

Synthesis of Quinolines Using Nano-Flake ZnO as a New Catalyst under Solvent-Free Conditions

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Catalytic activity of nano-flake ZnO for synthesis of quinoline derivatives and their related polyheterocycles under solvent-free conditions has been studied. Nano-flake ZnO has been successfully synthesized by conventional heating of a solution approach using ZnOAc.2H₂O and Urea. This method is simple, cost-effective, and environmentally benign and the catalyst can be reused for several times.

Keywords: Quinoline, Nano ZnO, Friedlander reaction, Solvent-free

INTRODUCTION

The reaction of 2-aminoaryl ketones with a secondary carbonyl compounds to give quinolines -also called Friedlander annulation- is a reaction which is well known [1]. Although this reaction has been known for more than a century, it is still the most useful method for the synthesis of quinoline derivatives.

Quinolines are widely occurring natural alkaloids known for a wide range of pharmacological properties being used such as anesthetic, tumorcidal angina pectoris, antihypertensive and antibacterial activities, antimalarial drugs and also act as insecticidal agents [2]. In addition, these compounds are well-known ligands for the preparation of OLED phosphorescent complexes [3] and they are valuable synthons used for the preparation of nano and mesostructures with enhanced electronic and photonic properties [4].

Generally, Friedlander reaction is carried out by base or acid catalysts to yield quinolines. In many cases acid catalyzed Friedlander condensations have been found to be more

effective. Acid catalysts such as HCl [5], H₂SO₄ [5d,6], *p*-toluenesulfonic acid, [7] sulfamic acid, [8] heterogeneous solid acids, [9] phosphoric acid, [10] heteropoly acids, [11] dodecylphosphonic acid [12] and *etc.* were widely employed for this condensation. In addition, microwaves [7,13], ionic liquids [14], gold compounds [15], triflates [16] and *etc.* were also employed as promoters and catalysts. Also, Friedlander reaction is carried out by heating a mixture of the reactant at high temperatures ranging from 150-220 °C in the absence of a catalyst [17].

Most of the previously reported synthesis methods suffer from poor yields, long reaction times, harsh conditions, use of stoichiometric and/or relatively expensive reagents, difficulties in work-up, and using toxic/polar solvent leading to complex isolation and recovery procedures. Moreover, the main disadvantage of almost all previous methods is that the catalyst cannot be recovered; also, in the cases where the catalyst can be recovered, the preparation of the catalyst needed a special and also hazardous material and tedious procedures [12,14]. For these reasons, the use of a neutral and heterogeneous solid catalyst under solvent-free condition, which can be prepared *via* commercially and inexpensive

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starting materials and simple procedure have drawn the attention.

Over recent years, nanometer inorganic oxides have attracted interest throughout the scientific community. Their electronic, magnetic, optical, biological, mechanical and catalytic properties make nanometer materials attractive alternatives to their bulky materials [18]. Of them, the special catalytic activities of nanomaterials intrigued our interest. Because of the larger specific surface area, the metal oxide nanoparticles have a high surface activity, which results in a more robust catalytic activity than bulk metal oxides. However, to the best of our knowledge, little study has been carried out and no report about Friedlander synthesis of quinolines catalyzed by nanometer materials can be found in the literature. In addition, we have also recently shown that nanometal oxides specially, ZnO, can successfully catalyze the organic transformations. The reactions investigated are Knoevenagel condensation and synthesis of β -phosphono Malonates [19,20].

In continuation of our ongoing studies on metal oxides as catalysts [21], here we report an efficient and ecofriendly process for the synthesis of quinolines using Friedlander heteroannulation method in the presence of the nano ZnO as catalyst the method is mild, non-volatile, non-corrosive (compared with the other acid catalysts), and efficiently solid under solvent-free condition as green reaction media.

EXPERIMENTAL

Chemicals were purchased from Fluka, Merck, B.D.H. and Aldrich Chemical Companies. Progress of the reactions was followed by TLC using silica gel polygrams SIL G/UV 254 plates. IR spectra were recorded on a Perkin Elmer 781 and an Impact 400 D Nicolet FTIR spectrophotometers. NMR spectra were recorded on a Bruker DPX 250 MHz instrument. Mass spectra were obtained on a Shimadzu GCMS0QP 1000EX at 20 and/or 70 eV. Elemental analyses were performed on Thermo Finnigan, Flash EA 1112 series microanalyzer by the head of the CHN lab.

Catalyst Preparation

Commercial ZnO, [CM-ZnO, Merk-8849] was purchased from Merck. Samples of conventionally prepared ZnO, nano-

flake prepared ZnO [NF-ZnO (20-30 nm)], and nano-particle prepared ZnO, [NP-ZnO (35+5 nm)] were synthesized and characterized as reported in our previous works [19,20].

In a typical experiment for the synthesis of NF-ZnO, Zn(OAc)₂.2H₂O (10 mmol) and CO(NH₂)₂ (0.2 mol) were dissolved in 200 ml deionized water at room temperature to form a transparent solution. Then the mixture was refluxed for 12 h. It was cooled by cold water to stop the reaction. The product was centrifuged and washed with deionized water and absolute ethanol and dried at 80 °C for 8 h. The NF-ZnO was obtained by calcining the precursor in a furnace in air at 400 °C for 2 h [19,20].

In a typical experiment for the synthesis of NP-ZnO, Zn(OAc)₂.2H₂O (10.98 g) was treated with absolute ethanol (300 ml) at 60 °C. After dissolving the salt, oxalic acid dehydrate (12.6) which was dissolved in ethanol (200 ml) at 50 °C was added slowly under of stirring. A thick white gel formed, which was kept for drying at 80 °C. The solid was calcined at 500 °C for 2 h to yield ZnO nanoparticles [20].

General Procedure for Synthesis of Quinoline Derivatives

To a mixture of 2-aminoaryl ketone (1 mmol) and α -methylene carbonyl compound (1.5 mmol), nano-falke ZnO (NF-ZnO) (0.008 g, 10 mol%) was added. The mixture was heated in an oil bath at 100 °C and the reaction was monitored by TLC. After the reaction was complete, EtOAc was added to the reaction mixture and centrifuged to separate the catalyst. The organic solvent was removed under reduced pressure. After purification by chromatography on silica gel (solvent:n-hexane/ethyl acetate, 70/30) the product was obtained. All Products are known and were characterized by ¹H NMR, IR and mass spectral data which were found to be identical with those described in references and for new compounds the complete spectroscopic data are described as bellow.

Compound 3c. Light yellow solid, ¹H NMR, (CDCl₃) ppm: 7.37-8.19 (9H, m, ArH), 5.44 (2H, s, -COOCH₂Ph-), 2.64 (3H, s, ArCH₃), 2.56 (3H, s, ArCH₃); ¹³C NMR (CDCl₃) ppm: 15.8, 26.2, 64.9, 120.1, 121.9, 123.1, 126.6, 128.1, 128.5, 129.2, 129.4, 129.6, 137.7, 141.0, 147.9, 154.9, 169.8; MS (70 eV) *m/z*: 291 (M⁺); Anal. Calcd. for C₁₉H₁₇F₃NO₂: C, 78.33; H, 5.88. Found: C, 78.13; H, 5.70.

Compound 3h. Light yellow solid, ¹H NMR, (CDCl₃)

ppm: 7.86-7.92 (2H, m, ArH), 7.52 (1H, m, Ar-H), 7.37 (1H, m, Ar-H), 2.92-2.96 (1H, m, H-12), 2.46 (3H, s, -Me), 2.13-2.23 (1H, m, H-13_{exo}), 1.89-2.01 (1H, m, H-14_{endo}), 1.24-1.33 (5H, m, Me and H-13_{endo}, H-14_{exo}), 0.98 (3H, s, Me), 0.50 (3H, s, Me); ¹³C NMR (CDCl₃) ppm: 165.3(C-2), 141.2 (C-4), 134.8 (C-10), 131.5 (C-11), 128.9 (C-9), 128.7 (C-5), 128.5 (C-8), 127.9 (C-6), 127.3 (C-7), 54.0 (C-12), 53.6 (C-15), 53.1 (C-1), 31.7 (C-14), 24.5 (C-13), 20.2 (C-16), 18.4 (C-17), 9.9 (C-18) 9.5 (C-19); MS (70 eV) *m/z*: 251 (M⁺); Anal. Calcd. for C₁₈H₂₁N: C, 86.01; H, 8.42. Found: C, 85.89; H, 8.34.

Compound 3i. Light yellow solid; ¹H NMR (CDCl₃) ppm: 7.90-7.96 (2H, m, ArH), 7.63 (1H, m, Ar-H), 7.46 (1H, m, Ar-H), 2.63 (3H, s, -Me), 2.58 (3H, s, Me); ¹³C NMR (CDCl₃) ppm: 14.2, 23.7, [110.5, 117.1, 124.5, 132.2 (q, -CF₃)], 112.2, 120.8, 123.9, 126.2, 129.2, 130.0, 146.7, 146.9, 153.4, 188.5; MS (70 eV) *m/z*: 253 (M⁺); Anal. Calcd. for C₁₃H₁₀F₃NO: C, 61.66; H, 3.98. Found: C, 61.60; H, 3.87.

Compound 3j. Light yellow solid; ¹H NMR (CDCl₃) ppm: 7.23-7.33 (4H, m, ArH), 3.95-4.03 (2H, m, -OCH₂CH₃), 2.33 (3H, s, ArCH₃), 1.13 (3H, t, *J* = 7.05 Hz, -OCH₂CH₃); ¹³C NMR (CDCl₃) ppm: 15.3, 17.2, 64.7, [108.1, 115.2, 122.3, 128.9 (q, -CF₃)], 119.2, 124.5, 124.8, 128.8, 131.3, 134.6, 145.3, 147.6, 148.9, 171.3; MS (70 eV) *m/z*: 283 (M⁺); Anal. Calcd. for C₁₄H₁₂F₃NO₂: C, 59.37; H, 4.27. Found: C, 59.12; H, 4.00.

Compound 4j. Light yellow solid; ¹H NMR (CDCl₃) ppm: 7.50-7.93 (4H, m, ArH), 4.39 (2H, m, -OCH₂CH₃), 2.60 (3H, s, ArCH₃), 1.31 (3H, t, *J* = 7.05 Hz, -OCH₂CH₃); ¹³C NMR (CDCl₃) ppm: 15.4, 17.5, 65.1, [107.5, 115.1, 122.5, 129.2 (q, -CF₃)], 100.2, 162.5, 124.8, 128.9, 130.4, 130.9, 132.7, 141.7, 151.4, 185.0; MS (70 eV) *m/z*: 283 (M⁺); Anal. Calcd. for C₁₄H₁₂F₃NO₂: C, 59.37; H, 4.27. Found: C, 59.20; H, 4.03.

Compound 3r. Light yellow solid, ¹H NMR (CDCl₃) ppm: 7.13-8.09 (9H, m, ArH), 2.89-2.91 (1H, m, H-12), 2.10-2.13 (1H, m, H-13_{exo}), 1.83-2.00 (1H, m, H-14_{endo}), 1.14-1.31 (5H, m, Me and H-13_{endo}, H-14_{exo}), 0.92 (3H, s, Me), 0.53 (3H, s, Me); ¹³C NMR (CDCl₃) ppm: 10.1, 18.3, 20.3, 24.5, 31.7, 53.1, 53.9, 54.1, 121.1, 125.1, 126.0, 127.0, 127.2, 128.7, 129.1, 129.4, 132.5, 138.2, 145.7, 146.4, 174.9; MS (70 eV) *m/z*: 313 (M⁺); Anal. Calcd. for C₂₃H₂₃N: C, 88.13; H, 7.40. Found: C, 88.02; H, 7.32.

Compound 3s. Light yellow solid; ¹H NMR (CDCl₃)

ppm: 7.40-8.50 (9H, m, ArH), 5.25 (2H, m, -OCH₂CH₃), 1.96 (3H, t, *J* = 7.06 Hz, -OCH₂CH₃); ¹³C NMR (CDCl₃) ppm: 15.3, 65.8, [107.1, 119.2, 122.3, 128.8 (q, -CF₃)], 116.0, 122.5, 126.4, 126.9, 127.7, 128.1, 128.2, 128.5, 128.7, 130.9, 137.5, 148.0, 161.2; MS (70 eV) *m/z*: 345 (M⁺); Anal. Calcd. for C₁₉H₁₄F₃NO₂: C, 66.09; H, 4.09. Found: C, 66.02; H, 4.00.

Compound 4s. Light yellow solid; ¹H NMR (CDCl₃) ppm: 7.13-7.28 (9H, m, ArH), 4.00 (2H, m, -OCH₂CH₃), 1.08 (3H, t, *J* = 7.06 Hz, -OCH₂CH₃); ¹³C NMR (CDCl₃) ppm: 15.5, 66.9, [108.2, 121.1, 123.5, 129.0 (q, -CF₃)], 119.3, 126.0, 126.6, 127.1, 127.8, 128.2, 128.4, 128.8, 129.1, 133.3, 137.8, 149.3, 201.5; MS (70 eV) *m/z*: 345 (M⁺); Anal. Calcd. for C₁₉H₁₄F₃NO₂: C, 66.00; H, 4.05. Found: C, 66.09; H, 4.09

RESULTS AND DISCUSSION

In view of the importance of the nano-ZnO as novel catalyst and as a part of our continuing efforts toward the synthesis of biologically important quinolines and related polyheterocycles, we became interested in the possibility of developing the Friedlander synthesis. For this purpose, α-amino acetophenone (**1a**) was reacted with ethylacetoacetate (**2a**) in the presence of various metal oxides as shown in Scheme 1, and Table 1. Two kinds of nanocrystalline ZnO powders with varying in size and shape were synthesized: nanoflake ZnO, NF-ZnO (20-30 nm), and nanoparticle ZnO, NP-ZnO (30-40 nm). They were fully characterized by XRD, SEM, and FT-IR as reported previously [19,20].

From Table 1, it can be seen that in the presence of some other metal oxides examined in the synthesis of quinoline **3a**, the reaction hardly proceeded even after long reaction times. Also, in order to examine the solvent effect and in our quest for the deployment of a benign reaction medium, the reaction was explored in toluene, THF, CH₃CN and water. The reaction in organic solvents required relatively longer reaction times and afforded low yields of the product (Entries 2-4), while, the reaction in aqueous media was failed (Entry 5).

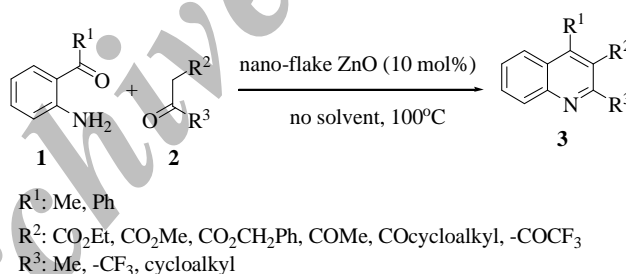
As it is obvious from Table 1, the nanoflake ZnO (10 mol%) afforded the best results. Consequently, all further studies were conducted using this type of catalyst under solvent-free conditions (Scheme 1). The results are summarized in Table 2.

According to Table 2, various 1,3-dicarbonyl compounds

Table 1. Optimization of the Synthesis of Quinoline **3a**^a


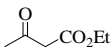
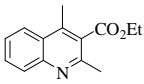
Entry	Catalyst	Solvent	Time (h)	Yield (%) ^b
1	Nano-flake ZnO (10 mol%)	None	4	98
2	Nano-flake ZnO (10 mol%)	Toluene	24	trace
3	Nano-flake ZnO (10 mol%)	THF	24	trace
4	Nano-flake ZnO (10 mol%)	CH ₃ CN	24	trace
5	Nano-flake ZnO (10 mol%)	H ₂ O	24	0
6	Nano-flake ZnO (5 mol%)	None	12	85
7	Nano-flake ZnO (2 mol%)	None	24	67
8	Nano-flake ZnO (20 mol%)	None	4	95
9	Nano-particle ZnO (10 mol%)	None	12	80
10	Commercially ZnO (10 mol%)	None	11	90
11	Commercially MgO (10 mol%)	None	24	40
12	Commercially TiO ₂ (10 mol%)	None	8	75
13	Commercially CaO (10 mol%)	None	24	73

^aConditions: a mixture of **1a** (1.0 mmol) and **2a** (1.5 mmol) and catalyst were heated in an oil bath at 100 °C. ^bIsolated yield.



Scheme 1. Synthesis of quinolines catalyzed by nano-flake ZnO

Table 2. Synthesis of Poly-Substituted Quinolines **3** under Solvent-Free Conditions

Entry	Substrate 1	Substrate 2	Quinoline 3	Type of catalyst	Time (h)	Yields (%) ^a	M.P. (°C) (lit.)
1	 1a	 2a	 3a	CM-ZnO ^b	11	90	oil (oil) ¹⁴
				NF-ZnO ^c	4	98 (1 st use)	
						95 (2 nd use)	
						95 (3 rd use)	

Synthesis of Quinolines Using Nano-Flake ZnO as a New Catalyst

Table 2. Continued

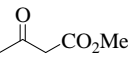
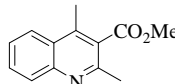
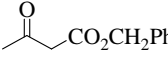
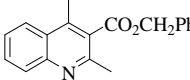

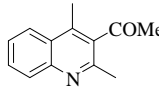

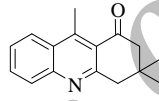

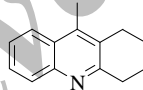

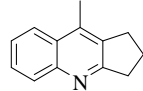

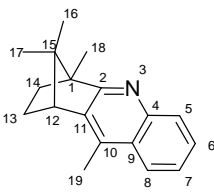
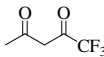
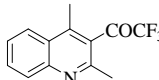
2	1a			CM-ZnO	5 ^d	60	oil (oil) ^{9b}
		2b	3b	NF-ZnO	5	95	
3	1a			CM-ZnO	5 ^d	82	54-57
		2c	3c	NF-ZnO	2.5	95	
4	1a			CM-ZnO	12	50	oil (oil) ¹⁴
		2d	3d	NF-ZnO	7	67	
5	1a			CM-ZnO	12	62	103-105 (105-106) ⁷
		2e	3e	NF-ZnO	3.5	83	
6	1a			CM-ZnO	12	50	76-78 (78) ¹⁴
		2f	3f	NF-ZnO	5.5	62	
7	1a			CM-ZnO	12	50	56-58 (60) ¹⁴
		2g	3g	NF-ZnO	6	65	
8	1a			CM-ZnO	48	36	197-199
		2h	3h	NF-ZnO	12	60	
9	1a			CM-ZnO	12	86	154-157
		2i	3i	NF-ZnO	3	95	

Table 2. Continued

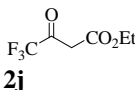
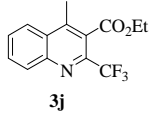
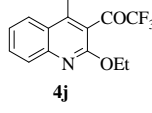
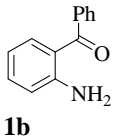
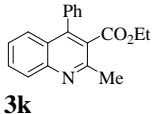
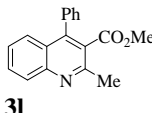
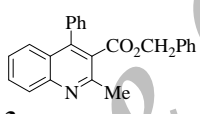
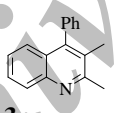
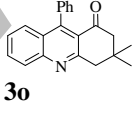
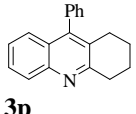
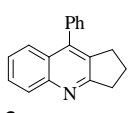
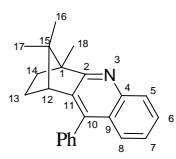
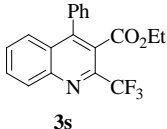
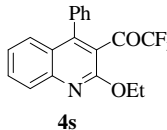
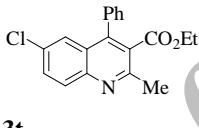
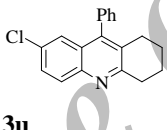
10	1a	 2j	 3j	CM-ZnO	5 ^d	70 (3j:4j ,57:43) ^e	86-88
			 4j	NF-ZnO	5	(3j:4j ,78:22) ^e	97-100
11	1b	 1b	 2a	CM-ZnO	6	65	96-98 (93)12
				NF-ZnO	3.5	85	
12	1b	2b	 3l	CM-ZnO	5d	70	131-133 (132-34)9b
				NF-ZnO	4	92	
13	1b	2c	 3m	CM-ZnO	10	84	90-92 (90-93)12
				NF-ZnO	2	95	
14	1b	2d	 3n	CM-ZnO	12	43	111-113 (112-15)12
				NF-ZnO	5	62	
15	1b	2e	 3o	CM-ZnO	12	57	189-191 (190-92)9a
				NF-ZnO	3	75	
16	1b	2f	 3p	CM-ZnO	12	47	138-140 (138-41)12
				NF-ZnO	4	63	
17	1b	2g	 3q	CM-ZnO	12	50	133-135 (133-35)12
				NF-ZnO	5	67	
18	1b	2h	 3r	CM-ZnO	48	20	>200
				NF-ZnO	10	62	

Table 2. Continued

19	1b	2j	 3s	CM-ZnO	12	82	165-167
						(3s:4s , 85:15) ^e	
			 4s	NF-ZnO	2	98	192-194
						(3s:4s , 92:8) ^e	
20	1c	2a	 3t	CM-ZnO	4	75	102-104
				NF-ZnO	2	92	(102-04) ¹²
21	1c	2f	 3u	CM-ZnO	10	50	157-159
				NF-ZnO	3.5	75	(163) ¹⁴

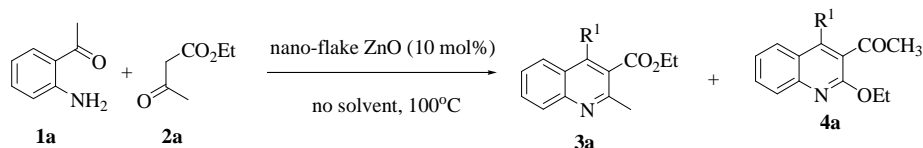
^aYields are the isolated compounds. ^bCM-ZnO means commercial ZnO. ^cNF-ZnO means nanoflake ZnO. ^dBy increasing the reaction time to 24 h, the reaction yield was not increased. ^eThe ratio of two regioisomers were determined by ¹H NMR of the crude products mixture before isolation by column chromatography.

including alkyl acetoacetates, acetyl acetone, cyclic β -diketone such as 5,5-dimethylcyclohexandione (dimedone) and cyclic ketones reacted with 2-aminoaryl ketones to give the corresponding quinolines without any side product. All the compounds were well characterized by melting point, IR, ¹H NMR, ¹³C NMR, and mass spectroscopy analyses. Their elemental analyses were in conformity with their structures. The respective quinolines and polyheterocycles (**3a-u**) were obtained in high regioselectivity and could be isolated in excellent yields in all cases.

Theoretically, the Friedlander reaction with unsymmetrical 1,3-diones such as ethyl acetoacetate (**2a**) can have two possible routes for cyclization, giving rise to two regioisomers (**3a**) and (**4a**) (Scheme 2). Depending upon the nature of catalyst, the route of cyclization can be changed [11]. To our surprise, the NF-ZnO promoted Friedlander reaction with unsymmetrical 1,3-diones afforded regiospecifically the

regioisomer **3** only in excellent isolated yields (Entries 1-3, 9, 11-13 and 20). No trace of the isomeric **4** could be detected either on TLC or in ¹H NMR of the crude product mixture before purification.

1,1,1-Trifluoro-2,4-pentanedione (**2i**) gave exclusively the regioisomers (**3i**) (Entry 9). This can be rationalized by the preferred hydrate formation rather than imine/enamine formation of the carbonyl group next to the CF₃ group in (**2i**). However, the condensation of 2-aminoarylketones **1a,b** with ethyl-4,4,4-trifluoro-3-oxobutanoate (**2j**) led to regioisomeric mixtures of quinolines **3** and **4**, respectively (Entries 10, 19). In this case, the two carbonyl groups presents in (**2j**) had similar reactivity, where the actual mechanism seems to be that the enamine formation may proceed in the condensation step; however, in this case, it is rather an iminoether. Interestingly, five and six membered ketones (**2f,2g**) and camphore (**2h**) reacted with 2-amino aryl ketones to afford the



Scheme 2. Friedlander reaction with ethyl acetoacetate (2a) giving rise to two regioisomers, (3a) and (4a)

Table 3. Comparison of Catalytic Activity of NF-ZnO with the other Selected Catalysts or Reagents Used for the Synthesis of Quinoline 3a

Entry	Catalyst/reagent	Solvent	Temp. (°C)	Time (h)	Yield (%) ^a
1	Y(OTf) ₃ ^{16a}	CH ₃ CN	r.t.	6.0	83
2	NaHSO ₄ ·SiO ₂ ^{9a}	none	70	4.0	80
3	Amberlyst-15 ^{9b}	EtOH	reflux	2.5	87
4	HCl ^{13a}	HCl	Microwave	6.0	60
5	Nano-flake ZnO (10 mol%)	None	100	4.0	98

^aIsolated yield.

corresponding tricyclic quinolines in moderate yields (Entries 6-8, and 16-18).

In Table 2, the catalytic activity of the NF-ZnO is compared with that of the CM-ZnO. The NF-ZnO indeed displayed the highest activity and regioselectivity (see entries 10, 19), compared to that of CM-ZnO. The NF-ZnO has Lewis acid sites (Zn²⁺) and Lewis base sites (O²⁻) [22]. Thus, in the Friedlander synthesis, an Lewis base site (O²⁻) of NF-ZnO can be taken up the proton of α -methylene group, and the Lewis acid moiety (Zn²⁺) can be activated the carbonyl group for the imine formation.

Furthermore, the catalyst can also be reused. As shown in Table 2, Entry 1, the yields of 3a in second and third uses of the catalyst were almost same as that in the first use. In every case, >90% of the NF-ZnO was easily recovered from reaction mixture by adding EtOAc and centrifuged to separate the catalyst.

A comparison of the present protocol, using nano flake ZnO, with some previously known protocols is collected in Table 3 to compare their results with those of the present protocol; as is obvious the proposed protocol shows superiority over the previous ones.

CONCLUSIONS

The nano-flake ZnO provides an efficient new catalyst for the regiospecific synthesis of quinolines *via* Friedlander annulation. We have developed a green approach to Friedlander synthesis of quinolines that requires neither harsh conditions nor the use of hazardous acids, or bases. The catalyst can be recovered and reused without any loss of activity. Two kinds of nano ZnO compounds were synthesized, characterized and screened for this heterocyclization reaction. The efficacy of the catalyst for this reaction has been correlated to the acidity sites of the NF-ZnO in terms of basicity sites. The moderate reaction conditions, absence of a solvent and recyclability of the catalyst make the proposed protocol an environment friendly methodology for scale-up.

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