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Microwave-Assisted One-Pot Synthesis Of Octahydroquinazolinone Derivatives Using Rice Husk Under Solvent Free Condition

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Abstract

In the presence of microwave irradiation and an absence of solvents, rice husk is an excellent catalyst to prepare the octahydroquinazolinone derivatives from Condensation of aldehydes in a single pot and three components, dimedone, and urea/thiourea. This approach has various advantages, including a moderate reaction, a clean operation, and a high yield with a quick reaction time.

Keywords: Biginelli reaction; Rice Husk; octahydroquinazolinone derivatives; microwave-irradiation.

1. Introduction:

The Biginelli reaction has recently been used to prepare octahydroquinazolinones by using dimedone instead of dicarbonyl compounds with open chains. It is possible to synthesize these octahydroquinazolinones piqued the interest of researchers due to their antibacterial and calcium antagonist activities Prokaryotic organisms such as staphylococcus aureus (S. aureus), E.coli, and pseudomonas.[1-3]

Quinazolinone derivatives can be synthesized using several different ways. Aldehydes react via reaction of $SOCl_2$ with 2-aminobenzylamine in benzene or xylene refluxing solvent, followed by removal of water via azeotropes,[4] refluxing in ethanol/acetic acid mixture[5], and alkali medium. Only a few studies have been conducted to preparation of octahydroquinazolinone derivatives using various catalytic reagents such as TMSCl,[6] Nafion-H,[7] Conc.H2SO48, and ionic liquid[9]. It is also feasible to synthesize octahydroquinazolinone derivatives in 100 percent ethanol, but yields are low (19-69 percent).[2] These methods, on the other hand, have one or more disadvantages, such as harsh reaction conditions, longer time for reaction, limited yields, and the utilization of potentially harmful substances and costly catalysts. As a result, developing a clean, high-yielding, and ecologically sustainable strategy remains desirable.

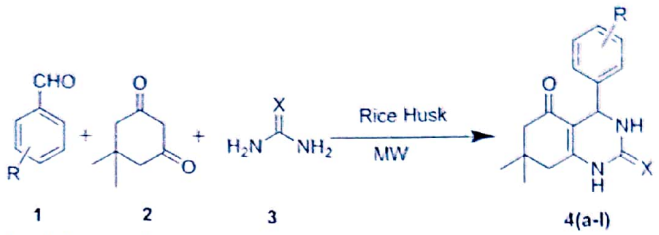
Rice husk comprises cellulose, hemicelluloses, lignin, silica, solubility and moisture as a thin yet abrasive covering that covers the edible rice kernel in nature. Approximately 80 million tonnes of rice husks are produced worldwide each year., with developing countries producing more than 97 percent of the husk.[10] Rice husk has been used in a wide range of industries and chemicals over the years. An intact rice husk's ability to hold metal ions like zinc (II), for example, has been investigated.[11-12] It has been found that the sorption capacity of metal ions as well as several other pollutants can be improved in rice.[13,14] Potential raw materials for the ceramics, cement, and silica industries include rice husk and rice husk ash.[15-17] Rice husk has not yet been used in chemical processes as a readily available and environmentally friendly reagent, to the best of our knowledge, despite the applications listed above.

To increase yields, selectivity, and the conditions for experimentation, 'non-classical' techniques in organic synthesis have recently been invented.[18] Microwave technology, especially when combined with Organic synthesis can be carried out more quickly and efficiently in solvent-free environment.[19–22] However, the use of inorganic solid supports and microwave irradiation in "dry medium" synthesis is possible. Has recently sparked a lot of attention. The synthesis of a wide range of chemical compounds with improved purity and simpler manipulation and set-up has been made possible using solid acid in combination with microwave heating. Environmentally friendly practices can be clearly seen in their design.[23] A survey of the literature reveals that multiple octahydroquinazolinone derivatives have been prepared using conditions of Biginelli reaction and various types of aldehydes, although there are comparatively few references using microwave irradiation.

As part of our ongoing research into developing methods for various chemical transformations,[24-26] we'd like to share a simple yet extremely effective method for making octahydroquinazolinone derivatives. [*] By using microwave irradiation and solvent-free condensation reactions between aromatic aldehydes, dimedone, and urea

in one pot with Rice Husk as catalyst, it is possible to obtain this result. **(Scheme 1)**

2. Results



Scheme 1. Preparation of octahydroquinazolinone derivaties

Rice husk catalyzed the synthesis of benzaldehyde (1a), dimedone (2), and urea (3) It is frequently used as a model reaction to examine the effects of microwave radiation and solvent-free circumstances.

We've looked at several different catalysts for the model process. When the reaction was carried out for a longer period, the product yield was reduced with cellulose sulfuric acid, alum, KH_2PO_4, acidic Al_2O_3, amberlite-IR 120, and H_3NSO_3 in the microwave irradiation conditions. Even though the same reactions were done under microwave irradiation and rice husk was used as a catalyst, the process took a long time to get high product yields in a short time (Table 1, Entry 6).

It was also shown that catalyst concentration had a significant impact in this experiment. Catalyst concentrations were adjusted to 5, 7, 10, and 12 mol percent in this experiment. The results showed that even after a longer reaction time, the yield of the product was lower when the reaction was takes place with a 5 or 7 mol% catalyst. As a result of this, we were able to get high product yields in a short amount of time when the catalyst concentration was 10%. To maintain consistent product production, the catalyst concentration had to be increased to 12 mole percent. Therefore, it looks that using 10% catalyst is the best option. The collected data is summarized in a report (Table 2).

There are a lot of different microwave power settings used during this workup such as 180, 360, 540, and 720 W, were also examined. High power irradiation had a lower yield than low power irradiation, which required more time. Thus, irradiation at 360 W appears to yield better results (Table 3, Entry 2).

Rice husk was used as a catalyst in the microwave-irradiated synthesis of different substituted aldehydes, dimedone, and urea/thiourea to see if this strategy was universally applicable. The results are shown in Table 4. Different aromatic aldehydes with different electron-donating or electron-withdrawing functional groups didn't have a big effect on the amount of products made or the time it took to make them. It was found that urea reactivity with aromatic aldehydes was a lot faster than thiourea reactivity with aromatic aldehydes. Table 4 shows the current method's results.

Finally, rice husk is an affordable, readily available, and effective catalyst to produce octahydroquinazolinone derivatives. Solvent-free reaction conditions, short reaction durations, easy product isolation, and excellent yields are all advantages of this approach. It is our belief that this method will be an important addition to the current synthesis of octahydroquinazolinone derivatives. \

Table 1. Using a simulated reaction to screen potential catalysts[a]

Entry	Catalysts	Time (min)	Yield[b] (%)
1	Cellulose sulfuric acid	12	35
1	Alum	12	47
2	KH_2PO_4	12	50
3	Al_2O_3	12	64
4	Amberlite IR-120	12	64
5	H_3NSO_3	12	66
6	Rice husk	12	95

[a] In the absence of any solvent, and after being microwave-irradiated', benzaldehyde, dimedone, and urea are

reacted. [b]Single-source output.

Table 2. Effect of catalyst concentration on model reaction[a]

Entry	Catalyst (mol%)	Yield[a] (%)
1	5	52
2	7	65
3	10	95
4	12	95

In the absence of solvent, microwave irradiation and benzaldehyde[a], dimedone, and urea react in rice husk. [b]Single-source output.

Table 3. Effect of Microwave Irradiation Powers on Octahydroquinazolinone Derivatization Synthesis **4a**[a]

Entry	Power (W)	Time (sec)	Yield (%)[b]
1	180	70	77
2	360	50	95
3	540	40	85
4	720	30	80

[a]1a (1 mmol) was reacted with dimedone (1 mmol) and urea (1.5 mmol) in presence of Rice husk catalyst(10 mol %) under microwave irradiation. [b]Isolated yield

Table 4 Use of Rice husk catalyst for microwave-irradiation-induced production of octahydroquinazolinone derivatives[a]

Entry	RCHO	X	Time (min)	Yield[b] (%)	M.p (°C)
4a	H	O	6	95	290-292
4b	4-Cl	O	5	90	>300
4c	3-OMe, 4-OH	O	8	88	193-194
4d	3-NO_2	O	7	92	298-299
4e	3-OMe	O	8	86	248-249
4f	3-Cl	O	7	85	282-284
4g	4- NO_2	O	5	92	302-304
4h	4-F	O	7	90	134-136
4i	H	S	10	88	283-285
4j	4-OMe	S	12	83	275-276
4k	3-Cl	S	10	85	275-276
4l	4-Br	S	11	86	286-288

[a]Reaction Condition: **1 (a-l)** (1 mmol), **2** (1 mmol), **3** (1.5 mmol) Microwave-irradiated rice husk (10 mole percent). [b]Self-sufficient. We used spectroscopic approaches such as infrared spectroscopy, one-dimensional nuclear magnetic resonance (NMR), and mass spectroscopy to comprehensively describe all of the synthesised products.

The synthesis of octahydroquinazolinone derivatives: general techniques:-

A mixture of aromatic aldehydes **1(a-l)** (1 mmol), dimedone **2** (1 mmol) urea/thiourea **3** (1.5 mmol), and Rice husk(10 mol%) was stirred for 1-2 min. and the resulting mixture was irradiated in a microwave oven at 360 W, as time shown in Table 4. The Completion of the reaction was monitored by TLC (ethyl acetate: hexane, 7:3). After completion, the reaction mixture was cooled and dichloromethane (25 mL) was added. Organic solvent was evaporated under reduced pressure and solid was dried and crystallized from ethanol, to afford the pure corresponding octahydroquinazolinone derivatives **4(a-l)** in an excellent yield. All the products were confirmed by comparisons with authentic samples, IR, ^{1}H NMR and mass spectra.

Spectroscopic data:

7,7-Dimethyl-4-phenyl-4,6,7,8-tetrahydro-1H,3H-quinazoline-2,5-dione (4a): Mp 291-292°C, IR (KBr) ν_{max} 3323(br), 3256(br), 2961(br), 1710(s), 1677(s), 1611(vs), 1448(w), 1371(s), 1231(s), 761(s), 690(w), 565(w), 487(w), 430(w) cm^{-1}. ^1H NMR (400MHz, $CDCl_3$ + DMSO-d_6), δ 0.93 (s, 3H, Me); 1.09 (s, 3H, Me); 2.18 (q, J =16.0Hz, 2H, CH_2); 2.39 (q, J =16.7Hz, 2H, CH_2); 5.26 (d, J =2.8Hz,1H, CH); 7.32-7.22 (m, 5H, Ar); 7.47 (s, 1H, NH); 9.40 (s, 1H, NH); MS (ESI) m/z 271 (M+1).

4-(4-Chloro-phenyl)-7,7-dimethyl-4,6,7,8-tetrahydro-1H,3H-quinazoline-2,5-dione (4b): Mp >300°C. IR (KBr) ν_{max} 3246 (br), 2961 (br), 1696 (vs), 1615 (vs), 1488 (s), 1376 (s), 1240 (s), 808 (w), 765 (w), 565 (s), 510 (w) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6), δ 0.97 (s, 3H, Me); 1.10 (s, 3H, Me); 2.20 (q, J = 17.5 Hz, 2H, CH_2); 2.38 (q, J = 17.5 Hz, 2H, CH_2); 5.29 (d, J =2.8 Hz, 1H, CH); 7.22-7.29 (m, 4H, Ar); 7.55 (s, 1H, NH); 9.37 (s, 1H, NH); MS (ESI) m/z 305 (M+1).

7,7-Dimethyl-4-(4-nitrophenyl)-4,6,7,8-tetrahydro-1H,3H-quinazoline-2,5-dione (4g): Mp 301-303°C; IR (KBr) ν_{max} 3327(br), 3247(br), 2966(br), 1669(s), 1625(vs), 1377(m), 1229(s), 830(w), 762 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$ + DMSO-d_6), δ 0.87 (s, 3H, Me); 1.05 (s, 3H, Me); 2.15 (q, J =16.7Hz, 2H, CH_2); 2.33 (q, J=17.4Hz, 2H, CH_2); 5.41 (d, J =2.8Hz, 1H, CH); 7.51 (d, J =8.36Hz, 2H, Ar); 8.10 (d, J =8.36Hz, 2H, Ar); 7.53 (s, 1H, NH); 9.45 (s, 1H, NH); MS (ESI) m/z 316 (M+1).

4-(4-Methoxyphenyl)-7,7-dimethyl-2-thioxo-2,3,4,6,7,8-hexahydro-1H-quinazolin-5-one (4j): Mp 276-277°C; IR (KBr) ν_{max} 3260(br), 3159(br), 2954(br), 1640(vs), 1585(vs), 1377(s), 1250(m), 1169(s), 1025(m), 828(w), 770(w), 550 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$ + DMSO-d_6), δ 0.98 (s, 3H, Me); 1.09 (s, 3H, Me); 2.15 (q, J =16.0Hz, 2H, CH_2); 3.12 (s, 2H, CH_2); 3.69 (s, 3H, OCH_3), 5.18 (d, J =2.7Hz, 1H, CH); 6.80 (d, J =8.7Hz, 2H, Ar); 7.26 (d, J =8.6Hz, 2H, Ar); 9.420 (s, 1H, NH); 10.35 (s, 1H, NH); MS (ESI) m/z 317 (M+1).

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