Supporting Information

Supplementary Material

One-pot multicomponent synthesis of highly functionalized bio-active pyrano[2,3-c]pyrazole and benzylpyrazolyl coumarin derivatives using ZrO_2 nanoparticles as reusable catalyst

Arijit Saha, Soumen Payra and Subhash Banerjee*

Content:

ESI-1: Method for the preparation of Catalyst

(i) Method for the preparation of tetragonal ZrO_2 NPs:[1]

ZrO_2 nanoparticles (NPs) have been synthesized by dissociation of $ZrO_2Cl_2.8H_2O$ in a basic medium (pH~10) at low temperature without adding any stabiliser. For synthesizing ZrO_2 NPs, 40 ml 0.05*M* NaOH solution in distilled water was slowly added in 100 ml 0.01*M* solution of $ZrO_2Cl_2.8H_2O$ in methanol-water (1:1) at ~5 ^oC with continuous stirring. After completion of the reaction (~1 hour) the sol solution was refluxed at 100^oC for 24 hours with vigorous stirring. Sequentially, the solid and solution phases were separated by centrifugation and the solids were washed with dilute solution of NH_4NO_3 until negative test for chloride ion followed by washed with de-ionized water (4x10 ml) and ethanol (2x5 ml). As prepared solids were dried well and then calcined at 500 ^oC for 4 hours. The formation of nano-sized particles was confirmed by powder XRD, TEM and SEM studies.

(ii) Method for the preparation of monoclinic ZrO_2 NPs:[1]

Monoclinic ZrO_2 nanoparticles were prepared following the above mentioned protocol and calcined the solid sample at 900 ^oC for 4 hrs. The formation of pure monoclinic phase was determined from powder XRD study.

(iii) Method for the preparation of SiO_2-ZrO_2Cl_2 Lewis acid catalyst:

A mixture of hydrous zirconium oxychloride (2 g), silica-60-120 mesh (10 g), chloroform (20 ml) and one drop of conc. HCl was refluxed for 2 h with continuous stirring and then aging for another 3 h at room temperature. The solid residue was separated by simple filtration and then catalyst (SiO_2-ZrO_2Cl_2) was completely dried in oven before use.

ESI-2: Characterization of ZrO_2 nanoparticles

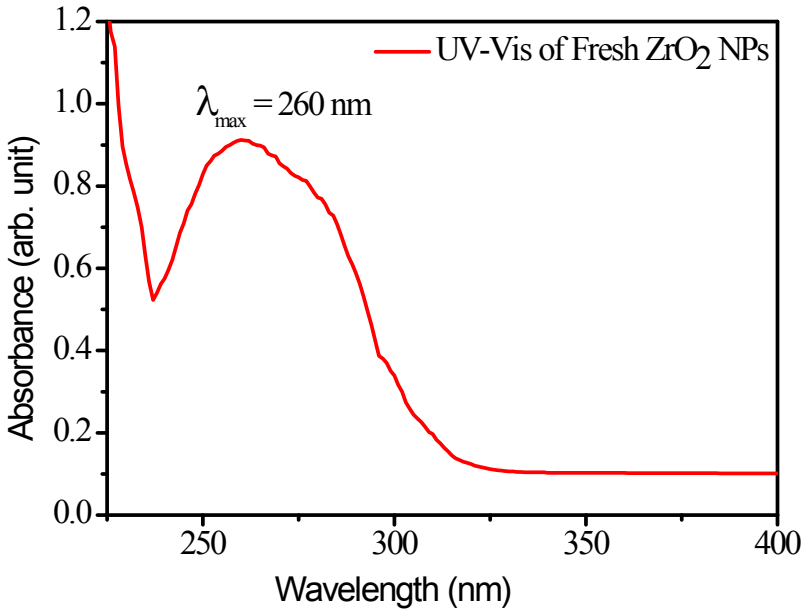


Figure S1 UV-Vis spectrum of fresh ZrO_2 NPs.

TEM Study: TEM study was in JEOL TEM 2100, Japan instrument

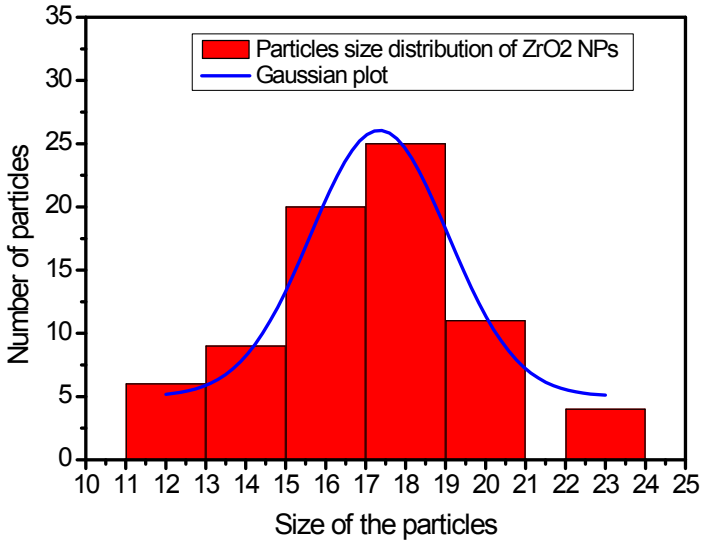


Figure S2 Size distribution of NPs obtained from TEM study.

Dynamic Light Scattering (DLS) Study:

The DLS experiment was performed in Malvern instrument. The uniform distribution of particle size was obtained from DLS study with average particle size of 25 nm. As DLS gives hydrodynamic radius of particles a little larger average particle size was observed in DLS study.

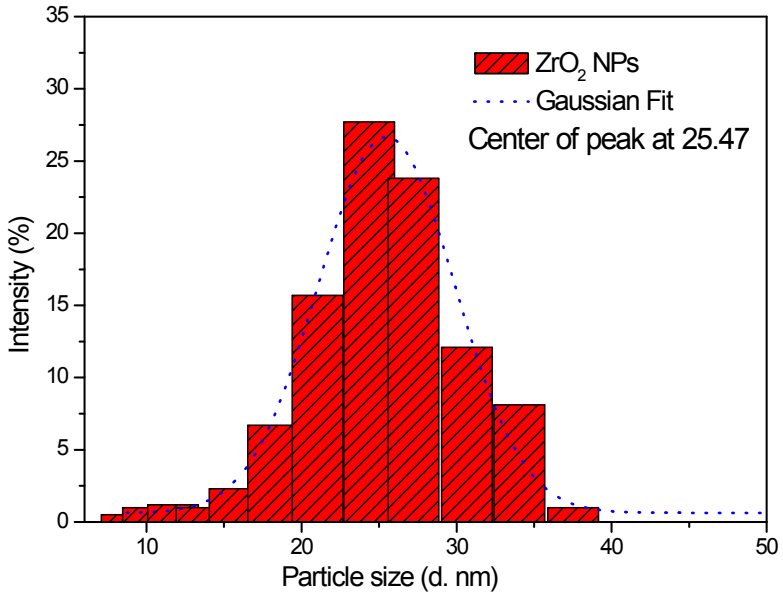


Figure S3 Size distribution of ZrO_2 NPs obtained from DLS study.

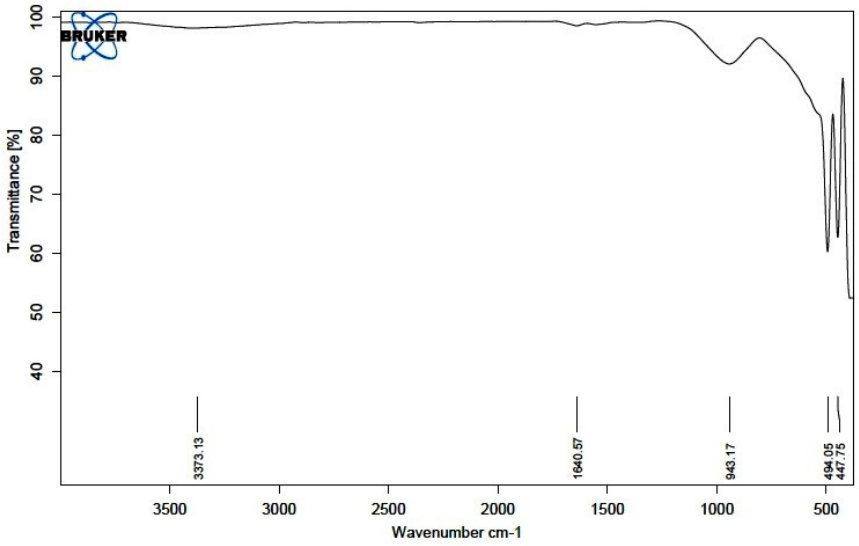


Figure S4 FT-IR spectra of fresh ZrO_2 NPs.

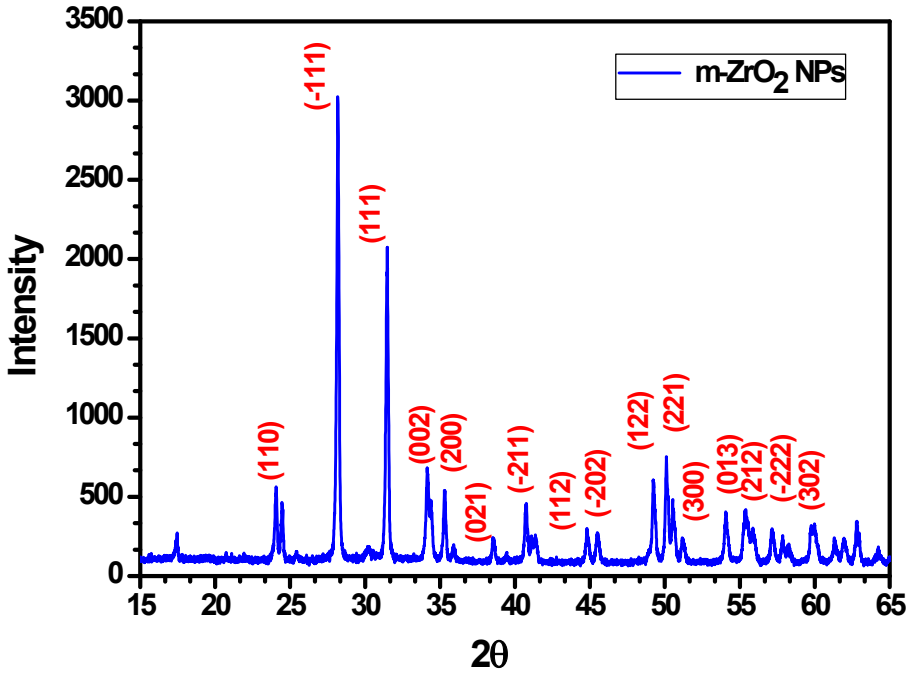


Figure S5 Powder XRD pattern of monoclinic ZrO_2 NPs.

ESI-3: Table 1. Size effect on the yield of the reaction for the preparation of compounds pyrano[2,3-c]pyrazoles derivative (entry 2, Table 2).

Average Size of ZrO_2 NPs	Time (min.)	Yield (%)
~ 5 nm^2	30	94
~ 18 nm	30	92
~ 45 nm^3	30	90

ESI-4: General method for the preparation of pyrano[2,3-*c*]pyrazoles derivatives:

A mixture of substituted hydrazine (1 mmol), ethyl acetoacetate (1 mmol), aryl aldehyde (1 mmol), malononitrile (1 mmol) and ZrO_2 NPs (10 mol%) in 2 ml ethanol-H_2O (6:1) was stirred at room temperature for a appropriate period of time until the reaction mixture solidified. The reaction was monitored by checking TLC. After completion of the reaction, solvent was removed under reduced pressure from the reaction mixture sequentially the solid crude product was stirred with 5 ml methanol at 60 ^oC for 5 min followed by the catalyst was separated by simple filtration. Then methanol was removed under reduced pressure and the solid compound was purified by recrystallization from absolute ethanol without using any column chromatography to give pure pyrano[2,3-c]pyrazole derivative. The prepared compounds were identified by their melting point determination and further characterized by FT-IR and ^1H NMR (300 MHz Bruker) studies.

ESI-5: General method for the synthesis of benzylpyrazolyl coumarin derivatives:

A mixture of substituted hydrazine (1 mmol), ethyl acetoacetate (1 mmol), aryl aldehyde (1 mmol), 4-hydroxycoumarin (1 mmol) and ZrO_2 NPs (10 mol%) in 2 ml ethanol-H_2O (1:1) was stirred at room temperature for a required period of time until the reaction mixture solidified. The completion of the reaction was indicated by checking TLC. After completion of the reaction, solvent was removed under reduced pressure from the reaction mixture sequentially the solid crude product was stirred with 5 ml methanol at 60^oC for 5 min. followed by the catalyst was separated by simple filtration. Then methanol was removed under reduced pressure and the solid compound was purified by recrystllization from absolute ethanol without using any column chromatography to give pure benzylpyrazolyl coumarin derivatives. The product was identified by melting point determination and then further characterized by FT-IR and ^1H NMR studies.

ESI-6: Reusability of the catalyst:

Procedure: The recovered catalyst from the reaction mixture during the synthesis of pyrano[2,3-*c*]pyrazole derivative was then washed with hot methanol (10 ml) followed by hot ethanol (2 ml) and finally dried well and reused for subsequent runs. The catalytic activity and tetragonal plane of ZrO_2 NPs remain unchanged even after 10^{th} cycles.

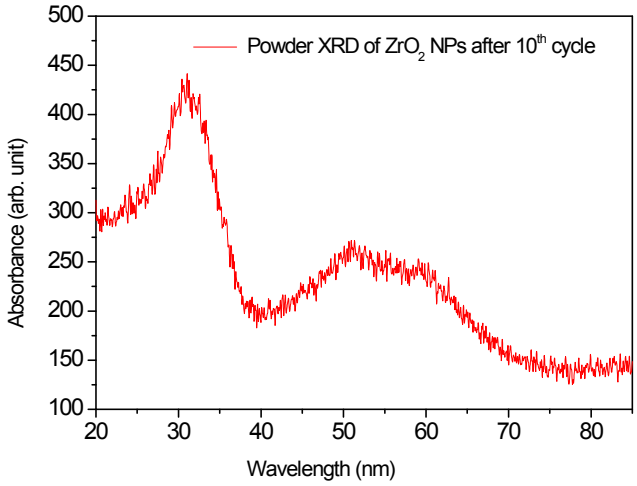


Figure S6 Powder XRD pattern of recycled ZrO_2 NPs after 10^{th} cycle.

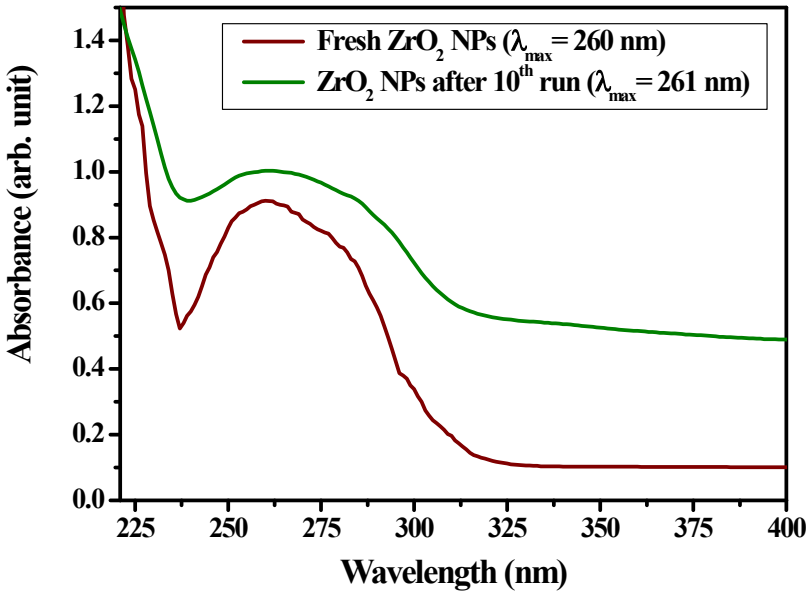


Figure S7 UV-Vis spectra of fresh ZrO_2 NPs and after 10^{th} run.

ESI-7: Comparison of FT-IR spectra of fresh and reused ZrO_2 NPs

The fresh ZrO_2 showed a distinctive broad band between 3600 and 3200 cm^{-1} and a broad band around 1600 cm^{-1}, which are assigned to the O–H modes of chemisorbed water and/or terminated hydroxides at the surface.[4,5]

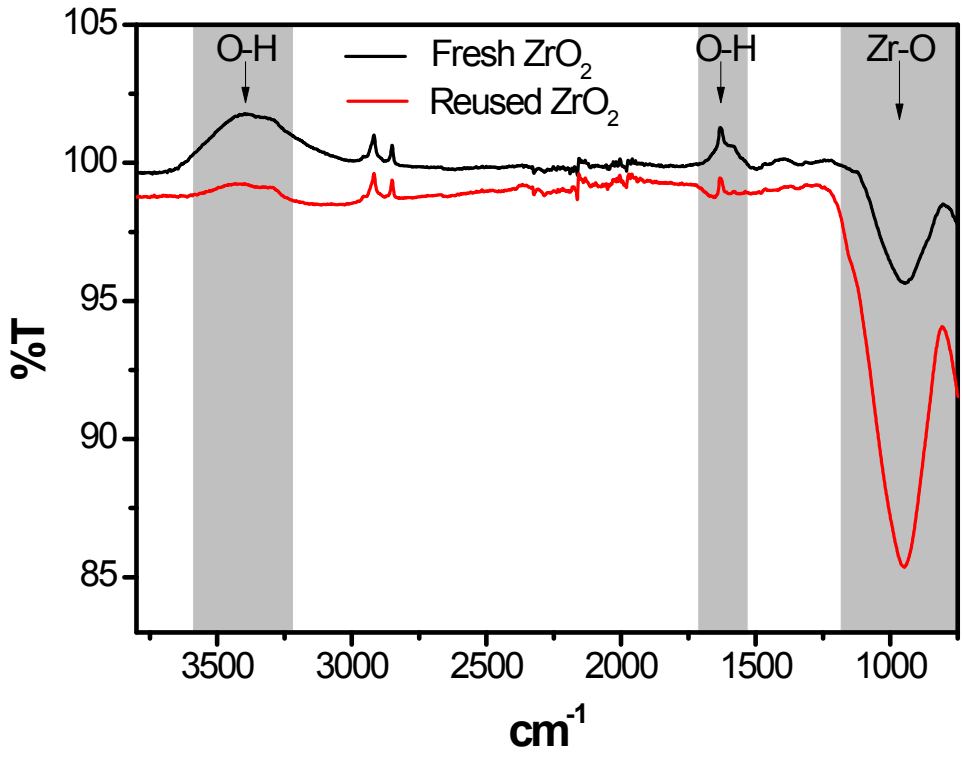
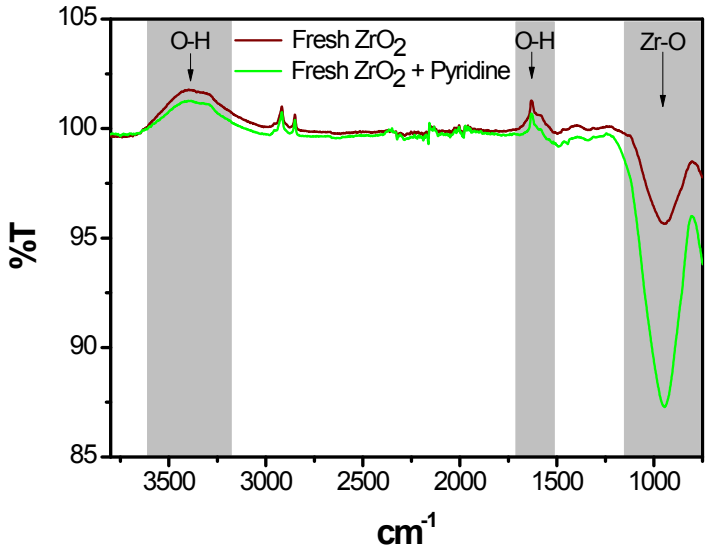
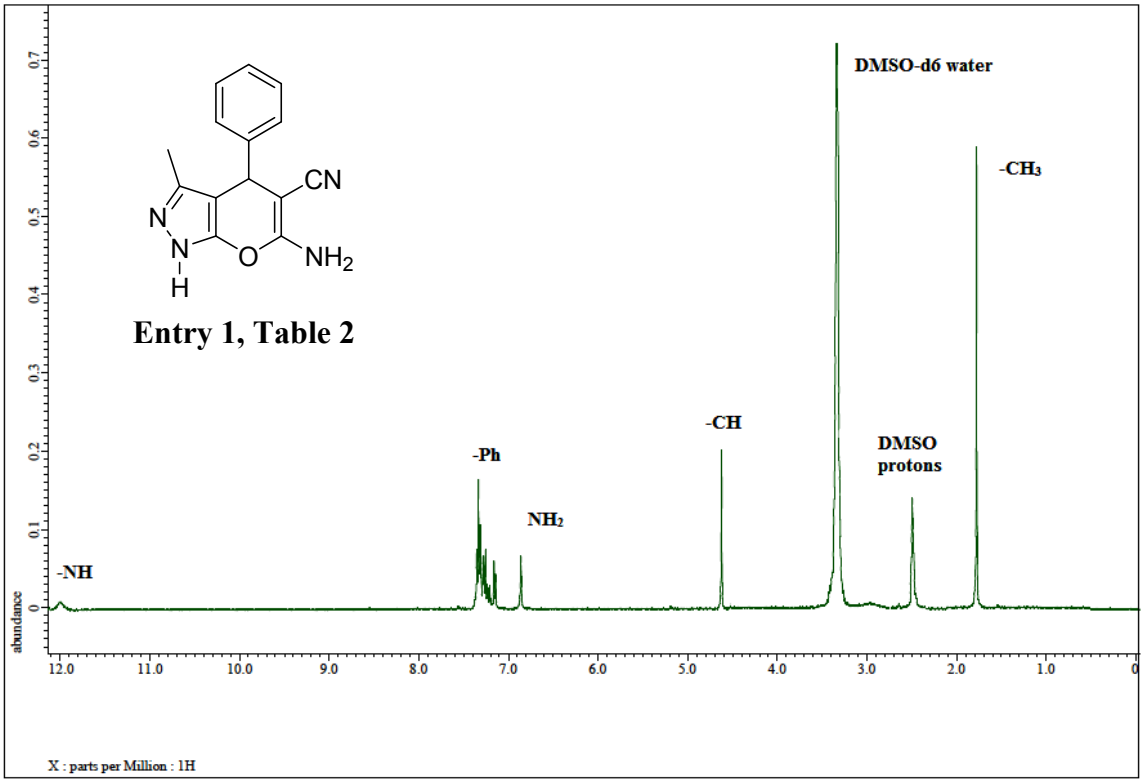


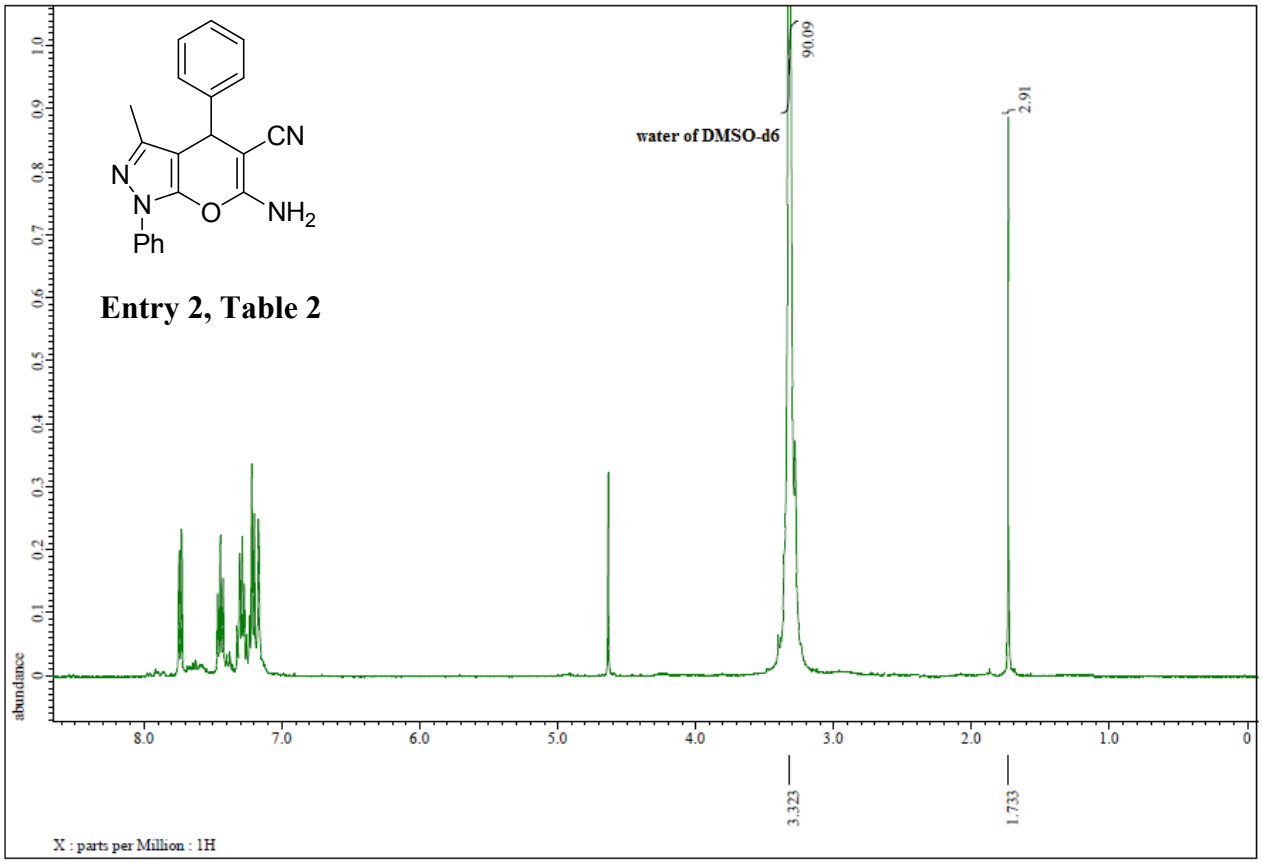
Figure S8 FT-IR spectra of fresh (black line) and reused (red line) ZrO_2 NPs.

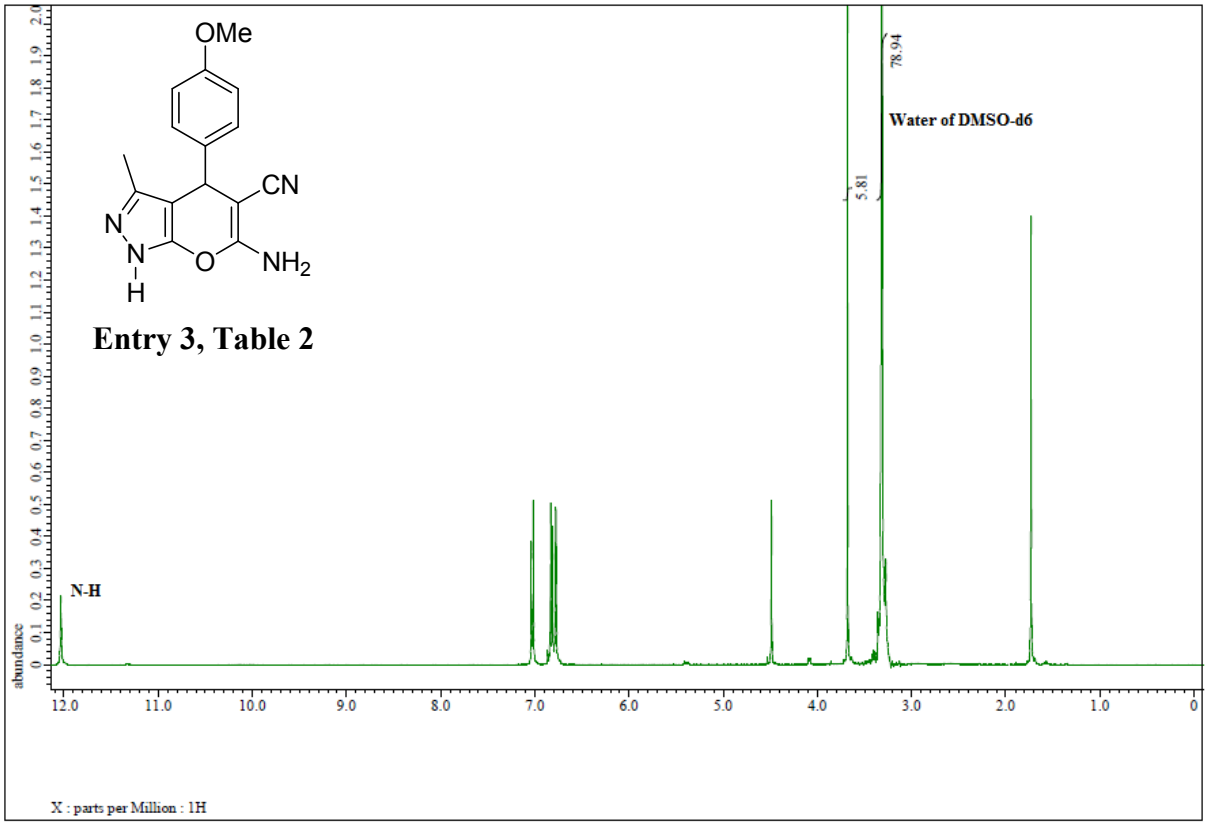
ESI-8: IR Based Absorption Experiment:

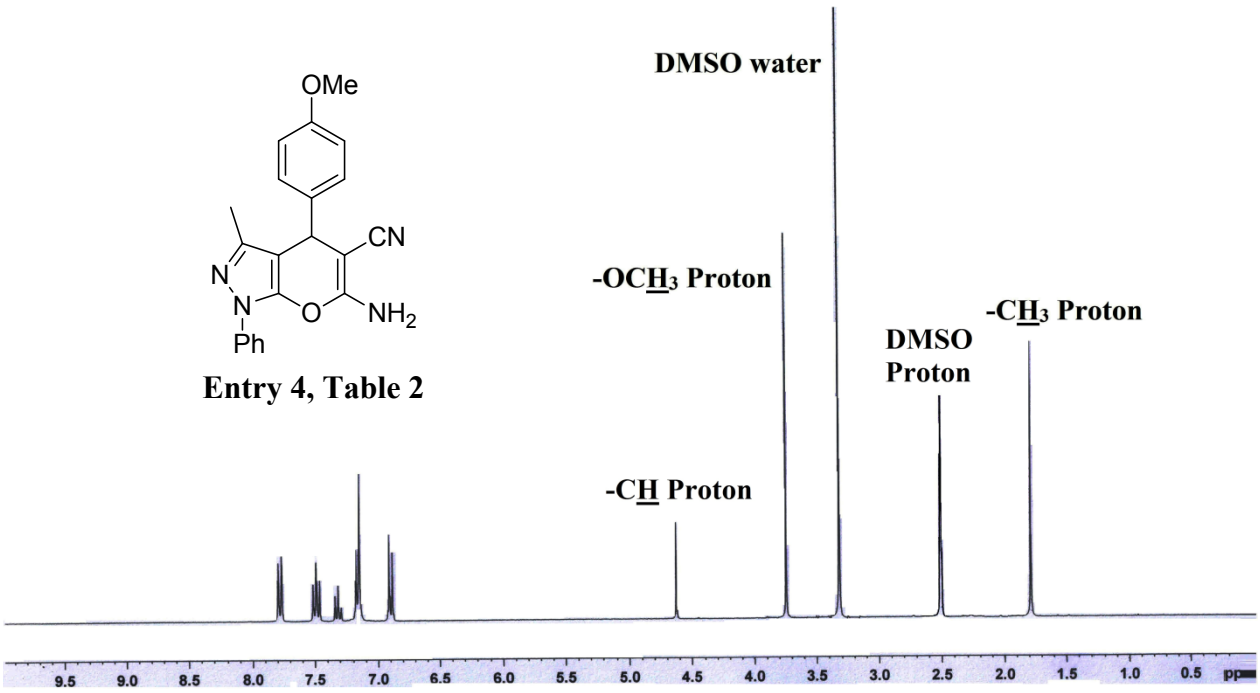


ESI 9: Representative ^{1}H NMR Spectra of pyranopyrazoles and benzylpyrazolyl cumarins. ^{1}H NMR Spectra of entries 1, 2, 3, 5, Table 2 were recorded in JEOL 300 MHz instrument and all other NMR spectra were recorded in Bruker 400 MHz NMR instrument. DMSO-d6 was used as solvent for all the NMR study.

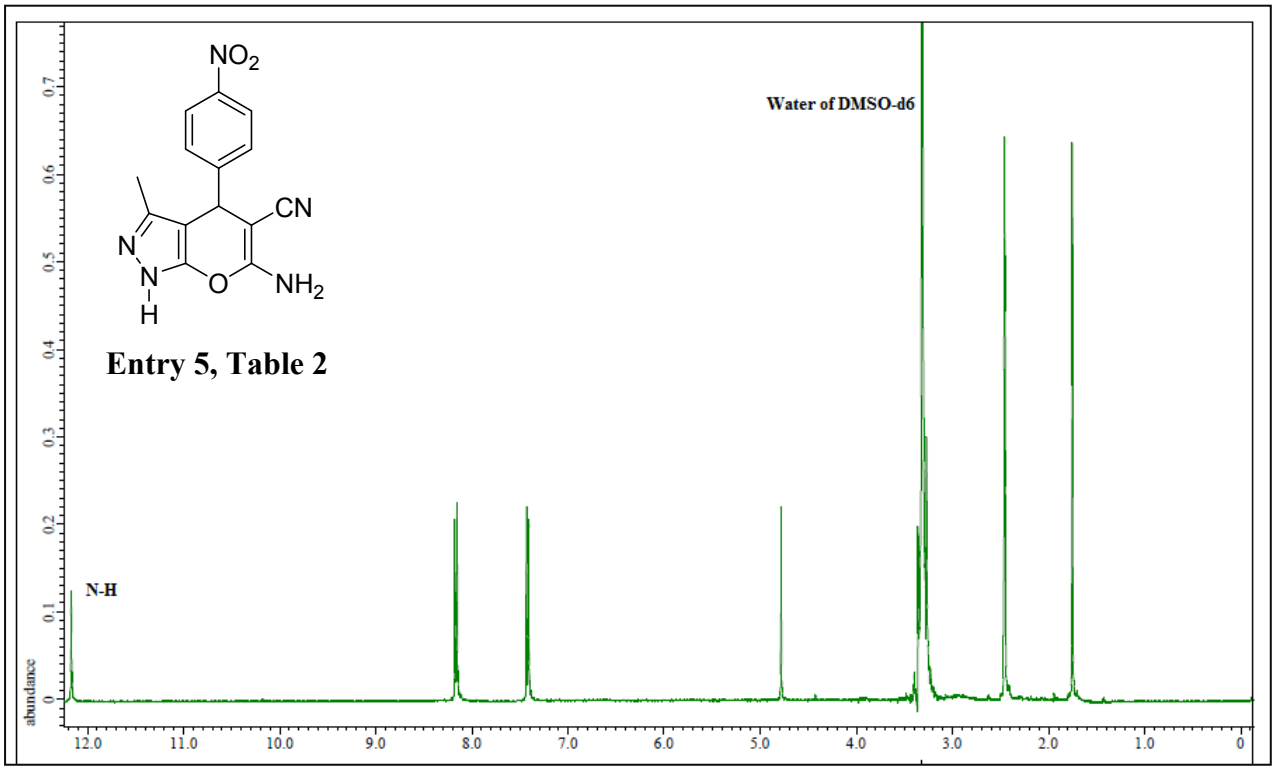


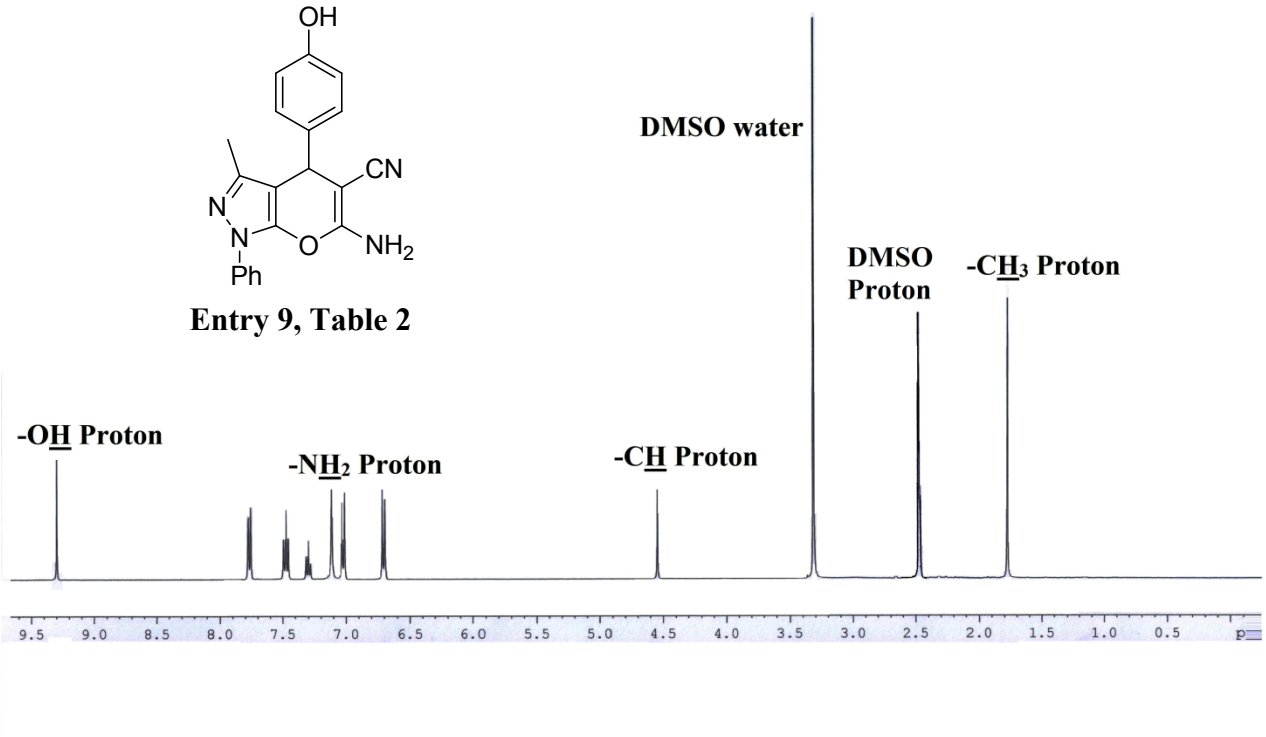

CN
N
N
O
NH2
Ph
Entry 2, Table 2
water of DMSO-d6
90.09
2.91
abundance
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
3.323
1.733
X : parts per Million : 1H


OMe
CN
N
N
H
O
NH2
Entry 3, Table 2
78.94
Water of DMSO-d6
5.81
N-H
abundance
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H

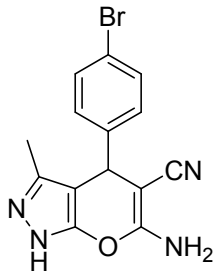


Entry 4, Table 2

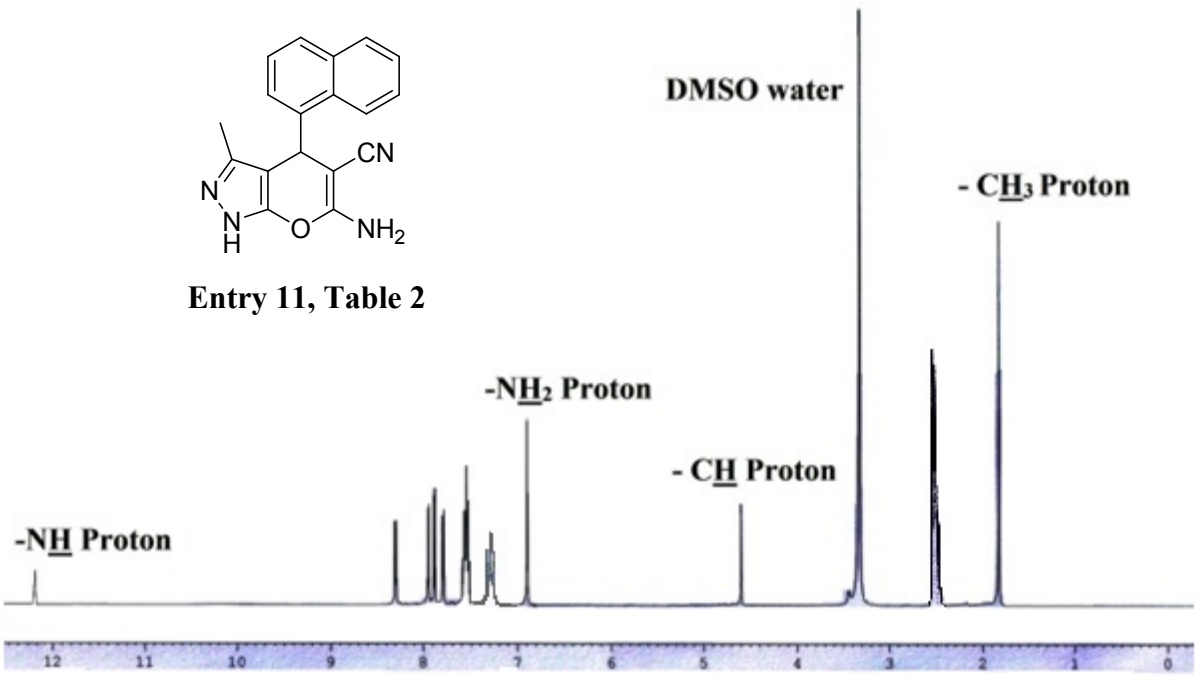

NO2
CN
N
N
H
O
NH2
Entry 5, Table 2
Water of DMSO-d6
N-H
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0



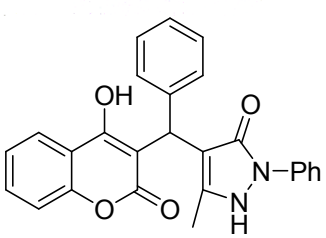
Entry 9, Table 2



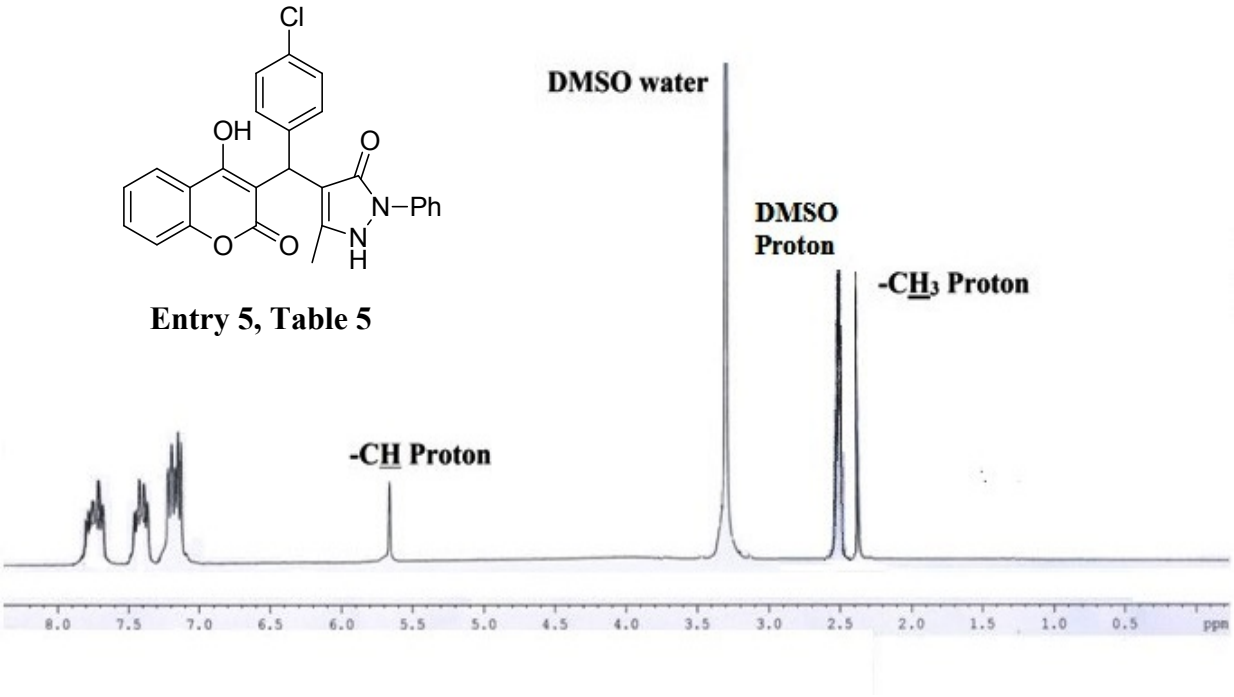
Entry 10, Table 2



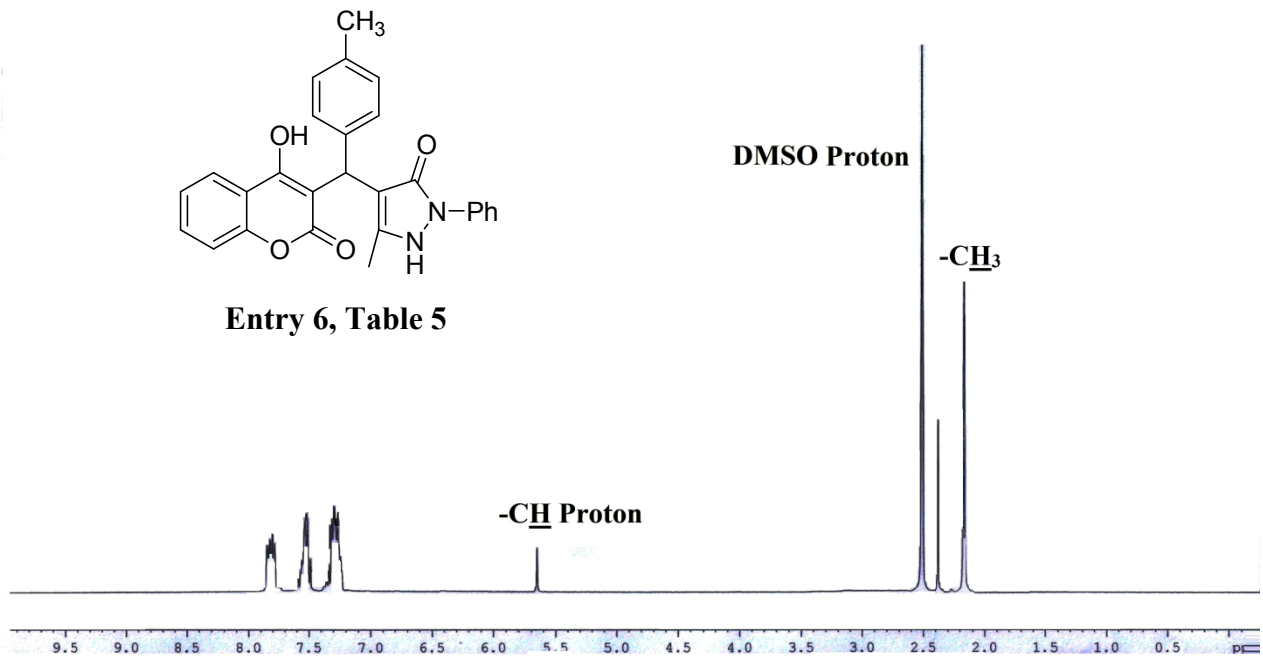
Entry 11, Table 2



Entry 2, Table 5



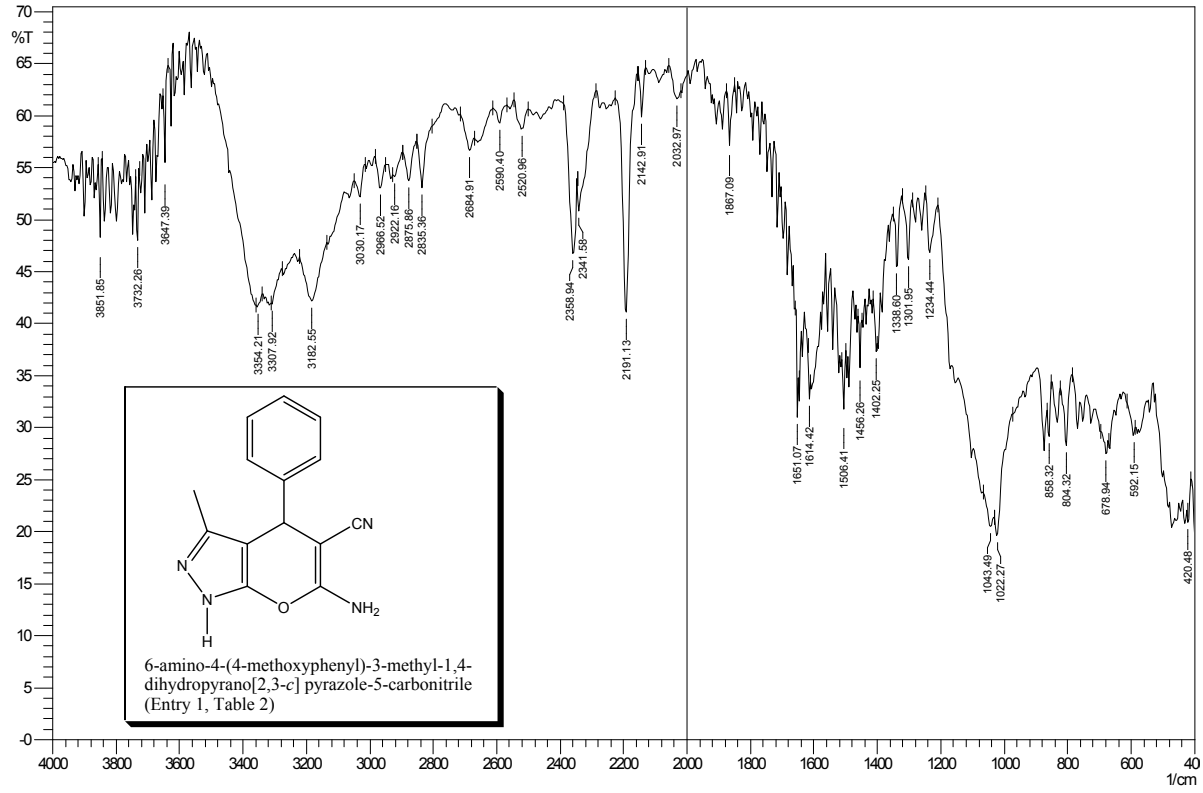
Entry 5, Table 5



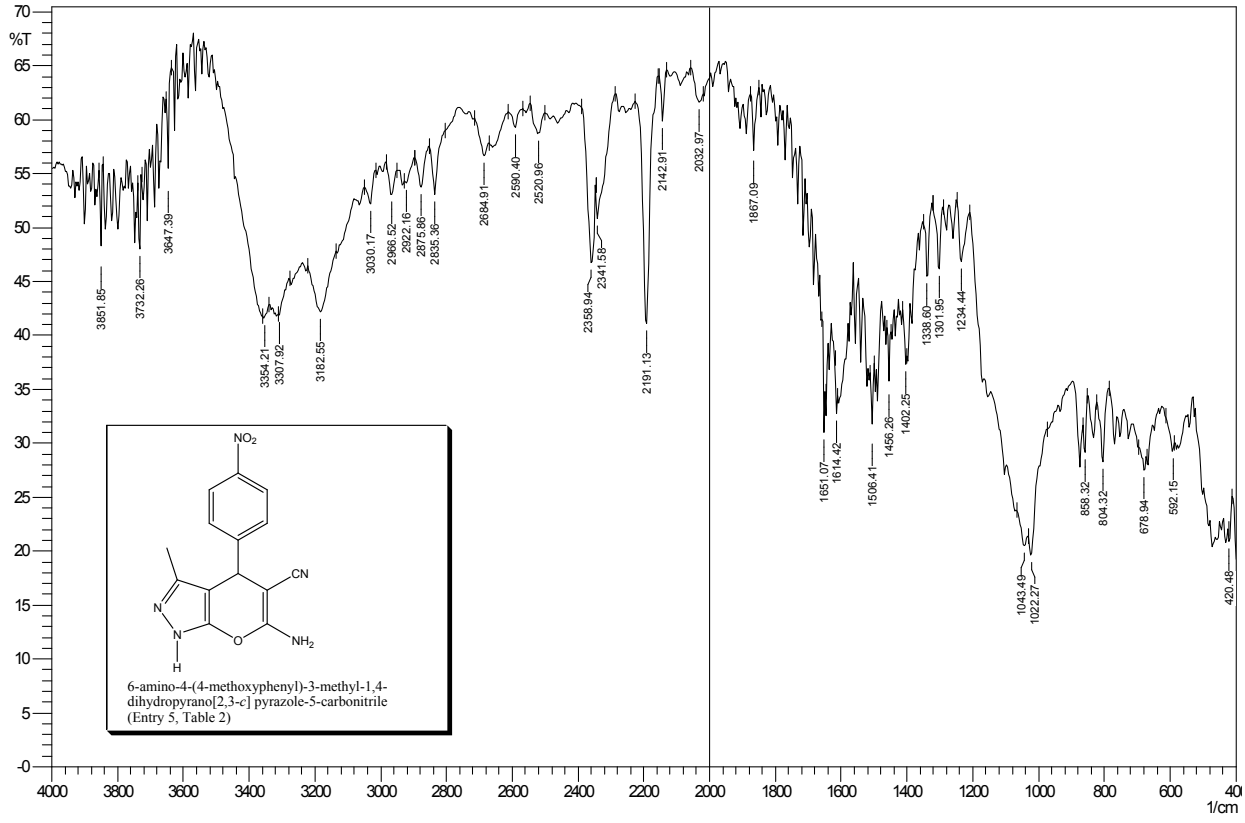
Entry 6, Table 5

ESI 10: Few representative Furrier Transform Infra Red Spectra of Pyrano[2,3-c]pyrazole derivatives

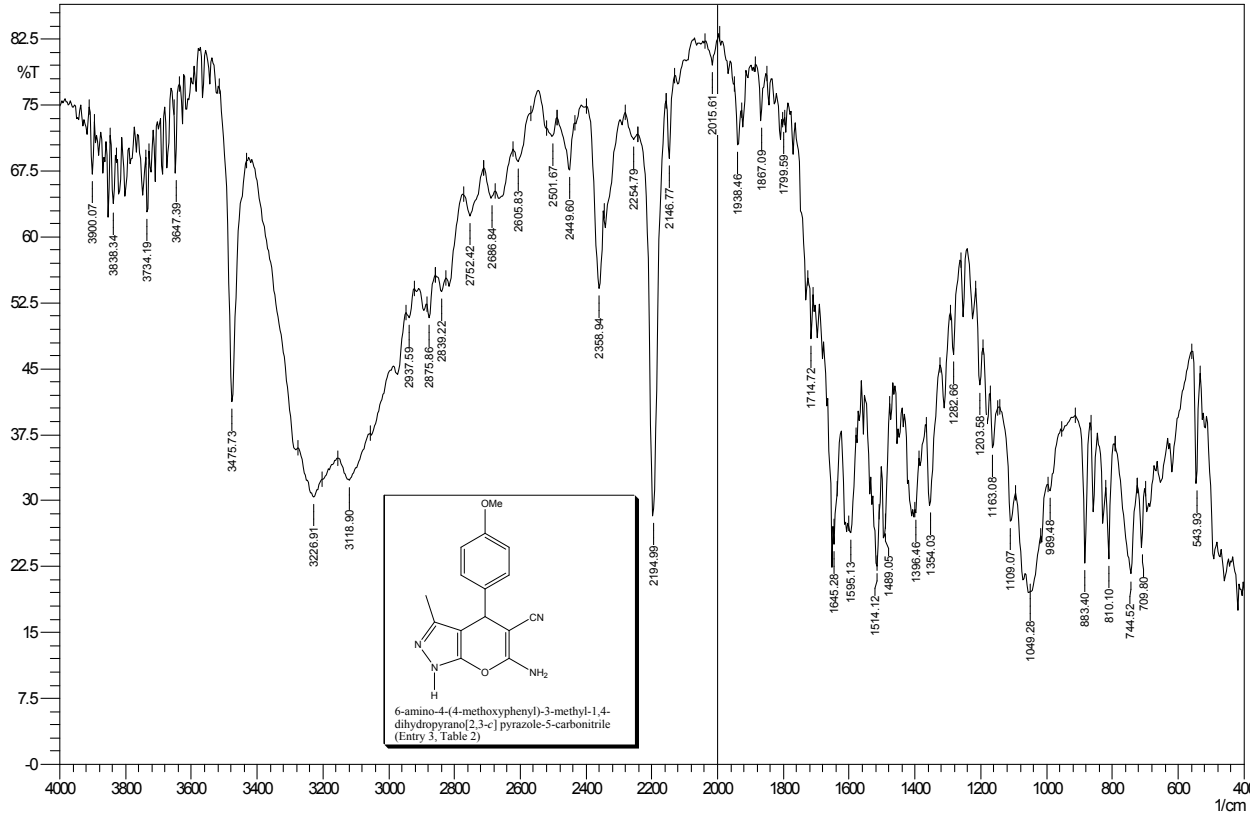
Furrier Transform Infra Red Spectrum of 6-amino-1,4-dihydro-3-methyl-4-phenylpyrano [2,3-c]pyrazole-5-carbonitrile



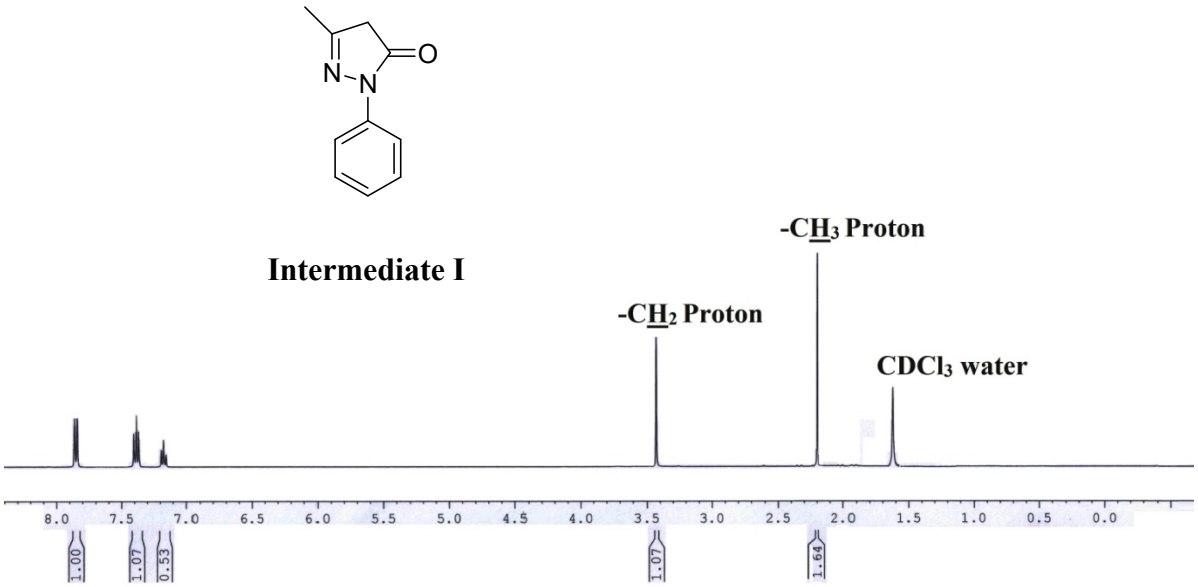
Furrier Transform Infra Red Spectrum of 6-amino-3-methyl-4-(4-nitrophenyl)-1,4-dihydropyrano[2,3-c]pyrazole 5-carbonitrile

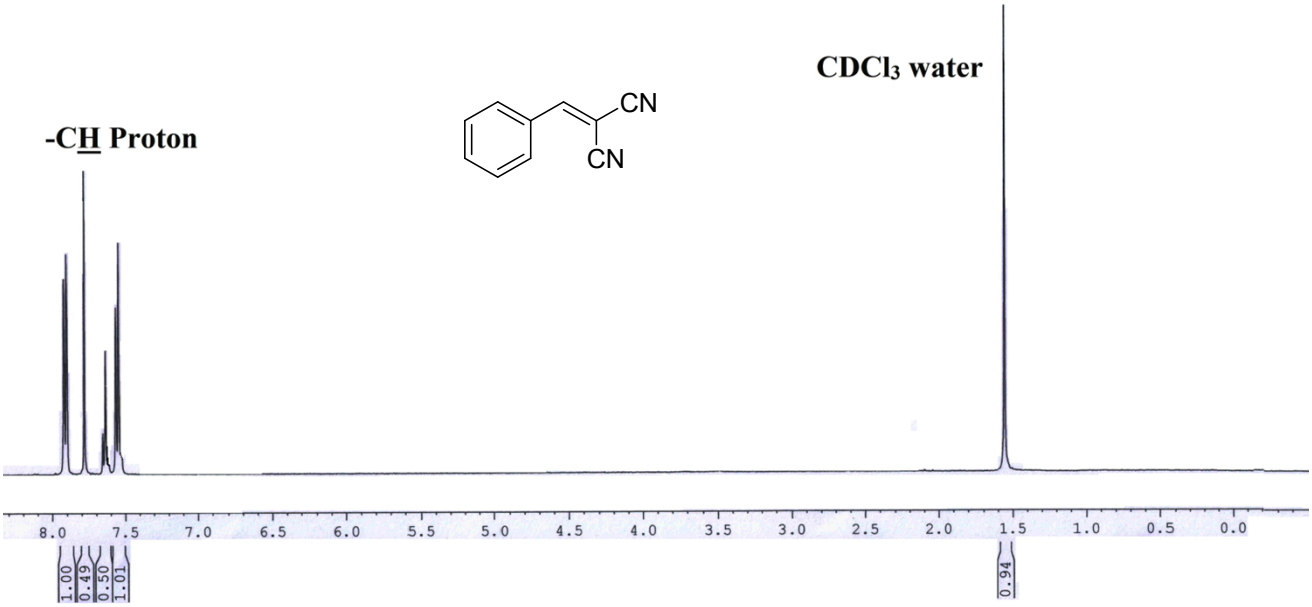


Furrier Transform Infra Red Spectrum of 6-amino-4-(4-methoxyphenyl)-3-methyl-1,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile



ESI-11: ^{1}H NMR spectra of Intermediates (I & II). The spectra were recorded in a Bruker 400 MHz NMR instrument and $CDCl_3$ was used as solvent.




-CH Proton
CN
CN
CDCl3 water
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.00
0.49
0.50
1.01
0.94

References:

1. Qaiser, M.; Adeel, A.; Humaira, M. S.; Amir, H. *J. Sol-Gel Sci. Technol.*, **2013**, *67*, 670.
2. R. Malakooti, H. Mahmoudi, R. Hosseinabadi, S. Petrovb and A. Miglioric *RSC Adv*., 2013, **3**, 22353
3. A. Opalinska, I. Malka, W. Dzwolak, T. Chudoba, A. Presz and W. Lojkowski, Beilstein J. Nanotechnol. 2015, 6, 27.
4. K. Nakanishi, Infrared Absorption Spectroscopy: Practical, Holden-Day, San Francisco, 1962.
5. K. Nakamoto, Infrared and Raman Spectra of Inorganic and Coordination Compounds, Wiley, New York, 1997.