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Synthesis of diazepines using magnetically yttrium doped ZnOnanocatalyst

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Abstract:
Yttrium-doped ZnO nanoparticles were synthesized by co-precipitation method to investigate structural, optical and antibacterial properties. X-ray diffraction analysis confirms hexagonal (wurtzite) structure with average crystallite size between 16 and 30 nm which is used as catalyst in synthesis of different substituted diazepine derivatives. The structures of the synthesized compounds have been confirmed on the basis of ^{1}HNMR, IR and Mass spectral analysis.

Keywords: Synthesis**,** Diazepine, Nanocatalyst,co-precipitation method.

Introduction:

Heterocyclic compounds are often considered privileged structures in medicinal chemistrydue to their biological effects. The benzodiazepines are one of the important classes of therapeutic agents for example, various benzodiazepines have anticonvulsants, antihypnotic and anxiolytic activities.[1]Benzodiazepinesserve as cholecystokinin A and B antagonits,[2]opioid receptor ligands,[3]platelet-activating factor antagonists,[4]HIV trans-activator (Tat) antagonists,[5]HIV reverse transcriptase inhibitors.[6]Benzodiazepines having effect on central nervous system for example clozapine[7], olanzapine[8]and quetiapine[9]are used in the clinic for treating schizophrenia, while lonazepam[10], diazepam[11], lorazepam[12], nitrazepam[13]and oxazepam[14]are used as antianxiety drugs. We have made an attempt to synthesize novel substituted benzodiazepines derivatives by using Yttrium-doped ZnO nanoparticles as catalyst.The Nanocatalyticalorganic synthesis (MAOS) is one of theconventional techniques used nowadays in the laboratory and is superior in many ways to traditional heating for the synthesis of novel compounds.[15-20]

Advantages of Nanocatalystic reactions over the conventional reactions

The practicaladvantages are:

1. Reduction in reaction temperatures.
2. Increases in reaction rates over 10-10,000 times.
3. Increased yields of 10-30% on an average.
4. Increased selectivity in the product.
5. Minimum side reactions due to rapid quenching.
6. Reduced solventusage createsless wastage.

Experimental Section:

For the synthesis of substituted diazepine derivatives the chemicals o-phenylenediamine and acetophenonewere purchased from Sigma Aldrich chemicals Pvt. Ltd, Mumbai, India. The solvents were reagent grade and purified by recrystallisation and distillation. The IR spectra were recorded Shimadzu FT-IR-8400 instrument using KBr pellet method at department of chemistry, Dayanand College, Solapur. The mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct Injection Probe technique and the ^{1}H NMR was determined in DMSO-d_6 solution on a Bruker Ascend-TM 400 MHz-NMR spectrometer in S.A.I.F. Division, Indian Institute Of Technology, Bombay.

Synthesis of Y-doped ZnONPs :

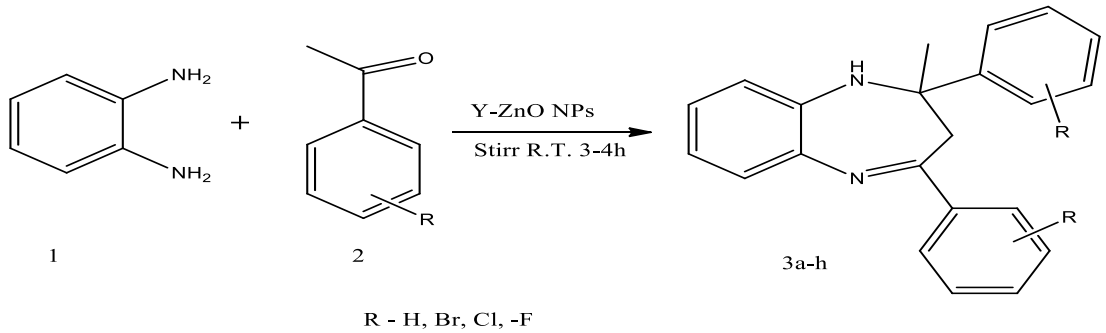
Samples with compositional formula Zn1-xYxO, with x = 0.00, 0.05, 0.10 and 0.15 were prepared by co-precipitation route in an alcoholic medium. In this procedure, zinc acetate dehydrate dissolved in methanol (100 mL) and NaOH in methanol (100 mL) were prepared and added by stirring with heating at 52 oC for 2 h. The precipitate separated from the solution by filtration, washed several times with distilled water and ethanol then dried in air at 127 ^{o}C to obtain ZnO nanoparticles.

The samples obtained were annealed at 450 ^{o}C for 8 h. For the synthesis of Y-doped ZnO nanoparticles, zinc acetate dehydrate and yttrium acetate tetrahydrate were dissolved in methanol (100 mL) and NaOH in methanol (100 mL) were prepared and added by stirring with heating at 52 ^{o}C for 2 h. The precipitate separated from the solution by filtration, washed several times with distilled water and ethanol then dried in air at 127 oC to obtain Y-doped ZnO nanoparticles. The samples were annealed at 450 ^{o}C for 8 h. The crystalline structure, phase purity and size of the nanoparticles were determined by XRD (Philips PW-3710). Optical properties of the samples were recorded using UVis spectrophotometer (Jasco) in the range 200-800 nm.

General procedure for 3a-h:

Yttrium-doped ZnO nanoparticles (5mol %) was added to a mixture of *o*-phenylenediamine**1** (1mmol) and acetophenone**2a-h** (2.2 mmol) in DCM solvent and stirred it at room temperature for 3-4 hrs. After completion of the reaction, monitored by TLC, the reaction mixture was cooled to room temperature and dissolved in 10 mL ethyl acetate. Organic layer was separated, dried over anhydrous sodium sulphate and filtered.

Filtrate was concentrated under reduced pressure to get crude product, which upon trituration in n-hexane gives title compound as off-white solid. The solid compound obtained was dried under vacuum. The Yttrium-doped ZnONPs was then separated by external magnetic field. The 3 separated Yttrium-doped ZnO NPs was washed with ethyl acetate and dried.



Scheme 1: synthesis of different substituted diazepine derivatives using Yttrium-doped ZnO NPs

Spectral Data of synthesized compounds:

1. White solid. IR (KBr): 3278, 3060, 1632, 1465 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.50 (t, *J* = 7.2 Hz, 4H), 7.20-7.07 (m, 7H), 7.02-6.90 (m, 2H), 6.75-6.78 (dd, *J* = 7.5, 1.1 Hz, 1H), 3.3 (Bs, 1H), 3.04 (d, *J* = 12.2 Hz, 1H), 2.90 (d, *J* = 12.2 Hz, 1H), 1.67 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 166.7, 146.6, 141.1, 138.5, 137.1, 128.7, 127.6, 126.3, 125.0, 125.1, 125.3, 123.4, 120.6, 120.4, 72.7, 42.1, 28.8. ESI- MS: *m/z* 313 $[M + H]^{+\cdot}$ Anal. Cacld for $C_{22}H_{20}N_2$: C, 83.58; H, 6.44; N, 8.96. Found: C, 84.46; H, 6.38; N, 8.78.
2. Pale Yellow solid. IR (KBr): 3490, 3024, 1680, 1492, 750 cm-1. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.50-7.44 (m, 4H), 7.31-7.24 (m, 1H), 7.21-7.16 (m, 4H), 7.06-7.01 (m, 2H), 6.80-6.75 (m, 1H), 3.40 (s, 1H), 3.06 (d, *J* = 12.3 Hz, 1H), 2.80 (d, *J* = 13.5, 1H), 1.70 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 165.1, 144.7, 138.8, 136.6, 135.1, 132.0, 127.5, 127.38, 127.31, 1260, 126.6, 121.0, 120.5, 72.5, 40.9, 28.7. ESI- MS: *m/z* 381, $[M+H]^{+\cdot}$ Anal. Cacld for $C_{22}H_{18}C_{l2}N_2$: C, 69.30; H, 4.76; N, 7.35. Found: C, 69.53; H, 4.64; N, 7.44.
3. Light Orange solid. IR (KBr): 3276, 3080, 1600, 1470, 1345 cm-1. ^1H NMR ($CDCl_3$, 100 MHz): δ = 8.40 (s, 1H), 8.15 (s, 1H), 8.10 (d, *J* = 8 Hz, 1H), 7.98-7.95 (m, 3H), 7.41-7.31 (m, 3H), 7.17- 7.07 (m, 2H), 6.92-6.90 (dd, *J* = 7.1 Hz, 1.1 Hz, 1H), 3.50 (s, 1H), 3.27 (d, *J* = 12.5 Hz, 1H), 3.01 (d, *J* = 12.5, 1H), 1.86 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 163.1, 148.0, 147.1, 147.0, 141.4, 138.2, 136.1, 131.5, 130.9, 128.5, 128.2, 127.9, 126.4, 123.4, 121.4, 121.2, 120.6, 120.8, 73.1, 40.8, 28.9. ESI- MS: *m/z* 403 [M + H]+. Anal. Cacld for $C_{22}H_{18}N_4O_4$: C, 64.66; H, 4.50; N, 13.90. Found: C, 65.60; H, 4.60; N, 13.84.
4. Brown solid. IR (KBr): 3371, 2978 cm-1. ^1H NMR ($CDCl_3$, 100 MHz): δ = 7.45-7.25 (m, 9H), 7.10-7.02 (m, 2H), 6.80-6.78 (m, 1H), 3.40 (s, 1H), 3.06 (d, *J* = 13 Hz, 1H), 2.87 (d, *J* = 13 Hz, 1H), 1.70 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 165.2, 145.5, 141.0, 137.3, 136.7, 130.5, 130.4, 127.8, 127.7, 126.6, 125.8, 123.7, 121.2, 121.6, 121.3, 72.7, 42.0, 28.9. ESI-MS: *m/z* 468.99 [M + H]+. Anal. Cacld for $C_{22}H_{18}Br_2N_2$: C, 55.20; H, 3.85; N, 5.95. Found: C, 55.12; H, 3.80; N, 5.75.

Conclusions:

Pure and yttrium-doped ZnO nanoparticles were synthesized by the co-precipitation method. The average crystalline size is in the range 16- 30 nm. We have successfully synthesized the diazapine derivatives using *o*-phenylenediamine andacetophenone in DCM solvent at room temperature. In the overall reaction protocol present an atom economy scheme as H_2O as is the only byproduct. All reactions are carried out at room temperature which presents itself an additional environmentally benign synthetic advantage. The 8 derivatives (**3a-h)** were synthesized and characterized for their structure elucidation by using physical, analyical and Spectral data (NMR, Mass).

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