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Zeolite Catalysed Method for the Preparation of 2,3-dihydroquinazolin-4(1H)-ones

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Abstract

The reaction of isatoic anhydride, amines and aldehydes in the presence of a microporous zeolite gave 2,3-dihydroquinazolin-4(1H)-one derivatives with good to excellent yield. The yield depends on the structure of the aldehyde and/or amine compound.



KEYWORDS: Heterogeneous catalysis, zeolites, quinazolines, multicomponent reaction, isatoic anhydride.

INTRODUCTION

Nowadays a major challenge for chemists in the synthetic organic chemistry is the development of environmentally more benign synthetic methods. An important tool in this work is the elaboration of heterogeneous catalytic processes. Among the catalysts

developed, natural, artifical or modified mineral-type catalysts have great importance, since they are generally non-toxic, non-corrosive and often recyclable or even reusable.

In the frame of our work in the field of heterogeneous catalysis, we investigated the catalytic properties of a zeolite-type small pore size adsorbent, Ersorb-4 (E4) and its more acidic derivative (E4a). Ersorb-4 (E4) is a clinoptylolite-type zeolite material with high silicon content (Si/Al ratio 5:1). The original mineral was modified with ionic exchanges and with other water-phase technologies followed by a thermal treatment yielding a Ca-K mixed cation-based adsorbent with 4Å pore size. The chemical composition of E4 is described in Table 1. It has a specific surface area of 40 m^2/g (determined by the BETmethod with nitrogen at the temperature of liquid nitrogen). Due to the high Si/Al ratio it has high acid-proof property; its crystalline structure does not change even after a longtime treatment in hot 4 N hydrochloric acid. E4 has a slightly surfacial acidic character (the pH of its aqueous suspension is 4,87). The high silicon content yields high chemical resistance. It is stable until 500-600 °C. It can adsorb small molecules such as water, hydrochloric acid, ammonia, methanol or hydrogen sulfide. It has several advantages, e.g. environmentally-friendly, non-toxic, inexpensive, recoverable and/or reusable. The small pore size does not allow the adsorption of molecules larger than methanol in the pores. Based upon this adsorption ability, E4 has been used as large spectral drying agent (molecular sieve) in both gaseous and liquid phases, suitable for the dehydration of gaseous hydrochloric acid or even liquid chlorine and sulfur-dioxide.

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E4a is obtained from E4 with ionic exchanges and other treatments. This provides a change in the surfacial acidity of the material, so that a more acidic (pH 4.35) version of E4 was achieved. During these treatments the amount of iron and aluminium does not change significantly but a considerable change in calcium magnesium and potassium content (Table 1) can be observed. The clinoptylolite-structure does not modify, which has been proved by the XRD profile of the materials. (Figure 1.).

The acidity of E4 and E4a have been determined by pyridine adsorption method. Thus, in E4 the amount of Lewis and Brønsted acid sites are 14 and 16 μ mol/g, respectively, while in E4a the corresponding values are 17 and 25 μ mol/g, respectively^[1].

During our research work with E4 a number of simple methods were elaborated for the preparation of different heterocycles, *e.g.* dihydro-^[2] and tetrahydroisoquinolines^[3], 1,5-benzodiazepines^[4], 1,2-dihydroquinolines^[1], etc. E4a was successfully applied in the synthesis of 3,4-dihydro-pyrimidin-2(1H)-ones in the multicomponent Biginelli reaction^[5]. Continuing this work we investigated the condensation of isatoic anhydride with amines and aldehydes yielding 2,3-dihydroquinazolin-4(1H)-ones. This reaction was recently examined using *i.a.* strontium(II) chloride hexahydrate,^[6] Fe₃O₄ nanoparticles,^[7] citric acid,^[8] ZnO nanoparticles,^[9] acetic acid,^[10] sulfuric acid and silica gel,^[11] montmorillonite K10,^[12] L-proline^[13] or Amberlyst-15^[14] under microwave irradiation, a Lewis acid-surfactant-combined catalyst, zinc(II) perfluorooctanoate,^[15] ionic liquid [Hmim][NO₃],^[16] or Bi(NO₃)₃·5H₂O.^[17] Some of these catalysts are expensive, not reusable and/or harmful for the environment.

RESULTS AND DISCUSSION

First the optimal reaction conditions were examined. The reaction of isatoic anhydride, butylamine and benzaldehyde was chosen as model reaction (Scheme 1). The results are summarized in Table 2.

The best results were obtained in ethanol using E4a (Table 2, entry 4); the desired quinazoline **4a** was obtained almost quantitatively. Using these conditions the reaction of different amines and aldehydes were examined (Scheme 2, Table 3). Good results were obtained when n-butylamine and aromatic aldehydes were used (Table 3, entries 1-6), except in case of 2-chlorobenzaldehyde (Table 3, entry 7), probably because of steric hindrance.

Aniline gave also the expected products in ethanol with variable yield (Table 3, entries 8-10). In toluene the expected product was obtained with poorer yield (Table 3, entry 8) or only the appropriate Schiff's base **5i** could be isolated (Table 3, entry 9).

Aralkyl amines (2-phenylethylamine and 3-phenylpropylamine) and benzaldehyde also gave the appropriate 2,3-dihydroquinazolin-4(1H)-one derivatives (Table 3, entries 11 and 12), in case of 3-phenylpropylamine with excellent yield.

ortho-Substituted aniline derivatives gave only the appropriate Schiff's bases (**5m**, **5n**), probably because of steric hindrance (Table 3, entries 13 and 14), the expected product was not obtained even after longer heating (Scheme 3).

We also tried to investigate the stereochemical aspects of the reaction. But from the mixture of (R)-1-phenyl-ethylamine, isatoic anhydride and benzaldehyde (Table 3, entry 15) only 2-amino-N-(1-phenylethyl)benzamide **60** could be isolated after column chromatography (Scheme 4).

The workup of the reaction mixture was very easy, the catalyst was filtered out and the solvent was evaporated.

An important factor in the characterization of a heterogeneous catalyst is the recyclability or reusability. We tested the reusability of E4 in the reaction of isatoic anhydride, benzaldehyde and *n*-butylamine. Thus, the catalyst filtered out from the reaction mixture was washed with acetone, dried at 110 °C for 4 h and reused. The yields obtained in the 2^{nd} and 3^{rd} experiments were 93 and 91%, respectively.

In summary, a heterogeneous catalytic method was developed for the the preparation of 2,3-dihydroquinazolin-4(1H)-one derivatives. This microporous zeolyte catalysed reaction provides a simple and environmentally benign alternative for the multicomponent reaction of isatoic anhydride, amines and aldehydes. The experimental and work-up procedure is simple. Excellent yields have been obtained with n-butylamine

or aralkyl amines and aromatic aldehydes, varibale results were obtained with aniline derivatives.

The yields are comparable with the yields obtained with other methods. Some examples are shown in Table 4.

EXPERIMENTAL

The commercial chemicals were purchased from Merck-Hungary Ltd. except E4 and E4a, which are the products of Erdőkémia-ker Ltd., Hungary. ¹H NMR spectra were recorded on a BRUKER Avanche-300 instrument using TMS as an internal standard in CDCl₃. GC-MS spectra were made on Shimadzu GC-2010, GC-MS QP2010S instruments. Thin layer chromatography was carried out using Merck Kieselgel 60 F_{254} plates with eluents hexane:acetone 4:1 or hexane:acetone 2:1, detection either by UV light at 254 nm or by heating after spraying with phosphoromolybdic acid solution. Column chromatography was carried out on Merck Kieselgel 63–200 mesh with hexane-acetone 4:1 or 2:1 eluents. Melting points are uncorrected and were measured on Gallenkamp instrument. Elemental analyses data of the new compounds were found to be in good agreement (±0.3%) with the calculated values.

Pretreatment Of The Catalyst

Before each experiment the sample of E4a was powdered and heated at 100 °C for 1h.

A Typical Protocol For The Reaction

A mixture of 0.82 g (5 mmol) of isatoic anhydride, 5 mmol of the appropriate amine, 5 mmol of the aldehyde and 0.5 g E4a in 10 cm^3 ethanol was heated at 80 °C for 10-20 h (as indicated in Table 2). The solid was filtered off, washed with the same solvent, the filtrate was evaporated. Pure products were obtained by column chromatography (Kieselgel, hexanes:acetone 4:1).

3-Butyl-2-Phenyl-2,3-Dihydroquinazolin-4(1H)-One (4a)

Yield 95%, white solid, mp 127-130 °C (ethanol; lit. 127-128°C^[18]); ¹H NMR (300 MHz, CDCl₃^[15]) δ (ppm): 0,84 (t, 3H); 1,26-1,29 (m, 2H); 1,52-1,57 (m, 2H); 2,68-2,77 (m, 1H); 3,88-3,98 (m, 1H); 4,45 (s, 1H); 5,71 (s, 1H); 6,48 (d, 1H); 6,80 (t, 1H); 7,20-7,33 (m, 6H); 7,93 (d, 1H); ¹³C NMR (75 MHz, CDCl₃^[19]) δ (ppm): 13.9, 20.5, 30.4, 44.7, 72.5, 112.3, 114.6, 115.8, 117.6, 119.4, 119.9, 127.1, 129.6, 133.8, 142.8, 145.1, 161.4; Anal. Calcd. for C₁₈H₂₀N₂O: C 77.14, H 7.14, N 10.00%, found: C 77.23, H 7.19, N 9.74%.

SUPPORTING INFORMATION

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REFERENCES

1. Hegedüs, A.; Hell, Z.; Vargadi, T.; Potor, A.; Gresits, I. A new simple synthesis of 1,2-dihydroquinolines via cyclocondensation using zeolite catalyst. *Catal. Lett.* **2007**, *117*, 99-101.

 Hegedüs, A.; Hell, Z.; Potor, A. A new, environmentally-friendly method for the Bischler-Napieralski cyclization using zeolite catalyst. *Catal. Commun.* 2006, *7*, 1022-1024.

 Hegedüs, A.; Hell, Z. One-step preparation of 1-substituted tetrahydroisoquinolines via the Pictet-Spengler reaction using zeolite catalysts. *Tetrahedron Lett*.
 2004, 45, 8553-8555.

4. Hegedüs, A.; Hell, Z.; Potor, A. A simple environmentally-friendly method for the selective synthesis of 1,5-benzodiazepine derivatives using zeolite catalyst. *Catal. Lett.* **2005**, *105*, 229-232.

Hegedüs, A.; Hell, Z.; Vigh, I. Convenient One-Pot Heterogeneous Catalytic
 Method for the Preparation of 3,4-Dihydro-pyrimidin-2(1H)-ones. *Synth. Commun.* 2006, 36, 129-136.

 Wang, M.; Zhang, T. T.; Liang, Y.; Gao, J. J. Strontium chloride-catalyzed onepot synthesis of 2, 3-dihydroquinazolin-4(1*H*)-ones in protic media *Chinese Chem. Lett*.
 2011, *22*, 1423-1426.

Zhang, Z. H.; Lue, H. Y.; Yang, S. H.; Gao, J. W. Synthesis of 2,3Dihydroquinazolin-4(1*H*)-ones by Three-Component Coupling of Isatoic Anhydride,
Amines, and Aldehydes Catalyzed by Magnetic Fe₃O₄ Nanoparticles in Water. *J. Comb. Chem.* 2010, *12*, 643-646.

 Ghorbani-Choghamarani, A.; Taghipour, T. Green and One-Pot Three-Component Synthesis of 2,3-Dihydroquinazolin- 4(1H)-Ones Promoted by Citric Acid as Recoverable Catalyst in Water. *Letters in Org. Chem.* 2011, *8*, 470-476.

9. Yavari, I.; Beheshti, S. ZnO nanoparticles catalyzed efficient one-pot threecomponent synthesis of 2,3-disubstituted quinazolin-4(1*H*)-ones under solvent-free conditions. *J. Iranian Chem. Soc.* **2011**, *8*, 1030-1035.

10. Karimi-Jaberi, Z.; Arjmandi, R. Acetic acid-promoted, efficient, one-pot synthesis of 2,3-dihydroquinazolin-4(1H)-ones. *Monatsh. Chemie* **2011**, *142*, 631-635.

 Salehi, P.; Dabiri, M.; Zolfigol, M. A.; Baghbanzadeh, M. A Novel Method for the One-Pot Three-Component Synthesis of 2,3-Dihydroquinazolin-4(1*H*)-ones. *Synlett* 2005, 1155.

12. Salehi, P.; Dabiri, M.; Baghbanzadeh, M.; Bahramnejad, M. One-Pot, Three-Component Synthesis of 2,3-Dihydro-4(1*H*)-quinazolinones by Montmorillonite K-10 as an Efficient and Reusable Catalyst. *Synth. Comm.* **2006**, *36*, 2287-2292.

13. Kumari, K.; Raghuvanshi, D. S.; Singh, K. N. Microwave assisted eco-friendly protocol for one pot synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones in water. *Indian J. Chem., Sect B: Organic Chemistry Including Medicinal Chemistry* **2012**, *51*, 860-865.

 Surpur, M. P.; Singh, P. R.; Patil, S. B.; Samant, S. D. Expeditious One-Pot and Solvent-Free Synthesis of Dihydroquinazolin-4(1H)-ones in the Presence of Microwaves. *Synth. Comm.* 2007, *37*, 1965-1970.

 Wang, L. M.; Hu, L.; Shao, J. H.; Yu, J.; Zhang, L. A novel catalyst zinc(II) perfluorooctanoate [Zn(PFO)₂]-catalyzed three-component one-pot reaction: Synthesis of quinazolinone derivatives in aqueous micellar media. *J. Fluor. Chem.* 2008, *129*, 1139-1145.

Mohammadpoor-Baltork, I.; Khosropour, A. R.; Moghadam, M.;
 Tangestaninejad, S.; Mirkhani, V.; Soltani, M.; Mirjafari, A. One-pot synthesis of 2,3-

disubstituted-2,3-dihydroquinazolin-4(*1H*)-ones using [Hmim][NO₃]: An eco-friendly protocol. *J. Het. Chem.* **2011**, *48*, 1419-1427.

17. Mohammadpoor-Baltork, I.; Khosropour, A. R.; Moghadam, M.;

Tangestaninejad, S.; Mirkhani, V.; Baghersad, S.; Mirjafari, A. Efficient one-pot synthesis of 2,3-dihydroquinazolin-4(1H)-ones from aromatic aldehydes and their one-pot oxidation to quinazolin-4(3H)-ones catalyzed by Bi(NO₃)₃·5H₂O: Investigating the role of the catalyst. *C. R. Chimie* **2011**, *14*, 944-952.

18. Song, Z.; Liu, L.; Wang, Y.; Sun, X. Efficient synthesis of mono- and disubstituted 2,3-dihydroquinazolin-4(1H)-ones using aluminum methanesulfonate as a reusable catalyst. *Research on Chemical Intermediates* **2012**, *38*, 1091-1099.

19. Sharma, M.; Pandey, A. K. Prem, M. S. A. Greener Protocol for Accessing 2,3-Dihydro/spiroquinazolin-4(1*H*)-ones: Natural Acid-SDS Catalyzed Three-Component Reaction. *Synlett* **2012**, *23*, 2209-2214.

Table 1 Chemical composition of E4 and E4a

Component (w/w%)	E4	E4a
SiO ₂	73.0	76.7
Al ₂ O ₃	11.2	12.2
Fe ₂ O ₃	1.7	1.19
K ₂ O	5.2	2.87
Na ₂ O	0.38	0.34
CaO	2.20	0.53
MgO	0.44	0.13

Entry	Catalyst	Solvent	Reaction time	Yield ^{a} (%)
			(h)	
1	E4	toluene	10	30
2	E4a	acetonitrile	7	40
3	E4a	toluene	10	35
4	E4a	ethanol	10	98 (95 ^b)

^{*a*}Crude product

^bRecrystallized product

Table 3 Multicomponent reaction of isatoic anhydride with different amines and

aldehydes

Entry	R ¹	R^2	Reaction	Product	Yield ^a /%
			time/h		
1	<i>n</i> -C ₄ H ₉	Н	10	4a	95
2	<i>n</i> -C ₄ H ₉	3-OCH ₃	11	4b	98
3	<i>n</i> -C ₄ H ₉	4-NO ₂	11	4c	96
4	<i>n</i> -C ₄ H ₉	3-NO ₂	11	4d	97
5	<i>n</i> -C ₄ H ₉	4-OCH ₃	14	4e	93
6	<i>n</i> -C ₄ H ₉	4-Cl	10	4f	75
7	<i>n</i> -C ₄ H ₉	2-Cl	10	4g	50
8	C ₆ H ₅	Н	10	4h	76 (22) ^b
9	C ₆ H ₅	3-NO ₂	10	4i (5i) ^b	95 (-) ^{b,c}
10	C ₆ H ₅	4-OCH ₃	14	4j	78
11	C ₆ H ₅ -(CH ₂) ₂	Н	17	4k	60
12	C ₆ H ₅ -(CH ₂) ₃	Н	15	41	96
13	2-C(CH ₃) ₃ -C ₆ H ₄	Н	20	5m	
14	$2-Br-C_6H_4$	Н	15	5n	_b,c
15	(<i>R</i>)-(+)-	Н	24	60	_ ^c
	CH(CH ₃)C ₆ H ₅				

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^aIsolated yield

^bIn toluene

^cNot determined

Table 4. Comparison of the yield obtained with referred values

	Compound	Yield	Referred yield	Referred conditions
1	4 a	95	75 ^[6]	aq. ethanol, 6 h, reflux
2	4d	97	92 ^[17]	neat, 80 °C, 1 h
3	4h	76	80 ^[7]	water, 2 h, reflux, 15
4	4j	78	88 ^[7]	mol% catalyst

Figure 1. XRD profiles of E4 (upper diagram) and E4a (lower diagram)



Scheme 1



Scheme 2



Scheme 3



Scheme 4

