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Application of novel, efficient and agro-waste sourced catalyst for Knoevenagel condensation reaction

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A greener, economic and eco-friendly method for Knoevenagel condensation of aromatic aldehyde, salicylaldehyde with active methylene compounds like malononitrile and Meldrum's acid to synthesize benzyldinmalononitrile and 3-carboxy coumarin derivatives respectively is demonstrated. The reaction has been carried out in the absence of external base using agro-waste sourced green catalyst WENBA {Water Extract of Nilgiri Bark Ash (Eucalyptus)} as an efficient natural catalytic medium. WENBA is a novel, ecologically safe and inexpensive green catalyst obtained from the agro-waste feedstock. The synthesized compounds benzyldinmalononitrile and 3-carboxy coumarin (2-oxo-2H-1-benzopyran) backbone have multiple applications in medicinal chemistry for the synthesis of bioactive molecules. Thus, a wide number of methodologies have been developed for the synthesis of this class of organic molecules. However, some of the methods reported are associated with hazardous materials and are toxic to the environment. They have longer reaction times, poor yields, and with lower purity of final isolated compound. In spite of a large number of methodologies available for this bioactive molecule synthesis, there is still demand for the development of newer reagents, which give environmentally friendly protocols, mild reaction conditions, inexpensive catalyst and final product isolation in pure form with good yields.

Keywords: Agro-waste, Knoevenagel reaction, Benzyldinmalononitrile, Coumarin-3-carboxylic acid, room temperature

Environmental issues associated with many of the organic reactions have created a huge challenge for the researchers to establish eco-friendly, sustainable or greener approaches for the existing organic transformations^{1,2}. The use of aqueous media instead of volatile organic solvents has got huge attention in organic reactions. Recently, eco-friendly, green and benign approaches have gained huge attention to carry out the organic transformation at ambient temperature. The use of hazardous reagents as catalysts during reaction seriously affects the human health and extremely damages to our environment. Nowadays, various water extract catalytic approaches have also given more attention due to its clean, simple, safe, economic and high yielding advantages³. These room temperature reactions being highly greener in their approach which strongly also fulfil the principles of 'Green Chemistry'⁴.

Coumarin-3-carboxylic acid represents as a prominent heterocycle with wide variety of applications showed in biological activities and in material science. The reported literature reveals that, coumarin-3-carboxylic acids how potential effects in

terms of medicinal application such as anti-coagulant⁵, anti-bacterial⁶, anti-inflammatory⁷, anti-HIV⁸ and neuro protective agents⁹. They have also been employed as prominent intermediates for the synthesis of various pharmacologically potential compounds such as β -lactams¹⁰, isoureas¹¹ and tetrahydropyridones¹². The ester and amide derivatives of coumarin-3-carboxylic acids are well known for their efficient anti-cancer¹³ properties which include the inhibition of tumour cell growth and invasion *in vitro* and *in vivo*¹⁴. The coumarin-3-carboxylic acids have not just focused to biological activities apart from that, they have also employed in triplet oxygen sensitizers¹⁵, cosmetics, perfume industries, pharmaceuticals¹⁶, also in the production of insecticide, optical brighteners¹⁷, as fluorescent probes¹⁸ and laser dyes¹⁹. They have also been extensively used as a ligand in metal-coumarin preparation and showed prominent bio-applications^{20,21}.

The above mentioned and several other applications have gained promising importance, which has made coumarin-3-carboxylic acids as an important objective for the researchers. The previous reported method adopted the synthesis of

coumarin-3-carboxylic acid by condensing various *o*-hydroxybenzaldehyde with ethylcyanoacetate, malononitrile or malonic acid²²⁻²⁶ catalyzed using piperidine²⁷, L-proline²⁸ and also variety of ionic liquids have been reported²⁹. Recently, researchers have reported better methodology for the synthesis of coumarin-3-carboxylic acid by condensing *ortho*-hydroxybenzaldehyde with Meldrum's acid has been proven to be more superior to previous combinations in terms of yield and simplicity of the reaction condition. Since coumarin derivatives have wide range of applications gave insight to chemist develop variety of synthetic methodologies. The various synthetic protocols available for its synthesis, some of the important reactions are Pechman condensation^{30,31}, Perkin reaction³², Knoevenagel condensation³³, Wittig reaction³⁴⁻³⁶, Baylis-Hillman reaction^{37,38}. In spite of many reactions reported, the Pechmann and Knoevenagel reactions are regularly employed for the synthesis of coumarins due to the simple reaction conditions and isolation of product in good yield. The development of newer methodologies to facilitate coumarin synthesis *via* Knoevenagel condensation is an intense area of research at present. Therefore, many techniques have been introduced for new methodologies that are simple reaction, solvent-free, inexpensive catalyst and environment benign.

Thus, researchers have been established many efficient catalytic approaches for the condensation of *o*-hydroxybenzaldehyde with Meldrum's acid which has been accepted as one of the best combination of substrates for the synthesis of 3-carboxy coumarins. The various catalysts reported such as ammonium acetate³⁹, potassium phosphate⁴⁰, stannous chloride⁴¹, ferrous chloride⁴², clays²⁵, lithium salt²⁶, triethylamine⁴³, silica sulphuric acid⁴⁴, choline chloride⁴⁵, 1,1,3,3,-N,N,N',N'-tetramethylguanidinium trifluoroacetate ionic liquid (TMGT)⁴⁶, piperidinium acetate⁴⁷.

Among various C-C bond formation reactions, widely employed and one of them which has got many industrial application is Knoevenagel condensation^{48,49}. This reaction proceeds by condensing aldehyde with active methylene compounds like malononitrile or ethylcyanoacetate which leads to alkenes. The product have been recognized by wide range of applications in chemical synthesis includes therapeutic drugs, cosmetics, insecticides, polymers and many more divisions⁵⁰. The Knoevenagel condensation reaction usually catalyzed by Lewis acid or base. In literature method reveals that

variety of catalytic approaches have been adopted for the Knoevenagel condensation of aldehyde with active methylene compound such as microporous polyurethane⁵¹, basic ionic liquid⁵², functionalized ionic liquids⁵³⁻⁵⁵, functionalized silica gel⁵⁶, diammonium hydrogen phosphate⁵⁷, Xonothite silica gel⁵⁸, Zn(OAc)₂⁵⁹, K₁₀-ZnCl₂⁶⁰, AlPO₄-Al₂O₃⁶¹, cetyltrimethyl ammonium bromide⁶², KF-Al₂O₃⁶³, ZnCl₂⁶⁴, K₃PO₄⁶⁵, I₂-K₂CO₃⁶⁶, CdI₂⁶⁷, Al₂O₃⁶⁸, natural catalyst⁶⁹, MgBr₂.OEt₂⁷⁰, GaCl₃⁷¹. In spite of these many catalytic approaches, some of the methods have advantages, and most of the method suffer from various disadvantages such as longer reaction time, harsh condition, elevated temperature, need for excess reagents, lower yields, tedious workup and mainly expensive catalyst, lead to several side products, usage of hazardous organic solvents and most of the method ask for chromatographic purification of adducts. Therefore, there is huge demand to establish clean, simple, efficient and high yielding approaches to follow green chemistry principles are still in demand in organic synthesis.

Present chemists are more interested to develop eco-friendly, simple, efficient and economic approach methods as an important tool for many synthetic transformations, which employ various natural feedstock extracts, which are well known for their non-hazardousness, no usage of organic solvent, and replace many organic and inorganic based catalysts. At present literature reported so many homogenous catalytic approaches, which follow green chemistry principle established for various organic transformations such as Suzuki coupling, Henry reaction, Dakin reaction and Ipso-hydroxylation in WERSA⁷²⁻⁷⁵, Suzuki coupling, Dakin reaction and peptide bond formation using WEB⁷⁶⁻⁷⁸, heterocyclization using BFE (*Aeglemarmelos*)⁷⁹, Sonogashira coupling reaction employing WEPBA⁸⁰, Suzuki cross coupling reaction using Eichhorniacrassipes (Water hyacinth)⁸¹, and recently our group has reported Knoevenagel condensation using WEPBA⁸² and WEB⁸³. And also our group has recently focused on the green synthesis of pharmacologically potent heterocyclic molecules such as 2-aryl benzimidazoles using WEPBA^{84a}, 2-amino-4H-chromenes using WEPBA^{84b} and 4-Benzylidene-2-(2-fluorophenyl) Oxazol-5(4H)-one derivatives using ESP^{84c}. Thus all these findings inspired us to generate a novel catalytic media using water extract of nilgiri bark ash (WENBA). In this regard our group has established

a novel, efficient and economic catalytic media, which plays dual role being catalyst as well solvent, low cost, abundantly available, natural feedstock extract for the green method synthesis of 3-carboxy coumarins and benzylidinemalononitriles at chromatographically pure is described.

Results and Discussion

Researchers are interested recently for the development of efficient, safer catalyst of green and sustainable processes derived from the natural 'feedstocks' as an alternative to hazardous organic solvents or metal based catalysts for the synthesis of organic compounds. Keeping present demand, and in continuation of our interest in exploring the applications of natural feedstock catalysts for the organic transformation. Herein, we wish to report a WENBA extract as an efficient and eco-friendly catalyst for the synthesis of 3-carboxy coumarins and arylidinemalononitriles based on multi component reaction (MCR) strategy is described. The extracted WENBA catalyst act as a non-conventional base with

a pH of 12.06, highly active with good to excellent product isolation in a short reaction time at RT. To the best of our knowledge, this is the first report on the use of WENBA catalyst for the synthesis of 3-carboxy coumarins and arylidinemalononitriles. The catalytic media is extracted from the ash of Nilgiri bark (Eucalyptus) available in Indian continent was employed for the extraction. It has many medicinal significance also, the species of Eucalyptus are cultivated widely in the tropical and temperature in world, including the Americas, Europe, Africa, Mediterranean Basin, the middle east, china and the Indian continent. The physico-chemical studies using EDX analysis of WENBA extracted revealed that, it is rich in Ca, Mg, K, Na, Cu, O and C in the range of 0.15 – 60.70 % (Figure 1 and Figure 2). The pH of the extracted solution was also examined using pH meter and found pH 12.06. The elemental analysis has also been carried out for WENBA using ESICO Microprocessor Flame Photometry 1382. The elemental analysis using flame photometry is also carried out by preparing standard solutions of

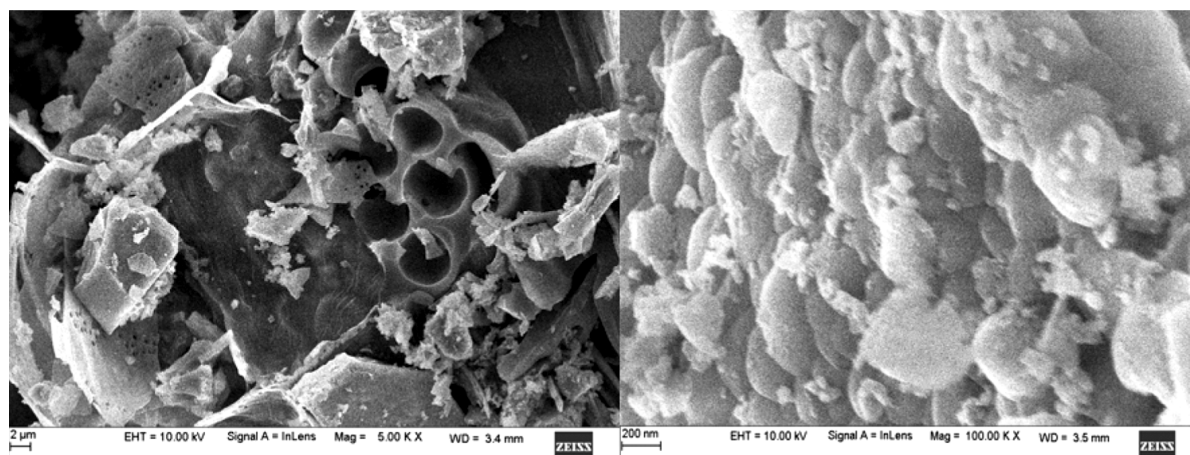


Figure 1 — SEM images of Nilgiri bark ash

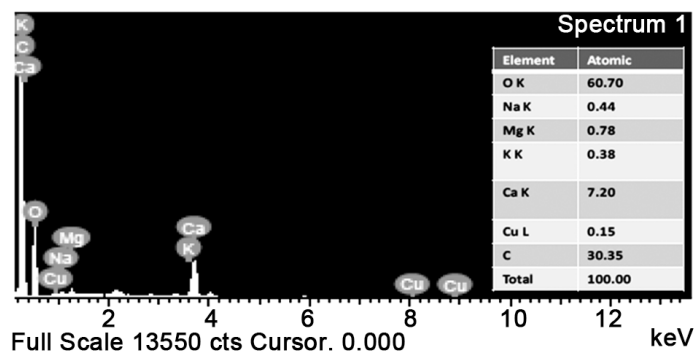
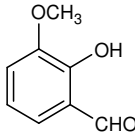
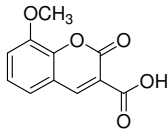
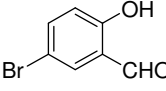
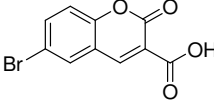
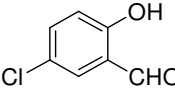
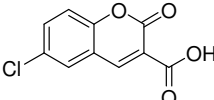
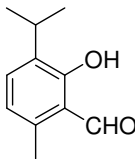
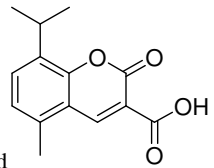
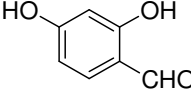
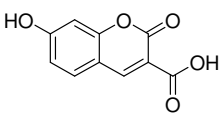
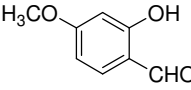
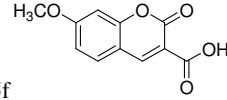
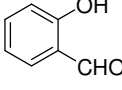
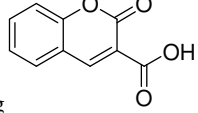


Figure 2 — EDX spectrum of Nilgiri bark ash

respective metal salts KCl for K, NaCl for Na, MgCO₃ for Mg and CaCO₃ for Ca detection, these respective salt standard solutions are prepared such as 40ppm, 60ppm, 80ppm for standardization purpose. Further, 10% of WENBA solution is employed for the flame photometry analysis, which reveals the presence of 17.55ppm of K, 16.53ppm of Na and 26.3ppm of Mg and 44.2ppm of Ca in the WENBA, which is in comparable with the elemental data obtained from EDX analysis of WENBA. In view of this data of natural feedstock extract having alkaline nature, it may serve as a better alternative to harmful corrosive catalyst used in organic transformations. For the present study, bark of nilgiri was collected from

local area and species was authenticated. The collected dried bark was broken into small pieces manually with a knife and burnt bark to ash directly using burner on a container. The resulted bark ash (10 gm) was suspended in distilled water (100 mL) stirred mixture for one hour at RT, filtered to get clear solution, the resulted light yellow coloured filtrate is named as WENBA. To check the applications of the extracted WENBA, we attempted the Knoevenagel condensation reaction in 10% WENBA in the absence of any other ligand or solvent or promoters. To carry out this synthetic method, a model reaction (Table I, entry 1) of *o*-vanillin (1mmol), Meldrum's acid (1mmol) and (5 mL) at RT stirring method. The

Table I — Synthesis of 3-carboxy coumarins with physical data

Compd	Salicylaldehyde	Product ^a	Time (h)	Yield ^b (%)	m.p. (°C)	
					Obsd.	Lit.
3a		5a 	3	90	213-215	215-216 ⁸⁵
3b		5b 	3	89	191-193	193-195 ⁸⁵
3c		5c 	3	88	122-123	122-123 ⁸⁵
3d		5d 	3.5	90	167-169	166-168 ⁹²
3e		5e 	3	88	261-263	260-262 ⁸⁵
3f		5f 	3.5	89	192-194	192-194 ⁸⁵
3g		5g 	3	90	188-190	189-191 ⁸⁵

(Contd.)

Table I — Synthesis of 3-carboxy coumarins with physical data (Contd.)

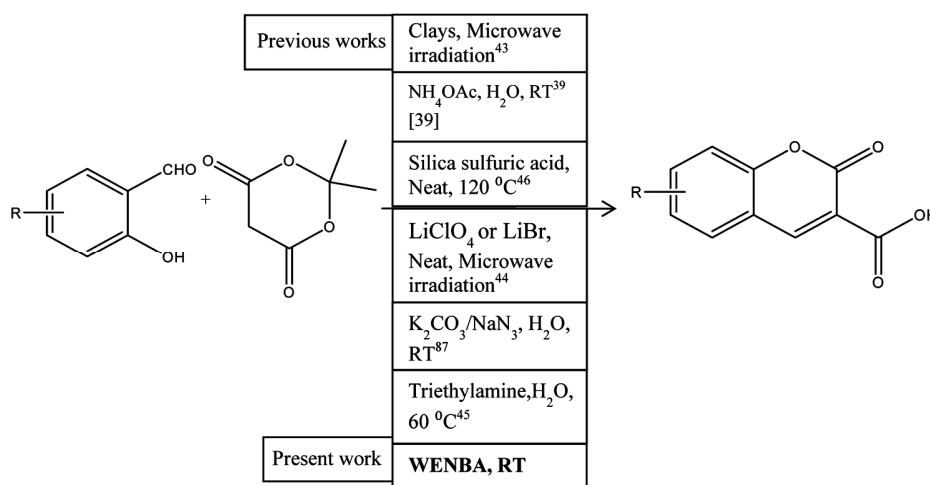
Compd	Salicylaldehyde	Product ^a	Time (h)	Yield ^b (%)	m.p. (°C)	
					Obsd.	Lit.
3h		5h 	3	91	198-200	199-202 ⁸⁵
3i		5i 	3.5	90	203-205	204-206 ⁹²
3j		5j 	3.5	89	209-211	210-212 ⁹²
3k		5k 	3	89	190-192	190-192 ⁹²
3l		5l 	3.5	87	206-208	206-208 ⁸⁵

^a All the products were characterized by FT-IR, ¹H and ¹³C NMR, and LC-MS.

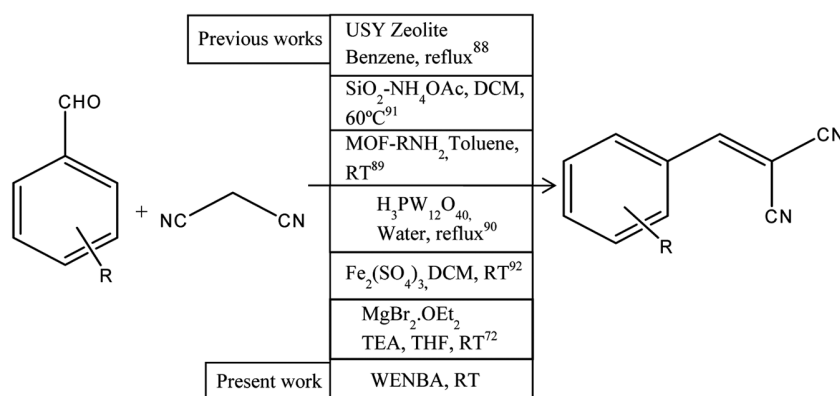
^b Yields refer to the isolated yields.

model reaction at RT revealed that, the highest isolation of the product with pure form took of about 3hrs to complete. So, the method optimization revealed that, RT stirring method in presence of WENBA required lesser time with solvent free and no catalyst is an example of a greener protocol synthesis. Further to check the amount of catalytic media required for the 1 mmol scale reaction, selected 3 mL, 5 mL and 7 mL of 10% WENBA in a separate reaction on model reactants, the reaction revealed 5 mL of catalyst is the minimal amount required for the reaction at RT. The 5 mL WENBA gave better product isolation compare to 3 mL of catalyst in reaction, but in the case of 7 mL catalytic media not observed any increase in its product isolation. So, we came to conclusion that, the minimal catalytic media required for the present work is 5 mL for 1 mmol scale reaction and used throughout in this present reaction. To extend generality of this model reaction,

we prepared a range of coumarin derivatives (5a-5l, Table I, Scheme I, Scheme II) by reacting with various substituted salicylaldehyde derivatives (3a-3l) with Meldrum's acid under optimized reaction conditions. As shown in Table I, substituted salicylaldehydes with groups carrying either electron donating or electron withdrawing reacted successively and gave the expected product in good to excellent yields. In addition, the synthesis of 5a derivative was also performed with 10 mmol scale of salicylaldehyde and Meldrum's acid, the final product isolated in good yield of 88% indicating that this method could also be used for the large scale synthesis without any side product formation. In all the cases, the single product isolated in pure form and was characterized by FT-IR, ¹H, ¹³C-NMR and mass spectrometry. Inspired by these excited results obtained for the coumarin-3-carboxylic acid cyclization, we extended the present protocol for the synthesis of aryldinmalononitriles



Scheme I — Previous work vs present work for the synthesis of 3-carboxy coumarin derivatives



Scheme II — Previous work vs present work for the synthesis of benzylidene malononitrile derivatives

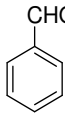
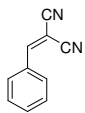
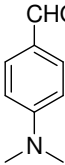
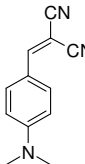
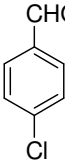
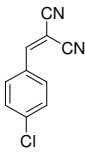
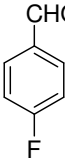
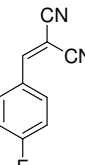
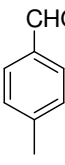

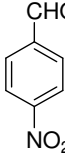
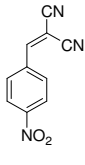
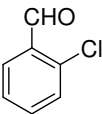
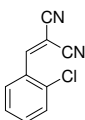
(6a-1) by reaction of various substituted benzaldehyde derivatives (4a-1) with malononitrile (Table II).

Further, we also examined the present method compatibility on electron donating and electron withdrawing groups substitution on benzaldehyde, the results revealed that, the present method reacted successively with malononitrile and gave the expected products in high yields (Table II). The final product isolated in pure form and examined its homogeneity by FT-IR, ¹H-, ¹³C NMR and mass spectrometry. The acceleration of coumarin and arylidene malononitrile formation using WENBA (Scheme III) is currently not well understood. The EDX data revealed that, WENBA contains Ca, K, Na as major constituents along with the host of other trace elements. Therefore, it is believed that carbonates of Ca, Na, and K of WENBA get transformed into corresponding oxides on burning and then into hydroxides during water extract which may act as a basic catalyst for the

present reaction. To compare the catalytic activity of WENBA, here we compared the catalytic activity some of synthetic alkali/carbonates for the model reactions (Table III). In Table III WENBA catalyzed reaction showed better catalysed with respect to time and product yield compare to other catalyzed (Table III, entry 1-3). This reaction suggested that, the strong alkalinity of WENBA (Table III, entry 4) in presence of other mineral salts is promoting the reaction efficiently.

The plausible mechanism (Scheme IV) for the 3-carboxy coumarin formation initiates by Knoevenagel condensation between salicylaldehyde and Meldrum's acid. In the beginning hydrogen of active methylene site of Meldrum's acid can be abstracted by the agro-waste natural basic catalyst (1) by forming carbanion for further attack on the carbonyl aldehyde proceeds *via* nucleophilic substitution, which further promotes ring opening

Table II — Synthesis of benzylidinemalonitrile derivatives with physical data

Compd	Aldehyde	Product ^a	Time (min)	Yield ^b (%)	m.p. (°C)	
					Obsd.	Lit.
4a		6a 	55	93	81-83	83-84 ⁸⁸
4b		6b 	45	89	181-183	180 ⁶⁹
4c		6c 	60	88	159-161	158-160 ⁸⁸
4d		6d 	45	85	121-123	122-124 ⁹⁰
4e		6e 	55	87	113-115	114 ⁹⁰
4f		6f 	60	89	159-160	158-161 ⁸⁸
4g		6g 	60	85	95-96	94-95 ⁹¹

(Contd.)

Table II — Synthesis of benzylidene malonitrile derivatives with physical data

Compd	Aldehyde	Product ^a	Time (min)	Yield ^b (%)	m.p. (°C)	
					Obsd.	Lit.
4h		6h 	55	90	136-138	137-138 ⁹¹
4i		6i 	50	88	117-119	116 ⁶⁹
4j		6j 	55	81	158-160	159 ⁶⁹
4k		6k 	50	80	141-142	140 ⁶⁹
4l		6l 	55	84	155-157	156 ⁶⁹

^a All the products were characterized by FT-IR, ¹H and ¹³C NMR and LC-MS.

^b Yields refer to the isolated yields.

mechanistic way of Meldrum's acid (2,3,4,) finally by cyclization of *ortho*-phenolic -OH (5) group of salicylaldehyde resulted in the formation of 3-carboxy coumarin (6). Further we checked the purity of the final product using several spectroscopic techniques. For this, the model reaction of *o*-vanilin and Meldrum's acid for the synthesis of 8-methoxycoumarin-3-

carboxylic acid (8-methoxy-2-oxo-2*H*-1-benzopyran-3-carboxylic acid) in pure form, which is directly taken for spectral analysis without further purification. The structure determining peaks observed in FT-IR using KBr pellets: 3410 (br, s, OH), 3055 (Aromatic CH), 2923 (CH vinylic), 1749 (C=O, ester) 1669 (C=O, acid) 1621, 1572 (C=C) cm⁻¹. ¹H NMR at 400 MHz, DMSO



Scheme III — Preparation of WENBA and its catalyzed synthesis of coumarin-3-carboxylic acid and arylidenemalononitrile derivatives

Table III — Comparison of different carbonates of Na, K, Ca and WENBA catalyst for the synthesis of coumarin-3-carboxylic acids^a and arylidenemalononitriles^b

Entry	Catalyst	pH ^c	Time (h)	Yield ^d (%)	Time	Yield ^d (%)
1	Na ₂ CO ₃	11.86	5	48	3 h	49
2	CaCO ₃	11.07	5	32	4 h	37
3	K ₂ CO ₃	11.58	6	64	2 h	68
4	WENBA	12.06	3	91	55min	93

^aReaction conditions: *o*-Vanillin (1.0 mmol), Meldrum's acid (1.0 mmol) in presence of catalyst (10%, 5 mL) at RT.

^bReaction conditions: benzaldehyde (1.0 mmol), malononitrile (1.0 mmol) in presence of catalyst (10%, 5 mL) at RT.

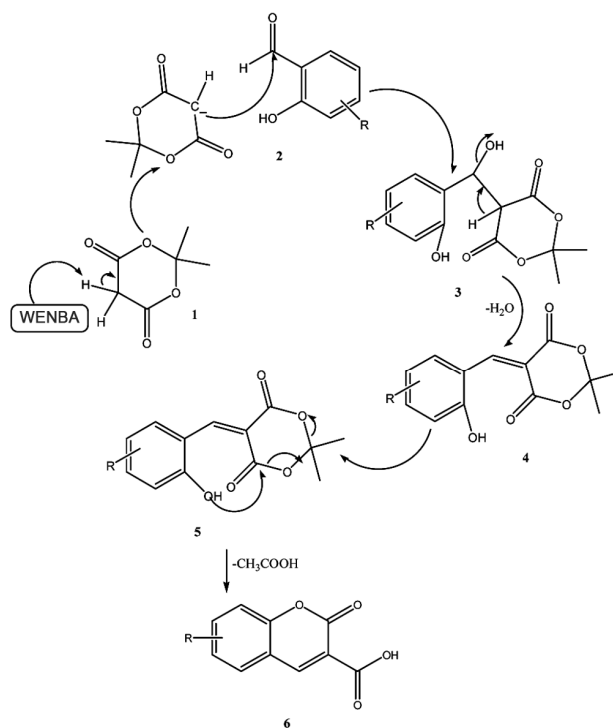
^cpH of 10% solution of alkaline salts

^dIsolated yields

(d₆) as a solvent and TMS as an internal standard, showed proton variations at 8.715 (1H, s, C₄-H), 7.32-7.46 (m, Ar-3H), 3.31 (s, C₈-OCH₃). In ¹³C NMR: δ: 163.92 (C₃-COOH), 156.39 (C-8a), 148.52 (C₈-OCH₃), 146.18(C-7), 143.75(C-5), 124.70(C-6), 121.04(C-3), 118.43(C-8), 116.19(C-4a) 56.12 (C₈-O-CH₃) peaks are observed. Mass spectrometry data is observed using LC-MS which give strong m/z peak at 221.01 [M+H]⁺ and theoretically C₁₁H₈O₅ requires 220.17.

Material and methods

All the reagents and chemicals were purchased from Sigma-Aldrich and used as received without further purification. IR spectra were recorded on KBr disks on a Shimadzu FT-IR, ¹H- and ¹³C NMR spectra were recorded on a Bruker spectrometer using TMS as an internal standard. The elemental analysis is



Scheme IV — Plausible mechanism for the synthesis of coumarin-3-carboxylic acid

carried out for WENBA using ESICO Microprocessor Flame Photometry 1382. LC-MS spectra were recorded in Waters; Synapt G2 High detection Mass spectrometry. SEM images are obtained using VEGA3, TESCAN (CZECH REPUBLIC) equipment followed by EDX by data by BRUKER nano, GmbH, D-12489 (Germany) equipment with Accelerating Voltage from 0 to 30 kV. The progress of the reaction

was monitored by TLC. Melting points were determined in open capillaries and were uncorrected.

Preparation of catalyst WENBA

Preparation of water extract of nilgiri (*Eucalyptus*) bark ash (WENBA) is carried out by burning dried agro waste nilgiri bark to ash. After that, 10 g of ash was suspended in 100 mL of distilled water and stirred for one hour at RT. The suspension was then filtered and a light yellow coloured filtrate is denominated as WENBA.

Typical experimental procedure for the synthesis of coumarin-3-carboxylic acid derivatives (5a-5l):

A mixture of salicylaldehyde (1 mmol), 2,2-dimethyl-1,3-dioxane-4,6-dione (1 mmol) followed by addition of 5 mL of WENBA were mixed and reaction mixture was stirred at RT for respective time till completion of the reaction, after reaction completion monitored by TLC, reaction mixture is acidified with dilute hydrochloric acid and solid product formed is collected by filtering and washed several times with water to obtain almost pure coumarin-3-carboxylic acid. The homogeneity of the compound is confirmed by ^1H NMR, ^{13}C NMR and mass spectrometry. Melting point of the obtained products is very much compared to the literature data.

Typical experimental procedure for the synthesis of arylidinemalononitrile derivatives (6a-6l):

A mixture of aldehyde (1 mmol), malononitrile (1 mmol) followed by addition of 5 mL of WENBA were mixed and reaction mixture was stirred at RT for respective time till completion of the reaction, after reaction completion monitored by TLC, product precipitated is filtered and washed several times with water to obtain almost pure arylidenemalononitrile derivatives. The homogeneity of the compound is confirmed by ^1H NMR, ^{13}C NMR and mass spectrometry. Melting points of the obtained products are very much compared to the literature data.

Selected spectral data of 2-oxochromene-3-carboxylic acid derivatives

(5a) 8-Methoxy-2-oxo-2H-chromene-3-carboxylic acid: Pale yellow solid, m.p. 213-215°C. FT-IR (KBr) ν : 3410, 3055, 2923, 1749, 1669, 1621, 1572 cm^{-1} ; ^1H NMR (DMSO- d_6), δ : 8.715 (1H, s, C₄-H), 7.32-7.46 (m, Ar-3H), 3.31 (s, C₈-OCH₃). ^{13}C NMR (100 MHz, DMSO- d_6): δ 163.92 (C₃-COOH), 156.39(C-8a), 148.52 (C₈-OCH₃), 146.18(C-7), 143.75(C-5), 124.70(C-6), 121.04(C-3), 118.43(C-8),

116.19(C-4a) 56.12 (C₈-O-CH₃). LC-MS: m/z Found: 221.01 [M+H]⁺, C₁₁H₈O₅ requires 220.17.

(5b) 6-Bromo-2-oxo-2H-chromene-3-carboxylic acid: Pale creamy solid, m.p. 191-193°C. IR (KBr) ν : 3603, 1742, 1710, 1609, 1551, 1473, 1343, 1030, 806 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6): δ 8.68 (1H, s, C₄-H), 8.17 (1H, d, J = 2 Hz, Ar-H), 7.86-7.88 (1H, dd, J = 8.8 and 2.4 Hz, Ar-H), 7.40-7.43 (1H, d, J = 8.8 Hz, Ar-H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 163.68 (C₃-COOH), 156.05 (C=O), 153.44 (C-8a), 146.72 (C-4), 136.27 (C-7), 131.91 (C-5), 119.83 (C-6), 119.67 (C-3), 118.35 (C-8), 116.14 (C-4a); LC-MS: m/z Found: 269.95 [M+H]⁺, C₁₀H₅BrO₄ requires 269.04.

(5c) 6-Chloro-2-oxo-2H-chromene-3-carboxylic acid: Pale yellow solid, m.p. 122-123°C. IR (KBr) ν : 3638, 3198, 1748, 1674, 1618, 1222, 1133, 980, 833 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6): δ 8.88 (1H, s, C₄-H), 7.92 (1H, d, J = 2.4 Hz, Ar-H), 7.69 (1H, dd, J = 8.8 and 2.4 Hz, Ar-H), 7.38 (1H, d, J = 8.8 Hz, Ar-H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 165.35 (C₃-COOH), 157.99 (C=O), 154.29 (C-8a), 146.22 (C-4), 133.69 (C-6), 129.02 (C-7), 128.97 (C-5), 121.59 (C-8), 119.69 (C-3), 118.65 (C-4a); LC-MS: m/z Found: 225.90 [M+H]⁺, C₁₀H₅ClO₄ requires 224.59.

(5g) 2-oxochromene-3-carboxylic acid: White solid, m.p. 188-190°C. FT-IR (KBr) ν : 3056, 2930, 2781, 1744, 1684, 1568, 1452, 1227, 1042, 833, 770 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 7.36-7.82 (m, 3H, Ar-H), 7.88-7.92 (dd, J = 8.0 Hz & J = 2.0 Hz, 1H, Ar-H), 8.75 (s, 1H, C₄-H), 13.23 (s, 1H, OH); ^{13}C NMR (100 MHz, DMSO- d_6): δ 165.99 (C₃-COOH), 156.37 (C=O), 152.72 (C-8a), 148.22 (C-4), 133.26 (C-8), 131.14 (C-5), 124.85 (C-6), 118.12 (C-3), 117.65 (C-4a), 115.09(C-7) LC-MS: m/z Found: 191.03 [M+H]⁺, C₁₀H₆O₄ requires 190.15.

(5h) 6,8-Dichloro-2-oxo-2H-chromene-3-carboxylic acid: Creamy solid, m.p. 198-200°C. IR (KBr) ν : 3566, 3176, 1783, 1699, 1578, 1286, 1022, 956 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6): δ 8.61 (1H, s, C₄-H), 8.02 (1H, d, J = 2.0 Hz, Ar-H), 8.13 (1H, d, J = 2.0 Hz, Ar-H); ^{13}C NMR (100 MHz, DMSO- d_6): δ 164.05 (C₃-COOH), 155.23 (C=O), 149.56 (C-8a), 147.55 (C-4), 133.36 (C-7), 128.67 (C-6), 128.56 (C-5), 122.34 (C-8), 120.82 (C-3), 120.57 (C-4a); LC-MS: m/z Found: 260.06 [M+H]⁺, C₁₀H₄Cl₂O₄ requires 259.04.

(5l) 6,8-Dibromo-2-oxo-2H-chromene-3-carboxylic acid: Yellow solid, m.p. 206-208. IR (KBr) ν : 3550, 3266, 2789, 1788, 1694, 1615, 1544, 1359, 1259,

1232, 979, 799, 694 cm^{-1} . $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$): δ 8.49 (1H, s, $\text{C}_4\text{-H}$), 8.21 (1H, d, $J = 2.0$ Hz, Ar-H), 8.16 (1H, d, $J = 1.6$ Hz, Ar-H); $^{13}\text{C NMR}$ (100 MHz, $\text{DMSO-}d_6$): δ 165.02 ($\text{C}_3\text{-COOH}$), 149.99 (C=O), 145.02 (C-8a), 137.60 (C-4), 131.42 (C-7), 126.35 (C-5), 122.36 (C-6), 116.79 (C-3), 110.33 (C-8 and C-4a); LC-MS: m/z Found: 348.90 $[\text{M}+\text{H}]^+$, $\text{C}_{10}\text{H}_4\text{Br}_2\text{O}_4$ requires: 347.94.

Selected spectral data of arylidinemalononitrile derivatives

(6a) Benzylidenemalononitrile: Light yellow crystals, m.p. 81–83°C. FT-IR (KBr) ν : 3034 cm^{-1} (HC=C), 2214 cm^{-1} (CN), 1589 cm^{-1} (C=C). $^1\text{H NMR}$ (300 MHz, CDCl_3): 7.93–7.96 (d, $J=8.5$ Hz, 2 H, phenyl), 7.81 (s, 1 H, CH), 7.54–7.68 (m, 3 H, phenyl) ppm. $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 160.02, 134.91, 131.07, 129.41, 113.62, 112.55, 82.98.

(6b) [4-(Dimethylamino)benzylidene]malononitrile: Orange crystals, m.p. 181–183°C; FTIR (KBr) 3436 (HC=C), 2924.7 (HC-C), 2207 (CN), 1618, 1526 (C=C), 1359, 1186 b (C-N) cm^{-1} ; $^1\text{H NMR}$ (300 MHz, CDCl_3) d: 7.74 (2H, d, 9.15 Hz, 2.88 Hz), 7.46 (1H, s, C=CH), 6.69 (2H, d, 9.22 Hz & 2.82 Hz), 3.17 (6H, s, N-Me_2); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) d: 157.98, 154.13, 133.81, 119.29, 115.94, 113.94, 111.58, 71.79, 40.03. LC-MS: m/z Found: 198.69 $[\text{M}+\text{H}]^+$, $\text{C}_{12}\text{H}_{11}\text{N}_3$ requires: 197.23.

(6c) (4-Chlorobenzylidene)malononitrile: Colorless crystals, m.p. 159–161°C. FTIR (KBr) ν : 2222 (CN), 1587 (C=C). $^1\text{H NMR}$ (300 MHz, CDCl_3): d = 7.88 (d, $J = 8.4$ Hz, 2H, phenyl), 7.67 (s, 1H, CH), 7.54 (d, $J = 8.4$ Hz, 2H, phenyl) ppm. LC-MS: m/z Found: 189.90 $[\text{M}+\text{H}]^+$, $\text{C}_{10}\text{H}_5\text{ClN}_2$ requires: 188.61.

(6d) (4-Fluorobenzylidene)malononitrile: White solid, m.p. 121–123°C. $^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 7.99$ (dd, $J = 8.7, 5.2$ Hz, 2H), 7.78 (s, 1H), 7.25 (dd, $J = 14.2, 5.8$ Hz, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3): δ 164.82, 158.42, 133.51, 133.42, 127.41, 117.32, 117.10, 113.62, 112.55, 82.36. LC-MS: m/z Found: 173.63 $[\text{M}+\text{H}]^+$, $\text{C}_{10}\text{H}_5\text{FN}_2$ requires: 172.15.

(6f) (4-Nitrobenzylidene)malononitrile: m.p. 158–159°C; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm): 8.43 (d, $J = 8.84$, 2H), 8.11 (d, $J = 8.84$, 2H), 7.95 (s, 1H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ (ppm): 156.9, 151.4, 136.8, 134.3, 126.6, 112.8, 113.5, 86.5. LC-MS: m/z Found: 200.19 $[\text{M}+\text{H}]^+$, $\text{C}_{10}\text{H}_5\text{N}_3\text{O}_2$ requires: 199.16.

(6g) (2-Chlorobenzylidene)malononitrile: m.p. 95–96°C yield: 85% $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm): 7.87 (d, $J = 7.84$, 2H), 7.75 (s, 1H), 7.73 (d,

$J = 7.84$, 2H); $^{13}\text{C NMR}$ (CDCl_3) δ (ppm): 158.7, 133.8, 132.9, 128.6, 129.7, 113.8, 112.4, 82.7. LC-MS: m/z Found: 189.72 $[\text{M}+\text{H}]^+$, $\text{C}_{10}\text{H}_5\text{ClN}_2$ requires: 188.61.

(6i) (4-Methoxybenzylidene)malononitrile: Pale yellow crystals, yield: 88%, m.p. 115–11°C, FT-IR (KBr) 2223 (CN), 1597 (C=C). $^1\text{H NMR}$ (300 MHz, CDCl_3): d = 7.90–7.92 (d, $J = 8.5$ Hz, 2H, phenyl), 7.65 (s, 1H, CH), 7.26 (d, $J = 8.5$ Hz, 2H, phenyl), 3.91 (s, 3H, OCH_3) ppm. $^{13}\text{C NMR}$ (CDCl_3) δ (ppm): 164.81, 158.81, 133.42, 128.88, 124.03, 115.12, 114.37, 114.39, 113.3, 79.67, 78.62, 77.31, 76.99, 55.77. LC-MS: m/z Found: 183.23 $[\text{M}+\text{H}]^+$, $\text{C}_{11}\text{H}_8\text{N}_2\text{O}$ requires: 184.19.

Conclusion

Our group has established a simple, efficient, eco-friendly green approach for the Knoevenagel condensation of aromatic aldehydes and salicylaldehydes with active methylene compounds like malononitrile and Meldrum's acid to synthesize benzylidinemalononitrile derivatives and 3-carboxy coumarins respectively in the absence of external base using agro-waste sourced green catalyst WENBA. The catalyst plays dual role being catalyst as well solvent media which made it to call as catalytic media. The advantages of the present approach are: it is an environmentally benign, inexpensive protocol, excellent yield, easier workup and shorter reaction time. The final product isolated was completely analysed for its purity using different spectroscopic techniques.

Conflict of interest

The author(s) confirm that this article content has no conflict of interest.

Supplementary Information

Supplementary information is available in the website <http://nopr.niscair.res.in/handle/123456789/60>.

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References

- Mulvihill M J, Beach E S, Zimmerman J B & Anastas P T, *Annu Rev Environ Resol*, 36 (2011) 271.
- Esmailpour M & Sardarian A Z, *Iran J Sci Technol*, 37 (2013) 277.

- 3 (a) Rossini G, Ballini R & Sorrenti P, *Synthesis*, 12 (1983) 1014; (b) Ballini R & Bosica G, *J Org Chem*, 62 (1997) 425.
- 4 (a) Shore G, Morin S & Organ G, *Angew Chem Int Ed*, 45 (2006) 2761; (b) Kappe C O & Stadler A, *Microwaves in Organic and Medicinal Chemistry* (Wiley-VCH, Weinheim) (2005) 182; (c) Comer E & Organ M G A, *J Am Chem Soc*, 127 (2005) 8160.
- 5 Van Schie R M, Wadelius M, Kamali F, Daly A K, Manolopoulos V G, De Boer A, Barallon R, Verhoef T I, Kirchheiner J & Haschke-Becher E, *Pharmacogenomics*, 10 (2009) 1687.
- 6 Lin C M, Huang S T, Lee F W, Sawkuo H & Lin M H, *Bioorg Med Chem*, 14 (2006) 4402.
- 7 Modranka J N, Nawrot E & Graczyk J, *Eur J Med Chem*, 41 (2006),1301.
- 8 Kirkiacharian S, Thuy D T, Sicsic S, Bakhchinian R, Kurkjian R & Tonnaire T, *Il Farmaco*, 57 (2002),703.
- 9 Ali M Y, Jannat S, Jung H A, Jeong H O, Chung H Y & Choi J S, *Chem Biol Interact*, 252 (2016) 93.
- 10 Bonsignore L, Cottiglia F, Elkhaili H, Jehl F, Lavagna S M, Loy G, Manna F, Monteil H, Pompei D & Secci D, *Il Farmaco*, 53 (1998) 425.
- 11 Bonsignore L, De Logu A, Lavagna S M, Loy G & Secci D, *Eur J Med Chem*, 29 (1994) 479.
- 12 Jonsson D, Erlandsson M & Uden A, *Tetrahedron Lett*, 42 (2001) 6953.
- 13 Elinos-Baez C M, Leon F & Santos E, *Cell Biol Int*, 29 (2005) 703.
- 14 Kempen I, Hemmer M, Counerotte S, Pochet L, de Tullio P, Foidart J M, Blacher S, Noel A, Frankenne F & Piroette B, *Eur J Med Chem*, 43 (2008) 2735.
- 15 Specht D P, Martic P A & Farid S, *Tetrahedron*, 38 (1982) 1203.
- 16 (a) Meuly W C & Kirk-Othmer, *Encyclopedia of Chemical Technology* (John Wiley and Sons, New York) 7 (1979) 196; (b) Stuart D M, Hruschka J K & Kirk-Othmer, *Encyclopedia of Chemical Technology* (John Wiley and Sons, New York) 16 (1979) 951; (c) Taylor W I, Chant B, Van-Loveren G & Kirk-Othmer, *Encyclopedia of Chemical Technology* (John Wiley and Sons, New York) 4 (1979),15
- 17 Zaharadnik M, *The Production and Application of Fluorescent Brightening Agents* (John Wiley and Sons, New York) (1992).
- 18 Peroni E, Caminati G, Baglioni P, Nuti F, Chelli M & Papini A M, *Bioorg Med Chem Lett*, 12 (2002) 1731.
- 19 Murra R D H, Mendez J & Brown S A, *The Natural Coumarins, Occurrence, Chemistry and Biochemistry* (John Wiley and Sons, New York) (1982).
- 20 Karaliota A, Kretsi O & Tzougraki C, *J Inorg Biochem*, 84 (2001) 33.
- 21 Creaven B S, Egan D A, Kavanagh K, McCann M, Noble A, Thati B & Walsh M, *Inorg Chim Acta*, 359 (2006) 3976.
- 22 Watson B T & Christiansen G E, *Tetrahedron Lett*, 39 (1998) 6087.
- 23 Maggi R, Bigi F, Carloni S, Mazzacani A & Saroti G, *Green Chem*, 3 (2001) 173.
- 24 Shirokova E A, Segal G M & Torgov I V, *Bioorganicheskaya Khimiya*, 14 (1988) 236.
- 25 Bandgar B P, Uppalla L S & Kurule D S, *Green Chem*, 1 (1999) 243.
- 26 Bandgar B P, Uppalla L S & Sadavarte V S, *J Chem Res*, 1 (2002) 40.
- 27 Creaven B S, Egan D A, Kavanagh K D, McCann M, Noble A, Thati B & Walsh M, *J Inorg Biochem*, 101 (2007) 1108.
- 28 Karade N N, Gampawar S V, Shinde S V & Jadhav W N, *Chin J Chem*, 25 (2007) 1686.
- 29 Darvatkar N B, Deorukhkar A R, Bhilare S V, Raut D G & Salunkhe M M, *Synth Commun*, 38 (2008) 3508.
- 30 Li T S, Zhang Z H, Yang F & Fu C G, *J Chem Res Synops* (1998) 38.
- 31 Khaligh N G, *Catal Sci Tech*, 2 (2012) 1633.
- 32 Vilar S, Quezada E, Santana L, Uriarte E, Ya'nez M, Fraiz N, Alcaide C, Cano E & Orallo F, *Bioorg Med Chem Lett*, 16 (2006) 257.
- 33 Bogdal D J, *Chem Res Synop* (1998) 468.
- 34 Shockravi A, Shargi H, Valizadeh H H & Heravi M M, *Phosphorus Sulfur Silicon Relat Elem*, 177 (2002) 2555.
- 35 Valizadeh H & Vaghefi S, *Synth Commun*, 39 (2009) 1666.
- 36 Yavari I, Hekmat-Shoar R & Zonouzi A, *Tetrahedron Lett*, 39 (1998) 2391.
- 37 Kaye P T S & Musa M A, *Synthesis*, 2002 (2002) 2701.
- 38 Kaye P T S, *Afr J Sci*, 100 (2004) 545.
- 39 Jr A J, Dias R L A, Castilho M S, Oliva G & Corre'a A G, *J Braz Chem Soc*, 16 (2005) 763.
- 40 Undale K A, Gaikwad D S, Shaikh T S, Desai U V & Pore D M, *Indian J Chem*, 51B (2012) 1039.
- 41 Karami B, Farahi M & Khodabakhshi S, *Helv Chim Acta*, 95 (2012) 455.
- 42 He X, Shang Y, Yu Z, Fang M, Zhou Y, Han G & Wu F, *J Org Chem*, 79 (2014) 8882.
- 43 Pan W Y, Xiao Y M, Xiong H Q & Lu C W, *Res Chem Intermed*, 42 (2016) 7057.
- 44 Hekmatshoar R, Rezaei A & Bheshtiha S Y S, *Phosphorus Sulfur Silicon Relat Elem*, 184 (2009) 2491.
- 45 Harishkumar H N, Mahadevan K M, Kiran Kumar H C & Satyanarayan N D, *Org Commun*, 4 (2011) 26.
- 46 Shaabani A, Ghadari R, Rahmati A & Rezayan A H, *J Iran Chem Soc*, 6 (2009) 710.
- 47 Song A, Wang X & Lam K S, *Tetrahedron Lett*, 44 (2003) 1755.
- 48 Tietze L F & Beifuss U, *Comprehensive Organic Synthesis*, 2 (1991) 341.
- 49 Jones G, *Org React*, 15 (1967) 204.
- 50 (a) Meuly W C & Kirk-Othmer, *Encyclopedia of Chemical Technology*, 3 (1979) 196; (b) Stuart D M & Hruschka J K, *Ibid*, 16, 951; (c) Taylor W I, Chant B & van Loveren G, *Ibid*, 4, 15.
- 51 Dey S K, Amadeu N & Janiak C, *Chem Commun*, 52 (2016) 7834.
- 52 Gao G, Lu L T, Zou J, Gao Y, Liu M & He U, *Chem Res Chin*, 23 (2007) 169.
- 53 Lai G, Peng J, Li J, Qiu H, Jiang J, Jiang K & Shen Y, *Tetrahedron Lett*, 47 (2006) 6951.
- 54 Liu Y, Peng J, Zhai S, Li J, Mao J, Li M, Qiu H & Lai G, *Eur J Inorg Chem* (2006) 2947.

- 55 Gao G, Gao J, Zhou W, Lu L & He M, *Chin Chem Lett*, 17 (2006) 1293.
- 56 Angeletti E, Canepa C, Martinetti G & Venturello P, *Tetrahedron Lett*, 29 (1988) 2261.
- 57 Saeed B, Morteza B, Shohreh H & Peyman S, *Synth Commun*, 36 (2006) 2549.
- 58 Chalais S, Laszlo P & Mathy A, *Tetrahedron Lett*, 26 (1985) 4453.
- 59 Liu X W, Jiang H & Gong H, *Chin J Org Chem*, 27 (2007) 131.
- 60 Li J, Xing C & Li T, *J Chem Technol Biotechnol*, 79 (2004) 1275.
- 61 Cabello J A, Campelo J M, Garcia A, Luna D & Marinas J M, *J Org Chem*, 49 (1984) 5195.
- 62 Wang S, Ren Z, Cao W & Tong W, *Synth Commun*, 31 (2001) 673.
- 63 Wang S, Li J, Yang W & Li T, *Ultrason Sonochem*, 9 (2002) 159.
- 64 Rao P S & Venkataratnam R V, *Tetrahedron Lett*, 32 (1991) 5821.
- 65 Li Y, *J Chem Res*, 2000 (2000) 524.
- 66 Ren Y & Cai C, *Synth Commun*, 37 (2007) 2209.
- 67 Dipak P & Jagir S S, *J Chem Soc Perkin Trans I* (1993) 739.
- 68 Texier-Boullet F & Foucaud A, *Tetrahedron Lett*, 23 (1982) 4927.
- 69 Patil S S, Jadhav S D & Deshmukh M B, *Indian J Chem*, 52B (2013) 1172.
- 70 Saeed Abaee M, Mohammad M, Mojtahedi M, Zahedi M & Khanalizadeh G, *ARKIVOC*, xv (2006) 48.
- 71 Muralidhar L & Girija C R, *J Saudi Chem Soc*, 18 (2014) 541.
- 72 Boruah P R, Ali A A, Chetia M, Saikia B & Sarma D, *Chem Commun*, 51 (2015) 11489.
- 73 Surneni N, Barua N C & Saikia B, *Tetrahedron Lett*, 57 (2016) 2814.
- 74 Saikia B & Borah P, *RSC Adv*, 5 (2015) 105583.
- 75 Saikia E, Bora S K & Chetia B, *RSC Adv*, 5 (2015) 102723.
- 76 Boruah P R, Ali A A, Saikia B & Sarma D, *Green Chem*, 17 (2015) 1442.
- 77 Konwar M, Ali A A & Sarma D, *Tetrahedron Lett*, 57 (2016) 2283.
- 78 Saikia B, Borah P & Barua N C, *Green Chem*, 17 (2015) 4533.
- 79 Shinde S, Damate S A, Morbale S, Patil M & Patil S S, *RSC Adv*, 7 (2017) 7315.
- 80 Dewan A, Sarmah M, Bora U & Thakur A J, *Appl Organometal Chem*, 31 (2017) e3646.
- 81 Sarmah M, Dewan A, Thakur A J & Bora U, *Chemistry Select*, 3 (2018) 5581.
- 82 Kantharaju K & Hiremath P B, *Int J Engg Tech Sci Res*, 4 (2017) 807.
- 83 Kantharaju K, Hiremath P B & Khatavi S Y, *Indian J Chem*, 58B (2019) 706.
- 84 (a) Kantharaju K & Hiremath P B, *Asian J Chem*, 30 (2018), 1634; (b) Hiremath P B, Kantharaju K, *Curr Microwave Chem*, 6 (2019), 30; (c) Hiremath P B, Kantharaju K & Pattanashetty S H, *Conference on Drug design and Discovery Technologies*, (2020), 123, *The Royal Society of Chemistry*.
- 85 Brahmachari G, *ACS Sustainable Chem Eng*, 3 (2015) 2350.
- 86 Luan Y, Qi Y, Gao H, Andriamitantoa R S, Zheng N & Wang G, *J Mater Chem A*, 3 (2015) 17320.
- 87 Wang H, Wang C, Yang Y, Zhao M & Wang Y, *Catal Sci Technol*, 7 (2017) 405.
- 88 Gupta R, Gupta M, Paul S & Rajive G, *Bull Korean Chem Soc*, 30 (2009) 2419.
- 89 Gill C, Pandhare G, Raut R, Gore V & Gholap S, *Bull Cat Soc India*, 7 (2008) 153.
- 90 Pasha M A & Manjula K, *J Saudi Chem Soc*, 15 (2011) 283.
- 91 Ren Z, Cao W & Tong W, *Synth Commun*, 32 (2002) 3475.
- 92 Bagul S D, Rajput J D & Bendre R S, *Environ Chem Lett*, 15 (2017) 725.