An efficient synthesis of perhydro[1,2,4]triazolo[1,2-a][1,2,4]triazole-1,5-dithiones catalyzed by TiO$_2$-functionalized nano-Fe$_3$O$_4$ encapsulated-silica particles as a reusable magnetic nanocatalyst

Javad Safari, and Leila Javadian

Immobilization of a nano-TiO$_2$ catalyst on the surface of a magnetic SiO$_2$ support was performed through the reaction of Fe$_3$O$_4$@SiO$_2$ composite with Ti(OCl)$_4$ via a simple process. The Fe$_3$O$_4$@SiO$_2$-TiO$_2$ nanocomposite was characterized using scanning electron microscopy (SEM), transmission electron microscopy (TEM), energy dispersive X-ray spectroscopy (EDS), X-ray diffraction (XRD), Fourier transform infrared spectra (FTIR), and vibrating sample magnetometer (VSM). The Fe$_3$O$_4$@SiO$_2$-TiO$_2$ nanocomposite has been found to be an efficient catalyst for the synthesis of perhydro[1,2,4]triazolo[1,2-a][1,2,4]triazole-1,5-dithiones from the condensation of various aldazines and potassium thiocyanate in acetonitrile solvent at room temperature. It has been found that the nanocatalyst was recycled for up to 6 cycles with minimal loss in catalytic activity. The purpose of this research was to provide an easy method for the synthesis of perhydrotriazolotriazole derivatives by a robust and magnetic recoverable catalyst.

1. Introduction

1,3-Dipolar cycloaddition or [3+2] cycloaddition reaction is fundamental processes in organic chemistry that offers a powerful synthetic methodology to achieve five-membered heterocyclic systems in stereo and regiocontrolled approach. The term “criss-cross” cycloaddition appeared in 1917 by Bailey and McPherson and the first paper described the cycloaddition of cyanic acid to benzalazine. Criss-cross cycloaddition reactions are a procedure for the synthesis of fused heterocyclic rings in an one pot arrangement that offer two fused five-membered rings. The formation of corresponding products was described by Huisgen as the result of fundamental processes in organic chemistry that offers a powerful synthetic methodology to achieve five-membered heterocyclic systems in stereo and regiocontrolled approach. They adopt the s-trans conformation due to steric interaction of the alkyl or aryl substitutions. So, this conformation does not suffer the drawbacks such as high catalyst loading, drastic conditions, low yields and long reaction times.

Since then, some papers have published listing examples of criss-cross cycloaddition reactions of aldazines and different dipolarophiles such as thiocyanate. In addition to aldazines, the current reactions have been reported for ketazines that offer two fused five-membered rings. Criss-cross cycloaddition reactions are a procedure for the synthesis of fused heterocyclic rings in an one pot arrangement that offer two fused five-membered rings. The formation of corresponding products was described by Huisgen as the result of fundamental processes in organic chemistry that offers a powerful synthetic methodology to achieve five-membered heterocyclic systems in stereo and regiocontrolled approach. They adopt the s-trans conformation due to steric interaction of the alkyl or aryl substitutions. So, this conformation does not suffer the drawbacks such as high catalyst loading, drastic conditions, low yields and long reaction times.

In recent decades, design of magnetically catalysts has attracted a great deal of attention due to simple separation of catalysts by a permanent magnetic field. A lot of materials such as FeCo, Fe$_3$O$_4$, NiFe$_2$O$_4$, Fe$_3$O$_4$, CoFe$_2$O$_4$ and black sand have the magnetic properties. Among them, Fe$_3$O$_4$ nanoparticles has been chosen because of its low toxicity and remarkable magnetic properties. Fe$_3$O$_4$ nanoparticles have emerged as supports for immobilization of catalyst which offer an easy separation of the catalyst without the need of conventional filtration method or tedious work-up processes. Beside the facile separation, a great feature of Fe$_3$O$_4$ nanoparticles is their surface modification that affords sometimes higher activity than their homogeneous systems. Fe$_3$O$_4$ core with shell of silica offers sites for surface modification with various compounds in catalyst application. Silica layer not only avoids the oxidation of the Fe$_3$O$_4$ by the outer atmosphere, but also prevents the aggregation induced by the magnetic dipolar attraction between magnetic nanoparticles. Also, silica enhances a better dispersion of magnetic nanoparticles in suspension. Magnetic nanoparticles have been used as catalysts or catalyst supports in many organic reactions including oxidation, reductions, multicomponent reactions and C-C couplings with a high level of activity. It is anticipated that the magnetic properties of catalyst would be useful to improve the performance of the [3+2] cycloaddition reaction and provide a support for the solid acid catalyst. On the other side, extensive attention has been directed toward the application of solid acids in organic synthesis because such reagents help prevent release of reaction residues into the environment. In this regard, nanostructure solid acids show higher...
activity than their bulk materials due to their particular chemical and physical properties especially large surface to volume ratio.\textsuperscript{35} As an extension of our researches on the application of magnetic solid acids in organic transformations, functionalization of Fe$_3$O$_4$ nanoparticles with TiO$_2$ has been studied to offer magnetic catalyst which combines the benefits of TiO$_2$ and Fe$_3$O$_4$ to afford greater potential applications. In which contribution, we hope to report an efficient method for the synthesis of perhydrotiazolotriazeolidithiones by the condensation of aldazines as 1,3-heterodienes with thiocyanate in [3+2] cycloaddition by a magnetically recyclable catalyst.

2. Experimental  

2.1. General  

All the commercially available reagents were obtained from Aldrich or Merk and were used without further purification.\textsuperscript{36} $^1$H and $^{13}$C NMR spectra were recorded on a Bruker DRX-400 spectrometer. Chemical shifts are expressed in $\delta$ parts per million. The IR spectra of the compounds were recorded on a Perkin Elmer FT-IR 550 spectrophotometer. All melting points (m.p.) were determined on an ElectroMk3 apparatus, expressed in °C and are uncorrected. Analytical thin layer chromatography (TLC) on silica gel plates containing UV indicator was employed regularly to follow the course of reactions and to confirm the purity of products. The sonication was performed in Shanghai Branson-BUG40-06 ultrasonic cleaner. The obtained nanoparticles were characterized by XRD on a Bruker D8 Advance X-ray diffraction (XRD) diffractometer (Cu-K$_\alpha$, radiation, $\kappa$ = 0.154056 nm and 40 kV voltage), at a scanning speed of 2° min$^{-1}$ from 10° to 100° (2$\theta$). Scanning electron microscope (SEM) was performed on a FEI Quanta 200 SEM operated at a 20 kV accelerating voltage. Magnetic properties were characterized by a vibrating sample magnetometer (VSM, MDKFD, University of kashan, Kashan, Iran) at room temperature. The samples for SEM were prepared by spreading a small drop containing nanoparticles onto a silicon wafer and being dried almost completely in air at room temperature for 2 h, and then were transferred onto SEM conductive tapes. The TEM images were recorded using a ZEISS EM10OC transmission electron microscope operated at a 80 kV accelerating voltage.

2.2. Preparation of Fe$_3$O$_4$@SiO$_2$ as a support  

First, Fe$_3$O$_4$ nanoparticles were prepared by chemical co-precipitation of FeCl$_3$ and FeCl$_2$[Fe]: $\text{Fe}^{3+} + 1:2$ in base solution as described in the literature.\textsuperscript{36} 37 Then, Fe$_3$O$_4$@SiO$_2$ composite were synthesized through the Stöber method using tetraethoxyorthosilicate as a silica source in a basic water/ethanol mixture at room temperature under continuous mechanical stirring.\textsuperscript{38} Briefly, 0.5 g of the Fe$_3$O$_4$ nanoparticles was dispersed in 20 ml of distilled water and 50 ml of ethanol under ultrasound irradiation and then concentrated aqueous ammonia (1 ml) was added. Finally, 0.2 ml of tetraethoxyorthosilicate diluted in ethanol (10 ml) was added drop-wise under continuous mechanical stirring. After stirring for 2 h, Fe$_3$O$_4$@SiO$_2$ nanoparticles were collected by magnetic separation and washed three times with water and ethanol. Finally, the magnetic product was dried at 70 °C for 6 h.

2.3. Preparation of catalyst  

A magnetically separable TiO$_2$ catalyst was prepared by dissolving 1.5 ml of Ti(OCH$_3$)$_4$ in 30 ml ethanol and adding this solution dropwise into a mixture containing 0.40 g of magnetic Fe$_3$O$_4$@SiO$_2$ in 10 ml water/ethanol. The mixture was refluxed at 90 C for about 2 h. Then, the magnetic sample was dried at 60 °C and calcined at 450 °C for 2 h to offer Fe$_3$O$_4$@SiO$_2$-TiO$_2$ nanocomposite.\textsuperscript{39}

2.4. A typical procedure for the synthesis of aldazines  

Aldazines were prepared by the method as described in the literature.\textsuperscript{40} A mixture of the aldehyde (2 mmol), hydrazine sulfate (1 mmol), and triethylamine (1 mmol) was heated at 60 °C for 3–5 min. The completion of the reaction was monitored by thin layer chromatography (petroleum ether:ethyl acetate= 7:3). After the completion of the reaction, the mixture was cooled on ice. The aldazine was collected by suction filtration. Then, it was washed with water, and dried under vacuum. The yellow solid was recrystallized from ethanol to afford the desired aldazineas cream to orange crystals.

2.5. A typical procedure for the synthesis of tetrahydro-[1,2,4]triazolo-[1,2-a][1,2,4]triazole-1,5-dithione derivatives  

In a typical experiment, KSCN (2 mmol), AcOH (0.18 mL), CH$_3$CN (6 mL) and catalytic amount of Fe$_3$O$_4$@SiO$_2$-TiO$_2$ nanocomposite (0.04 g) were stirred at room temperature. After stirring for 5 min, aldazine (1 mmol) was added to this mixture and the contents were stirred for an appropriate period while the progress of the reaction was followed by TLC using petroleum ether:ethyl acetate=7:3) as eluent. After completion of the reaction, the nanocatalyst was removed by an external magnet and reused. Then, cold water (50 mL) was added and the solid product was collected by filtration, was washed successively with CHCl$_3$, dried and recrystallized from ethanol to afford the pure product. The products were identified by comparison of their spectroscopic and physical data with those reported in the literature.

2.5.1. Spectral data for compounds  

2.5.1.1. Tetrahydro-3,7-diphenyl-[1,2,4] triazolo-[1,2-a][1,2,4]triazole-1,5-dithione (3a): white solid, m.p= 188-189 °C; $\text{Rf}$ (petroleum ether:ethyl acetate= 7:3 (v/v)) = 0.26; IR (KBr) / $\nu$ (cm$^{-1}$): 3385, 3180, 1500, 1251; $^1$H NMR (Acetone-$d_6$) / $\delta$ ppm: 6.81 (s, 2H, CH), 7.38-7.42 (m, 10H, Ar-H), 11.42 (s, 2H, NH); $^{13}$C NMR (DMSO-$d_6$) / $\delta$ ppm: 73 (CH), 126.25 (CH), 127.76 (CH), 128.31 (CH), 129.73 (CH), 184.1 (C=S) ppm; CH N

2.5.1.2. Tetrahydro-3,7-bis (3-nitrophenyl)-[1,2,4] triazolo-[1,2-a][1,2,4]triazole-1,5-dithione (3b): white solid, m.p= 190-191 °C; $\text{Rf}$ (petroleum ether:ethyl acetate= 7:3 (v/v)) = 0.15; IR (KBr) / $\nu$ (cm$^{-1}$): 3215, 1616, 1529, 1491, 1352, 1247, 1161; $^1$H NMR (Acetone-$d_6$) / $\delta$ ppm: 7.52 (s, 2H, CH), 7.80 (t, $J$ = 7.0 Hz, 2H, ArH), 8.00 (d, $J$ = 7.0 Hz, 2H, ArH), 8.31 (d, $J$ = 7.0 Hz, 2H, ArH), 8.39 (s, 2H, ArH), 10.38 (s, 2H, NH) ppm; $^{13}$C NMR (Acetone-$d_6$) / $\delta$ ppm: 72.0 (CH), 119.43 (CH), 122.55 (CH), 129.88 (CH), 133.76 (CH), 145.50 (CH), 148.60 (CH), 158.09 (CH), 184.11 (C=S) ppm; CHN$_{analysed}$ (%): C (58.89), H (4.29), N (17.18), S (19.63); CHN$_{found}$ (%): C (58.82), H (4.39), N (17.34), S (19.73).
2.5.1.4. Tetrahydro-3,7-bis (2-chlorophenyl)-[1,2,4] triazole [1,2-a] [1,2,4] triazole-1,5-dithione (petroleum ether:ethylacetate= 7:3 (v/v)) = 0.35; 13C NMR (DMSO-d6, 100 MHz) δ ppm: 55.73 (CH3), 77.03 (CH), 114.76 (CH), 127.67 (CH), 130.0 (C), 160.35 (C), 184.0 (C=S); ppm; CHNcalculated (%): C (55.96), H (4.46), N (14.51), S (16.58); CHNfound (%): C (55.93), H (4.76), N (14.72), S (16.68). 17

2.5.1.5. Tetrahydro-3,7-bis (chlorophenyl)-[1,2,4] triazole [1,2-a] [1,2,4] triazole-1,5-dithione (3d): white solid, m.p= 197 °C; Rf (petroleum ether:ethylacetate= 7:3 (v/v)) = 0.35; IR (KBr / cm-1): 3433, 3182, 2929, 1498,1251; 1H NMR (Acetone-d6, 400 MHz)/ δ ppm: 7.16 (s, 1H, CH), 7.34-7.36 (m, 1H, Ar-H), 11.48 (s, 1H, NH); 13C NMR (DMSO-d6, 100 MHz) δ ppm: 74.86 (CH), 128.14 (CH), 128.63 (CH), 130.62 (CH), 131.87 (CH), 132.48 (C), 134.01 (C), 185.19 (C=S) ppm; CHNcalculated (%): C (48.60), H (3.04), N (14.18), S (16.20); CHNfound (%): C (48.32), H (3.13), N (13.11), S (16.29), Cl (17.81). 17

2.5.1.6. Tetrahydro-3,7-bis (4-chlorophenyl)-[1,2,4] triazole [1,2-a] [1,2,4] triazole-1,5-dithione (3f): white solid, m.p= 194-195 °C; Rf (petroleum ether:ethylacetate= 7:3 (v/v)) = 0.35; IR (KBr / cm-1): 3438, 3168, 2925, 1492, 1249, 1157; 1H NMR (acetone-d6, 400 MHz)/ δ ppm: 7.07 (s, 1H, CH), 7.47-7.51 (m, 3H, Ar-H), 7.55 (s, 1H, Ar-H), 10.14 (s, 1H, NH); 13C NMR (DMSO-d6, 100 MHz) δ ppm: 76.62 (CH), 124.88 (CH), 126.39 (CH), 128.12 (CH), 131.84 (CH), 134.15 (C), 139.76 (C), 184.47 (C=S) ppm; CHNcalculated (%): C (48.60), H (3.04), N (14.18), S (16.20), Cl (17.72); CHNfound (%): C (48.32), H (3.13), N (13.11), S (16.29), Cl (17.81). 17

2.5.1.7. Tetrahydro-3,7-bis (3-hydroxyphenyl)-[1,2,4] triazole [1,2-a] [1,2,4] triazole-1,5-dithione (3g): white solid, m.p= 165-167 °C; Rf (petroleum ether:ethylacetate= 7:3 (v/v)) = 0.12; IR (KBr / cm-1): 3423, 3177, 2958, 1601, 1505, 1250; 1H NMR (Acetone-d6, 400 MHz)/ δ ppm: 6.95 (s, 4H, Ar-H), 7.24 (s, 1H, CH), 8.62 (s, 1H, OH), 9.97 (s, 1H, NH); 13C NMR (Acetone-d6, 100 MHz) δ ppm: 73 (CH), 112.08 (C), 113.88 (CH), 119.03 (CH), 124.00 (CH), 145.50 (CH), 151.09 (C), 184.0 (C=S) ppm; CHNcalculated (%): C (53.70), H (3.88), N (15.04), S (17.68), O (9.70); CHNfound (%): C (53.76), H (3.58), N (15.34), S (17.74), O (9.66). 17

2.5.1.8. Tetrahydro-3,7-bis (3-methoxyphenyl)-[1,2,4] triazole [1,2-a] [1,2,4] triazole-1,5-dithione (3h): white solid, m.p= 177-180 °C; Rf (petroleum ether:ethylacetate= 7:3 (v/v)) = 0.06; IR (KBr / cm-1): 3422, 2929, 1510, 1278, 1133; 1H NMR (Acetone-d6, 400 MHz)/ δ ppm: 3.81 (s, 6H, OCH3), 6.86 (s, 2H, CH), 6.97-7.40 (m, 6H, ArH), 7.89 (s, 2H, OH), 9.88 (s, 2H, NH) ppm; 13C NMR (Acetone-d6, 100 MHz) δ ppm: 55.40 (OCH3), 77.09 (CH), 111.54 (CH), 112.79 (CH), 130.32 (CH), 129.98 (C), 146.91 (C), 148.37 (C), 185.00 (C=S); CHNcalculated (%): C (51.52), H (4.29), N (13.35), S (15.55), O (15.29); CHNfound (%): C (51.34), H (4.83), N (12.88), S (14.98), O (15.97).
Figure 1. The XRD patterns of (a) Fe$_3$O$_4$, (b) Fe$_3$O$_4$@SiO$_2$, and (c) Fe$_3$O$_4$@SiO$_2$-TiO$_2$.

Figure 2. The EDAX of Fe$_3$O$_4$@SiO$_2$-TiO$_2$ nanocatalyst.

Figure 3. SEM image of the a) Fe$_3$O$_4$, b) Fe$_3$O$_4$@SiO$_2$, and c) Fe$_3$O$_4$@SiO$_2$-TiO$_2$ nanocatalyst. TEM image of the d) Fe$_3$O$_4$@SiO$_2$ and e) Fe$_3$O$_4$@SiO$_2$-TiO$_2$.

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) were recorded to understand morphological changes occurring on the magnetic catalyst and also the size and shape of the nanoparticles.

The SEM and TEM images of synthesized samples are shown in Figure 3. The SEM image of Fe$_3$O$_4$ MNPs have a mean diameter lower than 20 nm a nearly spherical shape (Figure 3a). Figure 3b shows that Fe$_3$O$_4$@SiO$_2$ nanoparticles keep the morphological properties of Fe$_3$O$_4$ MNPs except for a larger particle size and smoother surface. The TEM image shown in Fig. 3d demonstrates that silica is successfully coated on the Fe$_3$O$_4$NPs with a thin layer of different phase to form silica shell. So, Fe$_3$O$_4$@SiO$_2$ is nearly in core-shell structure.

Then, the chemical nature of the magnetic catalyst was surveyed. The SEM and TEM images in Fig. 3c and 3e show that Fe$_3$O$_4$@SiO$_2$-TiO$_2$ nanocatalyst have a larger particle size than Fe$_3$O$_4$@SiO$_2$ nanoparticles (about 30 nm in size) and nearly spherical shape. The nanocatalyst shows some aggregation, which was due to calcination at 450 °C.39
In order to explore the molecular structures of Fe₃O₄, Fe₇O₈@SiO₂, and Fe₇O₈@SiO₂-TiO₂, the FT-IR analysis was investigated. Figure 4 shows the FT-IR spectra recorded in the range of 4000–400 cm⁻¹. The main absorption peaks 3423 and 570 cm⁻¹ were assigned to O-H and Fe-O stretching vibration modes of pure Fe₇O₈ NPs, respectively (Figure 4a). The absorption peak of SiO₂-coated sample at 450 cm⁻¹ is due to the Si-O-Fe bond.

The bands at 1073 cm⁻¹ and 803 cm⁻¹ are characteristic peaks of the symmetrical and asymmetrical vibrations of Si-O-Si (Figure 4b). The peak at 451 cm⁻¹ is an indication of the presence of Si-O-Fe. Figure 4c show the IR spectra of TiO₂-modified Fe₇O₈@SiO₂ NPs. From this spectrum, the appearance of a new peak at 636 cm⁻¹ indicates the formation of Si-O-Ti surface structures and successful linking of the TiO₂ onto the Fe₇O₈@SiO₂ MNPs. There was no evidence for interaction between Ti and Fe in the IR spectra. It indicates that Fe₇O₈ is encapsulated by the SiO₂ layer well. So, the catalytic property of Fe₇O₈@SiO₂-TiO₂ is not reduced by this interaction.

The magnetization curves of Fe₇O₈, Fe₇O₈@SiO₂, and Fe₇O₈@SiO₂-TiO₂ were recorded in Figure 5. The magnetic property of the Fe₇O₈@SiO₂-TiO₂ magnetic catalyst were examined and were compared with the magnetic properties of Fe₇O₈ and Fe₇O₈@SiO₂. VSM study indicated a decrease in the magnetic saturation of Fe₇O₈@SiO₂-TiO₂ composite due to the non-magnetic nature of the shell NPs.

Room temperature specific magnetization versus applied magnetic field curve measurements of the Fe₇O₈@SiO₂-TiO₂ indicated the saturation magnetization value (Ms) of 31 emu g⁻¹, which is slightly lower than that of the Fe₇O₈@SiO₂ (46.94 emu g⁻¹) and uncoated Fe₇O₈ MNPs (55.70 emu g⁻¹).

3.2. Application of Fe₇O₈@SiO₂-TiO₂ nanocomposite as a heterogeneous catalyst in the synthesis of tetrahydro-[1,2,4]triazolo[1,2-a][1,2,4] triazole-1,5-dithione derivatives.

In this research, we tried to prepare tetrahydro-[1,2,4]triazolo[1,2-a][1,2,4] triazole-1,5-dithione derivatives from the reaction between aldehyde derivatives and potassium thiocyanate under mild conditions. Titanium dioxide anchored on the surface of the Fe₇O₈@SiO₂ nanoparticles and carried out successfully the cycloaddition reaction. Initially, in order to optimize the reaction conditions, the model reaction was proceeded from the condensation of benzaldehyde and potassium thiocyanate in a 1:2 ratio at room temperature for the synthesis of compound 3a using TiO₂, Fe₇O₈, or Fe₇O₈@SiO₂-TiO₂ as a catalyst. Fe₇O₈@SiO₂-TiO₂ acted as a highly efficient magnetic catalyst to synthesize perhydro[1,2,4]triazolo[1,2-a][1,2,4] triazole-1,5-dithione (3a) and afforded the product in higher yield and lower reaction time compared with other catalysts (Table 1). Also, other advantages of the current catalyst are simple separation and recoverable of Fe₇O₈@SiO₂-TiO₂ compared with reported catalysts. With notice to above results, the importance of Fe₇O₈@SiO₂-TiO₂ composite nanoparticles as a heterogeneous catalyst was revealed in this study and therefore it was selected as the efficient catalyst for further work.

Table 1: The synthesis of tetrahydro-3,7-diphenyl-[1,2,4] triazolo[1,2-a][1,2,4] triazole-1,5-dithione by various catalysts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Yield (%)</th>
<th>Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BF₃</td>
<td>85</td>
<td>21 [Ref. 16]</td>
</tr>
<tr>
<td>2</td>
<td>SbCl₅</td>
<td>88</td>
<td>21 [Ref. 16]</td>
</tr>
<tr>
<td>3</td>
<td>ZrCl₄</td>
<td>82</td>
<td>21 [Ref. 16]</td>
</tr>
<tr>
<td>4</td>
<td>TiCl₄</td>
<td>97</td>
<td>21 [Ref. 16]</td>
</tr>
<tr>
<td>5</td>
<td>TiO₂</td>
<td>97</td>
<td>31</td>
</tr>
<tr>
<td>6</td>
<td>Fe₇O₈ NPs</td>
<td>96</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>Fe₇O₈@SiO₂-TiO₂ NPs</td>
<td>98</td>
<td>17</td>
</tr>
</tbody>
</table>

The obtained results of the reaction to determine the optimum amount of magnetic catalyst are shown in Table 2. The reaction slowly proceeded in low yield without catalyst. The higher yield of the corresponding product was obtained in shorter time with an increase in the amount of magnetic nanocatalyst. As can be seen from Table 1, comparison of the results shows a better yield using 0.04 g of catalyst to synthesize of tetrahydro-[1,2,4] triazole[1,2-a][1,2,4] triazole-1,5-dithiones in the presence of Fe₇O₈@SiO₂-TiO₂. While a higher amount of the catalyst did not show any change in reaction time and yield of the corresponding product.

To demonstrate the advantage of the present work, we compared the results of Fe₇O₈@SiO₂-TiO₂ magnetic catalyst as a catalyst in the synthesis of tetrahydro-[1,2,4] triazole[1,2-a][1,2,4] triazole-1,5-dithiones in the presence of various solvents (Table 3). It can be...
seen from Table 2 that the present CH$_3$CN was found to be the most efficient solvent among tested solvents in term of reaction time of the desired products in the presence of Fe$_3$O$_4$-SiO$_2$-TiO$_2$.

Table 2. The synthesis of tetrahydro-3,7-diphenyl-[1,2,4] triazolo [1,2-a] [1,2,4] triazole-1,5-dithione under different amounts of the magnetic catalyst.*

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst loading (g)</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>blank</td>
<td>60</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>0.01</td>
<td>35</td>
<td>79</td>
</tr>
<tr>
<td>3</td>
<td>0.02</td>
<td>23</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>0.03</td>
<td>17</td>
<td>97</td>
</tr>
<tr>
<td>5</td>
<td>0.04</td>
<td>17</td>
<td>98</td>
</tr>
<tr>
<td>6</td>
<td>0.05</td>
<td>17</td>
<td>98</td>
</tr>
</tbody>
</table>

* Reaction condition: aldazine (1 mmol), KSCN (2 mmol) AcOH (0.18 mL) and CH$_3$CN (6 mL) at room temperature.

Table 3. The solvent effects on time and yield of tetrahydro-3,7-diphenyl-[1,2,4] triazolo [1,2-a] [1,2,4] triazole-1,5-dithione in the presence of magnetic catalyst.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DMSO</td>
<td>20</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>CH$_3$CN</td>
<td>17</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>H$_2$O</td>
<td>25</td>
<td>63</td>
</tr>
<tr>
<td>4</td>
<td>EtOH</td>
<td>25</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>CHCl$_3$</td>
<td>37</td>
<td>45</td>
</tr>
</tbody>
</table>

* Reaction conditions: aldazine (1 mmol), KSCN (2 mmol), AcOH (0.18 mL), Fe$_3$O$_4$-SiO$_2$-TiO$_2$ (0.04 g) and CH$_3$CN (6 mL) at room temperature.

After establishing the optimal conditions, the scope of the cycloaddition reaction between potassium thiocyanate and several aldehyde derivatives were carried out at ambient temperature according to the general experimental procedure (Table 4). As can be seen from this Table, benzaldazine bearing ortho substituent (Table 4, entry 4) slightly afford lower yield than benzaldazines bearing meta or para substituents. This is possibly due to the steric effect. There is more steric hindrance for the 2-substituted benzaldazine on the product formation than the 3- or 4-substituted benzaldazines.

In the case of aldehyde derivatives with a hydroxyl group at 2-position (Table 4, entries 9 and 10), the desired products were not synthesized. This is possibly due to tautomeric phenomena of these compounds.

Table 5. The cycloaddition reaction using the recycled Fe$_3$O$_4$-SiO$_2$-TiO$_2$ magnetic catalyst.

<table>
<thead>
<tr>
<th>Run</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield (%)</td>
<td>98</td>
<td>98</td>
<td>97</td>
<td>97</td>
<td>97</td>
<td>96</td>
<td>93</td>
</tr>
</tbody>
</table>
3.3. The proposed reaction mechanism

One of the significant advantage of the present catalyst is a large number of empty d-orbitals of the TiO$_2$ and the low amount of nanocatalyst used in the reaction. The magnetically separable TiO$_2$ catalyst show great catalytic activity. The features of the Ti centres on the surface of TiO$_2$ nanoparticles play an important role in increasing activation of thiocyanate. In fact, titanium dioxide grafted onto the Fe$_3$O$_4$@SiO$_2$ could catalyze the reaction by the coordination of the unfilled orbitals of TiO$_2$. Thus, it is obvious that Fe$_3$O$_4$@SiO$_2$-TiO$_2$ catalytic system increases the rate of reaction. The formation of the corresponding products can be explained by a proposed mechanism (Scheme 3). According to above reason, enhancing the electrophilic property of the thiocyanate has occurred using titanium dioxide supported on Fe$_3$O$_4$@SiO$_2$. Then, amidazone act as dipoles with two molecules of activated thiocyanate as a dipolarophile to form tetrahydro-[1,2,4] triazolo[1,2-a][1,2,4] triazole-1,5-dithiones.

1) KSCN + CH$_2$COOH $\rightarrow$ HSCN

2) HSCN + Fe$_3$O$_4$@SiO$_2$-TiO$_2$ $\rightarrow$ \( \text{N}_2\text{H}_2\text{SH} \)

3) \( \text{N}_2\text{H}_2\text{SH} \)

4) \( \text{N}_2\text{H}_2\text{SH} \)

Scheme 3. The proposed mechanism for the synthesis of tetrahydro-[1,2,4] triazolo[1,2-a][1,2,4] triazole-1,5-dithiones using Fe$_3$O$_4$@SiO$_2$-TiO$_2$.

Conclusions

In this research, we have been described the synthesis of tetrahydro-[1,2,4] triazolo[1,2-a][1,2,4] triazole-1,5-dithiones via condensation of different kinds of amidazone derivatives with potassium isothiocyanate using Fe$_3$O$_4$@SiO$_2$-TiO$_2$ composite nanoparticles as a magnetic nanocatalyst. The reaction in the presence of recent magnetic catalyst indicated a lot of significant advantages such as eco-friendly and recyclable catalyst, excellent product yields, low reaction times and simplicity of work-up.

Acknowledgements

The authors are grateful to University of Kashan for supporting this work by Grant 256722/XVI.

References

Graphical abstract:

An efficient synthesis of perhydro[1,2,4]triazolo[1,2-a][1,2,4] triazole-1,5-dithiones catalyzed by TiO$_2$-functionalized nano-Fe$_3$O$_4$ encapsulated-silica particles as a reusable magnetic nanocatalyst

Javad Safari and Leila Javadian

Immobilization of a nano-TiO$_2$ catalyst on the surface of a magnetic SiO$_2$ support was performed through the reaction of Fe$_3$O$_4$@SiO$_2$ composite with Ti(OC$_4$H$_9$)$_4$ via a simple process. The Fe$_3$O$_4$@SiO$_2$–TiO$_2$ nanocomposite was characterized using scanning electron microscopy (SEM), transmission electron microscopy (TEM), energy dispersive X-ray spectroscopy (EDS), X-ray diffraction (XRD), Fourier transform infrared spectra (FTIR), and vibrating sample magnetometer (VSM). The Fe$_3$O$_4$@SiO$_2$–TiO$_2$ nanocomposite has been found to be an efficient catalyst for the synthesis of perhydro[1,2,4]triazolo[1,2-a][1,2,4] triazole-1,5-dithiones from the condensation of various aldazines and potassium thiocyanate in acetonitrile solvent at room temperature. It has been found that the nanocatalyst was recycled for up to 6 cycles with minimal loss in catalytic activity. The purpose of this research was to provide an easy method for the synthesis of perhydrotriazolotriazole derivatives by a robust and magnetic recoverable catalyst.