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Ash of pomegranate peels (APP): A bio-waste heterogeneous catalyst for sustainable synthesis of α,α′-bis(substituted benzylidine)cycloalkanones and 2-arylidene-1-tetralones

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Abstract

α,α′-bis(substituted benzylidene)cycloalkanones were efficiently prepared from variously substituted aldehydes and cycloalkanones in water by using ash of pomegranate peels (APP) as a catalyst. The APP-catalyst was obtained from bio-waste by simple thermal treatment to dry peels of pomegranate fruit and formation of its active phase was confirmed by FT-IR, XRD, XRF, EDX, SEM, DSC-TGA and BET techniques. The analysis revealed that the present catalyst has basic sites which promote the synthesis of desired products. The main attractions of our protocol are utilization of highly abundant bio-waste-derived catalyst and good-to-excellent yield in shortest reaction time. This green protocol was further extended for structurally diverse 2-arylidene-1-tetralones by condensation of equimolar quantity of aromatic aldehydes and 1-tetralone at low temperature. The catalyst could be quantitatively recovered and reused effectively for five times.

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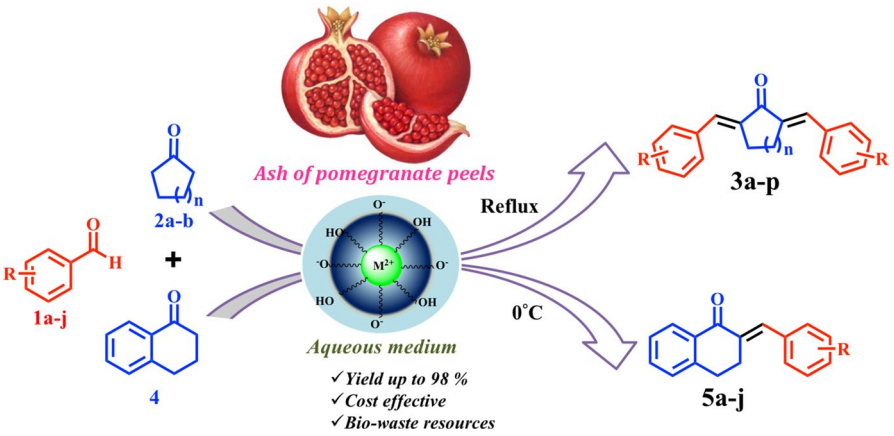
Graphic abstract



Keywords α,α′-Bis(substituted benzylidene)cycloalkanones · 2-Arylidene-1-tetralones · Bio-waste · Pomegranate peels · Natural catalyst

Introduction

In the modern era of synthetic chemistry, the synthesis of complex and diverse molecular architectures from simple and easily available starting materials while simultaneously meeting environmental and economic concerns is important from both industrial and academic points of view [1]. The development of proactive path for organic transformations with high efficacy and reduced environmental impact is an important goal in green chemistry and future sciences. While considering increasing environmental pollution and its intensive impact on living systems, the development of chemical processes using more environment-friendly chemicals, atom-efficient methods and energy-saving technologies eliminating waste production is the urgent requirement [2]. Furthermore, owing to typical reactivity and selectivity, reactions are preferred in green solvents like water because it is easily available, non-toxic and non-flammable solvent. Reactions in aqueous medium not only possess negative activation volume but also help in controlling exothermic reactions. Hence, organic transformations under aqueous conditions are preferred from both environmental and economical point of view [3].

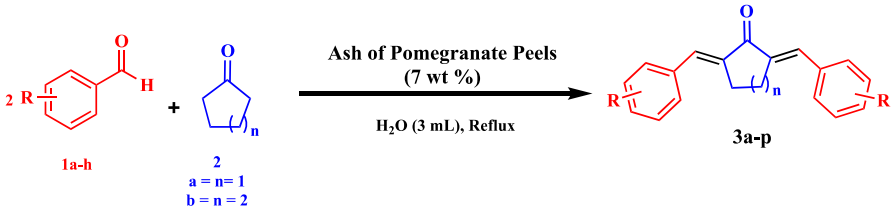
Bis-benzylidene cycloalkanone derivatives find a broad range of applications in the field of biology, medicinal chemistry and pharmacology. This structural motif is broadly represented by several types of natural products, manifesting diverse biological and pharmacological activities including pharmaceutical [4], agrochemical and perfume intermediates [5] as well as synthesis of liquid crystal polymers [6], also these are very important precursors to potentially bioactive pyrimidine derivatives [7], quinine reductase inducer derivatives [8],

cholesterol-lowering agents [9], antiparasitic agents [10], bis-spiropyrrolidines [11], cytotoxicity [12] histone acetyl transferase inhibitory activities [13] and many others.

On the account of widespread applicability of bis-benzylidene cycloalkanone derivatives, considerable attention has been focused on the development of clean, efficient and environment-friendly methodologies to synthesize these scaffolds via one-pot three-component reactions. The literature report revealed that very limited methodologies have been reported for the synthesis of bis-benzylidene cycloalkanone such as microwave [14], ultra-sound irradiation [15], basic catalyst [16], ionic liquids [17], micellar media [18], nano-materials [19], organometallic complexes [20] and polymer-supported catalyst [21]. Each of these methods has its own merit, but some of them suffer from demerits such as use of organic solvents, hazardous reagents, time-consuming processes, sometimes non-reproducible base catalysts and complications for the separation of homogeneous catalysts from the reaction mixture are the problems associated with these methods.

At present, synthetic processes involving bio-waste-derived catalysts are receiving much attention as a viable alternative for the development of green methodologies in organic transformations [22–24]. Bio-wastes are a better choice in certain conditions because of number of characteristics such as they are cheapest, obtained from renewable resources, a very simple procedure is followed in the preparation, the strategy involved also provides a high yield and good recyclability of the catalyst. Therefore, the objective of the present work is to explore the synthetic utility of bio-waste as a natural catalyst in organic transformations.

Interestingly, in recent years, various types of agro-waste biomass have been used as catalysts for numerous organic transformations [25, 26]. Nevertheless, to the best of our knowledge, there are no any reports in the literature where the agro biomass is exploited as a catalyst for cross-aldol condensation reaction. In continuation of our research program concerning the development of naturally sourced catalysts [27–30], we are going to utilize bio-waste pomegranate fruit peels after thermal treatment as an efficient catalyst for cross-aldol condensation. Herein, we report for the first time, a simple and environmentally benign route for the exclusive synthesis of a, a'-bis(substituted benzylidene)cycloalkanones via a cross-aldol condensation reaction (Scheme 1) using APP-catalyst as a heterogeneous solid catalyst in aqueous medium without addition of any external base.



Scheme 1 Synthesis of a, a'-bis(substituted benzylidene)cycloalkanones using APP-catalyst

Experimental procedure

Materials and methods

Except pomegranate fruit peels, all chemicals used in the study were purchased from *Sigma-Aldrich* and used without additional drying and purification. The formation of products was checked by TLC on precoated Merck silica gel 60 F254 aluminum sheets. IR spectrum was recorded in ATR technique on a Bruker ALPHA FT-IR spectrometer. XRD measurements were carried out on a Bruker AXS analytical instrument Pvt. Ltd. Germany, Model: D2 phaser with Cu Kα radiation (λ = 1.54060A°) at 40 mA, 45 kV a scan step time 10.3366 s, a start position 10.0184 and end position 99.9824 [2°Th]. SEM images were obtained on FEI, NOVA, NanoSem 450 equipment. Quanta 200 3D, FEI scanning electron microscope used for energy-dispersive X-ray spectroscopy (EDX) analysis. N_2-adsorption–desorption isotherms were obtained with a BELSORP surface area and porosity analyzer. XRF analysis of APP-catalyst was performed on X-ray fluorescence spectrometer (Pananlytical, USA). The thermal gravimetric analysis (TGA) was obtained using a TA SDT Q600 V20.9 Build 20 instrument in the presence of air at a linear heating rate of 10 °C min^{-1}. Proton and carbon-13 NMR spectra were measured with Avance-300 instrument in $CDCl_3$ and DMSO as a solvent with TMS as an internal standard.

Preparation of catalyst

During this study, pomegranate fruit peels (PFP) (Fig. 1a) were obtained from the dumping waste of local food processing industry and the APP-catalyst was obtained by thermal treatment in Muffle furnace. Initially, all attached impurities were removed by washing several times with tap water and left in open air for two hours. Later, they were transferred to the oven at 100 °C for drying. The dried peels (100 g) were manually broken into small pieces then convert to peels powder (Fig. 1b), which were treated at heating rate of 5 °C/min in muffle furnace up to 1000 °C and this temperature was maintained for 1 h. After thermal treatment, most of the organic materials were burnt out and got transformed into white soft ash (8.3 g). The resulting white ash (Fig. 1c) obtained was nominated as APP and utilized for cross-aldol condensation reaction.

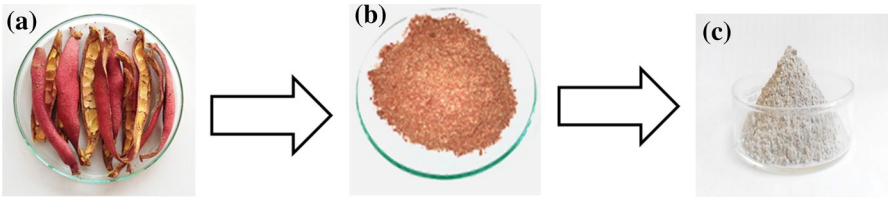


Fig. 1 **a** Dry pomegranate fruit peels, **b** peel powder, **c** APP-catalyst

Typical procedure for synthesis of 2, 6-bis(4-methoxybenzylidene)cyclohexanone (3j)

A mixture of 4-methoxybenzaldehyde (2 mmol) and cyclohexanone (1 mmol) in water (3 mL) was well stirred in the presence of APP-catalyst (7 wt%) under reflux condition until completion of the reaction (30 min) monitored by TLC. After completion of the reaction, the separated solid product was obtained by simple filtration followed by washing with distilled water (2x5 mL) and further purified by recrystallization from 96% ethanol. All other derivatives (3a–p) were synthesized by following same protocol and confirmed by spectral techniques.

Typical procedure for synthesis of 2-(4-methoxybenzylidene)-1-tetralone (5a)

An equimolar mixture of 4-methoxybenzaldehyde (1 mmol) and 1-tetralone (1 mmol) in water (3 mL) was magnetically stirred in the presence of APP-catalyst (7 wt%) at 0 °C temperature until completion of the reaction (4 h) monitored by TLC. Then, reaction mixture was kept in refrigerator overnight, the separated solid product was obtained by simple filtration and further purified by recrystallization from 96% ethanol. All other derivatives (5b-j) were synthesized by following same procedure and confirmed by spectral techniques.

Results and discussion

Catalyst Characterization

The agro-waste-derived ash catalyst was characterized by FT-IR, XRD, XRF, EDX, SEM and BET technique.

DSC-TGA analysis

The suitable modification temperature of PFP was determined by thermal gravimetric analysis (Fig. 2). The TGA result shows the temperatures at which the PFP decomposed when heated in a controlled environment to avoid any misleading oxidation reactions at a given temperature rate. The temperature ranged from 0 to 1000 °C depicting the decomposition of PFP.

Three distinct stages of weight loss were observed. In the first step, minor weight loss at temperatures below 103.02 °C was 6.73% occurred due to the loss of adsorbed moisture. Another weight loss occurred in the second step between 212.98 and 410.72 °C and was 61.21%, reflecting the decomposition of organic components. In the third step, weight loss between temperature ranges of 410.72-985.76 °C was due to the decomposition of metal carbonates. Finally, the 8.33% weight of

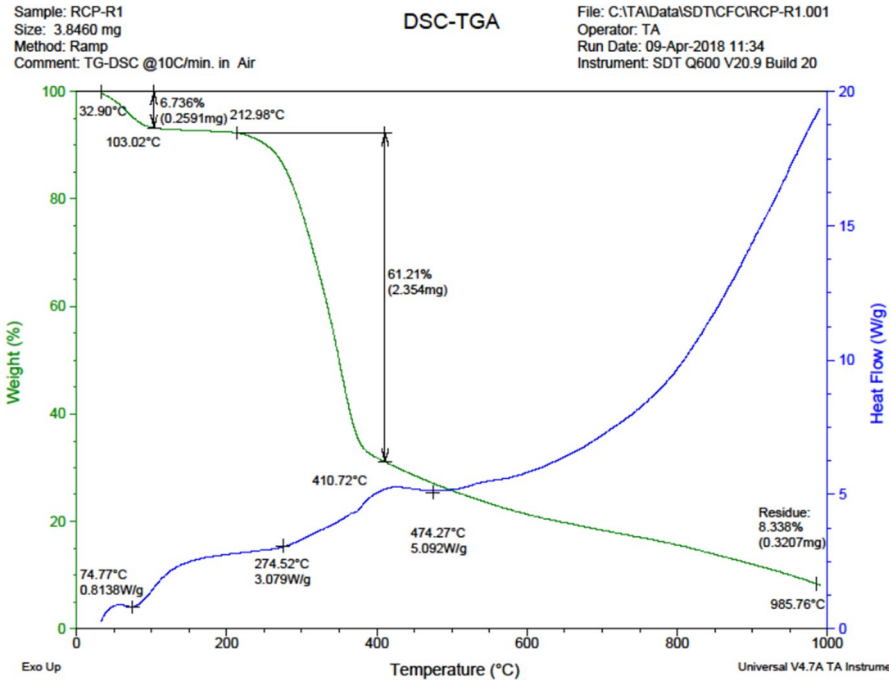


Fig. 2 DSC-TGA curves of parent PFP

residue remaining after the temperature of 985.76 °C was due to metal oxides and silica.

FT-IR analysis

The conversion of natural feedstock's PFP into APP-catalyst was confirmed by FT-IR analysis (Fig. 3). The observation of major absorption bands occurred at 694, 871, 1044, 1404 and 1687 cm^{-1} in parent PFP supports presence of metal carbonates (K_2CO_3, $CaCO_3$, $MgCO_3$). After thermal treatment at 1000 °C, absorption bands occurred at 606, 1022, 1509, 1687 and 1733 cm^{-1} clearly indicate the presence of metal oxides (K_2O, CaO, MgO).

XRD analysis

The XRD analysis of the APP-catalyst (Fig. 4) showed the characteristic peaks of metal oxides and carbonates present in the catalyst.

The peaks at $2\theta = 25.81$, 28.58, 31.86, 40.50 and 49.47 (JCPDS Reference No. 77-2176 and 87-0730) revealed the presence of the K_2O and K_2CO_3, while the intense peaks at $2\theta = 29.40$, 30.35, 39.40, 47.44, 32.54, and 53.03 (JCPDS Reference No. 47-1743, 37-1497) attributed to CaO and $CaCO_3$. The peak at $2\theta = 42.92$, and 62.31 (JCPDS Reference No. 04-0829, 75-1525) ascribed to MgO, and the peaks

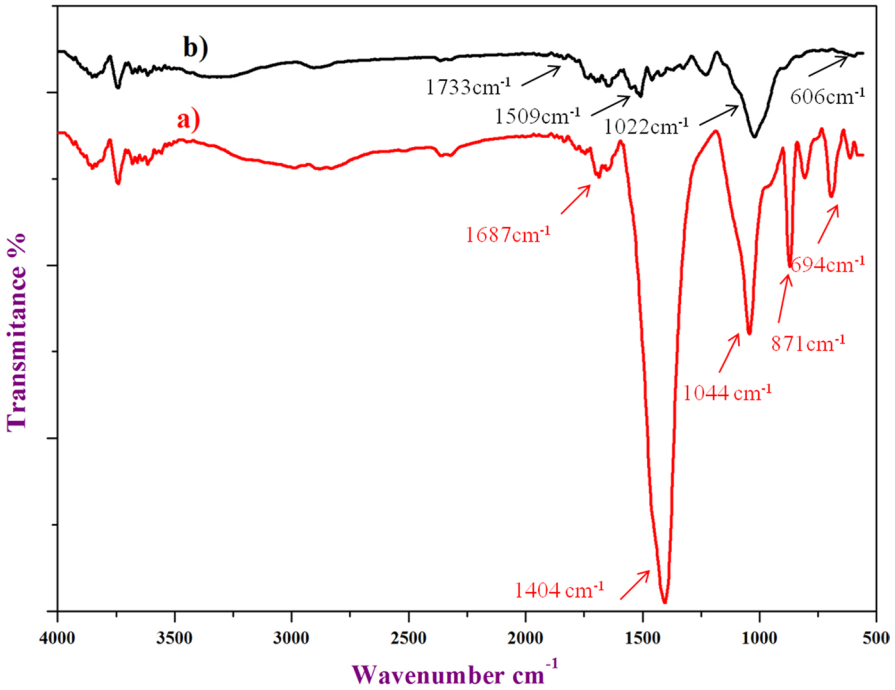


Fig. 3 FT-IR of **a** parent PFP, **b** APP-catalyst

at $2\theta = 25.36$, 33.05, 42.15, 50.68, 51.40 attributed to SiO_2, Fe_2O_3, P_2O_5, carbon and sulfur (JCPDS Reference No. 41-1413, 33-0664, 5-0488, 75-1621, 34-0941). Another peak was also observed at $2\theta = 17.92°$ due to metal hydroxides. Therefore, this active phase of the APP-catalyst was utilized for the conversion of reactant into the desired product.

XRF analysis

X-ray fluorescence (XRF) technique is one of the simplest, analytical methods to investigate the particular chemical composition of materials. The XRF analysis revealed that the fresh APP-catalyst was found to contain K_2O (25.1%), CaO (9.83%), MgO (4.59%) as major constituents while P_2O_5 (3.14%), Fe_2O_3 (0.10%), SiO_2 (0.56%), Na_2O (0.014%) as a minor constituents in the ash (ESI).

EDX analysis

The distribution of elements as based on the EDX analysis of the APP-catalyst is shown in Fig. 5. The report reveals a very high concentration of the oxides of potassium (K), calcium (Ca) and magnesium (Mg). It is believed that oxides of these elements in the presence of water produce corresponding metal hydroxides (KOH as a

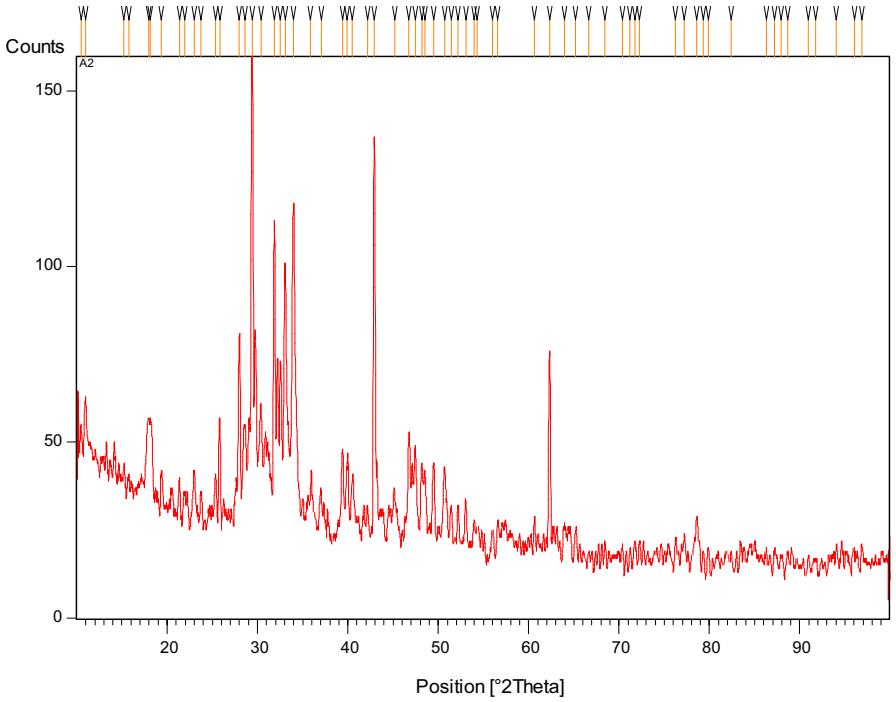


Fig. 4 X-ray diffraction patterns of APP-catalyst

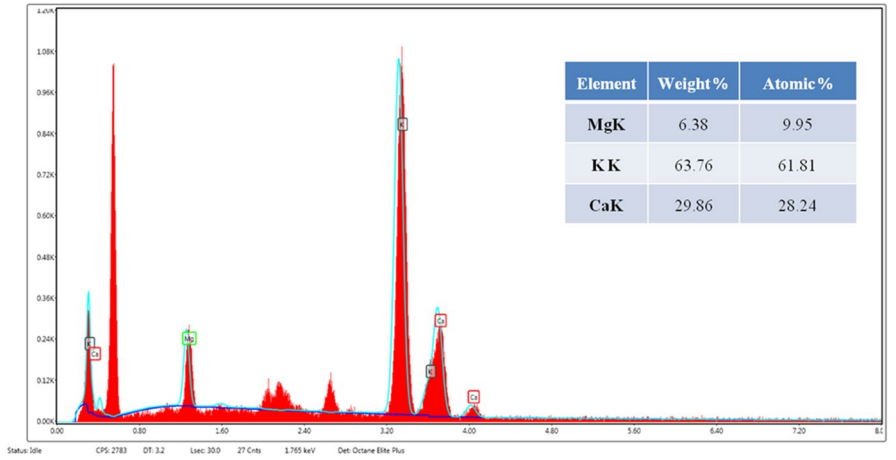


Fig. 5 EDX spectrum of APP-catalyst

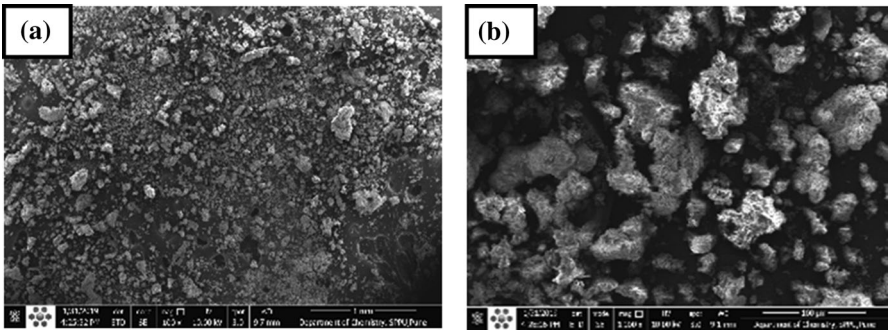


Fig. 6 SEM images of APP-catalyst **a** Normal view, **b** Magnified view

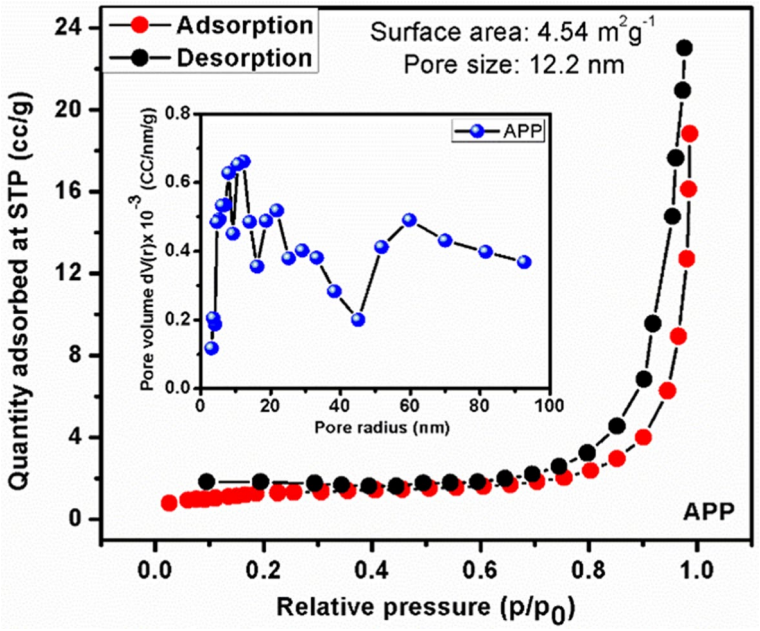


Fig. 7 BET isotherm and pore-size distribution curve (inset) of APP-catalyst

major constituent), which provides basic condition [31–33] to facilitate this cross-aldol condensation.

SEM analysis

The apparent morphology of APP-catalyst examined by SEM images is shown in Fig. 6. As observed from SEM micrographs, smaller and homogeneous particle size may be achieved with thermal treatment to parent PFP. In general, the smaller particle size of catalyst provides large contact area for catalyzing the reaction.

BET analysis

Figure 7 displays the N_2 adsorption–desorption isotherms and the corresponding pore-size distribution curve (inset) for freshly prepared APP-catalyst. The surface area of APP-catalyst was found to be 4.54 $m^2\ g^{-1}$ while the pore volume and pore radius are 0.037 ccg^{-1} and 12.2 nm, respectively. The pore-size distribution curve (inset) depicts mesopores of very uniform sizes. The isotherms of prepared APP-catalyst were type III isotherm with a H4-type hysteresis loop.

Optimization of reaction conditions

At the outset of the protocol, our goal was to identify the catalytic activity of the APP-catalyst for the synthesis of α,α′-bis(substituted benzylidene)cycloalkanones derivatives, and we defined the following criteria: a greener solvent system, a low catalyst loading, relatively low reaction temperature and good reaction yield in a short reaction time. With these goals in mind, the reaction conditions were optimized using 4-methoxybenzaldehyde (2 mmol) and cyclohexanone (1 mmol) as model reactants reacting at reflux condition and the observed results are summarized in Table 1. At first, the model reaction was examined under solvent-free conditions and in the water (3 mL) without any catalyst. It was found that the desired product, 3j was not observed on the TLC plate even after 3 h of stirring (Table 1, entries 1, 2). As the reaction requires a catalyst, the model reaction was performed using the APP-catalyst by varying the catalytic amounts (1–20 wt%) in water (3 mL). It was found that when increasing the amount of the catalyst from 1 to 5 and 7 wt% in water, the yield also increased (Table 1, entries 3, 4). A further increase in the catalyst amount (above 10 wt%) surprisingly reduced the yield (Table 1, entry 5), when the reaction was performed in 3 mL water. Therefore, 7 wt% of APP-catalyst in 3 mL water is sufficient to remarkably enhance the

Table 1 Optimization of reaction condition for synthesis of **3j**[a]

Entry	Ash catalyst (wt%)	Solvent (3 mL)	Time (min)	Yield[b] (%)
1	–	–	180	Nr[c]
2	–	H_2O	180	Nr[c]
3	APP (1)	H_2O	60	32 (43,70)[d]
4	APP (7)	H_2O	30	94
5	APP (10)	H_2O	60	92 (89, 86)[e]
6	APP (7)	EtOH	30	94
7	APP (7)	THF	60	56
8	APP (7)	DCM	60	51
9	APP (7)	CH_3CN	60	62
10	APP (7)	H_2O: EtOH (1:1)	30	94

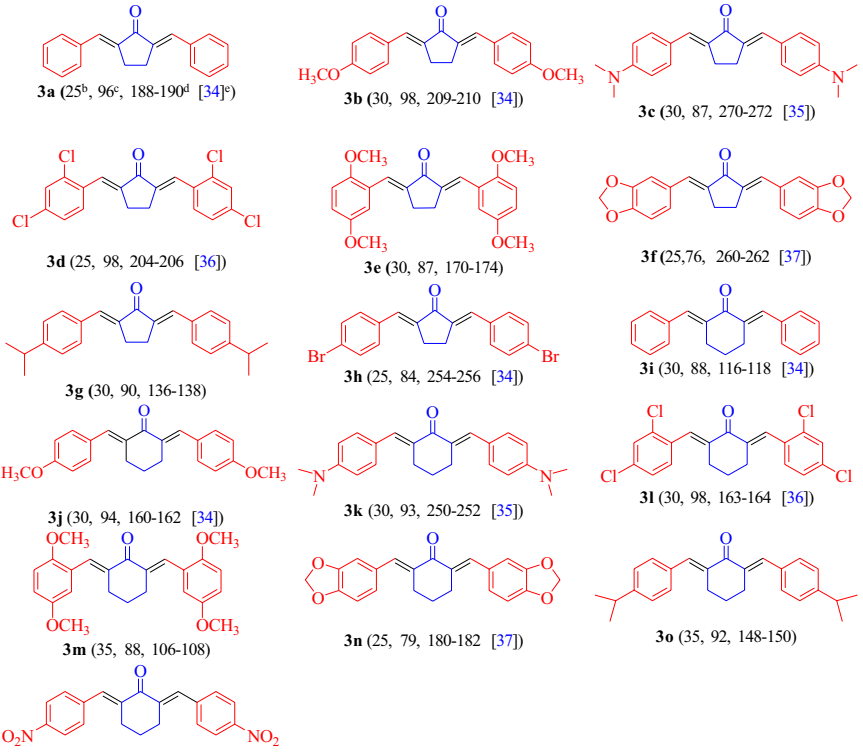
[a]Reaction conditions: 4-methoxybenzaldehyde (2 mmol), cyclohexanone (1 mmol), catalyst (wt%) and water (3 mL) at reflux condition, [b]isolated yield, [c]no reaction, [d]catalyst amount 3, 5 wt%, [e]catalyst amount 15, 20 wt%

reactivity of the reactants, and the corresponding product 3j was obtained in 94% yield within 30 min (Table 1, entry 4).

Optimization study was also performed with variation of the reaction medium. The model reaction was examined in different conventional organic solvents like EtOH, THF, DCM and CH_3CN. The results reveals that THF, DCM and CH_3CN afforded low-to-moderate yields (Table 1, entries 7–9) while pure EtOH and H_2O: EtOH solvent system shows equally good performance for this conversion (Table 1, entry 6 and 10). Thus, the best yield, cleanest reaction work-up was achieved employing 7 wt% of APP-catalyst in water (3 mL) at room temperature.

By reacting cyclopentanone and cyclohexanone with a variety of differently substituted aromatic aldehydes under optimized reaction conditions, we manage to prepared a range of α,α′-bis(substituted benzylidene)cycloalkanone derivatives. The results are shown in Table 2. As shown, aromatic aldehydes with substituent's carrying either electron-withdrawing or electron-donating groups reacted successfully and gave the expected products. The reactions were completed

Table 2 APP-catalyzed synthesis of α,α'-bis(substituted benzylidene)cycloalkanones **(3a–p)**[a]



[a]Reaction conditions: aryl aldehyde and cyclic ketone, catalyst (7 wt %) water (3 mL) at reflux condition, [b]time in min, [c]isolated yield in %, [d]melting point in ºC, [e]reference

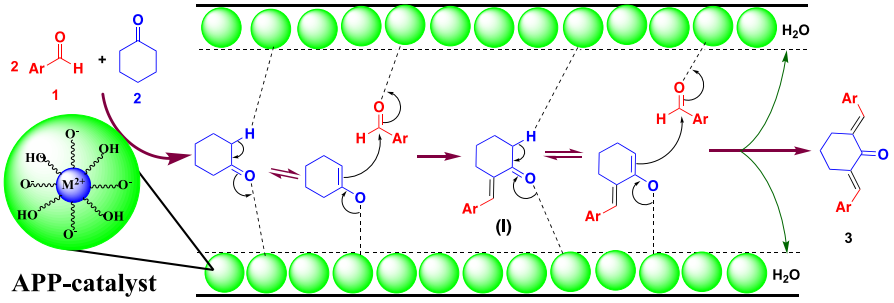
within 25-30 min with excellent yields. Melting point of all the synthesized products is compared with those reported in the literature [34–38].

Role of APP-catalyst

Although we did not investigate the reaction mechanism, the plausible mechanism for the α,α′-bis(substituted benzylidene)cycloalkanones (3) formation is depicted in Scheme 2. The APP-catalyst containing the mixture of metal oxides and carbonates is soluble to some extent in water which provides a number of Lewis basic sites ($O^{2-}$and OH) along with Lewis acid sites (M^{2+}) for the activation of reactants to forward the reactions in the proper direction. The carbonyl ketone (2) is activated by Lewis basic sites along with Lewis acid sites may be simultaneously increasing the driving force of aromatic aldehydes (1) to interact with activated ketone and eliminated water molecules to afford the targeted α,α′-bis(substituted benzylidene) cycloalkanones (3) product through formation of (*E*)-2-(argiomethylene)cyclohexan-1-one intermediate (I). As a result, of the overall effect there is a rate enhancement of the reaction.

Recycling of APP-catalyst

Next, we investigated the reusability of catalyst. The reusability of catalyst is important benefit for scale-up practical and industrial applications. A recycling experiment was conducted using the 4-methoxybenzaldehyde and cyclohexanone as a model reactants in water. After completion of the reaction, the solid product (3j) obtained was separated by simple filtration followed by washing with distilled water (2×5 mL). Whole filtrate containing APP-catalyst was collected separately and extracted with ethyl acetate. The recovered aqueous layer containing APP-catalyst was concentrated under vacuum to reduce 3 mL and directly used for the next cycle with fresh reactants. The results obtained in our experiment (Fig. 8) confirmed that the APP-catalyst could be reused up to fifth run with only negligible loss of activity. The presence of alkali metals in recycled catalytic system was evidenced by the



Scheme 2 Postulated role of APP-catalyst in the formation of α,α′-bis(substituted benzylidene)cycloalkanones

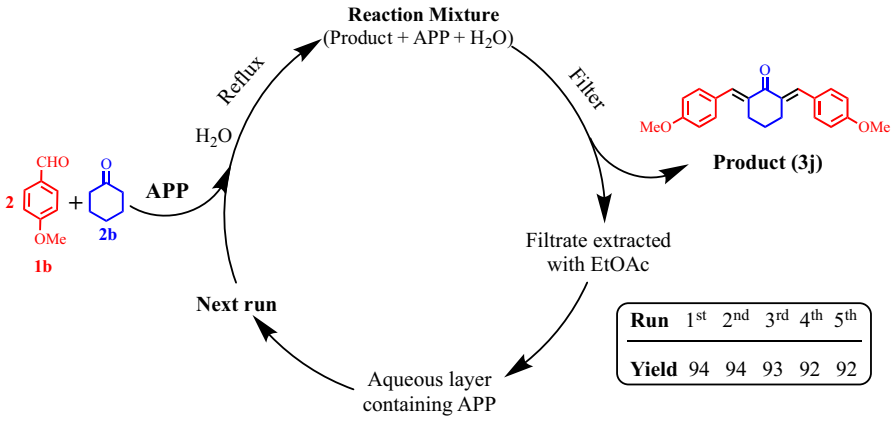


Fig. 8 Reusability of APP-catalyst

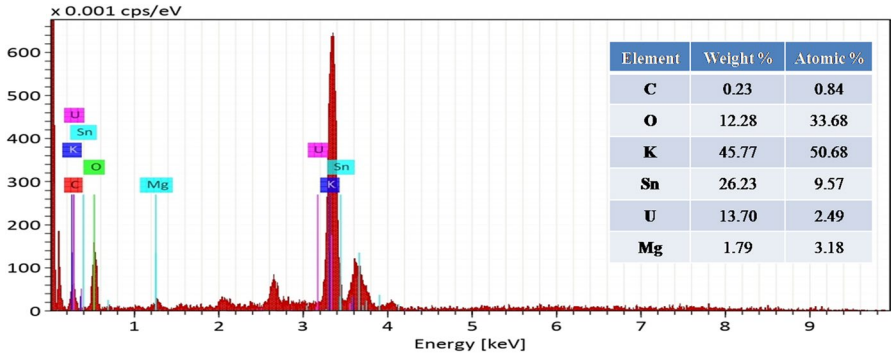
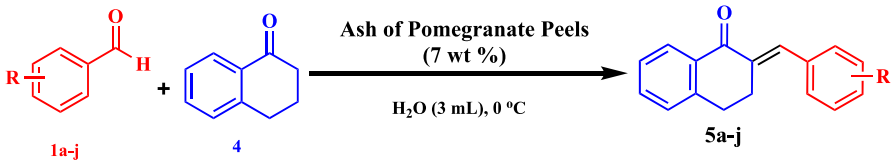


Fig. 9 EDX spectrum of recovered APP-catalyst



Scheme 3 Synthesis of 2-arylidene-1-tetralone derivatives

EDX analysis (Fig. 9), which revealed no appreciable change in the chemical composition of catalyst even after the fifth cycle.

Inspired by these tempting results obtained for condensation of aromatic aldehydes with cycloalkanones (Scheme 1) to afford the desired α,α′-bis(substituted benzylidene)cycloalkanones, we decided to check the feasibility of APP-catalyst for synthesis of 2-arylidene-1-tetralone under optimized reaction conditions (Scheme 3).

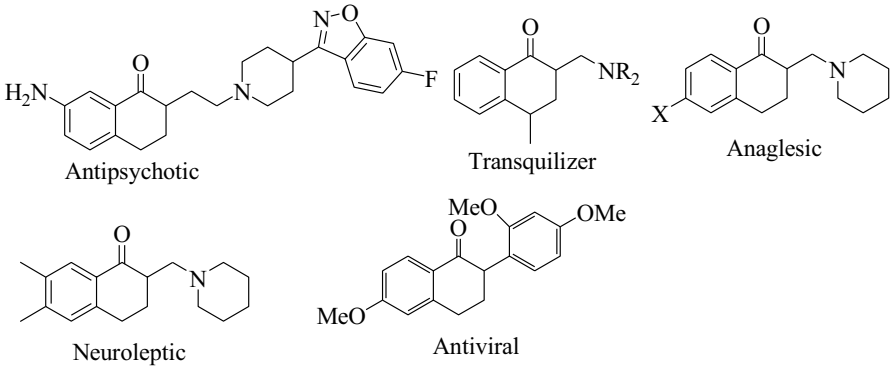


Fig. 10 Pharmaceutically important 1-tetralone derivatives

2-arylidene-1-tetralones exhibit important biological and pharmaceutical activities (Fig. 10) such as tranquilizer [39], antifungal [40], neuromuscular blocking agent [41], cytotoxic [42], inhibitory activity [43] and any others.

Unfortunately after 12 h, very trace amount of product was observed on TLC when equimolar quantity of aromatic aldehyde and 1-tetralone was reacted. A very few methods are reported in the literature where synthesis of 2-arylidene-1-tetralone has been synthesized by the condensation of 1-tetralone with aromatic aldehydes at various temperature conditions in the presence of different basic catalysts like NaOH (0 °C) [44], KOH (RT), [45], piperidine (RT) [46] and also acidic catalysts such as H_2SO_4, (reflux) [47], H_3PO_4, (80 °C) [48], HCl (RT) [49]. Therefore, we decided to optimize the reaction conditions for synthesis of 2-arylidene-1-tetralones.

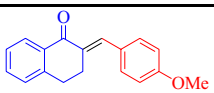
For optimization study, the reaction between equimolar quantity of 4-methoxybenzaldehyde and 1-tetralone in the presence of APP-catalyst (7 wt%) was performed at different temperature conditions and results are summarized in Table 3. From results, it reveals that excellent result was obtained after 4 h, when model reactants were stirred at 0 °C (Table 3, entry 7). Under the preceding optimized conditions, we decided to prepare variously substituted 2-arylidene-1-tetralone as

Table 3 Optimization of reaction temperature for synthesis of 2-(4-methoxybenzylidene)-1-tetralone **(5a)**[a]

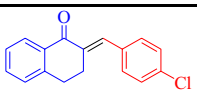
Entry	Temp (°C)	Time[b] (h)	Yields[c] (%)
1	Reflux	12	Trace
2	80	12	Trace
3	60	12	Trace
4	40	12	12
5	20	12	25
6	10	12	40
7	00	4	92
8	− 10	4	92

[a]Reaction conditions: 4-methoxybenzaldehyde and 1-tetralone, catalyst (7 wt%) water (3 mL), [b]time, [c]isolated yield

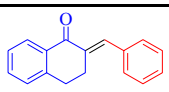
Table 4 APP-catalyzed synthesis of 2-arylidene-1-tetralone derivatives **(5a-j)**[a]



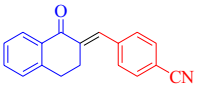
5a (4[b], 78[c], 92-94[d] [50][e])



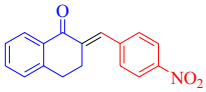
5b (4, 85, 120-122 [51])



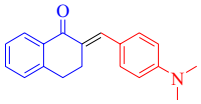
5c (5, 75, 96-98 [50])



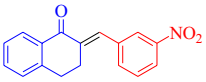
5d (4, 75, 160-162 [48])



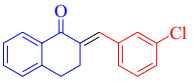
5e (3, 70, 182-184 [49])



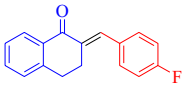
5f (4, 70, 35-37 [50])



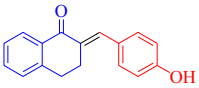
5g (3, 70, 118-120 [50])



5h (4, 82, 72-74 [50])



5i (3, 70, 106-108 [51])



5j (4, 65, 125-127 [52])

[a]Reaction conditions: aryl aldehyde and 1-tetralone, catalyst (7 wt %) water (3 mL) at room temperature, [b]Time in hr, [c]Isolated yield in %, [d]Melting point in ºC, [e]reference

the unique small drug-like molecules. As shown in Table 4, the results indicate that 1-tetralone bearing both electron-withdrawing and electron-donating groups can be involved efficient in this reaction to afford the desired products (5a-i) in high yields.

The reported methodologies (Table 5, entry 1–6) have used various catalysts for condensation of 4-methoxybenzaldehyde and cyclohexanone. These methodologies are convenient and afford the higher yield of product. However, these methodologies require chemicals which are hazardous for handling, some of the catalysts need toxic as well as corrosive chemicals for its synthesis, and their separation from the reaction mixture is much complicated. Compared to efficiency of the other reported methods, APP-catalyst found to be a suitable catalyst for the synthesis of 2, 6-bis(4-methoxybenzylidene)cyclohexanone (Table 5, entry 7).

Table 5 Comparison of APP-catalyst with some previously reported catalyst for synthesis of **3j**

Entry	Catalyst	Catalyst loading	Solvent (mL)	Temp. (°C)	Time	Yield (%)	References
1	I_2	0.3 mmol	CH_2Cl_2	R. T.	4.5 h	95	[53]
2	TiO_2/HOAc	0.6 mmol	EtOH	Reflux	6.15 min	90	[34]
3	NaOH	5.0 mmol	CTAB/H_2O	60 °C	8 h	95	[54]
4	Na/FAP	1 g	H_20	Reflux	3 h	80	[55]
5	$Cu(TFA)_2.4H_2O$	2.2 mmol	–	90 °C	6 h	85	[6]
6	SiO_2-OK	1.0 mmol	EtOH	Reflux	4 h	85	[56]
7	Ash of pomegranate peels	7 wt%	H_2O	Reflux	30 min	94	Present work

Conclusion

In conclusion, the present method reports green and highly efficient procedure for the synthesis of α,α′-bis(substituted benzylidene)cycloalkanones and 2-arylidene-1-tetralones under aqueous medium. Use of APP-catalyst obtained from renewable bio-waste, mild reaction conditions and simple work-up without involvement of any hazardous material quantify this method as an environmentally benign approach for this condensation. The catalyst is new, attractive and inexpensive which can contribute to the development of more benign catalytic processes, reduced environmental problems and proved to be a potential alternative to soluble bases.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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