



CALCINIZED EGGSHELL: A HIGHLY EFFICIENT CATALYST FOR THE SYNTHESIS OF PYRANO [2, 3-C] PYRAZOLES UNDER SOLVENT-FREE CONDITION

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Abstract: Pyrano pyrazoles are synthesized by hydrazine hydrate, ethyl acetoacetate, aromatic aldehyde and malononitrile using grinding method with calcinized eggshell catalyst. The calcinized eggshell catalyst was obtained from chicken eggshell waste. The calcinized eggshell is a safe, naturally available and inexpensive catalyst with high catalytic efficiency. The short reaction time, high yield, easy work-up, grinding technique, room temperature, solvent free, mild reaction condition and reusability of the catalyst are the advantages of this method. The scope of this reaction was to develop multicomponent organic reaction by using green catalyst at room temperature. The products were characterized by IR, ¹H NMR, ¹³C NMR and GC-MS techniques.

Keywords: Calcinized eggshell, room temperature, grinding method, pyranopyrazoles etc.

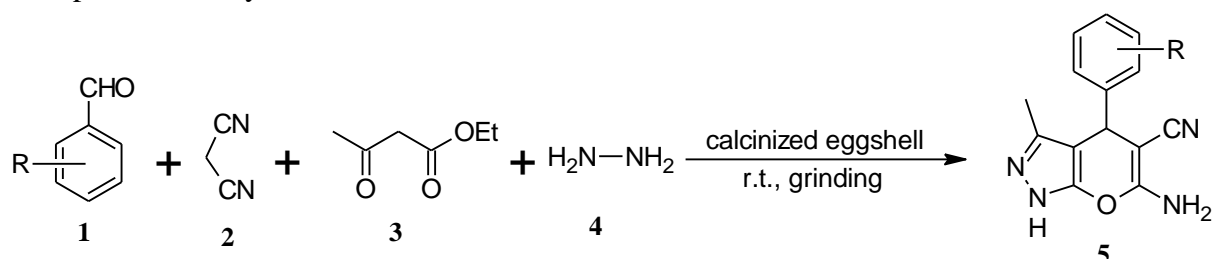
Introduction

Nowadays, there is an increasing interest towards green chemistry, resulting in new environmentally benign procedures such as one-pot multicomponent reactions and reusable heterogeneous naturally available catalystsⁱ. In designing a reaction according to green chemistry principles, it is a challenge to avoid harmful and hazardous organic solvents in multicomponent reactionⁱⁱ. The nanoporous materials are of great interest in various fields because of their catalytic, adsorbed and magnetic properties for their porous structuresⁱⁱⁱ. Pyranopyrazoles are an important heterocyclic compounds, which play a significant role in biologically active compounds^{iv}. Pyranopyrazoles are used as antifungicidal, analgesic, anti-inflammatory, anticancer, antimicrobial, inhibitors of human Chk1 kinase, insecticidal, vasodilator, molluscicidal and biodegradable agrochemicals^{v-viii}.

The pyranopyrazole derivatives are synthesized by the condensation of aldehyde, ethyl acetoacetate, malononitrile and hydrazine hydrate with L-proline^{ix}, trichloroacetic acid or ceric sulfate^x, Bronsted-acidic ionic liquid^{xi}, iodine^{xii}, silicotungstic acid^{xiii}, Fe₃O₄ nanoparticles^{xiv},

ZnS nanoparticles^{xv}, nano ZnO^{xvi}, sodium benzoate^{xvii}, nano-titania supported Preyssler-type heteropoly-acid^{xviii}, polyphosphoric acid supported on Ni_{0.5}Zn_{0.5}Fe₂O₄ nanoparticles^{xix} and polystyrene-supported p-toluenesulfonic acid^{xx}.

The naturally available eggshells have been utilized as treatment of osteoporosis^{xxi}, humidity adsorbent^{xxii}, catalyst in biodiesel production^{xxiii}, removal of chromium^{xxiv}, catalyst for lactose isomerization to lactulose^{xxv} and catalyst in organic reactions^{xxvi, xxvii}. Therefore, in present work calcinized eggshells are used as a catalyst in multicomponent synthesis of pyranopyrazole to explore its catalytic activities.



Results and Discussion

In continuation of our research^{xxvii-xxxiii}, herein we report the synthesis of pyranopyrazoles by grinding under solvent free condition using calcinized eggshell at room temperature. The reaction of benzaldehyde, hydrazine hydrate, ethyl acetoacetate and malononitrile was carried out as model reaction. The amount of catalyst required for reaction was optimized by carrying the reaction with calcinized eggshell catalyst at room temperature. It is found that the optimum amount of catalyst was 0.050 g to obtain the corresponding pyranopyrazoles. The large amount of catalyst did not affect the reaction (Table 1). After optimizing the reaction condition the variety of aromatic aldehydes with hydrazine hydrate, ethyl acetoacetate and malononitrile were employed under same reaction conditions to evaluate the scope of this reaction (Table 2). All reactions, delivered good product yields and accommodated a wide range of aromatic aldehydes bearing both electron-donating and electron-withdrawing substituents. In case of aromatic aldehydes the nature of substituents of aromatic aldehydes did not have appreciable effect on overall yields of the product. The electron deficient aldehydes gave excellent yield of products. The position (o, m and p) of the substituted aromatic aldehydes did not show any noticeable effect on either the reaction time or the yields.

Table-1 Optimization of amount of catalyst

Entry	Catalyst amount (g)	Time (min)	Yield (%)
1	0.010	29	80
2	0.020	25	81
3	0.030	20	83
4	0.040	16	86
5	0.050	12	90
6	0.060	12	90

7

0.070

12

90

The catalytic activity of calcinized eggshell was compared with other reported catalysts for the synthesis of pyranopyrazoles. The results show that calcinized eggshell catalyzed the reaction with high yield under solvent free condition at room temperature with grinding method (Table 3). As compare to other catalyst the calcinized eggshell has more catalytic activity. The recovered catalyst shows good results even after five runs (Table 4), it indicates that the catalyst was more efficient and reusable.

Table- 2 Synthesis of pyranopyrazole derivatives

Product	R	Time (min)	Yield (%)	M. P (°C)
5a	H	12	90	244
5b	3-NO ₂	15	91	192
5c	4-NO ₂	10	93	196
5d	4-Br	16	93	206
5e	2-OCH ₃	18	89	250
5f	4-OCH ₃	23	85	210
5g	4-CH ₃	23	83	201
5h	3-OH	14	79	224
5i	4-OH	21	90	224
5j	4-Cl	24	92	175
5k	Thiophene 2-carbaldehyde	12	88	241

Table-3 Comparison of calcinized eggshell with reported catalysts in the synthesis of pyranopyrazoles^a.

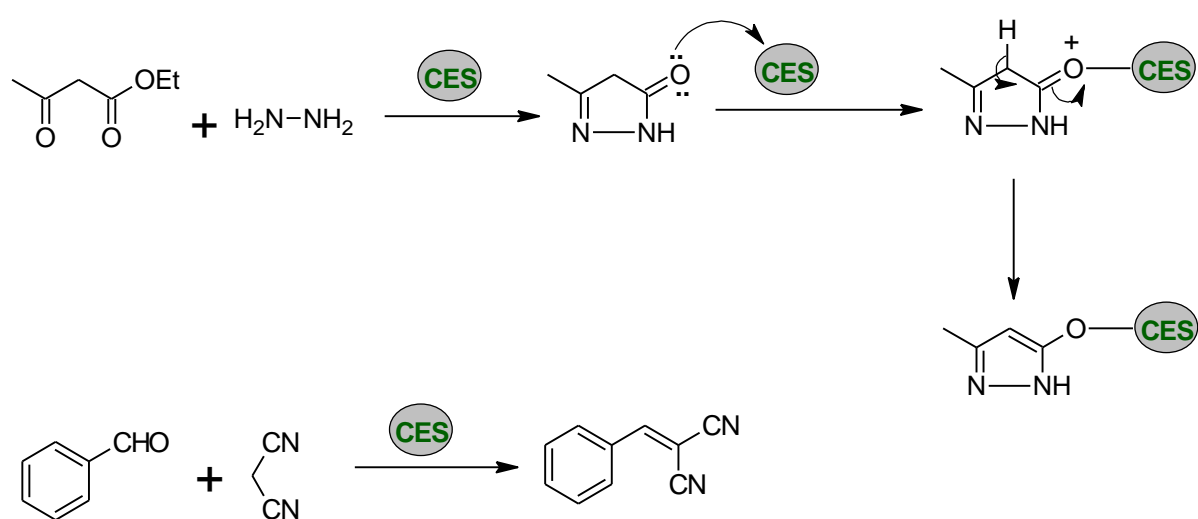
Entry	Catalyst	Time (min)	Yield (%)	Temperature (°C)	Ref.
1.	Bronsted-acidic ionic liquid	30	85	R. T.	xi
2.	Iodine	10	85	R. T.	xii
3.	H ₄ [SiW ₁₂ O ₄₀]	10	95	60	xiii
4.	ZnS nanoparticles	10	94	R. T.	xv
5.	Nano ZnO	90	87	70	xvi
6.	Sodium benzoate/water	50	85	R. T.	xvii
7.	Ni _{0.5} Zn _{0.5} Fe ₂ O ₄ @SiO ₂ -PPA	18	90	R. T.	xix
8.	polystyrene-supported p-toluenesulfonic acid	20	86	reflux	xx
9.	Calcinized eggshell	15	91	R. T.	Present work

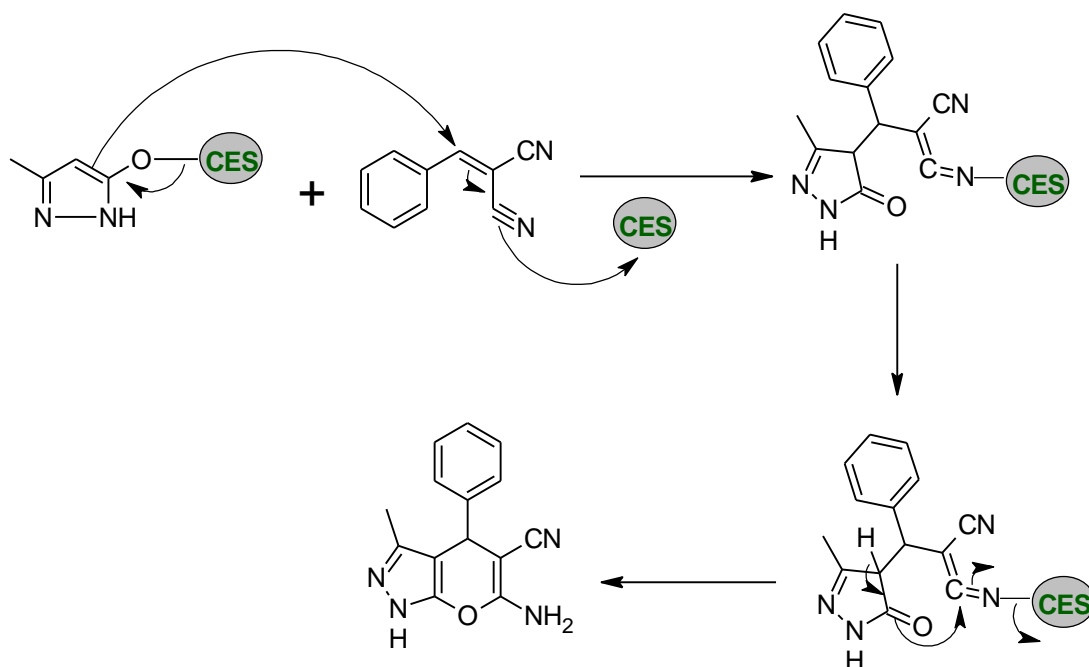
^aReaction conditions: ethyl acetoacetate (1.0 mmol), hydrazine hydrate (1.0 mmol), 3-nitro benzaldehyde (1.0 mmol) and malononitrile (1.0 mmol) in presence of calcinized eggshell.

Table-4 Reusability of calcinized eggshell catalyst^a

Cycles	Yields (%)
Initial	91
1	91
2	91
3	90
4	89
5	89

^aReaction conditions: ethyl acetoacetate (1.0 mmol), hydrazine hydrate (1.0 mmol), 3-nitro benzaldehyde (1.0 mmol) and malononitrile (1.0 mmol) in presence of calcinized eggshell.





Scheme 2: Proposed mechanism of the reaction

Experimental

The calcinized eggshells was obtained from waste chicken eggshells and characterized by different analytical techniques^{xxvii}. All chemicals were purchased from Loba Chemie and used without further purification. Melting points were determined by open capillary method. IR spectrum was recorded on Shimadzu 8400S spectrometer using potassium bromide pellets. ¹H NMR spectra were recorded on Bruker Avance II 400 MHz spectrometer in DMSO as a solvent and TMS as an internal standard. Mass spectra were determined on a Varian-Saturn GS/MS instrument.

Synthesis of pyrano[2, 3-c]pyrazoles

The aromatic aldehyde (1 mmol), malononitrile (1 mmol), ethyl acetoacetate (1 mmol), hydrazine hydrate (1 mmol) and calcinized eggshell were ground by mortar and pestle at room temperature (**Scheme 1**). The reaction was studied by thin layer chromatographic technique. The recrystallization of crude product was carried out by using ethanol. All products were identified by comparing their spectral and physical data with the authentic samples.

Selected spectral data:

Compound (Table 2, 5a): IR (KBr, cm⁻¹): 3370, 3307, 2190, 1609, 1591, 1441; ¹H NMR (400 MHz, DMSO-*d*₆, δ): 1.78 (s, 3H, CH₃), 4.58 (s, 1H, C-4), 6.85 (s, 2H, NH₂), 7.15-7.33 (m, 5H, Ar-H), 12.08 (s, 1H, NH); ¹³C NMR (100 MHz, DMSO, δ): 9.71, 36.24, 57.15, 97.56, 120.75, 126.67, 127.43, 128.36, 135.51, 144.39, 154.72, 160.82; M. F: C₁₄H₁₂N₄O; M. W: 252; MS (m/z): 253 (M+1)⁺.

Compound (Table 2, 5b): IR (KBr, cm⁻¹): 3381, 3288, 2192, 1626, 1510, 1451; ¹H NMR (400 MHz, DMSO-*d*₆, δ): 1.81 (s, 3H, CH₃), 4.95 (s, 1H, C-4), 6.91 (s, 2H, NH₂), 7.40-7.46 (m, 2H, Ar-H), 7.75 (d, 1H, Ar-H, *J* = 8.40 Hz), 7.87 (s, 1H, Ar-H), 12.11 (s, 1H, NH); ¹³C NMR (100 MHz, DMSO, δ): 9.71, 32.0, 59.1, 98.1, 121.8, 124.1, 127.2, 130.5, 134.6, 135.1, 141.2, 145.8, 147.5, 165.1; M. F: C₁₄H₁₁N₅O₃; M. W: 297; MS (m/z): 298 (M+1)⁺.

Compound (Table 2, 5c): IR (KBr, cm^{-1}): 3471, 3278, 3114, 2191, 1648, 1598, 1508, 1489; ^1H NMR (400 MHz, DMSO- d_6 , δ): 1.78 (s, 3H, CH_3), 4.87 (s, 1H, C-4), 7.41 (d, 2H, Ar-H, $J = 8.70 \text{ Hz}$), 7.43 (s, 2H, NH_2), 8.25 (d, 2H, Ar-H, $J = 8.70 \text{ Hz}$), 12.21 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO, δ): 9.3, 35.1, 96.1, 120.7, 123.2, 128.1, 135.3, 146.7, 151.3, 154.2, 161.3; M. F: $\text{C}_{14}\text{H}_{11}\text{N}_5\text{O}_3$; M. W: 297; MS (m/z): 298 ($\text{M}+1$) $^+$.

Conclusion

We have developed a green chemistry approach for one-pot synthesis of pyranopyrazoles using calcinized eggshell as an efficient catalyst by grinding method at room temperature. The advantages of this protocol are simple work up, excellent yield, solvent-free reaction, inexpensive and a green catalyst with high catalytic efficiency as a reusable catalyst.

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