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Sulfanilic Acid Supported on Magnetic Nanoparticles as a Green Catalyst for the Sonosynthesis of 1,4-Diazepines Containing Tetrazole Ring

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Magnetic nanoparticle-supported sulfanilic acid (MNPs-$PhSO_3H$) has been used as an efficient catalyst for the preparation of 1,4-diazepines containing tetrazole ring. The catalyst has been characterized by FT-IR (Fourier-transform infrared spectroscopy), SEM (scanning electron microscope), XRD (X-ray diffraction) and VSM (vibrating-sample magnetometer) and TGA (thermogravimetric analysis). The present synthetic protocol provides several advantages such as easy work-up, excellent yields, short reaction times, reusability of the catalyst and low catalyst loading. The present catalytic procedure is extensible to a wide diversity of substrates for the synthesis of a variety-oriented library of 1,4-diazepines containing tetrazole ring.

Keywords: 1,4-Diazepine, Magnetic nanoparticles, Ultrasonic irradiation, Heterogeneous catalyst

INTRODUCTION

The strategy of ultrasound as an energy source offers major advantages to promote organic reactions. Benefits further include shorter reaction times and higher yields over conventional methods [1-4]. The advantages of using cavitation (the creation, growth, and collapse of micrometer-sized bubbles that are formed when an acoustic pressure wave propagates through a liquid) as an energy source to promote organic reactions include shorter reaction times and higher yields when compared with conventional thermal heating methods (oil bath) [5-7]. Diazepines and benzodiazepines have various therapeutic applications. Many members of the diazepine family are widely utilized as antitumor [8], anti-schistosomal [9], and antidepressant [10-11]. Some other examples of benzodiazepine such prominent drug molecules as alprazolam, clonazepam, clorazepate, chlordiazepoxide, diazepam, estazolam, and lorazepam utilize with high bioavailability and a slower onset and prolonged effects [5-11]. Benzodiazepine derivatives are used as dyes for acrylic fibers [12]. Furthermore, benzodiazepines are valuable intermediates for the synthesis of fused ring compounds such as triazolo-, oxadiazolo-, oxazino- and furanobenzodiazepines [13-18]. Due to their wide range of pharmacological activity and industrial applications, the development of mild and efficient protocols for their preparation continues to be a challenging attempt in the synthetic organic chemistry [19-34]. The synthesis of tetrazoles have been developed in the presence of different catalysts including *p*-toluenesulfonic acid [35,36], $(NH_4)_2Ce(NO_3)_6$ [37], cadmium chloride [38] and tungstates [39]. The synthesis of 1,4-diazepines has been reported using sulfamic acid [40], $SbCl_3$-Al_2O_3 [41], iodine [42], gallium(III) triflate [43] and nanomagnetic catalyst under microwave irradiation [44]. However, a large number of the modified methods reported in the literature suffer from several drawbacks such as the use of a large amount of catalysts, unsatisfactory product yields and critical product isolation procedures. These disadvantages require the development of an efficient and practically useful process of preparation. The core/shell nanostructure is an ideal composite system that combines the advantages

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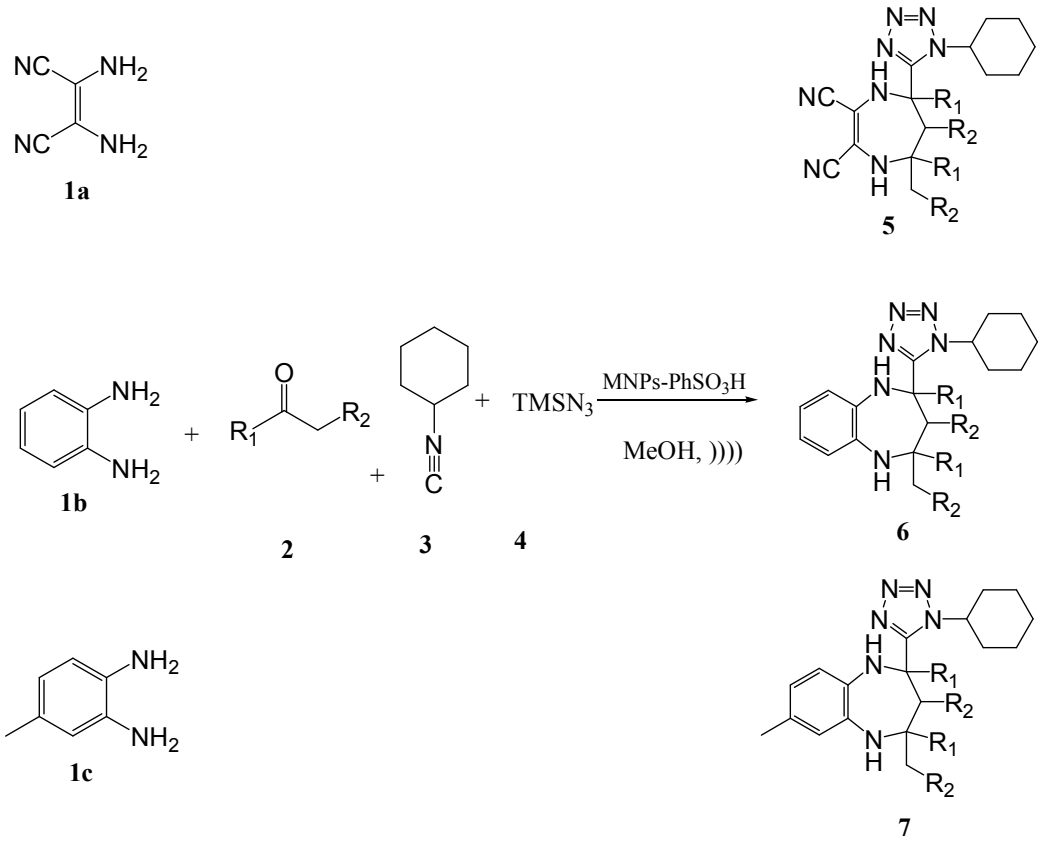


Scheme 1. Synthesis of 1,4-diazepines in the presences of MNPs-$PhSO_3H$ under ultrasonic irradiation

of both the core and the shell to offer enhanced physical and chemical properties. In recent years, magnetic nanoparticles (MNPs) have been extensively investigated as inorganic cores for the synthesis of organic/inorganic core-shell composite particles, due to their potential applications in many industrial and biological fields [45-50]. Magnetic nanoparticles have recently seemed as a new type of catalyst supports because of their easy preparation and functionalization, large surface area ratio, facile recovery and recyclability *via* magnetic force as well as low toxicity and price.

In continuing our efforts towards the development of efficient and environmentally benign magnetic nanocatalysts [51-52], herein, sulfanilic acid/Fe_3O_4 nanoparticles (MNPs-$PhSO_3H$) were prepared by a simple method as a highly efficient acid magnetic catalyst. Thus, we reported a simple, cost-effective, green and expeditious method for synthesis of new 1,4-diazepines containing tetrazole ring *via* a four-component reaction in higher yields and employing ultrasound as energy source (Scheme 1).

EXPERIMENTAL

Powder X-ray diffraction (XRD) was carried out on a Philips diffractometer of X'pert Company with monochromatized Cu Kα radiation (λ = 1.5406 Å). Microscopic morphology of catalyst was visualized by SEM (LEO 1455VP). The magnetic property of magnetite nanoparticle has been measured with a vibrating sample magnetometer (VSM) (Meghnatis Daghigh Kavir Co.; Kashan Kavir; Iran) at room temperature.

Preparation of the Magnetic Fe_3O_4 Nanoparticles (MNPs)

2.7 g of $FeCl_3 \cdot 6H_2O$ and 1.0 g of $FeCl_2 \cdot 4H_2O$ were sonicated in 100 ml of HCl (aq) in a three-necked bottom (250 ml) under N_2 atmosphere for 30 min. 150 ml of NaOH (1.25 M) was added into the solution with vigorous mechanical stirring under continuous N_2 atmosphere. The solution was heated at 70-80 ℃ for 1 h. The black precipitate formed was isolated by magnetic decantation, exhaustively washed with double-distilled water, and further washed twice with ethanol and dried at 60 °C in vacuum.

Silica Coated Magnetic Nanoparticles (Fe_3O_4@SiO_2 MNPs)

1.0 g of the MPs obtained above were homogeneously dispersed in a mixture of 50 ml of ethanol, 9 ml of water, and 1.0 ml of 28 wt% concentrated ammonia aqueous solution ($NH_3.3H_2O$), followed by the addition of 0.5 ml of tetraethylorthosilicate (TEOS). After vigorous stirring at room temperature for 16 h, the core-shell magnetic nanoparticles (Fe_3O_4@SiO_2 MNPs) were isolated by magnetic decantation to remove the unbounded silica particles and dried at room temperature at vacuum after being washed with deionized water, ethanol and acetone.

Preparation of Fe_3O_4@SiO_2-$(CH_2)_3Cl$ MNPs

1.0 g of the Fe_3O_4@SiO_2 MNPs was homogeneously dispersed in 50 ml of dry toluene under ultrasonic irradiation. (3-chloropropyl) trimethoxysilane (31 ml, 0.17 mol) was refluxed at 60 °C for 48 h under N_2 atmosphere. The unreacted materials were washed with toluene (3 × 8 ml). The toluene was removed under the reduced pressure at room temperature, followed by heating under high vacuum.

General Procedure for the Synthesis of Sulfanilic Acid Functionalized Fe_3O_4 Nanoparticles (MNPs-$PhSO_3H$)

1.0 g of the Fe_3O_4@SiO_2-$(CH_2)_3Cl$ MNPs was homogeneously dispersed in 50 ml of dry toluene under ultrasonic irradiation for 1 h. Subsequently, sulfanilic acid (11.5 mmol, 2 g) and Et_3N (11.5 mmol, 1.6 ml) were added and refluxed under N_2 atmosphere for 2 days. After the addition was completed, the mixture was shaken for 30 min and the brown solid (MNPs-$PhSO_3H$) was collected using an external magnet and washed with toluene and CH_2Cl_2 before being dried in an oven at 80 °C.

Typical Procedure for the Synthesis of 1,4-Diazepines Containing Tetrazole Ring

First, a solution of diamine compound (1 mmol) and ketone (2.2 mmol) in the presence of MNPs-$PhSO_3H$ (8 mg) was stirred for 4 min in 5 ml of MeOH at ambient temperature. After completion of the reaction, as indicated by TLC, cyclohexyl isocyanide (1 mmol) and trimethylsilyl azide (1.5 mmol) were added to the reaction mixture. Then, the resulting mixture was sonicated at 50 W powers for 15-20 min. After completion of the reaction and separation of the catalyst by a magnet, the product was filtered off, washed further with water, and then crystallized from acetone to give the pure product.

5-(1-Cyclohexyl-1H-tetrazol-5-yl)-4,5,6,7-tetrahydro-5,7,7-trimethyl-1H-1,4-diazepine-2,3-dicarbonitrile (5a). Colorless crystal, m. p.: 228-230 ℃; IR (KBr) cm^{-1}: 3351, 3317, 2931, 2855, 2219, 1588, 1487. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 1.25-1.68 (19H, m), 1.70 (1H, d, J = 14.2 Hz), 2.34 (1H, d, J = 14.2 Hz), 3.50 (1H, m), 5.55 (1H, br s), 5.82 (1H, br s). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 22.3, 25.2, 25.3, 25.6, 29.6, 32.1, 32.2, 32.8, 48.6, 54.6, 61.9, 110.1, 110.4, 117.5, 117.6, 152.5. Anal. Calcd. for $C_{17}H_{24}N_8$: C, 59.98; H, 7.11; N, 32.92; Found: C, 59.90; H, 7.19; N, 32.80.

2-(1-Cyclohexyl-1H-tetrazol-5-yl)-2,3,4,5-tetrahydro-2,4,4-trimethyl-1H-benzo [b] [1,4] diazepine (6a). Colorless crystal, m. p.: 238-239 ℃; IR (KBr) cm^{-1}: 3382, 2928, 1598, 1477. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 1.03-1.98 (m, 20 H), 2.80 (1H, d, J = 12 Hz), 3.98 (m, 1 H), 4.90 (br s, 1H), 5.87 (br s, 1H), 6.42-6.72 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 22.3, 25.3, 25.4, 25.7, 29.8, 32.2, 32.3, 32.9, 48.8, 54.5, 61.8, 114.5, 117.5, 117.9, 118.3, 132.2, 152.3. Anal. Calcd. for $C_{19}H_{28}N_6$: C, 67.03; H, 8.29; N, 24.68; Found: C, 67.09; H, 8.19; N, 24.55.

9a-(1-Cyclohexyl-1H-tetrazol-5-yl)-1,4,5a,6,7,8,9,9a octahydrospiro [benzo[e][1,4]diazepine-5,1'-cyclohexane]-2,3-dicarbonitrile (5b). Colorless crystal, m. p. > 300 ℃; IR (KBr) cm^{-1}: 3428, 3354, 2932, 2858, 2209, 1453. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 1.01-

1.98 (m, 28 H), 2.70 (m, 1H), 3.53 (m, 1H), 4.68 (s, 1H), 4.98 (s, 1H).^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 21.1, 21.4, 21.5, 23.9, 25.2, 25.6, 25.7, 26.0, 32.3, 32.6, 36.3, 38.6, 47.6, 48.2, 59.8, 65.0, 105.7, 113.4, 117.0, 118.0, 159.4. Anal. Calcd for $C_{23}H_{32}N_8$: C, 65.69; H, 7.67; N, 26.64; Found C, 65.54; H, 7.59; N, 26.69.

4a'-(1-Cyclohexyl-1H-tetrazol-5-yl)-1',2',3',4',4a',5', 10',11a'-octahydrospiro[cyclohexane-1,11'-dibenzo [b,e][1,4]diazepine] (6b). Colorless crystal, m. p.: 295-297 °C; IR (KBr) cm^{-1}: 3372, 2931, 2857, 1462, 1309. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 1.07-1.90 (m, 28 H), 2.65 (m, 1H), 3.38 (m, 1H), 4.64 (1H), 5.74 (1 H), 6.33-6.72 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 24.3, 24.4, 24.5, 24.8, 24.9, 25.0, 25.7, 28.9, 30.8, 32.2, 34.2, 37.8, 50.4, 57.1, 57.9, 58.1, 115.3, 117.6, 120.3, 120.8, 132.3, 137.6, 162.4. Anal. Calcd. for $C_{25}H_{36}N_6$: C, 71.39; H, 8.63; N, 19.98; Found C, 71.28; H, 8.52; N, 19.90.

5-(1-Cyclohexyl-1H-tetrazol-5-yl)-7-methyl-5,7-diphenyl-4,5,6,7-tetrahydro-1H-1,4-diazepine-2,3-dicarbonitrile (5c). Colorless crystal, m. p.: 262-264 °C; IR (KBr) cm^{-1}: 3343, 3059, 2932, 2854, 2216, 1569; ^{1}H NMR (400 MHz, DMSO-d$_6$) δ (ppm): 1.24-1.40 (6H, m), 1.66-173 (8H, m), 1.98 (1H, m), 3.83 (m, 1 H), 7.20-7.37 (m, 11H), 8.00 (1H, br s). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 31.3, 31.6, 32.2, 32.4, 35.4, 49.0, 50.2, 57.2, 58.4, 60.9, 117.6, 117.8, 124.6, 125.3, 126.1, 126.8, 128.0, 128.5, 140.1, 143.3, 148.3, 152.8, 158.2. Anal. Calcd. for $C_{27}H_{28}N_8$: C, 69.80; H, 6.08; N, 24.12; Found: C, 69.89; H, 6.01; N, 24.03.

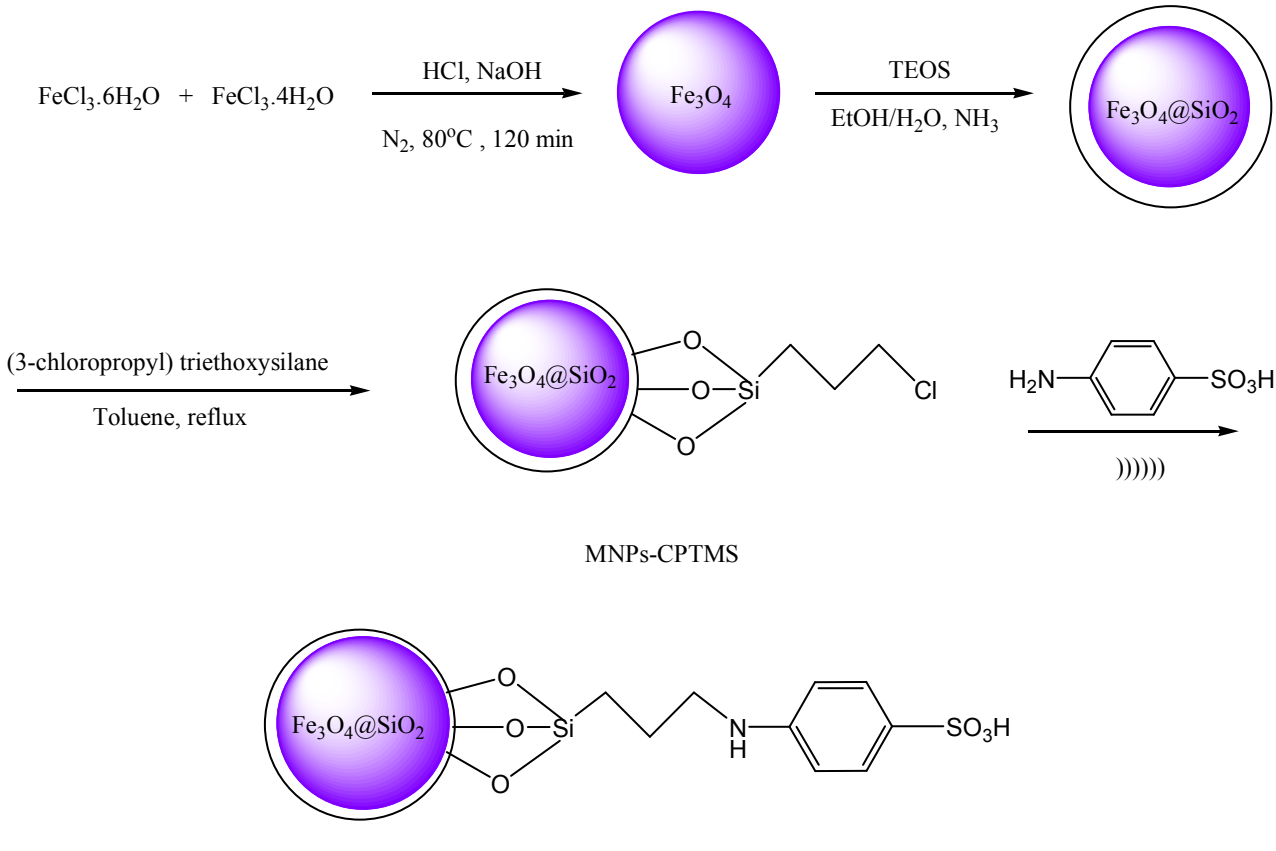
2-(1-Cyclohexyl-1H-tetrazol-5-yl)-4-methyl-2,4-diphenyl-2,3,4,5-tetrahydro-1H-benzo[b][1,4]diazepine (6c). Colorless crystal, m. p.: 292-295 °C; IR (KBr) cm^{-1}: 3368, 3054, 2935, 2859, 1596, 1445; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 0.9-1.97 (m, 14 H), 3.01 (d, 1 H, J = 12 Hz), 3.70 (d, 1 H, J = 12 Hz), 5.20 (s, 1 H), 5.32 (s, 1H), 6.34 (1 H, t, J = 8 Hz), 6.45 (1 H, t, J = 8 Hz), 6.62 (1H, t, J = 8 Hz), 6.71 (1 H, t, J = 8 Hz), 6.90-6.96 (m, 5 H), 7.14-7.23 (m, 5 H). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 24.2, 24.3, 24.5, 32.2, 32.4, 34.5, 48.4, 57.4, 57.8, 60.0, 118.0, 118.2, 122.8, 123.3, 126.4, 127.5, 127.7, 128.3, 129.8, 131.3, 131.5, 140.7, 141.3, 146.7, 157.7. Anal. Calcd. for $C_{29}H_{32}N_6$: C, 74.97; H, 6.94; N, 18.09; Found: C, 74.21; H, 7.01; N, 18.20.

2-(1-Cyclohexyl-1H-tetrazol-5-yl)-4-methyl-2,4-bis(4-nitrophenyl)-2,3,4,5-tetrahydro-1H-benzo[b][1,4] diazepine (6d). Yellow crystal, m. p. > 300 °C; IR (KBr) cm^{-1}: 3397, 3348, 3071, 2936, 2859, 1513, 1349, 752. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 0.5- 1.84 (m, 14 H), 3.25 (d, 1H, J = 15 Hz), 3.65 (d, 1H, J = 15 Hz), 3.90 (s, 1H), 5.40 (s, 1H), 6.35-6.48 (m, 2H), 6.80-6.85 (m, 2H), 7.17-7.19 (d, 2H, J = 8 Hz), 7.46-7.48 (d, 2H, J = 8 Hz), 7.71-7.73 (d, 2H, J = 8 Hz), 7.85-7.87 (d, 2H, J = 8 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 24.1, 24.2, 24.4, 32.2, 33.7, 40.4, 48.1, 57.4, 58.3, 60.1, 118.4, 118.8, 121.6, 122.3, 123.0, 123.8, 127.9, 131.1, 140.8, 145.0, 145.9, 149.1, 155.3, 157.2.Anal. Calcd. for $C_{29}H_{30}N_8O_4$: C, 62.80; H, 5.45; N, 20.20; Found: C, 62.78; H, 5.41; N, 20.25.

5-(1-Cyclohexyl-1H-tetrazol-5-yl)-5,7-bis(2-hydroxyphenyl)-7-methyl-4,5,6,7-tetrahydro-1H-1,4-diazepine-2,3-dicarbonitrile (5d). Colorless crystal, m. p.: 280-282 °C; IR (KBr) cm^{-1}: 3357, 3050, 2931, 2853, 2221, 1564, 1351, 1316, 1078, 756. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 1.11-1.98 (m, 16 H), 3.35 (1H, s, br), 3.80 (1H, s, br), 6.70-6.85 (m, 4H), 6.99-7.07 (m, 4H), 7.62 (s, 1H), 9.84 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 22.4, 24.6, 24.7, 25.2, 31.2, 31.7, 38.8, 40.08, 50.1, 54.2, 109.6, 110.7, 114.4, 115.2, 116.4, 117.8, 118.3, 118.4, 125.9, 126.8, 126.9, 127.15, 128.9, 152.3, 154.9. Anal. Calcd. for $C_{27}H_{28}N_8O_2$: C, 65.31; H, 5.68; N, 22.57; Found: C, 65.38; H, 5.61; N, 22.50.

2,4-Bis(4-chlorophenyl)-2-(1-cyclohexyl-1H-tetrazol-5-yl)-4-methyl-2,3,4,5-tetrahydro-1H-benzo[b][1,4] diazepine (6e). Yellow crystal, m. p. > 300 °C; IR (KBr) cm^{-1}: 3370, 3057, 2933, 2857, 1600, 1490, 1096, 751. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 0.8-1.98 (m, 13 H), 3.02 (d, 1H, J = 12 Hz), 3.54 (d, 1H, J = 12 Hz), 4.02 (m, 1H), 5.12 (1H, s, br), 5.24 (1H, s, br), 6.33-7.25 (12 H, m). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 24.2, 24.3, 24.5, 32.2, 32.4, 34.5, 48.4, 57.3, 57.9, 60.0, 118.0, 118.1, 122.8, 123.3, 126.4, 127.5, 127.7, 128.3, 129.8, 131.3, 131.5, 140.7, 141.3, 146.7, 157.7. Anal. Calcd. for $C_{29}H_{30}Cl_2N_6$: C, 65.29; H, 5.67; N, 15.75; Found: C, 65.19; H, 5.90; N, 15.55.

5-(1-Cyclohexyl-1H-tetrazol-5-yl)-7-ethyl-6-methyl-5,7-diphenyl-4,5,6,7-tetrahydro-1H-1,4-diazepine-2,3-dicarbonitrile (5e). Colorless crystal, m. p.: 268-270 °C; IR (KBr) cm^{-1}: 3360, 3065, 2932, 2855, 2215, 1575, 1546, 1316, 756. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 2.34-



Scheme 2. Synthesis of MNPs-$PhSO_3H$

2.40 (m, 2H), 3.86-3.88 (1H, m), 4.30 (1 H, s), 5.10 (1 H, s), 7.22-7.26 (5H, m), 7.32-7.40(5H, m). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 8.35, 24.7, 24.8, 25.2, 30.0, 31.3, 31.7, 38.7, 38.8, 49.9, 50.0, 59.3, 110.1, 110.5, 114.1, 117.6, 124.8, 124.9, 127.7, 128.5, 142.5, 151.6. Anal. Calcd. for $C_{29}H_{32}N_8$: C, 70.71; H, 6.55; N, 22.75; Found: C, 70.68; H, 6.52; N, 22.79.

2-(1-Cyclohexyl-1H-tetrazol-5-yl)-4-ethyl-3-methyl-2, 4-diphenyl-2,3,4,5-tetrahydro-1H-benzo[b][1,4]diazepine (6f). Yellow crystal, m. p.: 280-282 °C; IR (KBr) cm^{-1}: 3396, 3234, 3027, 2930, 2859, 1646, 1174, 756. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 0.95-1.90 (17H, m), 2.34-2.40 (m, 2H), 3.86-3.88 (1H, m), 4.02 (s, 1 H), 5.20 (s, 1 H), 7.22-7.26 (5H, m), 7.32-7.40 (5H, m), 7.85 (2H, s). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 8.37, 20.7, 24.3, 24.4, 24.6, 30.7, 30.8, 31.0, 52.1, 61.9, 114.5, 117.4, 118.4, 125.0, 125.5, 126.1, 126.2, 128.0, 128.1, 128.7, 134.9, 137.6, 141.4, 145.6, 154.9. Anal. Calcd. for $C_{31}H_{36}N_6$: C, 75.58; H, 7.37; N, 17.06; Found: C, 75.55; H, 7.34; N, 17.15.

4a'-(1-Cyclohexyl-1H-tetrazol-5-yl)-8'-methyl-1',2', 3',4',4a',5',10',11a'-octahydrospiro[cyclohexane-1,11'-dibenzo[b,e][1,4]diazepine](7). Colorless crystal, m. p. 245-247 °C; IR (KBr) cm^{-1}: 3372, 2930, 2858, 1601, 1460, 1311, 759. ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 0.95-2.20 (31H, m), 2.80 (1H, m), 3.50 (1H, m), 4.63 (1H, s), 5.61(1H, s), 6.31-6.58 (3H, m). ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 20.0, 20.1, 20.9, 21.0, 24.3, 24.5, 24.8, 24.9, 25.0, 25.2, 25.7, 30.7, 32.3, 34.2, 50.4, 57.1, 57.8, 115.4, 120.8, 121.2, 122.6, 126.0, 132.2, 135.9. Anal. Calcd. for $C_{26}H_{38}N_6$: C, 71.85; H, 8.81; N, 19.34; Found: C, 71.82; H, 8.75; N, 19.27.

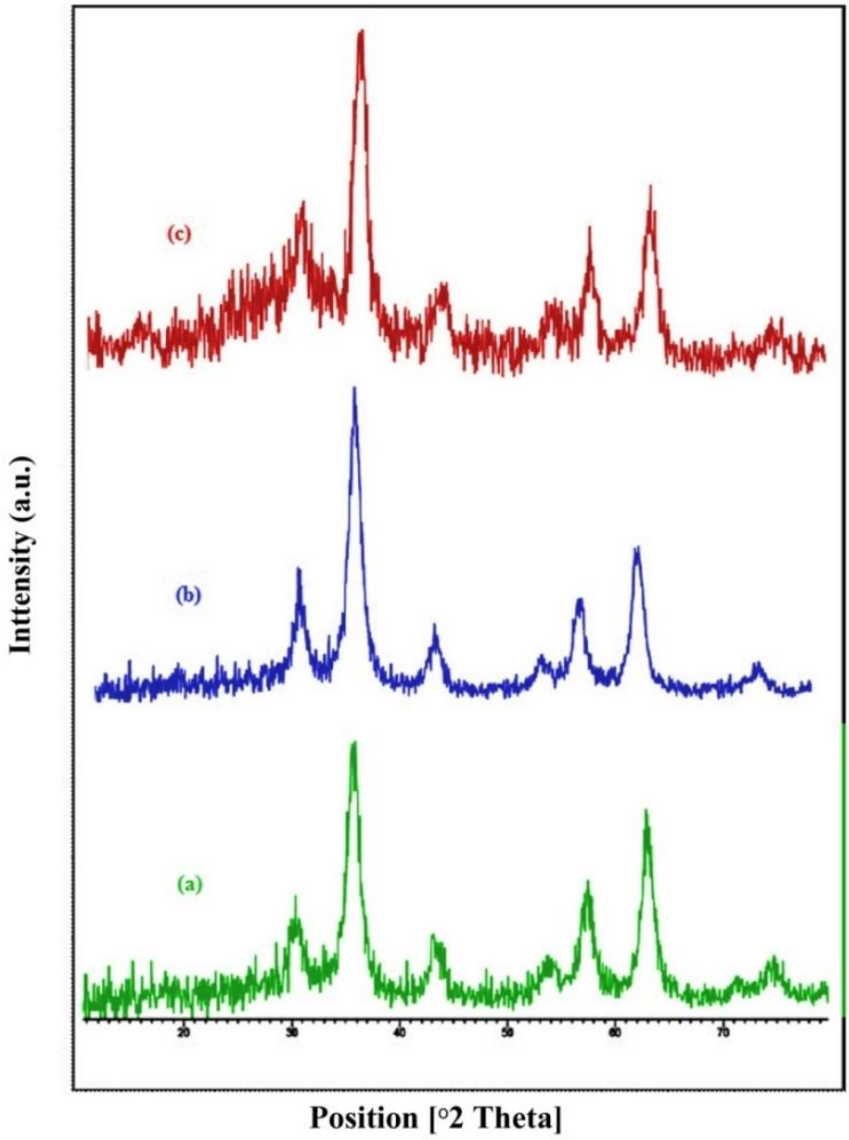


Fig. 1. XRD patterns of (a) Fe_3O_4, (b) Fe_3O_4@SiO_2 and (c) MNPs -$PhSO_3H$.

RESULTS AND DISCUSSION

Synthesis and Structural Analysis of MNPs-$PhSO_3H$

Magnetic Fe_3O_4 nanoparticles were prepared by chemical co-precipitation method and coated with 3-chloropropyltrimethoxysilane (CPTMS) by covalent bonds. The reaction of the supported CPTMS with sulfanilic acid in dry toluene under ultrasonic irradiation produced the sulfanilic acid functionalized magnetic nanoparticles (MNPs-$PhSO_3H$) (Scheme 2).

The catalyst was characterized by XRD, FT-IR, SEM, TGA and VSM techniques. Crystalline phases of Fe_3O_4, Fe_3O_4@SiO_2 and MNPs-$PhSO_3H$ were identified by XRD and the resultant patterns were shown in Fig. 1. The XRD patterns indicate that the three products (Figs. 1a, b, c)

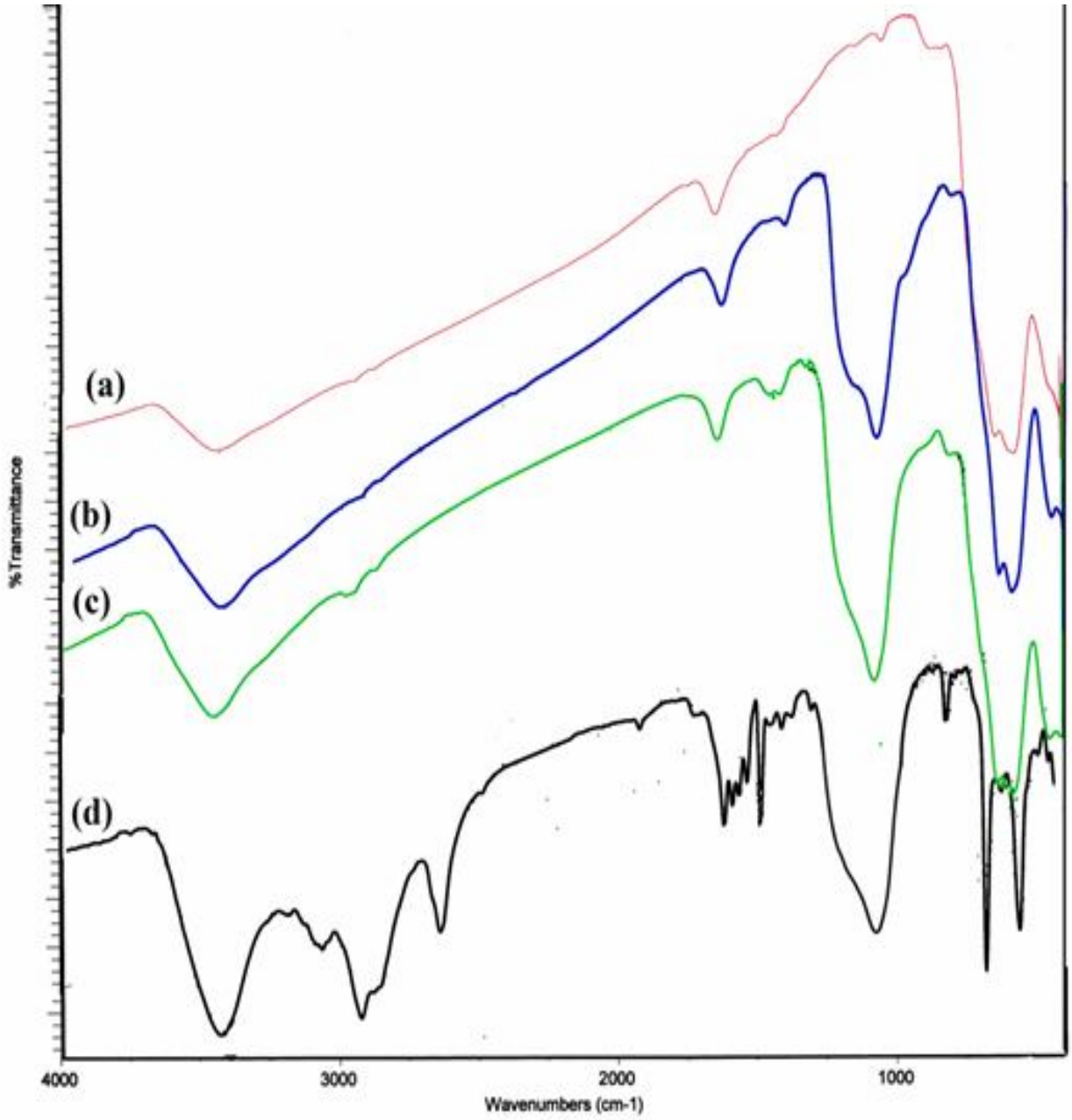


Fig. 2. FTIR spectra of (a) Fe_3O_4, (b) Fe_3O_4@SiO_2, (c) Fe_3O_4@SiO_2-$(CH_2)_3Cl$ and (d) MNPs -$PhSO_3H$.

represent similar diffraction peaks indicating that the coating agent does not significantly affect the crystal structure of the magnetite nanoparticles. The XRD results indicate that the Fe_3O_4 particles were successfully coated with the sulfanilic acid.

Successful surface modification of the Fe_3O_4@SiO_2-$(CH_2)_3Cl$ MNPs with sulfanilic acid was verified by the Fourier transform infrared (FT-IR) spectral analysis. FT-IR spectra of the bare magnetic Fe_3O_4 nanoparticles displayed the characteristic of Fe-O absorption around 575 cm^{-1}

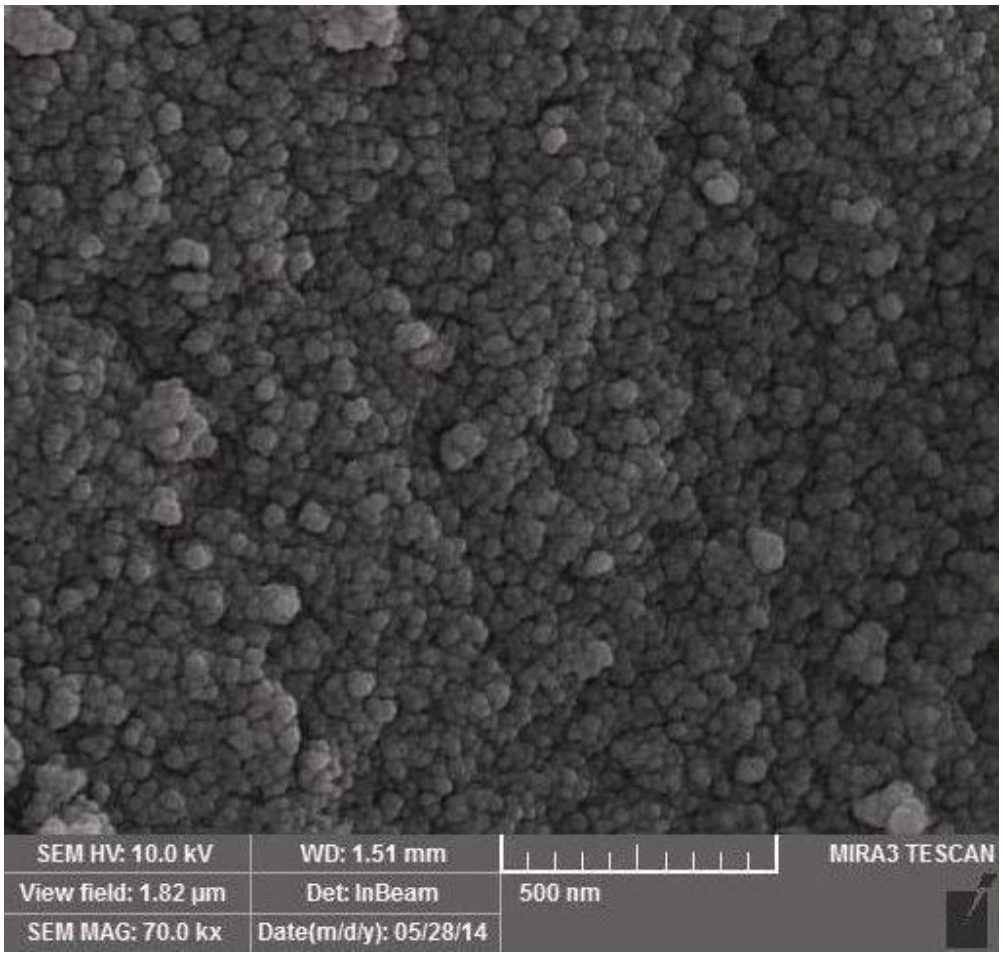


Fig. 3. SEM image of MNPs -$PhSO_3H$.

(Fig. 1a). Fe_3O_4@SiO_2 shows characteristic IR absorption bands at about 1090, 950, 800 and 465 cm^{-1} which are attributed to the asymmetric stretching, symmetric stretching, in plane bending and rocking mode of the Si-O-Si group, respectively. These results confirm the presence of SiO_2. The broad peaks in the range 3200-3500 cm^{-1} and the weak peak at 1620 cm^{-1} are due to the O-H stretching vibration mode and twisting vibration mode of H-O-H adsorbed in the silica shell, respectively. The presence of the anchored alkyl groups is confirmed by the weak aliphatic C-H symmetric and asymmetric stretching vibrations at 2926 and 2963 cm^{-1} in Figs. 1c and 1d. The peaks at 3100-3500 cm^{-1} are related to O-H (sulfonic acid group) and N-H (amide groups) in MNPs-$NHC_6H_4SO_3H$. The bands at 1540 cm^{-1} is related to the bending vibration of the N-H bond. The presence of sulfonyl group is also verified by the peaks appeared at 1215 and 1120 cm^{-1}. Thus, the above results indicate that the functional groups were successfully grafted onto the surface of the magnetic Fe_3O_4@SiO_2 nanoparticles.

The morphology of the nanocomposite was observed on scanning electron microscopy. Figure 3 displays the SEM micrograph of MNPs-$PhSO_3H$ nanocomposite. As can be seen, the nanocomposite has spherical morphology with the average particle size of about 40-45 nm.

The magnetic property of MNPs and MNPs-$PhSO_3H$ was characterized by VSM (Fig. 4). As expected, the bare MNPs showed the higher magnetic value (saturation

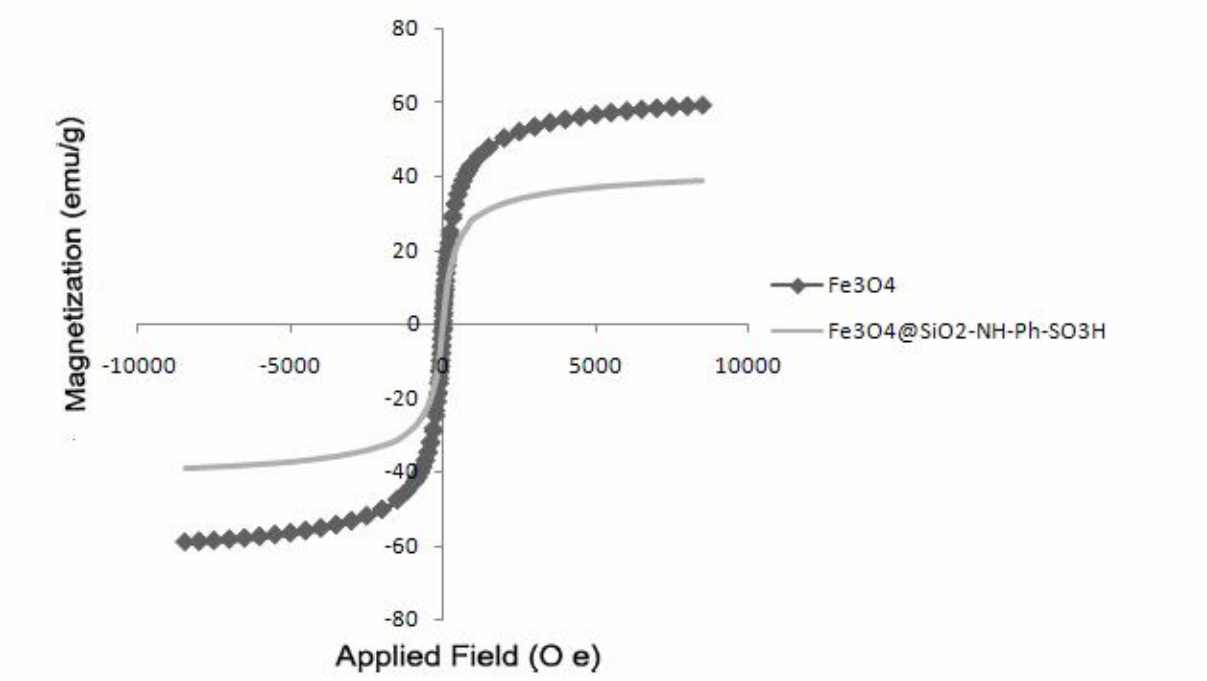


Fig. 4. VSM curves of (a) Fe_3O_4 and (b) MNPs-$PhSO_3H$.

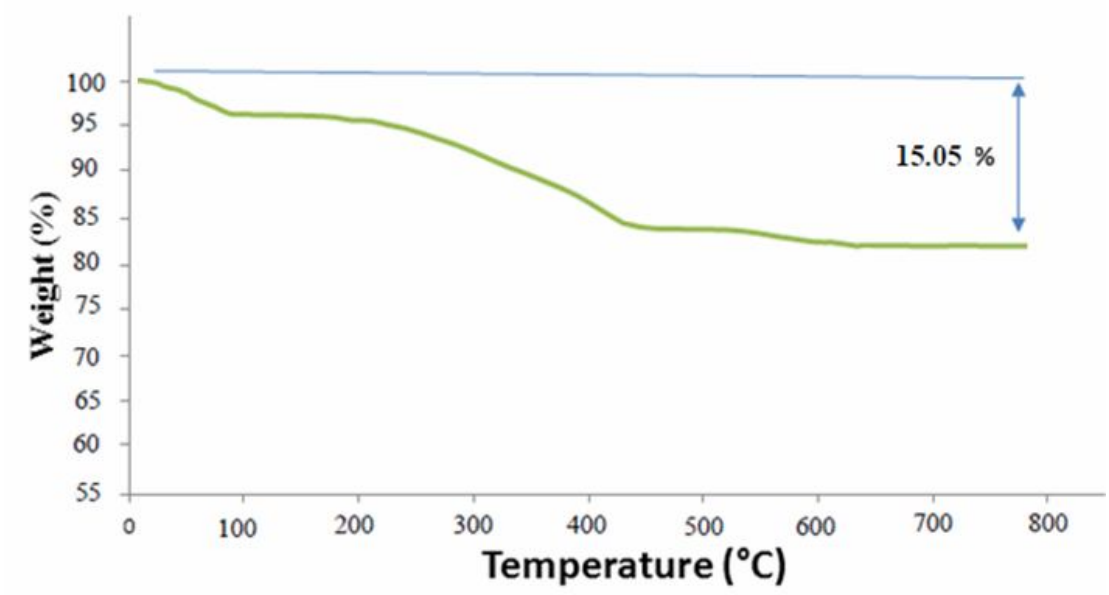


Fig. 5. TGA of MNPs-$PhSO_3H$.

magnetization, Ms) of 60.05 emu g^{-1}, the Ms value of MNPs -$PhSO_3H$ is decreased due to the silica coating and the layer of sulfanilic acid (39.45 emu g^{-1}).

The stability of the MNPs-$PhSO_3H$ catalyst was determined by thermogravimetric analysis (TGA) (Fig. 5). The weight loss at temperatures below 210 ºC is owing to the removal of physically adsorbed solvent and surface hydroxyl groups. The curve indicates a weight loss about

Table 1. Optimization of Different Conditions in the Synthesis of 1,4-Diazepines[a]

Entry	Catalyst	Solvent	Time (min)	Yield (%)[b]
1	-	MeOH	240	-
2	NiO (8 mol%)	MeOH	180	25
3	CuO (8 mol%)	MeOH	180	22
4	ZrP_2O_7 (8 mol%)	MeOH	180	36
5	$MgFe_2O_4$ (8 mol%)	MeOH	180	31
6	pTSA (8 mol%)	MeOH	180	50
7	MNPs-$PhSO_3H$ (.008 g)	Hexane	180	23
8	MNPs-$PhSO_3H$ (0.008 g)	toluene	180	29
9	MNPs-$PhSO_3H$ (0.008 g)	CH_3CN	180	36
10	MNPs-$PhSO_3H$ (0.002 g)	MeOH	180	55
11	MNPs-$PhSO_3H$ (0.004 g)	MeOH	180	63
12	MNPs-$PhSO_3H$ (0.006 g)	MeOH	120	80
13	MNPs-$PhSO_3H$ (0.008 g)	MeOH	120	84
14	MNPs-$PhSO_3H$ (0.01 g)	MeOH	120	84
15	MNPs-$PhSO_3H$ (0.008 g)	MeOH (40 W)[c]	15	86
16	MNPs-$PhSO_3H$ (0.006 g)	MeOH (50 W)[c]	15	88
17	MNPs-$PhSO_3H$ (0.008 g)	MeOH (50 W)[c]	15	92
18	MNPs-$PhSO_3H$ (0.01 g)	MeOH (50 W)[c]	15	92
19	MNPs-$PhSO_3H$ (0.008 g)	MeOH (60 W)[c]	15	92
20	-	MeOH (60 W)[c]	15	55

[a]2,3-Diaminomaleonitrile (1 mmol), acetone (2.2 mmol), cyclohexyl isocyanide (1 mmol), trimethylsilyl azide (1.5 mmol). [b]Isolated yield. [c]Ultrasonic irradiation.

10% from 150 to 500 ºC, due to the decomposition of the organic spacer grafting to the MNPs surface To evaluate the MNPs-$PhSO_3H$ catalyst described here, the catalytic activities of various catalysts for the synthesis of 1,4-diazepines containing tetrazole ring were examined under different conditions (Table 1). The following point for our experiments was to optimize the reaction conditions such as solvent and amount of catalyst for the production of 1,4-diazepine containing tetrazole ring derivatives (Table 1). By using different amounts of MNPs -$PhSO_3H$ (2, 4, 6, 8 and 10 mg); we found that 8 mg of MNPs -$PhSO_3H$ affords the product in 92% isolated yield (entry 10, 16, 17, 18). Increasing the amount of catalyst did not improve the yield (entry 18). It was noticed that the reaction is also possible

Table 2. Synthesis of 1,4-Diazepine Derivatives in the Presence of MNPs-$PhSO_3H$ under Heating and under Ultrasonic Irradiation

Entry	Diamine	Ketone	Product	Heating	Ultrasonic
				Time (h)/Yield (%)[a]	Time (min)-Yield (%)[a]
1	2,3-Diaminomaleonitrile	Acetone	5a	1/92	15/92
2	Orthophenylenediamine	Acetone	6a	1.5/90	25/91
3	2,3-Diaminomaleonitrile	Cyclohexanone	5b	1/91	15/92
4	Orthophenylenediamine	Cyclohexanone	6b	1.5/89	20/90
5	2,3-Diaminomaleonitrile	Acetophenone	5c	1/92	15/92
6	Orthophenylenediamine	Acetophenone	6c	1.5/90	20/91
7	Orthophenylenediamine	4-Nitroacetophenone	6d	1.5/90	25/91
8	2,3-Diaminomaleonitrile	2-Hydroxyacetophenone	5d	1/89	15/90
9	Orthophenylenediamine	4-Chloroacetophenone	6e	1.5/90	25/90
10	2,3-Diaminomaleonitrile	Ethylphenylketone	5e	1/90	15/91
11	Orthophenylenediamine	Ethylphenylketone	6f	1.5/89	20/90
12	4-Methylbenzen-1,2-diamine	Cyclohexanone	7	1.5/89	20/90

[a]Isolated yields.

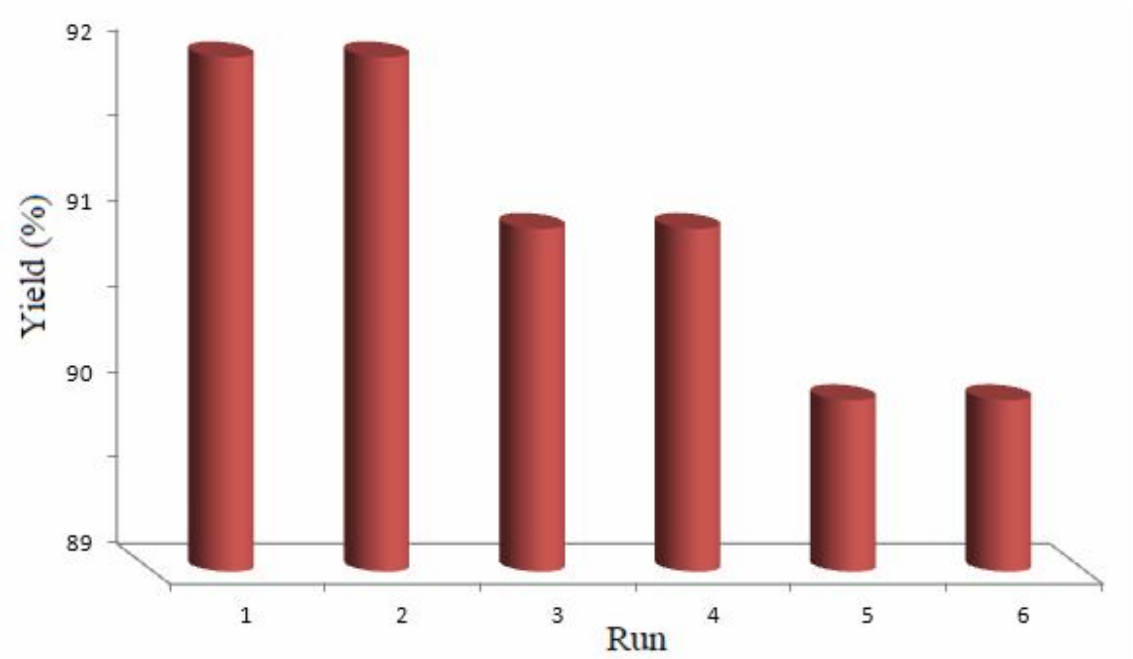
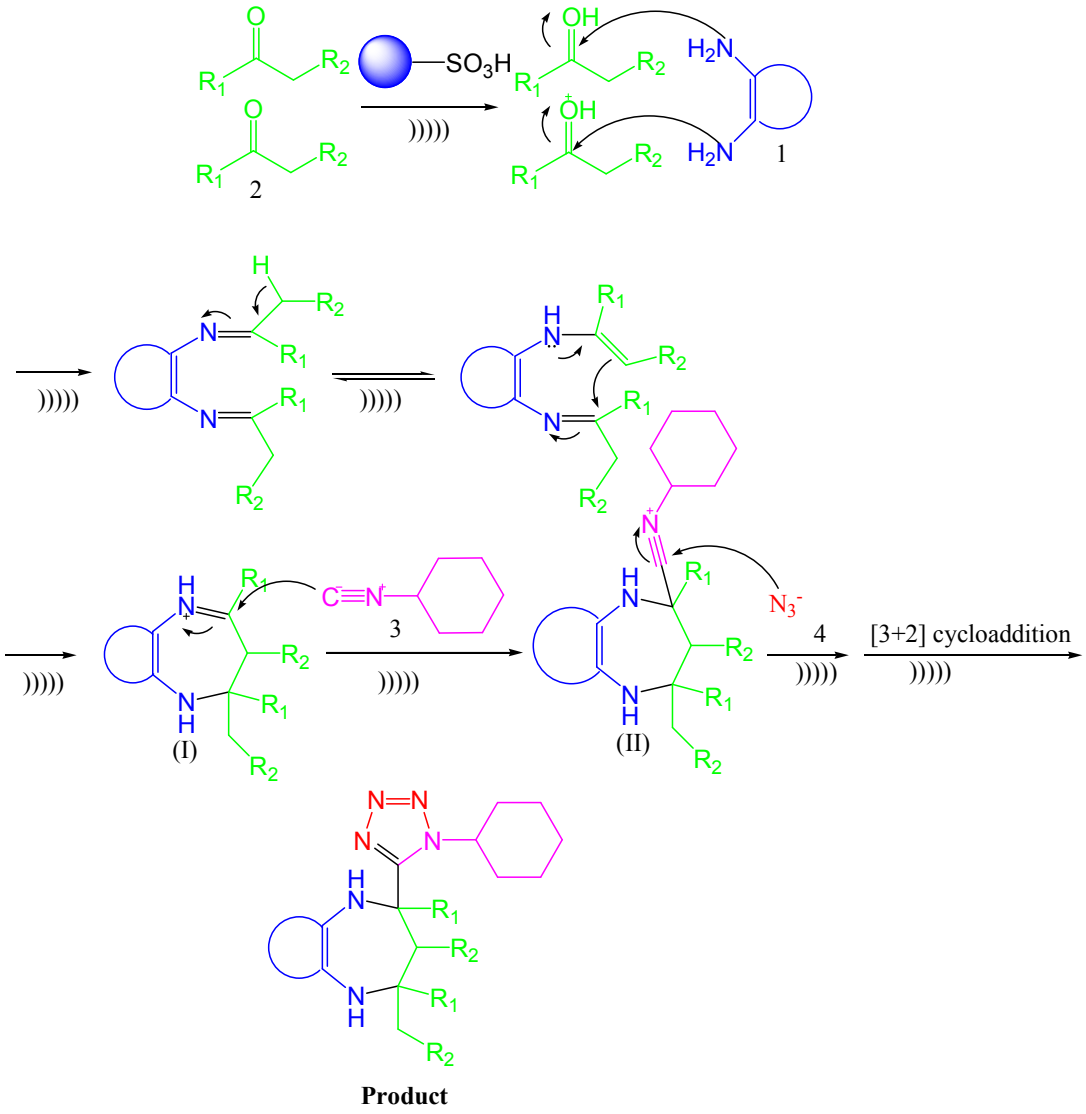


Fig. 6. Recycling of MNPs-$PhSO_3H$ as catalyst for the synthesis of 5a.



Scheme 3. Proposed mechanism for the synthesis of 1,4-diazepines

by MNPs-$PhSO_3H$ in *n*-hexane, toluene, MeOH, and CH_3CN; among the solvents used MeOH was found to be the best solvent as shown in Table 1.

We examined condensation reaction under ultrasonic irradiation without catalyst. When the reaction was examined without catalyst, the products were obtained in a moderate to good yields (Table 1). The results show that the sonication certainly affected the reaction of the system. To demonstrate the generality of this method, we performed all further reactions using MNPs-$PhSO_3H$ (8 mg) in MeOH under ultrasonic irradiation (50 W), and found that MNPs-$PhSO_3H$ can efficiently catalyze the reaction between different ketones, diamino compounds, cyclohexyl isocyanid and trimethylsilyl azide to afford excellent yield of the desired products. Also, the results of the comparison study between heating condition and ultrasonic irradiation performed to illustrate effect of sonication are listed in Table 2.

The possibility of recycling the catalyst was then examined. After completion of the reaction, the nanocatalyst

was separated by an external magnet. Dichloromethane (10 ml) was added to the residue, the catalyst was filtered and washed with dichloromethane and recycled six times. It was seen that the respective isolated yields for the six runs are found to be 92%, 92%, 91%, 91%, 90% and 90% respectively (Fig. 6).

As displayed in Scheme 3, ketone was first protonated in the presence of MNPs-$PhSO_3H$ and the enamine was generated. Then, the intramolecular attack of enamine produced the intermediate (I). In the following, the nucleophilic attack of the intermediate (I) by isocyanide was done and intermediate (II) produced. Then, attack of azid ion to intermediate (II) and, at the end, the product was performed by [3+2]-cycloaddition between C=N group and N_3. The synthesis of tetrazole in this approach is Ugi-azide reaction.

CONCLUSIONS

In conclusion, we have developed a new, rapid, and efficient method for the synthesis of 1,4-diazepines containing tetrazole ring by a one-pot four-component reaction under ultrasonic irradiation using MNPs-$PhSO_3H$ as an efficient, mild, and heterogeneous catalyst which could be reused for at least six times. The reaction is facile, simple, and environment-friendly.

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Supporting Information

Some characteristics of the MNPs-$PhSO_3H$ and spectra data of product are given in the Supporting Information available online.

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