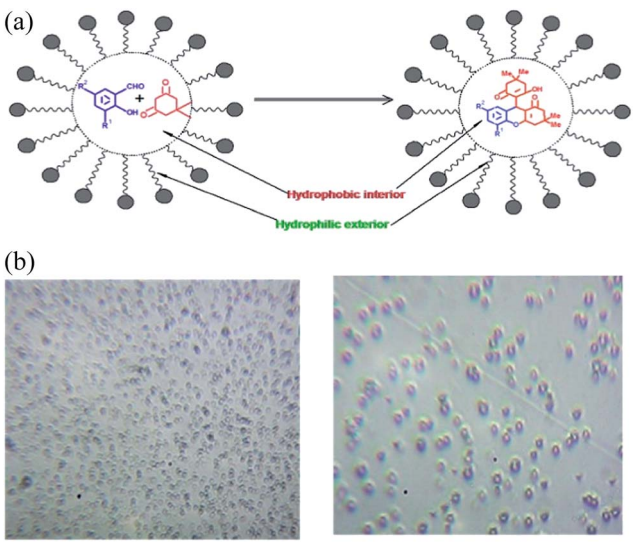


Fig. 2 (a) Mechanistic picture of role of micellae for benzopyran formation. (b) Optical micrograph of model reaction mixture normal view and magnified view.

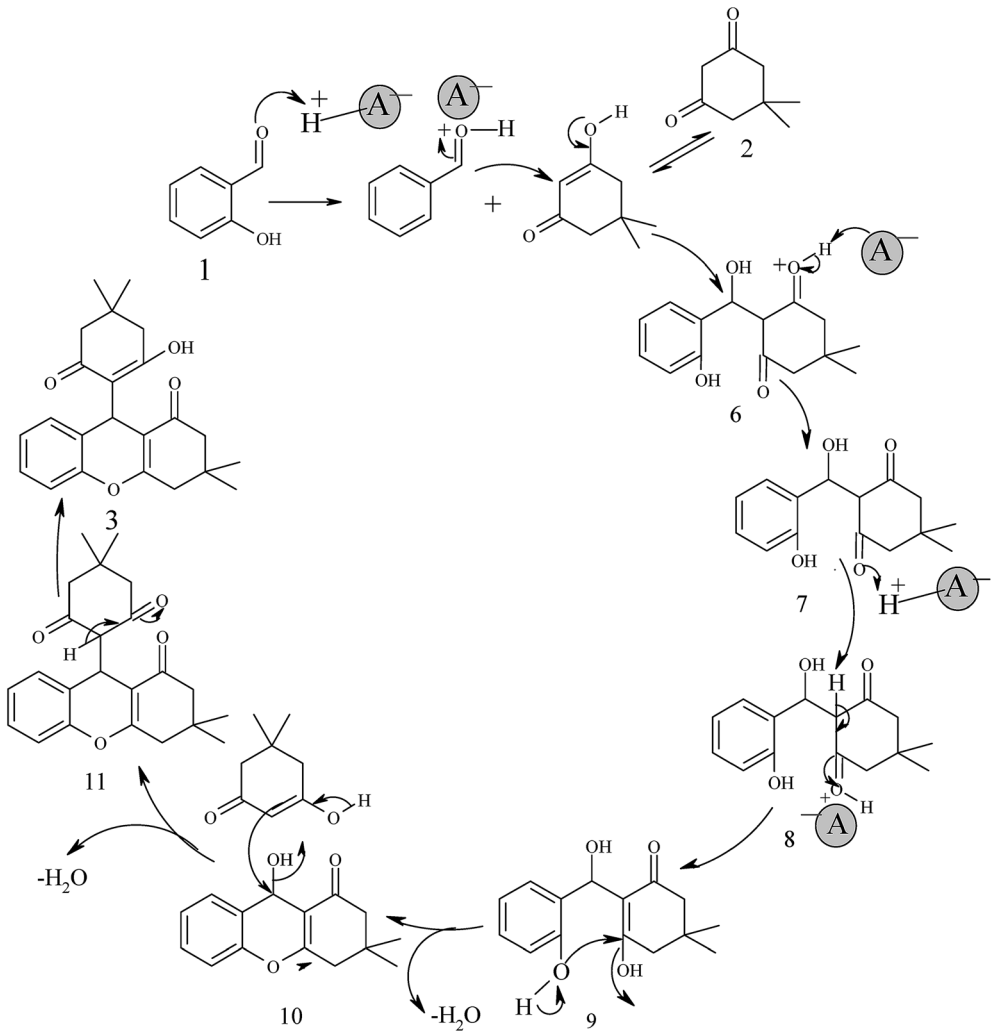
surfactant solutions, a drastic change occurs in physico-chemical properties such as conductivity, surface tension, turbidity *etc.*[33] To maintain better lemon extract : water composition for this cyclocondensation, we employed electrical conductivity method to determine the critical micelle concentration (CMC) and it was found to be 40% v/v (Fig. 3).

Then, we compared our catalytic data with that found in the literature. Comparison of the results shows a better catalytic activity of biosurfactant for synthesis of benzopyrans (Table 5).

In summary, we have introduced a highly efficient, straightforward bioorganic approach for benzopyran synthesis *via* Knoevenagel condensation and tandem Knoevenagel–Michael reaction which represents eco-friendly and environmental benign system. Simplicity of product separation, clean reaction profile, and utilization of biodegradable catalyst obtained from renewable resource provide attractive alternative to the previously reported methodologies. Therefore, this new acidic natural biosurfactant should thereby provide attractive alternative to the harmful corrosive acids. We expect that the methodology presented hereby will find great utility in academic and industrial applications in the near future.

Experimental

All the chemicals were commercially sourced from Sigma Aldrich and used without further purification. The melting points were determined on DBK programmable melting point apparatus and are uncorrected. Infrared spectra were measured with a Bruker FT-IR spectrophotometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC (300 MHz for ^{1}H NMR and 300 MHz for ^{13}C NMR) spectrometer using $CDCl_3$ as a solvent. The chemical shifts are expressed in δ parts per million (ppm) values with tetramethylsilane (TMS) as the



Scheme 3 Plausible mechanism for the reaction between salicylaldehyde **1** and 1,3-dimedone **2** catalyzed by acidic biosurfactant ($H^+\cdots A^-$).

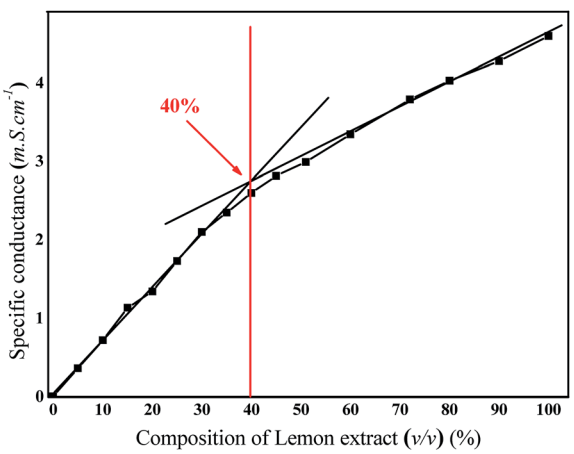


Fig. 3 Critical micellar concentration (CMC) obtained from plot of specific conductance against percentage composition of biosurfactant.

internal reference. The Equiptronics (Model EQ-664A) digital auto ranging conductivity meter was used for the measurement of critical micellar concentration. For the preparation of fruit extract, fresh *Citrus limonium* fruits were obtained from the local market, and species was authenticated by the Department of Botany. The small pieces of a fruit was pressed manually by domestic pressure to get turbid extract and filtered through filter paper and muslin cloth to get clean, pale-yellow-colored extract. This extract was stored below 5 °C temperature and found to be stable for several days.

Optical microscopy measurements: a drop of turbid reaction mixture was subjected to light microscopy measurement using an ordinary light microscope under 100× magnification.

Typical procedure for synthesis of 9-(2-hydroxy-4,4-dimethyl-6-oxo-cyclohex-1-enyl)-3,3-dimethyl-2,3,4,9-tetrahydroxanthen-1-one

In a 25 mL round bottom flask, salicylaldehyde (1.1 mmol), 1,3-dimedone (2.2 mmol) were placed in lemon extract : water (6 mL, 1 : 1, v/v) and reaction mixture was stirred at 80 °C

Table 5 Comparison of biosurfactant with other catalysts in the literature to synthesize benzopyran

Sr. no.	Catalyst	Solvent	Reaction condition	Yield (%)	References
1	KF/Al_2O_3	Ethanol	80 °C, 0.25 gm	83	27
2	Triethylbenzylammoium chloride (TEBA)	Water	90 °C, 0.1 g, 5 h	86	28
3	Cellulose sulfuric acid	Solvent free	RT, 0.08 g, grinding, 30 min	96	28 (cross ref.)
4	2,4,6-Trichloro-1,3,5-triazine	Solvent free	120 °C, 10 mol%, 2.5 h	93	29
5	*p*-TSA	Water	90 °C, 10 mol%, 30 min	83	30
6	Lemon juice	Water	80 °C, 3 mL, 40 min	96	Present work

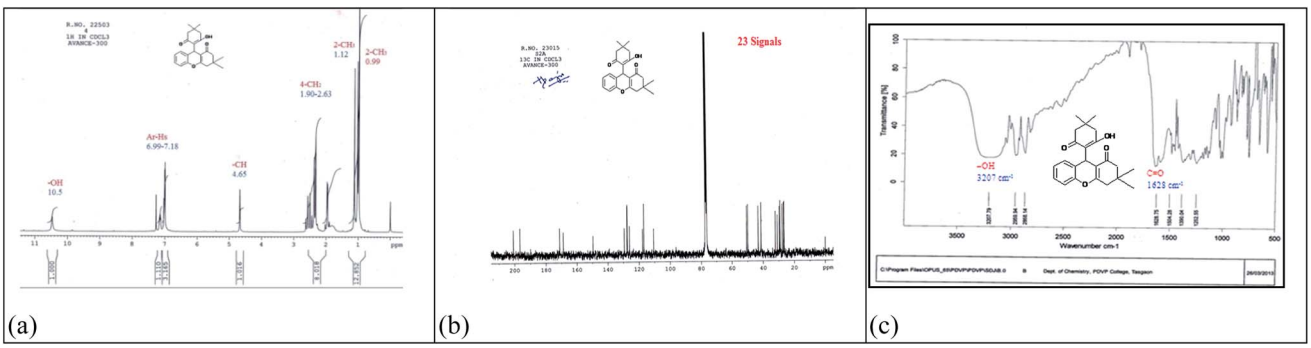


Fig. 4 (a) ^1H NMR ($CDCl_3$) spectrum of compound **3a**. (b) ^{13}C NMR ($CDCl_3$) spectrum of compound **3a**. (c) FT-IR spectrum of the compound **3a**.

temperature in preheated oil-bath till the completion of reaction as indicated by TLC (ethylacetate : hexane 4 : 6). The solid products was separated by simple filtration through a Buchner funnel, washed with cold water, and recrystalyzed from 96% ethanol (5 mL). The identity of the compound was ascertained on the basis of ^1H NMR, ^{13}C NMR, and FT-IR spectroscopy (Fig. 4a–c). The physical and spectroscopic data are in consistent with the proposed structure and is in harmony with the literature values.

Physical and spectroscopic data of selected compounds are as follow:

9-(2-Hydroxy-4,4-dimethyl-6-oxo-cyclohex-1-enyl)-3,3-dimethyl-2,3,4,9-tetrahydroxanthen-1-one. Yield: 96%; mp 215–218 °C; ^1H NMR (300 MHz, $CDCl_3$): d 10.50 (s, 1H, –OH), 7.08–7.16 (m, 1H, Ar–H), 6.93–7.01 (m, 3H, Ar–H), 4.65 (s, 1H, –CH), 2.54 (q, $J = 17.7$, 20.0 Hz, 2H, $–CH_2$), 2.35 (s, 2H, $–CH_2$), 2.30 (s, 2H, $–CH_2$), 1.93 (q, $J = 6.0$, 16.4 Hz, 2H, $–CH_2$), 1.14 (s, 3H, $–CH_3$), 1.03 (s, 3H, $–CH_3$), 1.00 (s, 6H, 2-CH_3); ^{13}C NMR (300 MHz, $CDCl_3$): d 200.40, 196.13, 170.53, 168.78, 151.04, 127.98, 127.52, 124.53, 118.31, 115.78, 111.07, 96.20, 50.58, 49.93, 43.24, 41.60, 32.33, 31.02, 29.85, 29.43, 27.79, 27.21, 26.42; IR (cm^{-1}): 3153, 2958, 1622, 1488, 1376, 1312, 1233, 1185, 1151, 1077, 1019, 762, 655, 582, 475; MS: 367 (M + 1), 389 (M + Na). Anal. calcd for $C_{23}H_{26}O_4$: C, 75.38; H, 7.15; O, 17.46. Found: C, 75.33; H, 7.15; HRMS *m*/*z* calcd for $C_{23}H_{26}O_4$: 366.0000, found 367.1918 (M + H), 389.1737 (M + Na).

3-Methoxy-9-(2-hydroxy-4,4-dimethyl-6-oxo-cyclohex-1-enyl)-3,3-dimethyl-2,3,4,9-tetrahydro-xanthen-1-one (Table 3, entry 2). Yield: 80%; mp 224–227 °C; ^1H NMR (300 MHz, $CDCl_3$): d 10.50 (s, 1H, –OH), 7.08–7.21 (m, 1H, Ar–H), 6.93–7.01 (m, 3H, Ar–H), 4.63 (s, 1H, –CH), 2.54 (q, $J = 17.7$, 20.0 Hz, 2H, $–CH_2$), 2.35 (s, 2H, $–CH_2$), 2.30 (s, 2H, $–CH_2$), 1.93 (q, $J = 6.0$, 16.4 Hz, 2H, $–CH_2$), 3.88 (s, 1H, $–OCH_3$), 1.14 (s, 3H, $–CH_3$), 0.93 (s, 9H, 3CH_3); ^{13}C NMR (300 MHz, $CDCl_3$): 200.40, 196.521, 170.554, 168.800, 147.081, 140.658, 125.203, 124.203, 119.760, 118.149, 110.887, 110.370, 56.058, 50.623, 49.930, 43.167, 41.533, 32.288, 30.887, 29.852, 29.051, 27.755, 27.162, 26.421.

7-Bromo-9-(2-hydroxy-4,4-dimethyl-6-oxo-cyclohex-1-enyl)-3,3-dimethyl-2,3,4,9-tetrahydro-xanthen-1-one (Table 3, entry 3). Yield: 92%; mp 248–251 °C; ^1H NMR (300 MHz, $CDCl_3$): d 10.15 (s, 1H, –OH), 7.21–7.24 (dd, $J = 1.9$, 6.8 Hz, 1H, Ar–H), 7.08 (s, 1H, Ar–H), 6.87 (d, $J = 8.7$ Hz, 1H, Ar–H), 5.02 (s, 1H, –CH–), 2.28–2.59 (m, 6H, 3-CH_2), 1.95 (s, 2H, $–CH_2$), 1.33 (s, 3H, $–CH_3$), 0.99–1.05 (m, 9H, 3-CH_3); ^{13}C NMR (300 MHz, $CDCl_3$ + DMSO): d 195.65, 164.328, 148.794, 130.563, 129.103, 127.741, 116.932, 115.413, 110.34, 50.27, 40.65, 40.33, 40.05, 39.78, 39.22, 38.94, 38.66, 31.35, 31.27, 28.93, 27.56, 26.30; IR (cm^{-1}): 3103, 2963, 1618, 1475, 1374, 1302, 1231, 1178, 1075, 1037, 884, 817, 657, 590, 478; MS: 445 (M + 1), 447 (M + 2). Anal. calcd for $C_{23}H_{25}BrO_4$: C, 62.03; H, 5.66; Br, 17.94; O, 14.37. Found: C, 62.03; H, 5.65. HRMS *m*/*z* calcd for: $C_{23}H_{25}BrO_4$: 445.0000, found 445.1003 $(M)^+$.

7-Chloro-9-(2-hydroxy-4,4-dimethyl-6-oxo-cyclohex-1-enyl)-3,3-dimethyl-2,3,4,9-tetrahydro-xanthen-1-one (Table 3, entry 5). Yield: 91%; mp 232–234 °C; ^1H NMR (300 MHz, $CDCl_3$): d 10.50 (s, 1H, –OH), 7.09 (dd, $J = 2.2$, 2.6 Hz, 1H, Ar–H), 6.91–6.97 (m, 2H, Ar–H), 4.61 (s, 1H, –CH), 2.52 (q, $J = 17.3$, 18.5 Hz, 2H, $–CH_2$), 2.37 (d, $J = 4.9$ Hz, 2H, $–CH_2$), 2.30 (s, 2H, $–CH_2$), 1.96 (s, 2H, $–CH_2$), 1.14 (s, 3H, $–CH_3$), 1.00–1.05 (m, 9H, 3-CH_3); IR (cm^{-1}): 3102, 2965, 2710, 1624, 1571, 1476, 1374, 1301, 1233, 1179, 1077, 1038, 1015, 879, 819, 657, 618, 591, 549, 469; MS: 401 (M + 1), 403 (M + 2). Anal. calcd for $C_{23}H_{25}ClO_4$: C, 68.91; H, 6.29; Cl, 8.84; O, 15.96. Found: C, 68.89; H, 6.24. HRMS *m*/*z*

calcd for $C_{23}H_{25}ClO_4$: 400.0000, found 401.1529 (M + H), 423.1328 (M + Na).

5-Bromo-7-chloro-9-(2-hydroxy-4,4-dimethyl-6-oxo-cyclohex-1-enyl)-3,3-dimethyl-2,3,4,9-tetrahydro-xanthen-1-one (Table 3, entry 6). Yield: 90%; mp 241–243 °C; ^{1}H NMR (300 MHz, $CDCl_3$): d 10.34 (s, 1H, –OH), 7.36 (d, J = 2.2 Hz, 1H, Ar–H), 6.90 (d, J = 2.0 Hz, 1H, Ar–H), 4.60 (s, 1H, –CH), 2.62 (q, J = 17.7, 18.5 Hz, 2H, $-CH_2$), 2.38 (d, J = 4.5 Hz, 2H, $-CH_2$), 2.31 (s, 2H, $-CH_2$), 1.97 (s, 2H, $-CH_2$), 1.16 (s, 3H, $-CH_3$), 1.00–1.05 (m, 9H, 3-CH_3); ^{13}C NMR (300 MHz, $CDCl_3$): d 196.47, 195.10, 163.43, 144.77, 128.68, 127.79, 127.41, 126.35, 112.78, 109.93, 108.78, 94.79, 49.58, 49.03, 39.81, 30.77, 28.24, 26.92, 26.03, 25.64, 25.17; IR (cm^{-1}): 3184, 2940, 1647, 1599, 1452, 1375, 1313, 1257, 1207, 1183, 1150, 1017, 887, 855, 803, 722, 662, 587, 475; MS: 479 (M^+), 481 (M + 2). Anal. calcd for $C_{23}H_{24}BrClO_4$: C, 57.58; H, 5.04; Br, 16.65; Cl, 7.39; O, 13.34. Found: C, 57.57; H, 5.04; HRMS m/z calcd for $C_{23}H_{23}ClBrO_4$: 478.0000, found 479.0618 (M + H), 481.0602 (M + 2) 501.0421 (M + Na), 503.0415 (M + Na + 2).

9-(2-Hydroxy-6-oxo-cyclohex-1-enyl)-2,3,4,9-tetrahydro-xanthen-1-one (Table 3, entry 7). Yield: 87%; mp 240–243 °C; ^{1}H NMR (300 MHz, $CDCl_3$): d 10.00 (s, 1H, –OH), 6.80–7.14 (m, 4H, Ar–H), 4.84 (s, 1H, –CH), 1.60–2.40 (m, 12H, 6-CH_2); IR (cm^{-1}): 2951, 2538, 1830, 1641, 1553, 1485, 1421, 1372, 1294, 1235, 1192, 1142, 1071, 993, 924, 850, 773, 564, 493 MS: 311 (M + 1). Anal. calcd for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85; O, 20.62. Found: C, 73.52; H, 5.84; HRMS m/z calcd for $C_{19}H_{18}O_4$: 310.0000, found 311.1295 (M + H), 333.1081 (M + Na).

7-Bromo-9-(2-hydroxy-6-oxo-cyclohex-1-enyl)-2,3,4,9-tetrahydro-xanthen-1-one (Table 3, entry 9). Yield: 88%; mp 238–240 °C; ^{1}H NMR (300 MHz): d 10.75 (s, 1H, –OH), 7.25 (d, J = 3.0 Hz, 1H, Ar–H), 7.09 (d, J = 2.2 Hz, 1H, Ar–H), 6.89 (dd, J = 5.2, 6.0 Hz, 1H, Ar–H), 4.57 (s, 1H, –CH), 1.76–2.85 (m, 12H, 6-CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): 202.18, 193.99, 167.43, 166.15, 148.45, 129.74, 129.28, 128.61, 126.86, 116.51, 116.10, 115.09, 47.57, 35.57, 35.02, 33.26, 26.02, 22.80, 18.95; IR (cm^{-1}): 3105, 2955, 1640, 1596, 1477, 1374, 1279, 1233, 1186, 1144, 1070, 981, 819, 763, 620, 530, 470; MS: 389 (M + 1) 391 (M + 2); anal. calcd. For $C_{19}H_{17}BrO_4$: C, 58.63; H, 4.40; Br, 20.53; O, 16.44, found: C, 58.63; H, 4.39; HRMS m/z calcd for $C_{19}H_{17}BrO_4$: 389.0000, found 391.0551 (M + 2).

7-Chloro-9-(2-hydroxy-6-oxo-cyclohex-1-enyl)-2,3,4,9-tetrahydro-xanthen-1-one (Table 3, entry 11). Yield: 94%; mp 242–244 °C; ^{1}H NMR (500 MHz, $CDCl_3$): d 10.76 (s, 1H, –OH), 7.09 (d, J = 6.3 Hz, 1H, Ar–H), 6.91–6.96 (m, 2H, Ar–H), 4.57 (s, 1H, –CH), 1.77–2.81 (m, 12H, 6-CH_2); ^{13}C NMR (300 MHz, $CDCl_3$ + DMSO-d6): 201.86, 193.94, 167.23, 165.96, 147.56, 127.13, 126.76, 125.61, 124.53, 115.52, 110.65, 99.74, 47.08, 35.47, 34.82, 33.05, 26.35, 22.69, 19.03; IR (cm^{-1}): 3110, 2954, 1645, 1596, 1477, 1416, 1375, 1280, 1239, 1188, 1141, 1068, 984, 917, 824, 576, 460; MS: 345 (M^+), 347 (M + 2). Anal. calcd for $C_{19}H_{17}ClO_4$: C, 66.19; H, 4.97; Cl, 10.28; O, 18.56, found: C, 66.18; H, 4.97.

5-Bromo-7-chloro-9-(2-hydroxy-6-oxo-cyclohex-1-enyl)-2,3,4,9-tetrahydro-xanthen-1-one (Table 3, entry 12). Yield: 91%; mp 238–240 °C; ^{1}H NMR (300 MHz, $CDCl_3$): d 10.44 (s, 1H, –OH), 7.30 (d, J = 2.6 Hz, 1H, Ar–H), 6.95 (d, J = 1.7 Hz, 1H, Ar–H), 5.04 (s, 1H, –CH), 1.93–2.12 (m, 4H, 2-CH_2), 2.25–2.51 (m, 8H, 4-CH_2); ^{13}C NMR (300 MHz, $CDCl_3$): 195.44, 163.90, 145.45, 129.31, 128.72, 127.93, 110.62, 109.50, 50.29, 40.33, 40.05, 39.77, 39.50, 39.2, 38.94, 38.76, 31.45, 31.3, 28.97, 27.56, 26.69, 26.20, 25.75, 29; IR (cm^{-1}): 49, 2887, 2526, 1651, 1560, 1452, 1363, 1279, 1245, 1185, 1133, 1063, 1007, 857, 765, 707, 538, 500, 438; MS: 423 (M^+), 425 (M^{+2}) anal. calcd for $C_{19}H_{16}BrClO_4$: C, 53.86; H, 3.81; Br, 18.86; Cl, 8.37; O, 15.11, found: C, 53.85; H, 3.81.

5-Methoxy-2,3-dihydro-9-(2-hydroxy-5-oxocyclopent-1-enyl)-cyclopenta[*b*]chromen-1(9*H*)-one (Table 3, entry 14). Yield: 84%; mp 257–260 °C; ^{1}H NMR (300 MHz DMSO): 2.29–2.36 (m, 6H, 3CH_2), 2.72–2.74 (m, 2H, CH_2), 3.82 (s, 3H, CH_3O), 4.58 (s, 1H, CH), 6.58–6.60 (m, 1H, ArH), 6.92 (dd, J = 8.0 Hz, J = 1.2 Hz, 1H, ArH), 6.99–7.03 (m, 1H, ArH), 11.80 (b, 1H, OH); IR (cm^{-1}): 3438, 3024, 2971, 2939, 1682, 1637, 1579, 1480, 1445, 1380, 1322, 1273, 1255, 1237, 1170, 1125, 1076, 825, 788, 739, 716.

7-Bromo-2,3-dihydro-9-(2-hydroxy-5-oxocyclopent-1-enyl)-cyclopenta[*b*]chromen-1(9*H*)-one (Table 3, entry 15). Yield: 86%; mp 280–282 °C; ^{1}H NMR (300 MHz DMSO): 2.26–2.43 (m, 6H, 3CH_2), 2.56–3.34 (m, 2H, CH_2), 5.01 (s, 1H, CH), 7.01–7.24 (m, 2H, ArH), 7.27 (d, J = 8.4 Hz, 1H, ArH), 10.60 (b, 1H, OH); IR (cm^{-1}): 3505, 2932, 2910, 1699, 1653, 1585, 1474, 1383, 1276, 1259, 1240, 1198, 1160, 1126, 1071, 1018, 818, 707, 659.

7-Nitro-2,3-dihydro-9-(2-hydroxy-5-oxocyclopent-1-enyl)cyclopenta[*b*]chromen-1(9*H*)-one (Table 3, entry 16). Yield: 89%; mp 265–268C °C; ^{1}H NMR (300 MHz DMSO): 2.34–2.41 (m, 6H, 3CH_2), 2.74–2.76 (m, 2H, CH_2), 4.72 (s, 1H, CH), 7.41 (d, J = 8.8 Hz, 1H, ArH), 7.87 (d, J = 2.4 Hz, 1H, ArH), 8.11 (dd, J = 8.8 Hz, J = 2.4 Hz, 1H, ArH), 12.06 (b, 1H, OH). IR (cm^{-1}): 3512, 2943, 2926, 1698, 1656, 1581, 1528, 1481, 1458, 1379, 1277, 1253, 1168, 1134, 1020, 929, 912, 840, 805, 748, 666.

7-Chloro-2,3-dihydro-9-(2-hydroxy-5-oxocyclopent-1-enyl)cyclopenta[*b*]chromen-1(9*H*)-one (Table 3, entry 17). Yield: 90%; mp 271–273 °C; ^{1}H NMR (300 MHz DMSO): 2.33–2.38 (m, 6H, 3CH_2), 2.71–2.73 (m, 2H, CH_2), 4.60 (s, 1H, CH), 7.01 (dd, J = 2.4 Hz, J = 1.2 Hz, 1H, ArH), 7.18 (d, J = 8.8 Hz, 1H, ArH), 7.27–7.30 (m, 1H, ArH), 12.00 (b, 1H, OH); IR (cm^{-1}): 3508, 2935, 2914, 1699, 1654, 1583, 1477, 1409, 1384, 1277, 1259, 1240, 1162, 1126, 1018, 819, 677.

7,8-h-ph-9-(2-Hydroxy-4,4-dimethyl-6-oxocyclohex-1-enyl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3h) (Table 4, entry 1). Yield: 95% mp 235–237 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.70 (s, 1H, OH), 7.78 (d, 1H, ArH), 7.73 (d, 2H, ArH), 7.48 (t, 1H, ArH), 7.39 (t, 1H, ArH), 7.27 (d, 1H, ArH), 5.27 (s, 1H, CH), 2.68 (AB_q, J = 17.6 Hz, 1H, CH_2), 2.57 (AB_q, J = 17.6 Hz, 1H, CH_2), 1.96 (AB_q, J = 16.4 Hz, 1H, CH_2), 1.83 (AB_q, J = 16.4 Hz, 1H, CH_2), 2.36–2.41 (m, 4H, 4CH_2), 1.17 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 0.72 (s, 3H, CH_3) ppm; ^{13}C NMR (300 MHz, $CDCl_3$) δ = 201.11, 196.85, 170.22, 169.09, 148.89, 131.26, 130.96, 158.54, 128.50, 126.71, 124.64, 122.87, 117.68, 116.59, 116.14, 111.08, 50.71, 49.98, 43.18, 41.37, 32.42, 30.62, 29.92, 29.33, 27.10, 26.37, 25.38 ppm; IR (KBr): 3182, 2941, 2862, 1643, 1593, 1464, 1373, 1315, 1261, 1235, 1061, 1026, 888, 813 cm^{-1}.

Conclusions

In conclusion, we developed a simpler, more convenient, and more efficient procedure for synthesis of benzopyran from the

various salicylaldehydes (or 2-hydroxy naphthaldehyde) and cyclic 1,3-diketones using catalytic amount of lemon extract as a green biosurfactant under mild reaction conditions. The use of the low-cost, biodegradable biosurfactant in replacement to toxic synthetic surfactants is a promising alternative for the organic transformations. Usability of the catalyst in aqueous medium caters to a more 'green' and eco-friendly solution towards benzopyran formation.

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