

Waste crab shell catalysed synthesis of dihydropyrano[c]chromenes

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Abstract

In present study we have applied green and sustainable route for synthesis of dihydropyrano[c]chromenes catalysed from waste crab shell. Waste crab shell on calcinations converts to calcium oxide which acts as base catalyst to promote formation of dihydropyrano[c]chromenes. Mild reaction media, green route of synthesis, better yield of products with short time are remarkable advantages of method. The method is applicable for synthesis of diversified dihydropyrano[c]chromenes starting from wide range of aldehydes. The products obtained are characterised by IR, ^{13}C , ^1H NMR studies.

Keywords: Dihydropyrano[c]chromenes, Crab shell, Sustainability.

Introduction

MCR, a powerful and virtually reliable target-guided synthetic approach, has extensively been used and applied for the rapid construction of molecular-level complex architectures and interest in it from different branches of science is expanding exponentially.¹ Multicomponent reactions—have become important tools for the rapid generation of molecular complexity and diversity with predefined functionality in chemical biology and drug discovery.² Heterocyclic rings are found in many naturally occurring compounds and they compose the core structures of many biologically active scaffolds as well as some industrial compounds.³⁻⁵

Dihydropyrano[3,2-c]chromenes are a class of important heterocycles, they can be used as cognitive enhancers for the treatment of neurodegenerative disease including amyotrophic lateral sclerosis, Huntington's disease, Alzheimer's disease, Parkinson's disease, AIDS associated dementia and Down's syndrome as well as for the treatment of schizophrenia and myoclonus⁶. In addition, aminochromene derivatives exhibit a wide spectrum of biological activities including antihypertensive and anti-ischemic behavior⁷⁻⁹.

Literature study reveals applications of silica gel 5.2-hydroxyethyl ammonium formate, $[\text{H}_3\text{N}^+-\text{CH}_2-\text{CH}_2-\text{OH}][\text{HCOO}^-]$ ¹⁰ as ionic liquid, *N*-propyl-imidazolium hydrogen sulfate ($[\text{Sipim}]\text{HSO}_4$) as a recyclable heterogeneous ionic liquid¹¹, thiourea dioxide¹², diammonium hydrogen phosphate¹³, [TBBDA] and [PBBS]¹⁴ as catalyst for synthesis of dihydropyrano[c]chromenes. Some recently introduced

catalysts for synthesis of 3,4-dihydropyrano[3,2-c]chromenes are DABCO promoted¹⁵, Piperidinium Benzene-1,3-Disulfonate Ionic Liquid¹⁶ and Ni(II)-functionalized Li^+ -Montmorillonite¹⁷.

In comparison to the above mentioned catalysts, CaO is cheaper and also possesses dynamic catalytic activity, provides favourable reaction condition and re-usability. Also calcium is available abundantly in natural sources like shells and bones. A study with Li doped CaO derived from egg shell for biodiesel production has been reported previously¹⁸. A report¹⁹ on transesterification of soybean oil to biodiesel using CaO as a solid base showed that the life time of CaO is longer than that of $\text{K}_2\text{CO}_3/\gamma\text{-Al}_2\text{O}_3$ and $\text{KF}/\gamma\text{-Al}_2\text{O}_3$ catalyst.

Boey et al²⁰ show usage of calcined crab shells for biodiesel production through central composite design approach. By the study of advantages of CaO catalyst in different organic transformation, we herein employed CaO derived from waste crab shell for three component reaction between aromatic aldehyde, malononitrile and 4-hydroxy coumarin for synthesis of dihydropyrano[c]chromenes.

Material and Methods

All the chemicals used are commercially available and were used without purification. ^1H and ^{13}C NMR spectra were recorded on Avance-300 Bruker NMR spectrophotometer in CDCl_3 and DMSO. IR spectra were obtained using potassium bromide pellets on Bruker ALPHAFT-IR spectrometer. Melting points were measured on open capillary method on DBK-programmable melting point apparatus. Purity of the substrates and completion of reactions were checked by thin layer chromatography (TLC) using Merck silicagel 60 F₂₅₄ plates.

Preparation of catalyst: The waste crab shell were collected from local market washed thoroughly with hot water to remove adhesive impurities and dried in oven at 80-90°C for 24 hrs. It was then calcined at 800°C temperature at heating rate 10 degree min^{-1} for 3 hr in Muffle furnace which got transformed into white soft powder, which was used as catalyst.

Catalyst characterization: After modification by calcinations, absorption bands of CO_3^{2-} molecules shift to higher frequency and are observed at 1450, 1050 and 518 cm^{-1} . A sharp stretching band is observed at 3641 cm^{-1} due to OH group in IR spectrum of calcined crab shell, which is in raw crab shell displayed at 3480 cm^{-1} (Fig. 1). The XRD patterns of crab shell (Fig. 2) were obtained in reflection mode with

Cu K α radiation ($\lambda=1.5418 \text{ \AA}$) at 30 kV, 10 mA, a scan speed of $1.0 \text{ degree min}^{-1}$ and a scan range of $10\text{-}90^\circ$. The data was analyzed in the 2θ / degree range from 2° to 70° with the scanning step of 0.5 per sec. For raw crab shell powder (I), the main peak was observed at $2\theta=29.86^\circ$ and other peaks were observed at 23.25° , 31.74° , 36.12° , 39.61° , 43.32° , 47.64° , 48.63° , 57.53° , 61.61° , 64.83° and 65.80° which were characteristics of CaCO_3 . The peaks for the calcined crab shell (II) appeared at $2\theta=43.17^\circ$, 33.32° , 38.84° , 54.14° , 62.81° and 65.34° , which were characteristics of CaO .

General procedure for synthesis of 2-amino-4-(phenyl)-4,5-dihydro-5-oxopyrano[3,2-c]chromene-3-carbonitrile:

The reaction mixture contains aromatic aldehyde (5.0 mmol), 4-hydroxy coumarin (5.0 mmol) and malononitrile (5.0 mmol) to which catalyst (15 wt.%) was added and the

reaction was carried out in solvent ethanol:water(1:1). Then the reaction mixture was stirred at 80°C on preheated oil bath for appropriate time. The progress of reaction was monitored by TLC (n-hexane: ethyl acetate, 6:4). The crude product 4 obtained after cooling at room temperature was separated by filtration and washed with 10 mL of cold water twice to remove the catalyst and dried in vacuum. The pure products were obtained by recrystallization from ethyl alcohol.

Results and Discussion

We investigated calcium oxide sourced from waste crab shell as a catalyst to promote condensation between aromatic aldehydes (5.0 mmol), malononitrile (5.0 mmol) and 4-hydroxy coumarin (5.0 mmol) to synthesise dihydropyrano[c]chromenes (Scheme 1).

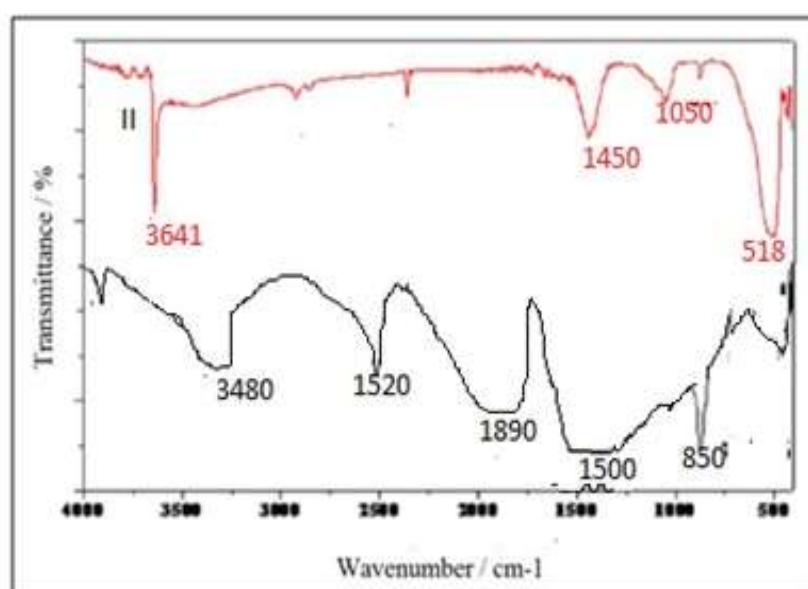


Fig. 1: Comparison of IR spectrum of raw crab shell powder to calcined crab shell powder (II)

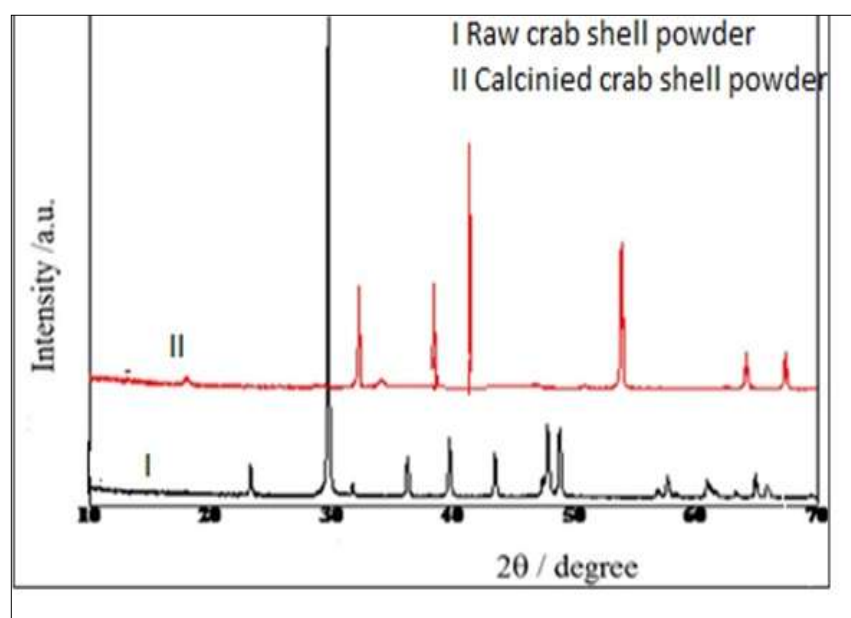


Fig. 2: XRD spectrum of crab shell powder

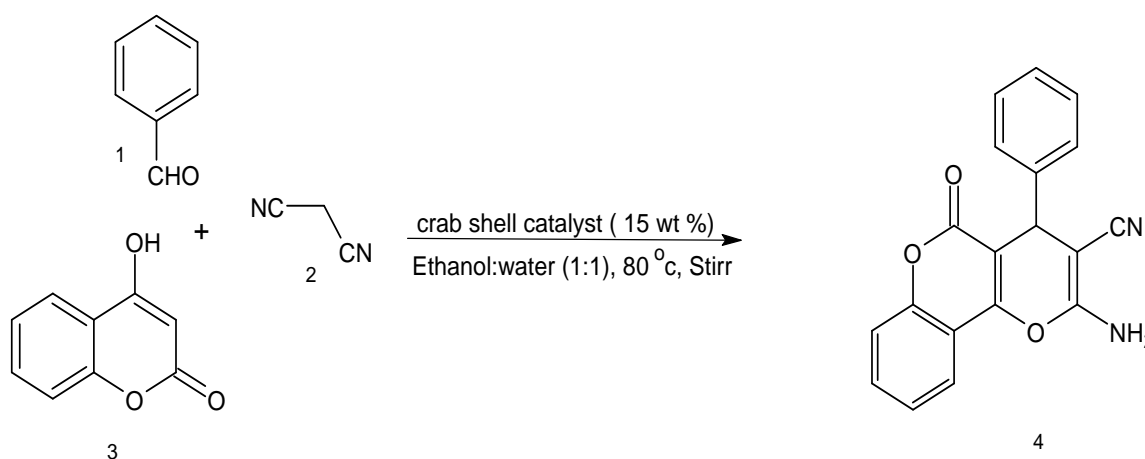
We employed this reaction as a template to optimize the reaction conditions and the results are summarized in table 1. When we examined effect of different solvents on product yield, we found that water, methanol, ethanol, toluene, THF and DCM were less effective (entry 1-6) than mixed solvent system ethanol:water (1:1, v/v, 5 mL) (entry 7). Upon examining the influence of the amount of catalyst on the reaction, it was found that 15 wt. % of crab shell catalyst was sufficient to promote the reaction (entry 9). In the presence of less than this amount, the yield dropped dramatically even on prolonged reaction (entry 8). When the amount of catalyst was increased over 15 wt. % equivalent, neither the yield nor the reaction time was improved (entry 10).

Using the optimized reaction conditions, a range of substituted dihydropyrano[*c*]chromenes (4a-i) was synthesized. This method was found to be equally effective for aromatic aldehydes bearing electron donating as well as electron-withdrawing substituents. The reaction proceeds very well in all cases affording the products in good to excellent yield (Table 2). All the products were isolated by recrystallization from 96% ethanol. The formation of pure

products as indicated by TLC and better yields of resulting products reveal the efficiency of proposed method.

To examine the reusability of catalyst, recycling experiments were carried out with substrates used in model reaction for four times. After filtration of the reaction mixture followed by evaporation of aqueous phase, catalyst was recovered quantitatively and then regenerated by heating at 400°C for 3 hrs before each new reuse. The results shown in table 3 indicate satisfactorily reusability of catalyst.

Physical and spectral data of selective compounds: 2-Amino-4-(phenyl)-4,5-dihydro-5-oxopyrano[3,2-*c*]chromene-3-carbonitrile(4a): MP: 260-262°C; IR (KBr): 3411, 3177, 2198, 1704, 1673, 1604 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ, 7.91 (d, 1H, ArH), 7.71 (t, 1H, ArH), 7.49 (t, 1H, ArH), 7.45 (d, 1H, ArH), 7.42 (s, 2H, NH₂), 7.33 (t, 2H, ArH), 7.28(m, 1H, ArH), 7.25 (d, 2H, ArH), 4.46 (s, 1H, CH) ppm; ¹³C NMR (DMSO-*d*₆): δ, 160.4, 158.8, 154.3, 153.0, 144.2, 133.8, 129.4, 128.5, 128.0, 125.5, 123.3, 120.1, 117.4, 113.8, 104.9, 58.8 ppm; Anal. calcd for C₁₉H₁₂N₂O₃: C, 72.15; H, 3.79; N, 8.86 %, found: C, 72.26; H, 3.67; N, 8.81 %.



Scheme 1: Synthesis of dihydropyrano[*c*]chromenes

Table 1
Optimization of reaction conditions for the synthesis of dihydropyrano[*c*]chromenes

Entry	Solvent ^a (5 mL)	Catalyst wt. %	Time (min)	Yield (%)
1	Water	15	90	72
2	Methanol	15	90	67
3	Ethanol	15	60	81
4	Toluene	15	120	45
5	THF	10	120	37
6	DCM	10	100	58
7	Ethanol:Water (1:1)	10	60	95
8	Ethanol:Water (1:1)	5.0	90	81
9	Ethanol:Water (1:1)	15	45	95
10	Ethanol:Water (1:1)	20	45	95

^aEntries in bracket indicates the ratio of ethanol and water on volume basis

Table 2
Synthesis of dihydropyrano[c]chromenes derivatives starting from different aldehydes

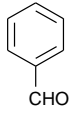
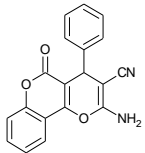
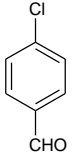
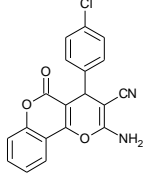
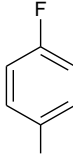
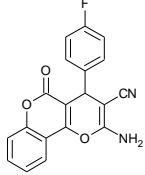
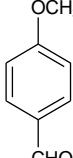
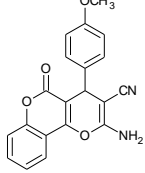
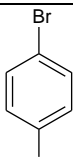
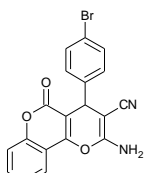
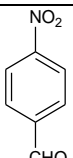
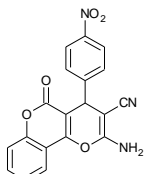
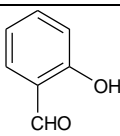
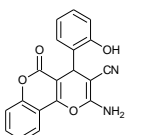
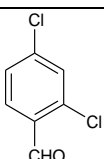
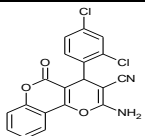
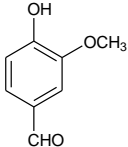
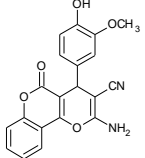
Entry	substrate	Time (Minutes)	Yield %	Product
4a		45	95	
4b		50	94	
4c		50	94	
4d		60	90	
4e		45	95	
4f		50	93	
4g		60	90	
4h		45	95	
4i		60	92	

Table 3
Reusability of catalyst

Recycle Number	1 st Run	2 nd Run	3 rd Run	4 th run
% yield	95	92	92	90

2-Amino-4-(4-chlorophenyl)-5-oxo-4H, 5H-pyrano[3,2-c]chromene-3-carbonitrile(4b): MP: 266-268°C; IR (KBr): 3144, 3008, 2852, 2200, 1695, 1613, 1568 cm⁻¹; ¹H NMR (CDCl₃+DMSO-*d*₆): δ, 8.07-8.09 (d, 1H, ArH), 7.85-7.87 (d, 1H, ArH), 7.53-7.58 (t, 1H, ArH), 7.43-7.46 (d, 4H, ArH), 7.25-7.31 (t, 1H, ArH), 6.69 (s, 2H, NH₂), 4.63 (s, 1H, CH) ppm; ¹³C NMR (DMSO-*d*₆): δ, 160.3, 158.9, 154.4, 153.0, 143.1, 133.8, 132.6, 130.4, 129.2, 123.3, 119.3, 117.3, 113.9, 104.4, 58.8, 36.4 ppm; Anal. calcd for C₁₉H₁₁N₂O₃Cl: C, 65.05; H, 3.14; N, 7.99 % found: C, 64.93; H, 3.07; N, 8.12 %

2-amino-4-(4-fluorophenyl)-5-oxo-4H, 5H-pyrano[3,2-c]chromene-3-carbonitrile(4c): MP: 260°C; IR (KBr): 3384, 3281, 2186, 1711, 1668, 1603, 1501 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ, 7.88 (d, 1H, ArH), 7.67 (t, 1H, ArH), 7.46 (t, 1H, ArH), 7.41 (d, 1H, ArH), 7.38 (s, 2H, NH₂), 7.31 (dd, 2H, ArH), 7.07 (dd, 2H, ArH), 4.47 (s, 1H, CH) ppm; ¹³C NMR (DMSO-*d*₆): δ, 162.2, 160.2, 159.4, 157.9, 153.4, 152.1, 139.4, 132.8, 129.6, 123.5, 119.0, 116.5, 115.1, 112.9, 103.8, 57.9, 36.3 ppm; Anal. calcd for C₁₈H₁₇FN₂O₂: C, 69.22; H, 5.49; N, 8.97 % found: C, 69.29; H, 5.42; N, 8.93 %

2-Amino-4-(4-methoxyphenyl)-4,5-dihydro-5-oxopyrano [3,2-c]chromene-3-carbonitrile(4d): MP: 245-247°C; IR (KBr): 3380, 3310, 3184, 2189, 1711, 1668, 1607 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ, 7.89 (d, 1H, Ar-H), 7.70 (t, 1H, ArH), 7.49 (t, 1H, ArH), 7.45 (d, 1H, ArH), 7.37 (s, 2H, NH₂), 7.18 (d, 2H, ArH), 6.87 (d, 2H, ArH), 4.40 (s, 1H, CH), 3.72 (s, 3H, OCH₃) ppm; ¹³C NMR (DMSO-*d*₆): δ, 160.4, 159.2, 158.8, 153.9, 152.9, 136.2, 133.66, 129.6, 125.5, 123.3, 120.2, 117.4, 114.7, 113.8, 105.1, 59.1, 55.9 ppm; Anal. calcd for C₂₀H₁₄N₂O₄: C, 69.36; H, 4.05; N, 8.09 % found: C, 69.27; H, 4.10; N, 8.02 %

2-Amino-4-(4-bromophenyl)-4,5-dihydro-5-oxopyrano [3,2 c]chromene-3-carbonitrile(4e): MP: 251-253°C; IR (KBr): 3370, 2165, 1705, 1670, 1612, 1371, 1057 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ, 7.91(d, 1H, ArH), 7.73 (t, 1H, ArH), 7.47-7.52 (m, 4H, ArH), 7.25 (d, 2H, ArH), 4.48 (s, 1H, CH) ppm; ¹³C NMR (DMSO-*d*₆): δ, 160.0, 158.3, 154.0, 152.6, 143.2, 133.5, 131.8, 130.5, 125.2, 123.0, 120.7, 119.5, 117.1, 113.4, 103.9, 57.8 ppm; Anal. calcd. for C₁₈H₁₇BrN₂O₂: C, 57.92; H, 4.59; N, 7.51 % found: C, 57.97; H, 4.50; N, 7.57 %

2-Amino-4-(4-nitrophenyl)-5-oxo-4H,5H-pyrano- [3,2-c] chromene-3-carbonitrile(4f): MP: 250-252°C; IR (KBr): 3476, 3421, 3369, 3323, 2190, 1711, 1666, 1609, 1518, 1379, 1292 cm⁻¹; ¹H NMR (DMSO-*d*₆): δ, 8.18 (d, 2H, ArH), 7.91 (d, 1H, Ar-H), 7.74 (t, 1H, ArH), 7.60 (d, 2H, ArH), 7.52 (t, 1H, ArH), 7.57 (s, 2H, NH₂), 7.47 (d, 1H, ArH), 4.68

(s, 1H, CH) ppm; ¹³C NMR (DMSO-*d*₆): δ, 160.4, 158.9, 154.8, 153.1, 151.6, 147.4, 134.0, 130.0, 125.6, 124.6, 123.4, 119.8, 117.5, 113.7, 103.6, 57.6 ppm; Anal. calcd for C₁₉H₁₁N₃O₅: C, 63.16; H, 3.05; N, 11.63 % found: C, 63.04; H, 3.16; N, 11.70%

2-Amino-4-(2,4-dichlorophenyl)-5-oxo-4H, 5H-pyrano [3,2-c]chromene-3-carbonitrile(4g): MP: 261-263°C; IR(KBr): 3411, 3396, 3177, 2197, 1786, 1767, 1712, 1666 cm⁻¹; ¹H NMR (CDCl₃+DMSO-*d*₆): δ, 7.83-7.86 (d, 1H, ArH), 7.52-7.57 (t, 1H, ArH), 7.24-7.33 (m, 3H, ArH), 7.12 (d, 2H, ArH), 6.51 (s, 2H, NH₂), 4.99 (s, 1H, CH) ppm; ¹³C NMR (DMSO-*d*₆): δ, 160.2, 159.0, 155.1, 153.1, 140.3, 134.3, 133.9, 133.3, 132.9, 129.7, 128.7, 125.6, 123.4, 119.4, 117.5, 113.7, 103.4, 57.1 ppm; Anal. calcd. for C₁₉H₁₀N₂O₃Cl₂: C, 59.22; H, 2.60; N, 7.27 % found: C, 59.14; H, 2.52; N, 7.37 %.

Conclusion

In conclusion, we have promoted green, cost effective and sustainable route for preparation of dihydropyrano[*c*]chromenes under mild reaction condition. Simplicity of procedure, fast reaction rate, pure and better yield of products with reusability of catalyst are prominent features of method.

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