One pot, Solvent-free synthesis of substituted 3,4-dihydropyrimidin-2(1H)-ones/thiones under microwave irradiation (CEM) using reusable nickel nanoparticles

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Abstract:

A library of 3,4-dihydropyrimidin-2(1H)-ones/thiones derivatives were synthesized via Biginelli condensation reaction of β -keto esters, aryl aldehydes and urea/thiourea under solvent-free conditions utilizing nickel nanoparticles under microwave irradiation (CEM Discover). The structures of the all compounds were elucidated with the aid of elemental analysis, IR, ¹H-NMR and Mass spectral data. Nickel nanoparticles can be recovered and reused five times without loss of their efficiency. Short reaction time, high yield of products and simple workup procedure, solvent-free conditions and reusability of the catalyst are the superior features of this protocol.

1. INTRODUCTION

3,4-dihydropyrimidinones (Biginelli compounds) derivatives in general are known to have a broad range of applications in medicinal, bio-organic, industrial as well as in the fields of synthetic chemistry. Some of these compounds are very active calcium channel blocker.^[1] Few derivatives of 3,4-dihydropyrimidinones like Amlodipine[1] and Nicardipine[2] are found to have antihypertensive activity.^[2] Dihydropyridine drugs exhibits cardiovascular activity. Their sulfur analogues (DHPMs) also have been reported to possess diverse pharmacological activities such as antiviral, antibacterial and antihypertensive activity.^[2] Thiourea compounds have found wide applications as pharmaceuticals, insecticides, preservatives, rodenticides, and otherwise also they are of commercial use in dyes, photographic films, textiles etc. They show a wide variety of physiological activities. Several alkaloids containing the dihydropyrimidine core unit, exhibiting interesting biological properties, have been isolated from marine source.^[3-5] Among these the crambine^[3] and batzelladine alkaloids^[4] were found to be potent HIVgp-120-CD4 inhibitors. 4-(3-hydroxyphenyl)-2-thione derivative ($\pm$) called monastrol[5] known as a novel cell-permeable lead molecule for the development of anticancer drugs.

Figure 1

Biginelli reaction is multicomponent reaction which involves condensation of ethyl acetoacetate, aryl aldehyde and urea/thiourea to give Substituted 3,4-dihydropyrimidin-2(1H)-ones/thiones (Scheme 1).

Scheme 1

This reaction was carried out in presence of various catalysts in different conditions,^[6] such as sulfonated-cyclodextrine, Cu(OTf)₂/MWI, Sulfated tungstate, Melamine trisulfonic acid, HCl/EtOH, N,N-Dichlorobis(2,4,6-trichlorophenyl)urea, H₃PO₃/Pd-Cat., *hν*/DMSO, TFA/THF/MWI, TMSCl/CAN, HCl or H₂SO₄ or TEBA, FeCl₃/Al-MCM, Ca(OCi)₂, BPAT-TfOH, *L*-(+)-tartaric acid-urea mixtures, AcOH, Mg(NO₃)₂, chloroacetic acid, PPA-SiO₂, gypsum, Nano-BF₃.SiO₂, Organocatalytic, HCl/MWI, Me₃SiCl, [Hmim]HSO₄-NaNO₃, NH₄VO₃/MWI, CeCl₃.7H₂O, Me₃SiCl/DMF, *p*-TSA.H₂O, TMSCl/DMF, Sm(ClO₄)₃, AcOH, TSIL, VitaminB1/EtOH, Cl₃CCO₂H, sulfamic acid, ultrasonic radiation, neat condition, PEG-400. Commonly synthesis of DHPMs via Biginelli reaction is done in reflux condition. The simple and direct method for the synthesis of DHPMs reported by Biginelli in 1893 involves the one-pot condensation of an aldehyde, a β-ketoester and urea under strongly acidic conditions¹⁴ but this method suffers from low yields especially in the cases of aliphatic and some substituted aromatic aldehydes. At present there are few general methods for synthesis of DHPMs involves the reflux of β-ketoesters, aryl aldehydes and urea, using catalytic acid in a protic solvent, but disadvantage of this method is it's a more time consumption method and gives low yield of product. All this discovered method require solvent, longer reaction time and isolation workup for the desired 3,4-dihydropyrimidones.

Now a days, Metal nanoparticles have attracted much attention in the fields of physics, chemistry, electronics and biology^{[7][8]} due to their unique electrical,^[9] chemical,^[10] optical^[11] and photo-electrochemical^[12] properties, which are strongly dependent on the sizes and shapes of metal

nanomaterial.^[12-14] These nanoparticles having a high specific surface area and a high surface to volume ratio.

Moreover, Microwave heating has emerged as a powerful technique to promote a variety of chemical reactions. Microwave reactions under solvent-free conditions are attractive in offering reduced pollution and offer low cost together with simplicity in processing and handling.^[15] We have used combination approach of these two things i.e. use of nickel nanoparticle under microwave irradiation to optimize synthesis of 3,4-dihydropyrimidinones (Biginelli compounds) derivatives. We have reported one pot synthesis which is a simple, efficient, environmentally safe and economical method for the preparation of DHMPs in solvent-free condition using nickel nanoparticles.

2. RESULTS AND DISCUSSION:

The use of heterogeneous and recyclable catalysts^[16-18] especially under solvent-free conditions presented itself as a remarkable technique toward environmentally clean synthesis of organic compounds. Therefore, we decided to investigate the efficiency of Ni-nano particle as a an efficient and reusable catalyst for the synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones derivatives under microwave irradiation as well as under solvent-free conditions (**Scheme 2**).

Firstly, we have synthesized Ni-nano particles according to previously reported method and it was characterized using XRD. From the XRD analysis and *Debye-Scherrer formula*, we got size of Ni-nano particles. The size of nano particle is 14 nm. Then the synthesis of compound **1** (**Table 1**) was selected as a model reaction to determine suitable reaction conditions. The reaction was carried out under microwave irradiation by employing benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea (1.5 mmol) and different amount of Ni-nanoparticles under solvent-free conditions. Initial experiment without catalyst produced very lower yield of product. Then the reaction was performed in the presence of 5 mol%, 10 mol% and 15 mol% of Ni-nanoparticles using different amount of urea (**Table 2**). In a Improvement of yield was observed when the amount of urea was increased from 1 equiv. to 1.5 equiv. (based on benzaldehyde) but the yield remained same with further increment of urea up to 2 equiv. Use of just 10 mol% of Ni-nanoparticles is sufficient to push the reaction into completion with excellent yield. Higher amount of the catalyst did not improve the result to a greater extent. Hence, an optimum of 0.10 equiv. (10 mol%) of Ni-nanoparticles and 1.5 equiv. of urea (based on benzaldehyde) in the reaction mixture was ideal for achieving the best yield. Methanol was also used as a solvent instead of solvent-free condition. However, in absence of solvent reaction proceeded efficiently in terms of product yield and reaction time.

Table 1: Synthesis of various dihydropyrimidinones using Ni-nanoparticle as catalyst

Compound	R	X	Microwave Irradiation time (Seconds)	Yield (%)	Melting point °C (Literature)
1	H	O	20	99	200-203 (200-202) ^[19]
2	4-Cl	O	30	98	210-212 (212-213) ^[20]
3	4-OCH ₃	O	50	99	201-203 (200-202) ^[19]
4	4-F	O	30	97	175-177 (174-176) ^[20]
5	4-NO ₂	O	40	98	183-185 (184-187) ^[19]
6	4-OH	O	30	99	224-226 (227-229) ^[19]
7	H	S	20	99	206-208 (202-210) ^[19]
8	4-Cl	S	30	97	180-182 (180-182) ^[21]
9	4-OCH ₃	S	40	95	152-154 (150-152) ^[19]
10	4-F	S	40	98	208-210 (209-210) ^[21]
11	3-NO ₂	S	50	99	206-208 (206-208) ^[19]
12	3-OH	S	30	99	184-185 (183-185) ^[19]

Table 2: Synthesis of dihydropyrimidinones under different conditions

Entry	Urea (mmol)	Catalyst (mol%)	Yield (%)
1	1	-	0
2	1	10	80
3	1.2	10	88
4	1.5	10	99
5	1.7	10	98
6	2.0	10	99
7	1.5	5	82
8	1.5	15	99
9	1.5	20	99

To evaluate the generality of this model reaction we then prepared a range of 3,4-dihydropyrimidin-2(1H)-ones/thione derivatives under the optimized reaction conditions. In all cases, aromatic aldehydes with substituents carrying either electron-donating or electron-withdrawing groups reacted successfully and gave the products in high yields. It was found that aromatic aldehydes with electron-withdrawing groups reacted faster than those with electron-donating groups.

The principle advantage of the use of heterogeneous catalysts in organic transformations is their reusability. Hence, we decided to study the catalytic activity of recycled Ni-nano particles in the synthesis of compound **1** under the optimized conditions. After the completion of the reaction, the catalyst was recovered according to the procedure mentioned in experimental section and reused for a similar reaction. The catalyst could be used at least five times with only slight reduction in the catalytic activity (**Table 3**).

Table 3: Reusability profile of Nickel nanoparticles

Run	% Yield of Product	Recovery of catalyst (%)
1	99	99
2	98	98
3	96	95
4	95	92
5	92	90

The merits of our protocol are: (a) unlike other metallic catalyst, our process extends the scope of reusability of the catalyst. The recycled catalyst was reused five times without loss of its activity; (b) Ni-nano particles was easily synthesized by inexpensive protocol; (c) high yielding process; (d) simple and efficient work up procedure; (e) solvent-free condition; (f) reaction under microwave irradiation (MWI); (g) shorter reactions times.

Scheme 3

As a normal curiosity of chemists after discover a reaction there were studies to find the expected pathway for that reaction. As Biginelli reaction involves condensation of three component aldehydes, β -keto esters and urea/thiourea, keeping these reactant's reactivity in mind possibly the reaction could proceed in a following way (**Scheme 3**). The mechanism involved nucleophilic attack of urea on the electron deficient carbon of the aromatic aldehyde resulted in formation of N-benzylidene-urea with removal of water molecule. Now, electrons available on nitrogen atom which was attached to benzylidene double bond were pulled by nickel nanoparticles so that nitrogen couldn't take part in further condensation i.e. only double bond electrons were available. On other site electrons on both oxygen atom of ethylacetoacetate also pulled by Nickel nanoparticles so active methylene group of ethyl acetoacetate adds to benzylidene double bond of N-benzylidene-urea resulted in formation of final product followed by dehydration.

3. Materials and Methods

All Starting materials and other reagents were purchased from commercial suppliers and were used without any further purification unless otherwise indicated. The reactions were assayed by thin layer chromatography (TLC) and terminated as judged by the consumption of starting material. Analytical thin-layer chromatography (TLC) was performed on silica gel G 60 F254 (Merck) plates and eluted with the appropriate solvent ratios (v/v). The melting points were recorded in optimeit automated melting point system and were uncorrected. IR spectra were recorded on a Perkin-Elmer 377 spectrophotometer, ^1H NMR spectra was measured in Bruker AV 400 MHz using CDCl_3 as a solvent and TMS as an internal standard. Mass spectra was recorded on Advion Expression CMS, USA. Elemental analysis was performed on the Vario MICRO cube, elementary CHN analyzer serial no.: 15084053. Here we have used the CEM Discover microwave system for synthesis. Its model no.: 908010 and made CEM Matthews. Inc, USA.

3.1. Preparation and characterization of nickel nanoparticles^[22]

Nickel nanoparticles were prepared using hydrazine hydrate as reducing agent by earlier reported method.

Take 0.5 g of nickel chloride in flask and dissolved it in 50 ml ethylene glycol by heating the solution at 60 °C. Then 2.25 ml hydrazine hydrate was added to above solution. Then 1.44 g of NaOH (1M) solution was added with stirring. The complete solution was kept under magnetic

stirrer for 1 h at 60 °C. After 1 hour reaction was completed and black nickel nanoparticles formed were collected, washed several times by ethanol and dried at the room temperature. The formation of nanoparticles was confirmed by XRD analysis.

Formation of nickel nanoparticles was confirmed by XRD analysis. XRD graph (**Figure 1**) shows two characteristic peaks at 2θ value **45.37 & 52.8** which were matched with standard data. ^[23-25] These peaks correspond to indices (1 1 1) and (2 0 0) respectively. The broad nature of peaks is indicative of their nano size.

Particle Size Calculation from XRD^[26]

Considering the peak at degrees, average particle size has been estimated by using *Debye-Scherrer formula*,

$$D = \frac{0.9 \lambda}{\beta \cos \theta}$$

Where ' λ ' is wave length of X-Ray (0.1541 nm),

' β ' is FWHM (full width at half maximum),

' θ ' is the diffraction angle &

'D' is particle diameter size.

Here, the values of different component in scherrer formulla obtained from XRD are as follows,

- 1) $2\theta = 45.3702$ & hence $\theta = 22.685$
- 2) $\beta = (45.3702 - 44.7649) \pi / 180 = 0.01056$ radians
- 3) $\lambda = 0.1541$

From the above calculation, the average diameter size of nickel nanoparticles is **14.25 nm**. The smaller size of Ni-nano particles having a higher surface to volume Ratio has promising features for the reaction response such as the shortest Reaction time, excellent product yields, simple work-up procedure, and purification of products by non-chromatographic methods.

3.2. Synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thiones using Ni-nano particle as a Reusable catalyst:

The aromatic aldehyde (1 mmol), ethyl acetoacetate (1 mmol), urea or thiourea (1.5 mmol) and nickel nanoparticles (10 mol%) were placed into a sealed glass ampoule (10 mL) and introduced in the center of the cavity of a CEM microwave oven. The reaction mixture were irradiated at 150 W (80 °C) for the time shown in **table 1**. The reaction progress was monitored by thin layer chromatography (TLC) using n-hexane:ethyl acetate (8:2) as a mobile phase, during the interval of each 10 second. After completion of the reaction, the mass was cooled to room temperature, the solid residue was dissolved in ethyl acetate, and the mixture was stirred for 5 min. The catalyst was filtered and washed with acetone, then dried in an oven at 100 °C for 2 h. The

combined organic filtrate was washed twice with water and brine solution followed by dried over anhydrous Na_2SO_4 . After vacuum distillation of the filtrate to the crude product was obtain almost in pure form. In some cases the crude product was further purified by recrystallization from ethanol. All of the desired pure product(s) were characterized by comparison of their physical data with those of known compounds, melting point, IR, ^1H -NMR and Mass spectroscopy.

5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (1): IR (KBr, cm^{-1}): 3233, 2954, 1730, 1690, 1206, 698. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 9.21 (s, 1H), 7.74 (s, 1H), 7.25 (m, 5H), 5.14 (s, 1H), 3.98 (q, $J = 7.1$ Hz, 2H), 2.25 (s, 3H), 1.09 (t, $J = 7.1$ Hz, 3H); EIMS m/z (%): 261.15 [$\text{M}^+ + 1$].

4-(4-Chlorophenyl)-5-ethoxycarbonyl-6-methyl-3,4-dihydropyrimidin-2(1H)-one (2): IR (KBr, cm^{-1}): 3230, 3091, 2974, 2935, 1700, 1642. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 1.10 (t, $J = 6.7$ Hz, 3H), 2.24 (s, 3H), 3.97 (q, $J = 6.7$ Hz, 2H), 5.14 (d, $J = 3.1$ Hz), 7.23-7.38 (m, 4H), 7.76 (s, 1H), 9.23 (s, 1H). EIMS m/z (%): 296.27 [$\text{M}^+ + 2$].

5-Ethoxycarbonyl-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (3): IR (KBr, cm^{-1}): 3206, 2956, 1740, 1679, 1245, 1180, 1040, 875. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 9.14 (s, 1H), 7.66 (s, 1H), 6.99 (m, 4H), 5.07 (s, 1H), 3.96 (q, $J = 6.8$ Hz, 2H), 3.70 (s, 3H), 2.23 (s, 3H), 1.09 (t, $J = 6.8$ Hz, 3H). EIMS m/z (%): 291.20 [$\text{M}^+ + 1$].

5-Ethoxycarbonyl-6-methyl-4-(4-fluorophenyl)-3,4-dihydropyrimidin-2(1H)-one (4): IR (KBr, cm^{-1}): 3240, 2980, 1730, 1640, 1230, 1150, 790. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 9.25 (s, 1H), 7.77 (s, 1H), 7.21 (m, 4H), 5.15 (s, 1H), 3.99 (q, $J = 7.1$ Hz, 2H), 2.26 (s, 3H), 1.09 (t, $J = 7.1$ Hz, 3H). EIMS m/z (%): 279.11 [$\text{M}^+ + 1$].

5-Ethoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (5): IR (KBr, cm^{-1}): 3232, 3108, 2977, 1701, 1641, 1591, 1522. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 9.37 (s, 1H), 8.20-7.50 (m, 4H), 7.91 (d, $J = 2.46$ Hz, 1H), 5.27 (d, $J = 1.6$ Hz, 1H), 3.98 (q, $J = 7.1$ Hz, 2H), 2.27 (s, 3H), 1.09 (t, $J = 7.1$ Hz, 3H). EIMS m/z (%): 306.40 [$\text{M}^+ + 1$].

5-Ethoxycarbonyl-6-methyl-4-(4-hydroxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (6): IR (KBr, cm^{-1}): 3510, 3276, 3125, 2970, 1682, 1642. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 9.30 (s, 1H), 9.11 (s, 1H), 7.64 (s, 1H), 6.67-7.0 (m, 4H), 5.02 (d, 1H, $J = 2.76$ Hz), 3.94 (q, 2H, $J = 6.90$ Hz), 2.21 (s, 3H), 1.06 (t, 3H, $J = 6.90$ Hz). EIMS m/z (%): 277.29 [$\text{M}^+ + 1$].

Ethyl-6-methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (7): IR (KBr, cm^{-1}): 3330, 3172, 3105, 2980, 1670, 1575, 1467. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 10.35 (s, 1H), 9.65 (s, 1H), 7.20-7.35 (m, 5H), 5.15 (d, 1H, $J = 3.57$ Hz), 3.98 (q, 2H, $J = 7.02$ Hz), 2.26 (s, 3H), 1.08 (t, 3H, $J = 7.02$ Hz). EIMS m/z (%): 277.35 [$\text{M}^+ + 1$].

Ethyl-4-(4-chlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (8): IR (KBr, cm^{-1}): 3230, 3091, 2974, 2935, 1700, 1642. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 10.40 (bs, 1H), 9.70 (bs, 1H), 7.35 (m, 4H), 5.10 (bs, 1H), 4.00 (q, $J = 7.2$ Hz), 2.31 (s, 3H), 1.10 (t, $J = 7.2$ Hz, 3H). EIMS m/z (%): 312.80 [$\text{M}^+ + 2$].

Ethyl-4-(4-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (9): IR (KBr, cm^{-1}): 3323, 3171, 3102, 2985, 1678, 1575, 1521, 1467, 1200. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 8.18 (bs, 1H), 7.96 (bs, 1H), 7.26 (d, $J = 8.6$ Hz, 2H), 6.89 (d, $J = 8.6$ Hz, 2H), 5.35 (s, 1H), 4.09 (q, $J = 7.2$ Hz, 2H), 3.77 (s, 3H), 2.42 (s, 3H), 1.17 (t, $J = 7.2$ Hz, 3H). EIMS m/z (%): 307.12 [$\text{M}^+ + 1$].

Ethyl-4-(4-fluorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (10): IR (KBr, cm^{-1}): 3327, 3176, 2982, 1673, 1614, 1573, 1464, 1370, 1322, 1280, 1268, 1209. ^1H NMR (DMSO- d_6 , 400 MHz) δ : 7.80 (brs, 1H), 7.28 (brs, 1H), 7.43 (d, $J = 8.6$ Hz, 2H), 7.23 (d, $J = 8.6$ Hz, 2H), 5.20 (s, 1H), 4.02 (q, $J = 7.2$ Hz, 2H), 2.30 (s, 3H), 1.10 (t, $J = 7.2$ Hz, 3H). EIMS m/z (%): 295.08 [$\text{M}^+ + 1$].

Ethyl-4-(3-nitrophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (11): IR (KBr, cm^{-1}): 3232, 3108, 2977, 1701, 1641, 1591, 1522. ^1H NMR (DMSO- d_6): δ = 10.50 (bs, 1H), 9.75 (bs, 1H), 7.85 (m, 4H), 5.30 (bs, 1H), 4.00 (q, $J = 7.2$ Hz, 2H), 2.38 (s, 3H), 1.11 (t, $J = 7.3$ Hz, 3H). EIMS m/z (%): 322.07 [$\text{M}^+ + 1$].

Ethyl-4-(4-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (12): IR (KBr, cm^{-1}): 3510, 3276, 3125, 2970, 1682, 1642. ^1H NMR (DMSO- d_6): δ = 10.10 (s, 1H), 9.65 (s, 1H), 7.64 (s, 1H), 6.67-7.0 (m, 4H), 5.02 (d, 1H, J = 2.76 Hz), 3.94 (q, 2H, J = 6.90 Hz), 2.21 (s, 3H), 1.06 (t, 3H, J = 6.90 Hz). EIMS m/z (%): 293.35 [$\text{M}^+ + 1$].

4. CONCLUSIONS

Ni-nanoparticle as a solid acid catalyst, showed high catalytic activity in the synthesis of 3,4-dihydropyrimidin-2(1H)-ones/thione *via* a one-pot three-component reaction of ethyl acetoacetate, aryl aldehydes and urea or thiourea under microwave irradiation as well as under solvent-free conditions. This procedure offers several advantages including mild reaction conditions, excellent yields of the products, ease of workup, reusability of catalyst, shorter reaction time, which makes it a useful and attractive protocol for the synthesis of these compounds. Furthermore, the catalyst could be recycled after a simple work-up, and reused at least five times with only slight reduction in its catalytic activity. It has also all advantages devoted to solvent-free reactions namely environmentally friendly conditions.

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References

- [1] C. O. Kappe, *Eur. J. Med. Chem.* 2000, 35, 1043.
- [2] G. C. Rovnyak, S. D. Kimball, B. Beyer, G. Cucinotta, J. D. Dimarco, J. Ougoutas, A. Hedberg, M. Malley, J. P. McCarthy, R. Zhang, S. Moreland, *J. Med. Chem.* 1995, 38, 119.
- [3] B. B. Snider, Z. Shi, *J. Org. Chem.*, 1993, 58, 3828.
- [4] A. D. Patil, N. V. Kumar, W. C. Kokke, M. F. Bean, A. J. Freyer, C. Debrosse, S. Mai, A. Truneh, D. J. Faulkner, B. Carte, A. L. Breen, R. P. Hertzberg, R. K. Johnson, J. W. Westly, B. C. M. Ports, *J. Org. Chem.*, 1995, 60, 1182.
- [5] a) Y. Kashman, S. Hirsh, O. J. Mc Connel, J. Ohtani, I. Takenori, H. Kakisawa, *J. Am. Chem. Soc.*, 1989, 111, 8925.
b) K. Ohtani, T. Kusumi, H. Kakisawa, Y. ashman, S. Hirsh, *J. Am. Chem. Soc.*, 1992, 114, 8472.
- [6] a) C. O. Kappe, *Tetrahedron* 1993, 49, 6937;
b) C. O. Kappe, *Acc. Chem. Res.*, 2000, 33, 879.
- [7] G. Schmid, *Clusters and Colloids: from Theory to Applications*, VCH, Weinheim, 1994.
- [8] A. Henglein, *Chem. Rev.*, 1989, 89, 1861.
- [9] A. Kumar, S. Mandal, P. R. Selvakannan, R. Pasricha, A. B. Mandale, M. Sastry, *Langmuir*, 2003, 19, 277.
- [10] A. Krolikowska, A. Kudelski, A. Michota, J. Bukowska, *Surf. Sci.*, 2003, 532, 227.
- [11] N. Chandrasekharan, P. V. Kamat, *J. Phys. Chem.*, 2000, B104, 10851.
- [12] J. A. Creighton, D. G. Eadon, *J. Chem. Soc., Faraday Trans.*, 1991, 24, 3881.
- [13] a) Z. B. Zhang, X. Z. Sun, M. S. Dresselhaus, J. Y. Ying, *Phys. Rev.*, 2000, B 61, 4850.
b) K. Liu, K. Nagodawithana, P. C. Searson, C. L. Chien, *Phys. Rev.*, 1995, B 51, 7381.
- [14] B. G. Biginelli, P. Gazz., *Chim. Ital.*, 1893, 23, 360.

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- [15] a) R. H. Vekariya, S.N. Panchal, K.D. Patel, H. D. Patel, *Current Microwave Chemistry*, 2015, 2, 61-68.
b) N. P. Prajapati, R. H. Vekariya, H. D. Patel, *International Letters of Chemistry, Physics and Astronomy*, 2015, 44, 81-89.
c) S. M. Prajapati, R. H. Vekariya, K. D. Patel, S. N. Panchal and H. D. Patel, *International Letters of Chemistry, Physics and Astronomy*, 2015, 44, 195-210.
- [16] R. H. Vekariya, H. D. Patel, *ARKIVOC*, 2015, (i), 70-96.
- [17] R. H. Vekariya, H. D. Patel, *Synthetic Communications*, 2014, 20, 1031–1054.
- [18] R. H. Vekariya, H. D. Patel, *ARKIVOC*, 2015, (i), 136-159.
- [19] N.Y. Fu, Y.F. Yuan, Z. Cao, S.W. Wang, J.T. Wang, C.Peppe, *Tetrahedron*, 2002, 58, 4801.
- [20] A.S. Paraskar, G.K. Dewkar, A. Sudalai, *TetrahedronLett.* 2003, 44, 3305.
- [21] B. B. F. Mirjalili, A. Bamoniri, A. Akbari, *Chinese Chemical Letters*, 2011, 22, 1, 45–48.
- [22] A.S. Lanje, S.J. Sharma, R.B. Pode. *Archives of Physics Research*, 2010: 1, 49-56.
- [23] X.M. Ni, X.B. Su, Z.P. Yang, H.G. Zheng, *Journal of crystal Growth*, 2003,252, 612.
- [24] Y. Hou, H. Kondoh, T. Ohta, S. Gao, *Applied surface Science*, 2005,241, 218.
- [25] D.E.Zhang, X.M. Ni, H.G. Zheng, Y. Li, X.J. Zhang, Z.P. Yang, *Materials Letters*, 2005,59, 2011.
- [26] S. S. Nath, D. Chakdar, G. Gope, D. K. Avasthi; *Journal of nanotechnology online*, 2008,4.

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