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Nanocrystalline $MgAl_2O_4$ as a Heterogeneous Nanocatalyst for the Synthesis of 2-Ketomethylquinolines Using Green Design Methodology

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Abstract

In this investigation, a facile and green sonochemical route has been developed for the synthesis of 2-Ketomethylquinolines by using 2-methylquinolines and several acyl chlorides in the presence of nanocrystalline $MgAl_2O_4$ as an efficient heterogeneous catalyst. The combination of nanocatalyst and ultrasonic process afforded corresponding ketomethyl quinolines in shorter reaction durations, and in high yields. This work consistently has the advantages of excellent yields, short reaction time, mild condition and work-up procedures. This method might be useful in the future for the preparation of similar derivatives.

1. Introduction

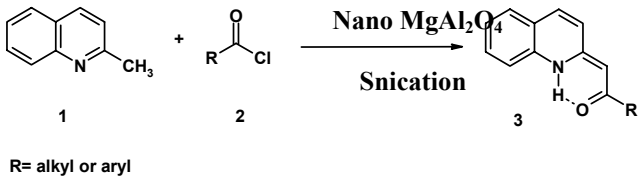
Heterogeneous catalysis has been known for many years and has become strategically vital for the efficient and ecofriendly organic synthesis over the past few decades [1, 2]. The heterogeneous catalysts are of various types, such as hydrotalcites, zeolites, mixed metal oxides, solid-supported catalysts, resins, etc [3]. ‘‘Nanocatalysis’’ is an important and emerging field in catalysis science, because of the small size (1–100 nm), the active metal atoms are exposed to the surface and thus minimize the specific cost per function [4].

Among the nanocatalysts, magnesium aluminate spinel, nano $MgAl_2O_4$ is an effective nanocatalyst in some organic reactions [5, 6]. It has catalytic properties because of its unique properties such as chemical inertness, high surface area, small crystallite size and more active sites. Nanocrystalline $MgAl_2O_4$ is an efficient nanocatalyst with high specific surface area, high activity and superior controlled selectivity [7].

Quinalidine derivatives are very important heterocyclic compounds, because of the applications of these compounds in heterocyclic synthesis and chemical transformations [8-10]. One of the main group of quinaldines, are 2-ketomethylquinolines. This class of compounds act as polydentate ligands to form stable complexes with different cations is well known [11]. Although several methods have been reported for the synthesis of 2-ketomethylquinolines, some of these methodologies have limitations in their general application such as long reaction times and high temperatures [12-15]. Therefore, the development of simple, clean, efficient, high-yielding, and environmentally friendly approaches using new nanocatalysts for the synthesis of 2-ketomethyl quinolines is an important task for organic chemists.

On the other hand, greener process involves mainly solvent-free reaction, microwave irradiation and solid phase synthesis using a catalyst and ultrasound irradiation [5]. Ultrasonic-assisted organic synthesis as a green synthetic process is a powerful technique that is being used more and more to accelerate chemical reactions. Sonication can be extremely efficient and it is applicable to a broad range of practical syntheses. The notable features of the ultrasound approach are enhanced reaction rates, formation of purer products in high yields, easier manipulation and considered a processing aid in terms of energy conservation and waste minimization which compared with traditional heating methods, this technique is more convenient taking green chemistry concepts into account [16].

In this investigation, we report an efficient and practical procedure for the synthesis of 2-ketomethylquinolines with 2-methylquinolines **(1)** and several acyl chlorides **(2)** using nanocrystalline magnesium aluminate as a heterogeneous catalyst under ultrasound irradiation (Scheme 1).



Scheme 1. synthesis of 2-ketomethylquinolines using $MgAl_2O_4$ nanocatalysts.

2. Experimental procedure

2.1. Chemicals and apparatus

Chemical reagents in high purity were purchased from the Merck Chemical Company. All materials were of commercial reagent grade. Melting points were determined in open capillaries using an Electrothermal Mk3 apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker DRX-400 spectrometer at 400 and 100 MHz respectively and reported as parts per million (ppm) downfield from tetramethylsilane as internal standard. FT-IR spectra were obtained with potassium bromide pellets in the range 400-4000 cm^{-1} with a Perkin-Elmer 550 spectrometer. A mass spectrum was recorded by a QP- 1100EX Shimadzu spectrometer. The purity determination of the substrates and reaction monitoring were accomplished by thin layer chromatography (TLC) on silica gel polygram SILG/UV 254 plates. The N_2 adsorption/desorption analysis (BET) was performed at -196 °C using an automated gas adsorption analyzer (Tristar 3000, Micromeritics). Transmission electron microscopy (TEM) was performed with a Jeol JEM- 2100UHR, operated at 200 kV. An ultrasound bath (water) dental scaler (with a frequency of 40 kHz and an output power of 200 W) was used.

2.2. Preparation of nanocrystalline $MgAl_2O_4$

Nanocrystalline magnesiumaluminate spinel was synthesized by means of a procedure reported elsewhere [7]. In short, stoichiometric amounts of magnesium nitrate and aluminum nitrate and desired

amount of CTAB were added to well stirring deionized water. Then, ammonia solution was added dropwise to the well stirring slurry for adjusting pH value around 9. After precipitation, the slurry was stirred for another 30 min and refluxed at 80 °C for 24 h under continuous stirring. The mixture then was cooled and filtered. The final product was dried at 100 °C for 24 h under flowing air and calcined at 700 and 800 °C. The crystallite sizes of the magnesium aluminate determined by TEM analysis was at 700 ºC were between 3–10 nm (Fig. 1). The pore volume was also calculated from the N_2 adsorption/desorption isotherm result, the approximately 1.10 cm^3g^{-1}. In addition the surface area is approximately 201 m^2g^{-1} [7].

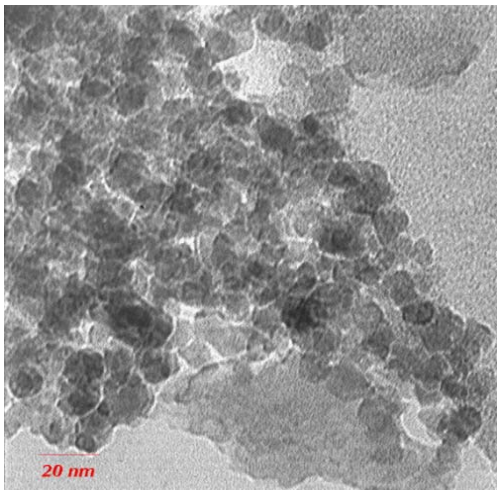


Fig. 1. TEM image of nanocrystalline $MgAl_2O_4$ [7]

2.3. General procedure for the synthesis of 2-Ketomethylquinolines by use of nanocrystalline $MgAl_2O_4$

An equimolar mixture of new distilled 2–methylquinoline (1 mL, 1.09 g) and new distilled benzoyl chloride (1 mL, 1.21 g) placed in an open glass container, then $MgAl_2O_4$ (5mmol%) in dry pet. ether (10 mL) was added to the container and was irradiated under ultrasound at 50 ˚C for the period of time (The reaction was monitored by TLC). The solvent was evaporated then the aqueous solution of sodium bicarbonat was added and was filtered or extracted with chloroform. The solid residue was chromatographed over a silica gel column (petrolium ether 60 ^oC (chlorophorm: ethyl acetate 4:1 v/v) or some of the product was obtained by recrystallization it from aqueous ethanol (90%). All the products are known and were identified by comparison of their physical and spectral data with those of authentic samples [17].

2.4. Spectroscopic data of selected compounds

*2-(1,2-dihydro-2-quinolinyliden)-1-phenyl-1-ethanone **(3a)***

IR (KBr) (υ_{max}/cm^{-1}): 1556 (C=C), 1590 (C=C), 1636 (C=O enaminone form); ^1H NMR (400 MHz, $CDCl_3$): δ_H 15.3 (s, 1H, NH), 7.3 (dd, 1H, *J*=8.38 Hz, enaminone form), 6.6-7 (m, 9H, C_9H_6N, C_6H_5), 6.43 (dd, 1H, *J*=9.2 Hz, enaminone form), 6.41 (s, 1H, CH, enaminone form), 5.9 (s, 2H, CH_2, imine form) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 183.81, 154.14, 136.05, 122.24, 118.18, 89.88 ppm.

*2-(1,2-dihydro-2-quinolinyliden)-1-(4-methylphenyl)-1-ethanone **(3b)***

IR (KBr) (υ_{max}/cm^{-1}): 1547 (C=C), 1623 (C=O enaminone form), 1730 (C=O imine form); ^1H NMR (400 MHz, $CDCl_3$): δ_H 15.7 (s, 1H, NH), 8.1 (dd, 1H, *J*=8.38 Hz, imine form), 6.4-7.9 (m, 8H, C_9H_6N, C_6H_5), 6.2 (dd, 1H, *J*=9.2 Hz, enaminone form), 6.2 (s, 1H, CH, enaminone form), 5.7 (s, 2H, CH_2, imine form), 2.5 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 183.87, 153.92, 122.23, 117.94, 89.56 ppm.

*1-(4-chlorophenyl)-2-(1,2-dihydro-2-quinolinyliden)-1-ethanone **(3c)***

IR (KBr) (υ_{max}/cm^{-1}): 1555 (C=C), 1592 (C=C),1632 (C=O enaminone form), 1725 (C=O imine form); ^1H NMR (400 MHz, $CDCl_3$): δ_H 15.4 (s, 1H, NH), 8.1 (dd, 1H, *J*=8.38 Hz, imine form),

6.6-8 (m, 8H, C_9H_6N, C_6H_5), 6.4 (dd, 1H, *J*=9.2 Hz, enaminone form), 6.2 (s, 1H, CH, enaminone form), 4.4 (s, 2H, CH_2, imine form) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 182.41, 154.13, 136.26, 122.08, 118.11, 89.59 ppm.

3. Results and discussion

In recent years, nanomaterials have emerged as powerful catalysts in various organic transformations [1, 2, 5]. Therefore, nanocatalysts are potential catalysts due probably to their high catalytic activities, low costs and ease of handling. In an initial study, we considered as a model reaction the condensation of 2–methyl quinolines and benzoyl chloride in dry petroleum benzine under reflux condition. Different catalysts such as $ZrCl_4$, CuCl, $AlCl_3$, BF_3/EtO_2, $SnCl_2$, $SnCl_4$, $MgAl_2O_4$ and nanocrystalline $MgAl_2O_4$ were tested to improve the yield for the specific synthesis of 2-Ketomethylquinoline. The results are presented in Table 1.

Table 1. Influence of different acid catalysts for the reaction of 2–methyl quinolines (1mmol) and benzoyl chloride (1mmol) under reflux condition.

Entry	Catalyst (mol%)	Time (h)	Yield[a] (%)
1	None	10	0-5
2	$ZrCl_4$ (3mol%)	4	60
3	CuCl (3mol%)	10	-
4	BF_3/EtO_2 (3mol%)	5	20
5	$SnCl_4$ (3mol%)	3	65
6	$AlCl_3$ (3mol%)	3	65
7	$MgAl_2O_4$ (3mol%)	3	70
8	Nano-$MgAl_2O_4$ (3mol%)	3	80
9	Nano-$MgAl_2O_4$ (4mol%)	3	85
10	Nano-$MgAl_2O_4$ (5mol%)	3	90
11	Nano-$MgAl_2O_4$ (6mol%)	3	90
12	Nano-$MgAl_2O_4$ (7mol%)	3	90

[a] Isolated yield of the pure compound.

Interestingly, when the reaction was carried out in the presence of (5 mol%) nanocrystalline $MgAl_2O_4$, it led to the desired product in 90% yield in 3 h (Table 1, Entry 10). The catalytic activity of nanocrystalline $MgAl_2O_4$ was evident when no product was obtained in the absence of the catalyst (Table 1, Entry 1). The reaction yield with increasing amount of nanocrystalline $MgAl_2O_4$ was not substantially increased. In conclusion, according to Table 1, nanocrystalline $MgAl_2O_4$ were the best catalyst in terms of reaction time, yields, and products purity for preparation of 2–ketomethylquinolines derivatives under heating method.

Subsequent efforts were focused on optimizing conditions for formation of 2-ketomethyl quinolines by the effect of ultrasonic irradiation on reaction in presence of $MgAl_2O_4$ nanocatalysts (Table 2). Compared with the heating method, the reaction time using ultrasound is sharply decreased from 3–5 h to 5–20 min.

It seems that the existence of $MgAl_2O_4$ as an acidic catalyst can accelerate this reaction by increasing the reactivity of quinoline derivatives. nano-$MgAl_2O_4$ used as nanocatalyst, shows a relatively large surface area, special active sites, and small crystalline size which can be controlled by its preparation process. The high activity of $MgAl_2O_4$ is not only because of their high effective surface. On the other hand, the high impact of these nanostructures is due to the high concentration of areas with low coordination and structural deficiencies in their surface. When the particle size decreases to nanoscale, defect is made in coordination of constituent atoms. Most atoms have a partial capacity and remain on the levels [5]. Therefore, the magnesium aluminate nanoparticles act as a mild lewis acid catalyst in the synthesis of 2-ketomethylquinolines.

Ultrasound provides an unusual mechanism for generating high-energy chemistry due to the

immense temperature, pressure and the extraordinary heating and cooling rates generated by the formation, growth and collapse of the cavitation bubbles in the reaction medium [10]. In all cases, the results show that the reaction times are shorter and the yields of the products are higher under sonication. Applying ultrasound irradiations in the heterogeneous systems involving immiscible liquid, the reaction between these species can only occur in the interfacial region between the liquids. Sonication process can be used to produce very fine emulsions and enhances mass transfer from immiscible liquids [18, 19] This phenomenon is possible because cavitational collapse at or near the interface disrupts it and implies jets of one liquid into the other to form the emulsion [20]. These can cause the reaction to take place rapidly.

Table 2. Preparation of several 2-ketomethylquinolines **3** from acyl chlorides **2** and 2-methyl quinoline **1** under ultrasound irradiation at 50 ˚C (method A) and reflux conditions (method B)[a]

Entry	R	Product[b]	Method A	Method B	Mp. (◦C)	
			Time (min)/ Yield (%)[c]	Time (h)/ Yield (%)[c]	Found	Reported[d]
1	Ph	**3a**	12/90	3/90	114-116	113
2	4-MeC_6H_6	**3b**	12/88	3/87	170-172	169
3	4-ClC_6H_6	**3c**	15/75	3/70	164-165	162
4	2-ClC_6H_6	**3d**	15/55	3/52	115-117	117
5	4-$MeOC_6H_6$	**3e**	15/86	4/77	153-155	153
6	4-BrC_6H_6	**3f**	12/89	3/80	163-165	164
7	4-$O_2NC_6H_6$	**3g**	5/52	3/50	179-181	177-178
8	3-BrC_6H_4	**3h**	12/89	5/85	127-129	129
9	$C_6H_5CH_2$	**3i**	20/43	5/40	82-83	81-83
10	CH_3	**3j**	20/10	5/10	68-70	69

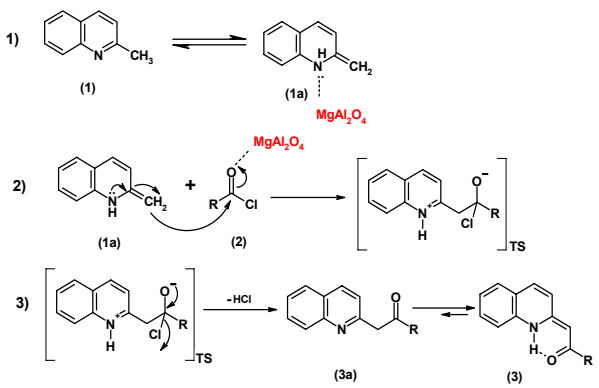
[a] 2-methyl quinoline (1 mmol), acyl chloride (1 mmol), nano-$MgAl_2O_4$ (5 mol%).

[b] All products were characterized by ^1H NMR, ^{13}C NMR, and IR.

[c] Isolated yields.

[d] Ref [17].

A plausible mechanism for the formation of 2-Ketomethylquinolines is envisaged in scheme **2**. A plausible mechanism for this reaction is that 2-methylquinoline **1** and acyl chlorides **2** are first activated by Lewis acidic catalyst and so can activaet the carbonyl group of acyl chloride. On the other hand, 2-methylquinoline is imine-enamine tautomerization that prefer enamine form **(1a)** in presence acidic catalyst. The reaction is thought to proceed through the nucleophilic attack of **1a** to the carbonyl group of acyl chloride **(2)** to afford the intermediate **TS.** The dipolar transition states **TS** occur resulting in generation 2-Ketomethylquinoline **(3a)** that is a ketoimine. Several studies have shown that these Ketomethylquinolines exist as equilibrium mixtures of the enaminone forms **(3)** and the unconjugated forms **(3a)** (keto-enol tautomerization). This class of compounds strongly prefer the enaminone forms **(3)** [21-23]



Scheme 2. Plausible mechanism of the reaction.

Aroyl chlorides were converted to the corresponding 2-ketomethylquinolines in good to excellent yields in in presence of $MgAl_2O_4$ nanocatalysts under ultrasound irradiation. (2–chlorophenyl)(2-quinolyl)methanone (Entry4, **3d**) was low yield than (4–choloro phenyl) (2 quinolyl)methanone (Entry 3, **3c**), because (2-chlorophenyl)(2-quinolyl)methanone has steric hindrance. In all ^{1}H NMR spectra NH group of the 2-ketomethylquinolines appeared around δ 14-16 as a broad singlet and in the IR spectra the C=O/C=C groups (enaminone form) were observed around 1610-1640 cm^{-1}. Proton vinillic appeared around δ 5-6 as a singlet and in IR spectra the C=C/C=O groups enaminone form) 1730-1700 cm^{-1}.

4. Conclusion

In summary, we have developed an efficient and convenient route to synthesis of 2-ketomethylquinoline derivatives by the reaction between 2-methylquinoline and acyl chlorides using a catalytic amount of nanocrystalline $MgAl_2O_4$ under ultrasound irradiation. The reported method is an interesting, easy and novel method, high yields of the products, ease of work-up conditions and low cost make the above method preferable to other existing methods.

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References

[1] M. Nasrollahzadeh, A. Ehsani, A. Rostami-Vartouni, Ultrason Sonochem. 21 (2014) 275-282.

[2] M. Salavati-Niasari, Inorg. Chim. Acta. 362 (2009) 2159-2166.

[3] (a) M. B. Gawande, R. K. Pandey and R. V. Jayaram, Catal. Sci. Technol. 2 (2012) 1113-1125; (b) A. Corma, J. Catal. 216 (2003) 298-312; (c) M. R. Othman, Z. Helwani, Martunus and W. J. N. Fernando, Appl. Org. Chem. 23 (2009) 335-346; (d) S. M. Mahajani and M. M. Sharma, Org. Process Res. Dev. 1 (1997) 97-105; (e) L. Delaude, P. Laszlo and K. Smith, Acc. Chem. Res. 26 (1993) 607-613; (f) M. B. Gawande, V. Polshettwar, R. S. Varma and R. V. Jayaram, Tetrahedron Lett. 48 (2008) 8170-8173.

[4] M. B. Gawande, P. S. Brancoa, R. S. Varma, Chem. Soc. Rev. 42 (2013) 3371-3393.

[5] J. Safari, S. Gandomi-Ravandi, Z. Akbari, Journal of Advanced Research. (2012) http://dx.doi.org/10.1016/j.jare.2012.09.001.

[6] J. Ahmad, M. E. Mazhar, M. Q. Awan, M. N. Ashiq, Physica B. 406 (2011) 3484-3488.

[7] E. Navaei Alver, M. Rezaei, H. Navaei Alver, Powder Technol. 198 (2010) 275-278.

[8] H. Loghmani-Khouzani, R. Gawinecki, M. M. Sadeghi, H. Mehrabi, B. Osmailowski, J. Iran. Chem. Soc. 2 (2005) 294-299.

[9] J. V. Greenhill, H. Loghmani-Khouzani, Spectrochim. Acta, Part A. 46 (1990) 803-808.

[10] H. Loghmani-Khouzani, H. Sabzyan, A Rezaei-Pooranari, Dyes and Pigments. 76 (2006) 447-454.

[11] J. Safari, M. Adib, F. Sheibani, Z. Sadeghi, Turk J Chem. 30 (2006) 673-679.

[12] A. E. M. Saeed, S. A. Elhadi, Synthetic Commu. 41 (2011) 1435-1443.
[13] E. S. H. El Ashry, A. A. Kassem, E. Ramadan, Adv. Heterocycl. Chem. 90 (2006) 1-123.
[14] R. Roussel, M. O. de Guerrero, J. C. Galin, Macromolecules. 19 (1986) 291-299.
[15] H. Loghmani-Khouzani,; H.Minaeifar; R. Gawinecki, J. Mol. Struct. 1032 (2013) 138-146.
[16] (a) J. Wang, Y. Zong, R. Fu, Y. Niu, G. Yue, Z. Quan, X. Wang, Y. Pan, Ultrason Sonochem. 21 **(**2011) 29-34; (b) J. T. Li, M. X. Sun, Y. Yin, Ultrason. Sonochem. 17 (2010) 359-362; (c) A. Bazgir, S. Ahadi, R. Ghahremanzadeh, H. R. Khavasi, P. Mirzaei, Ultrason. Sonochem. 17 (2010) 447-452.
[17] H. Loghmani-Khouzani, M. M. Sadeghi, J. Safari, A. Minaeifar, Tetrahedron Lett. 42 (2001) 4363-4364.
[18] D. Nagargoje, P. Mandhane, S. Shingote, P. Badadhe ,C. Gill, Ultrason. Sonochem. 19 (2012) 94-96.
[19] S. Sadjadi, H. Sepehrian, Ultrason Sonochem. 18 (2011) 480-483.
[20] D. N. Zhang, J.T. Li, Y.L. Song, H.M. Liu, H.Y. Li, Ultrason. Sonochem. 19 (2012) 475-478.
[21] E. Kolehmainen, B. Osmiałowski, T.M. Krygowski, R. Kauppinen, M. Nissinen, R. Gawinecki, J Chem Soc Perk T1. 2 (2000) 1259-1266.
[22] J. V. Greenhill, H. Loghmani-Khouzani, D. J. Maitland, J Chem Soc Perk T1. 1 (1991) 2831-2840.
[23] R. Gawinecki, B. Osmiałowski, E. Kolehmainen, M. Nissinen, J Mol Struct. 525 **(**2000**)** 233-239.