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FULL PAPER

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Fe_3O_4@SiO_2@propyl-ANDSA: A new catalyst for the synthesis of tetrazoloquinazolines

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In this paper, a mild and green protocol has been developed for the synthesis of quinazoline derivatives. The catalytic activity of 7-aminonaphthalene-1,3-disulfonic acid-functionalized magnetic Fe_3O_4 nanoparticles (Fe_3O_4@SiO_2@Propyl–ANDSA) was investigated in the one-pot synthesis of new derivatives of tetrahydrotetrazolo[1,5-a]quinazolines and tetrahydrobenzo[h]tetrazolo[5,1-b]quinazolines from the reaction of aldehydes, 5-aminotetrazole, and dimedone or 6-methoxy-3,4-dihyronaphtalen-1(2H)-one at 100 °C in H_2O/EtOH as the solvent. The catalyst was characterized before and after the organic reaction. Fe_3O_4@SiO_2@Propyl–ANDSA showed remarkable advantages in comparison with previous methods. Advantages of the method presented here include easy purification, reusability of the catalyst, green and mild procedure, and synthesis of new derivatives in high yields within short reaction time.

KEYWORDS
green chemistry, magnetic nanoparticles, nano catalyst, quinazoline derivatives

1 | INTRODUCTION

The synthesis of organic compounds *via* green, mild, and simple procedures is currently receiving significant attention of chemists. In this regard, multicomponent reactions have been emerged as highly valuable synthetic routes for the rapid synthesis of diverse and complex heterocyclic scaffolds.

In recent years, metal oxide nanostructures including iron have attracted a great deal of attention. They have been demonstrated to be applicable in catalyst technology which cannot be usually achieved by their bulk counterparts.[1]

The synthesis of new heterocyclic compounds has been always a subject of great interest, due to their wide applications. Quinazolines and their derivatives represent one of the most important classes of heterocyclic compounds possessing a wide range of pharmacological and biological activities.[2] 5-Amino-tetrazole is known to be a part of certain drugs such as Corazol, Cefazolin, and Cefoperazone.[3] Cefoperazone is an effective antibiotic[4] and Cefazolin is an antibiotic used for the treatment of a number of bacterial infections.[5]

The reaction of keto acid esters with a mixture of aromatic aldehydes and 5-amino-tetrazole is the main method used for the synthesis of these heterocyclic compounds.[6]

The reaction of methyl esters of acylpyruvic acids with 5-amino-tetrazole or 3-amino-1,2,4-tetrazole proceeds similarly to give quinazoline derivatives.[7] Furthermore, it has been found that fusion of various acetylacetate with a mixture of aromatic aldehydes and 5-amino-tetrazole affords dihydrotetrazolo[1,5-*a*]pyrimidine derivatives.[8] These methods have been accomplished in the presence of different catalysts such as *p*-TSA,[9] acetic acid,[10] and I_2.[11] Although these protocols find certain merits of their own, they still suffer from a number of disadvantages such as the use of expensive or toxic catalysts, high reaction temperatures, low product yields and long reaction times. Therefore, there is still a demand for simple and facile synthetic methods in order to obtain these heterocyclic compounds under green reaction conditions.

In the present study, an efficient procedure has been described for the synthesis of tetrahydrotetrazolo[1,5-*a*] quinazolines and tetrahydrobenzo[*h*]tetrazolo[5,1-*b*] quinazolines in excellent yields from the reaction of aldehydes, 5-aminotetrazole, and dimedone or 6-methoxy-3,4-dihyronaphtalen-1(2*H*)-one at 100 °C in H_2O/EtOH as the solvent. 7-Aminonaphthalene-1,3-disulfonic acid-functionalized Fe_3O_4 magnetic nanoparticles (Fe_3O_4@SiO_2@Propyl–ANDSA)[12] was utilized as a novel catalyst in these reactions (Figure 1). With its operational simplicity, green nature, and high yields the reaction will be acting as an attractive alternative for the synthesis of tetrazoloquinazolines.

2 | EXPERIMENTAL SETUP

2.1 | Chemicals and instruments

All commercially available chemicals were obtained from Merck and Fluka companies, and used without further purification unless otherwise stated. Nuclear magnetic resonance (NMR) spectra were recorded in DMSO-d_6 on Bruker Avancespectrometers of 90 MHz, 400 MHz for ^{1}H NMR and 75 MHz and 100 MHz for ^{13}C NMR using TMS as an internal standard; chemical shifts were expressed in parts per million (ppm). Mass spectra were recorded on a Shimadzu QP 1100 BX Mass Spectrometer. Melting points were determined on a Stuarf Scientific SMP3 apparatus. Elemental analyses, (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer. Fourier transform infrared (FT-IR) spectra were recorded with a Shimadzu 435-U-04 FT spectrophotometer from KBr pellets. Scanning electron microscopy (SEM) was performed on EM3200 instrument operated at 30 kV accelerating voltage. The qualitative analysis of Fe_3O_4@SiO_2@Propyl–ANDSA was performed by using energy-dispersive X-ray spectroscopy (EDX). Energy dispersive X-ray analysis of the prepared catalyst was performed on a FESEM-SIGM (Germany) instrument. To measure the magnetic attributes of the samples, vibrating sample magnetometry (VSM) was utilized (MDKFT instrument).

2.2 | Preparation of 7-aminonaphthalene-1,3-disulfonic acid-functionalized magnetic Fe_3O_4 nanoparticles (Fe_3O_4@SiO_2@propyl–ANDSA)

There are totally four major steps for the synthesis procedure of the magnetic Fe_3O_4@SiO_2@Propyl–ANDSA. Firstly, naked magnetic Fe_3O_4 nanoparticles were prepared through coprecipitation of iron(II) and iron(III) ions.[13] Secondly, the magnetic NPs were coated with a silica shell by using tetraethylorthosilicate (TEOS). Thirdly, the Fe_3O_4@SiO_2 nanoparticles were coated by (3-chloropropyl)-triethoxysilane, yielding the chloro functionalized nanoparticles (Fe_3O_4@SiO_2@Cl MNPs).[14] Finally, the Fe_3O_4@SiO_2@Cl nanoparticles reacted with 7-aminonaphthalene-1,3-disulfonic acid to yield Fe_3O_4@SiO_2@Propyl–ANDSA.[12] The acidic content of Fe_3O_4@SiO_2@Propyl–ANDSA was characterized by determination of H^+ of the catalyst through back titration with NaOH (0/1 mol/L). The mol% H^+ of catalyst was found to be 1.8 and 1.65 mol%, before and after recycling, respectively.

2.3 | General procedure for the synthesis of tetrazoloquinazolines using Fe_3O_4@SiO_2@propyl–ANDSA

A mixture of substituted benzaldehyde (1 mmol), 2-amino tetrazole (1 mmol), and dimedone (1 mmol) or 6-methoxy-3,4-dihydronaphtalen-1(2*H*)-one (1 mmol) in H_2O: EtOH (1:1) as the solvent (2 mL) and in the presence of Fe_3O_4@SiO_2@Propyl–ANDSA (0.2 g ~ 1.8 mol%) was stirred for appropriate time at 100 °C. After completion of the reaction, the nanocatalyst was separated using an external magnet. Subsequently, the solvent was evaporated and 95% EtOH (5 mL) was added. The precipitate was then filtered off and washed with cold

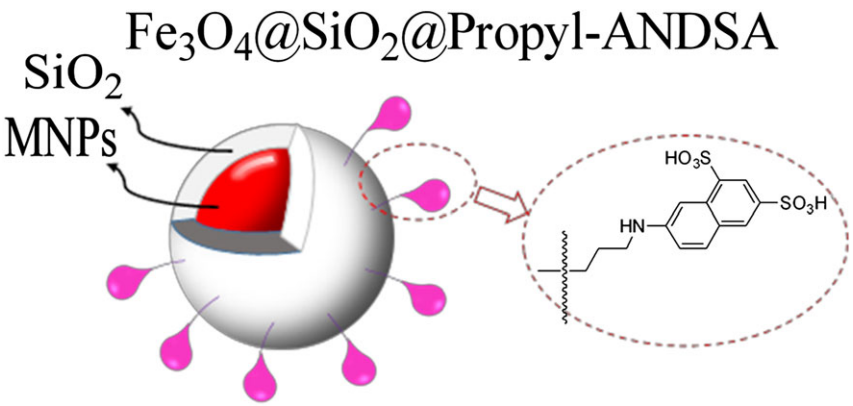


FIGURE 1 The structures of Fe_3O_4@SiO_2@Propyl–ANDSA.

ethanol. After drying, the pure product was obtained and characterized *via* different techniques.

2.4 | Analytical data of selected products

2.4.1 | 6,6-Dimethyl-9-(2-methoxyphenyl)-5,6,7,9-tetrahydrotetrazolo[1,5-a]quinazolin-8(4H)-one

White solid, **5b,** mp: 277-279 °C. ^{1}HNMR (90 MHz, DMSO-d_6): δ_H (ppm) 0.92 (s,CH_3, 3H), 1.04 (s, CH_3, 3H), 2.09 (s, CH_2, 2H), 2.52 (s, CH_2, 2H), 3.61 (s, OCH_3, 3H), 6.67 (s, CH, 1H), 6.88–7.42 (m, CH aromatic,4H), 11.47 (s, NH, 1H), ^{13}C NMR (75 MHz, DMSO-d_6): δ_c (ppm) 26.60, 29.13, 32.59, 50.34, 55.60, 55.92, 105.16, 112.09, 120.50, 127.86, 130.30, 130.66, 149.61, 151.17, 157.51, 193.22, ppm; Mass (m/z): 325, Anal. Calcd for $C_{17}H_{19}N_5O_2$: C, 62.75; H, 5.89; N, 21.52. Found: C,62.70; H, 5.91; N; 21.29.

2.4.2 | 6,6-Dimethyl-9-(3-methoxyphenyl)-5,6,7,9-tetrahydrotetrazolo[1,5-a]quinazolin-8(4H)-one

White solid, **5c,** mp: 232-233 °C. ^{1}HNMR (90 MHz, DMSO-d_6): δ_H (ppm) 1.01 (s,CH_3, 3H), 1.06 (s, CH_3, 3H), 2.20 (s, CH_2, 2H), 2.60 (s, CH_2, 2H), 3.71 (s, OCH_3, 3H), 6.56 (s, CH, 1H), 6.85–7.33 (m, CH aromatic,4H), 11.55 (s, NH, 1H), ^{13}C NMR (75 MHz, DMSO-d_6): δ_c (ppm): 27.39, 28.77, 32.74, 50.28, 55.54, 57.74, 105.97, 113.80, 119.64, 130.26, 142.31, 148.88, 151.04, 159.73, 193.48 ppm; Mass (m/z): 325, Anal. Calcd for $C_{17}H_{19}N_5O_2$: C, 62.75; H, 5.89; N, 21.52. Found: C, 62.80; H, 5.84; N, 21.54.

2.4.3 | 6,6-Dimethyl-9-(2,3-dichlorophenyl)-5,6,7,9-tetrahydrotetrazolo[1,5-a]quinazolin-8(4H)-one

White solid, **(5e)**, mp: 305-307 °C. ^{1}HNMR (90 MHz, DMSO-d_6): δ_H (ppm) 1.01 (s,CH_3, 3H), 1.05 (s, CH_3, 3H), 2.16 (s, CH_2, 2H), 2.58 (s, CH_2, 2H), 6.97 (s, CH, 1H), 7.38–7.61 (m, CH aromatic,3H), 11.72 (s, NH, 1H), ^{13}C NMR (75 MHz, DMSO-d_6): δ_c (ppm) 27.52, 28.64, 32.66, 50.23, 55.82, 104.71, 128.07, 129.74, 132.62, 133.67, 134.30, 136.50, 149.01, 151.83, 193.41, ppm; Mass (m/z): 364, Anal. Calcd for $C_{16}H_{15}$ Cl_2N_5O: C, 52.76; H, 4.15; N, 19.23. Found: C,52.74; H, 3.99; N, 19.24.

2.4.4 | 6,6-Dimethyl-9-(3-bromophenyl)-5,6,7,9-tetrahydrotetrazolo[1,5-a]quinazolin-8(4H)-one

White solid, **5f**, mp: 243-244 °C. ^{1}HNMR (90 MHz, DMSO-d_6): δ_H (ppm) 1.00 (s,CH_3, 3H), 1.04 (s, CH_3, 3H), 2.19 (s, CH_2, 2H), 2.60 (s, CH_2, 2H), 6.62 (s, CH, 1H), 7.24–7.54 (m, CH aromatic,4H), 11.65 (s, NH, 1H), ^{13}C NMR (75 MHz, DMSO-d_6): δ_c (ppm): 27.30, 28.60, 32.70, 50.10, 57.37, 105.48, 122.15, 126.61, 130.55, 131.40, 131.80, 143.11, 148.73, 151.68, 194.05, ppm; Mass (m/z): 373, Anal. Calcd for $C_{16}H_{16}$ BrN_5O: C, 51.35; H, 4.31; N, 18.71. Found: C,51.36; H, 4.23; N, 18.62.

2.4.5 | 3-Methoxy-7-(3-methoxyphenyl)-5,6,7,12-tetrahydrobenzo[h]tetrazolo[5,1-b]quinazoline

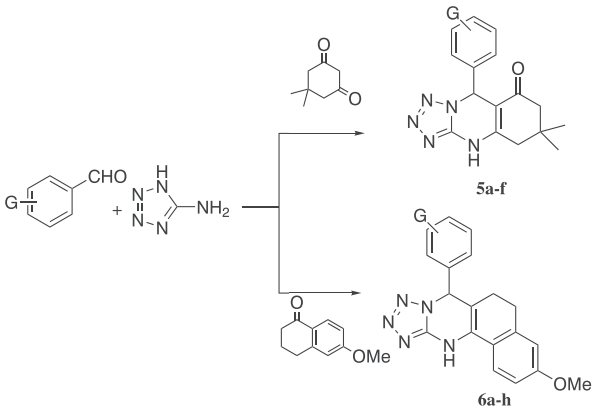
White solid, **6a**, mp: 258-260 °C. ^{1}HNMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.8 (ddd, J = 10.0, 6.4, 4.0 Hz, CH, 1H), 2.19 (t, J = 7.2 Hz, CH, 1H), 2.64 (t, J = 7.2 Hz, CH, 1H), 2.75 (ddd, J = 10.0, 6.4, 4.0 Hz, CH, 1H), 3.74 (s, OCH_3, 3H), 3.78 (s, OCH_3, 3H), 6.41(s, CH, 1H), 6.84 (ddd, J = 11.6, 9.2, 6.4 Hz, CH aromatic, 1H), 6.92–6.95 (m, CH aromatic, 4H), 7.32 (dd, J = 16.0, 8.0 Hz, CH aromatic, 1H), 7.65 (d, J = 8.8 Hz, CH aromatic, 1H), 10.40 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 24.06, 28.16, 55.62, 55.67, 56.18, 61.84, 104.07, 111.71, 114.02, 114.28, 119.89, 121.59, 123.88, 127.51, 130.74, 138.44, 141.41, 150.95, 159.76, 159.97 ppm; Mass (m/z): 361, Anal. Calcd for $C_{20}H_{19}N_5O_2$:C, 66.47; H, 5.30; N, 19.38. Found: C, 66.14; H, 4.72; N, 19.36.

2.4.6 | 3-Methoxy-7-(4-fluorophenyl)-5,6,7,12-tetrahydrobenzo[h]tetrazolo[5,1-b]quinazoline

White solid, **6b**, mp: 256-257 °C. ^{1}HNMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.80 (t, J = 6.4 Hz, CH, 1H), 2.16 (ddd, J = 16.0, 10.0, 8.0 Hz, CH, 1H), 2.65 (t, J = 7.2 Hz, CH, 1H), 2.72–2.80 (ddd, J = 16.0, 9.6, 6.0 Hz, CH, 1H), 3.3 (s, OCH_3, 3H), 6.50 (s, CH, 1H), 6.85 (ddd, J = 11.6, 7.6, 2.8 Hz, CH, 1H), 6.9 (ddd, J = 11.6, 7.6, 2.8 Hz, CH, 1H), 7.23(d, J = 8.8 Hz, CH aromatic, 2H),7.34 (d, J = 8.8 Hz, CH aromatic, 2H), 7.66 (d, J = 8.8 Hz, CH aromatic, 1H), 10.44 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 24.06, 28.15, 55.66, 61.15, 103.76, 111.71, 114.27, 116.23, 116.44, 121.56, 123.95, 127.71, 130.20, 130.29, 136.06, 136.08, 138.43, 150.87, 159.80, 161.40, 163.83 ppm; Mass (m/z): 349, Anal. Calcd for $C_{19}H_{16}$ FN_5O: C, 65.32; H, 4.62; N, 20.05. Found: C, 65.81; H, 4.26; N, 19.59.

2.4.7 | 3-Methoxy-7-(2-methoxyphenyl)-5,6,7,12-tetrahydrobenzo[h]tetrazolo[5,1-b] quinazoline

Cream solid, **6c**, mp: 270-272 °C. ^{1}HNMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.77 (ddd, J = 16.0, 10.2, 6.8 Hz, CH, 1H), 2.16 (ddd, J = 16.8, 10.2, 8.0 Hz, CH, 1H), 2.57 (ddd, J = 5.2, 3.6, 1.6 Hz, CH, 1H), 2.74 (ddd, J = 16.0, 10.0, 6.8 Hz, CH, 1H), 3.70 (s, OCH_3, 3H), 3.77 (s, OCH_3, 3H), 6.61(s, CH, 1H), 6.8 (ddd, J = 16.0, 8.4, 2.8 Hz, CH aromatic, 1H), 6.86 (ddd, J = 16.0, 8.4, 2.8 Hz, CH aromatic, 1H), 6.96(ddd, J = 8.4, 7.2, 6.4 Hz, CH aromatic, 1H), 7.00 (d, J = 8.0 Hz, CH, 1H) 7.21 (s, CH aromatic, 1H), 7.34 (ddd, J = 7.6, 2.4, 2.0 Hz, CH, 1H), 7.63 (d, J = 8.8 Hz, CH, 1H), 10.30 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 23.93, 28.19, 55.63, 56.31, 103.69, 111.64, 112.52, 114.21, 121.23, 121.89, 123.64, 127.32, 127.49, 129.48, 130.67, 138.30, 151.59, 157.67, 159.58 ppm; Mass (m/z): 361, Anal. Calcd for $C_{20}H_{19}N_5O_2$: C, 66.47; H, 5.30; N, 19.38. Found: C,65.94; H, 5.04; N, 19.33.



Reaction condition: Fe_3O_4@SiO_2@Propyl-ANDSA, H_2O/EtOH, 100 °C

SCHEME 1 One-pot synthesis of tetrahydrotetrazolo[1,5-*a*] quinazolines and tetrahydrobenzo[*h*]tetrazolo[5,1- *b*]quinazolines

2.4.8 | 3-Methoxy-7-(4-methylphenyl)-5,6,7,12-tetrahydrobenzo[h]tetrazolo[5,1-b] quinazoline

White solid, **6d**, mp: 257-258 °C. ^{1}HNMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.79 (ddd, J = 16.0, 10.0, 6.4 Hz, CH, 1H), 2.15 (ddd, J = 22.2, 16.8, 9.6 Hz, CH, 1H), 2.28

TABLE 1 Optimizing the reaction conditions for the synthesis of 9-(4-chlorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydrotetrazolo[1,5-a] quinazolin-8(4*H*)-one ***5a*** using Fe_3O_4@SiO_2@propyl–ANDSA as the catalyst

Entry	Catalyst	Conditions	Time (min)	Yield[a] (%)
1	-	100 °C	6	-[b]
2	$AlCl_3$ (5 mol%)	EtOH, reflux	5	Trace
3	MNPs@SiO_2-Pr-ANDSA (0.05 g)[c]	100 °C	10	80
4	MNPs@SiO_2-Pr-ANDSA (0.1 g)[c]	100 °C	10	86
5	MNPs@SiO_2-Pr-ANDSA (0.15 g)[c]	100 °C	10	90
6	MNPs@SiO_2-Pr-ANDSA (0.2 g)[c]	100 °C	5	94
7	MNPs@SiO_2-Pr-ANDSA (0.25 g)[c]	100 °C	5	90
8	MNPs@SiO_2-Pr-ANDSA (0.3 g)[c]	100 °C	5	85
9	MNPs@SiO_2 (0.2 g)[c]	100 °C	15	70
10	MNPs@SiO_2-Pr-ANDSA (0.2 g)[c]	90 °C	5	90
11	MNPs@SiO_2-Pr-ANDSA (0.2 g)[c]	110 °C	5	94
12	MNPs@SiO_2-Pr-ANDSA (0.2 g)[d]	120 °C	5	92
13	MNPs@SiO_2-Pr-ANDSA (0.2 g)[d]	130 °C	5	92
14	MNPs@SiO_2-Pr-ANDSA (0.2 g)[d]	100 °C	5	75
15	MNPs@SiO_2-Pr-ANDSA (0.2 g)	MeCN	5	80
16	MNPs@SiO_2-Pr-ANDSA (0.2 g)	H_2O	10	75
17	MNPs@SiO_2-Pr-ANDSA (0.2 g)	EtOH	5	88
18	Fe_3O_4@SiO_2-SO_3H[c]	100 °C	15	80

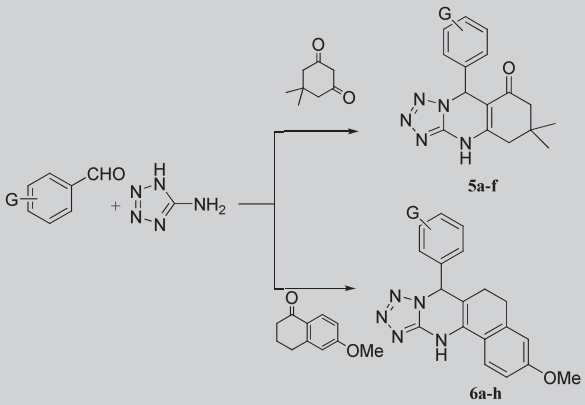
[a]Isolated yield.

[b]No reaction accrued.

[c]Reaction condition: 4-chlorobenzaldehyde (1 mmol), 2-aminotetrazole (1 mmol), and dimedone (1 mmol) in H_2O/EtOH (1:1).

[d]Reaction condition: 4-chlorobenzaldehyde (1 mmol), 2-aminotetrazole (1 mmol), and dimedone (1 mmol) in solvent-free condition.

TABLE 2 Synthesis of tetrahydrotetrazolo[1,5-*a*]quinazolines **5a–f** and tetrahydrobenzo[*h*]tetrazolo[5,1-*b*]quinazolines **6a–h** using Fe_3O_4@SiO_2@propyl–ANDSA[a]



Compd.	G	Time (min)	Yield[b] (%)	m.p.	m.p.[Ref]
5a	4-Cl	5	94	259–260	254–255[10]
5b	2-OMe	10	85	277–279	-------
5c	3-OMe	10	90	232–233	-------
5d	2,4-Cl_2	20	94	280–281	>270[10]
5e	2,3-Cl_2	30	92	305–307	-------
5f	3-Br	40	90	243–244	-------
6a	3-OMe	15	90	258–260	-------
6b	4-F	10	85	256–257	-------
6c	2-OMe	25	88	270–272	-------
6d	4-Me	20	90	257–258	-------
6e	3,4,5-$(OMe)_3$	55	85	262–263	-------
6f	2-Cl	70	85	272–274	-------
6g	4-OMe	35	85	243–245	-------
6h	3-Cl	8	90	258–259	-------

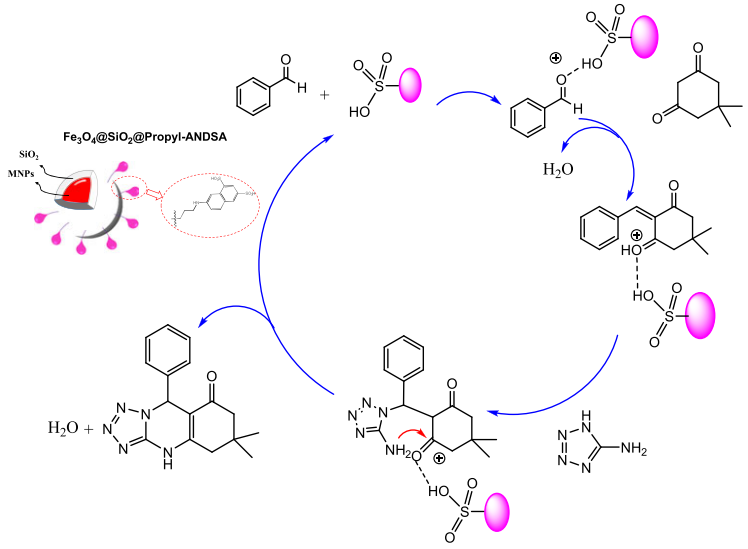
[a]Reaction condition: aldehydes (1 mmol), 5-aminotetrazole (1 mmol), and 6-methoxy-3,4-dihyronaphtalen-1(2*H*)-one (1 mmol), or dimedone (1 mmol).

[b]Isolated yield.

TABLE 3 Comparison of different methods in the synthesis of 6,6-dimethyl-9-aryl-5,6,7,9-tetrahydrotetrazolo[1,5-*a*]quinazoline-8(4*H*)-one **5a**

Entry	Catalyst	Solvent	Conditions	Time	Yield (%)	Ref.
1	I_2	Isopropyl alcohol	Reflux	10 min	92	[11]
2	*p*-TSA	Solvent-free	80 °C	6 min	88	[9]
3	Fe_3O_4@SiO_2@propyl–ANDSA	H_2O/EtOH (1:1)	100 °C	5 min	94	This work

(s, CH_3, 3H), 2.63 (ddd, J = 16.2, 10.2, 6.8 Hz, CH, 1H), 2.74 (ddd, J = 16.0, 10.0, 6.4 Hz, CH, 1H), 3.77 (s, OCH_3, 3H), 6.40 (s, CH, 1H), 6.83 (d, J = 2.4 Hz, CH, 1H), 6.87 (dd, J = 8.8, 2.8 Hz, CH, 1H), 7.19 (d, J = 8.4 Hz, CH aromatic, 2H), 7.22 (d, J = 8.4 Hz, CH aromatic, 2H), 7.64 (d, J = 8.8 Hz, CH, 1H), 10.38 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 20.69, 23.62, 27.67, 55.15, 61.21, 103.66, 111.18, 113.76, 121.07, 123.36, 126.86, 127.43, 129.47, 136.45, 137.88, 138.18, 159.22 ppm; Mass (m/z): 345, Anal. Calcd for $C_{20}H_{19}N_5O$: C, 69.55; H, 5.54; N, 20.28. Found: C,69.58; H, 5.54; N, 20.34.



SCHEME 2 The suggested mechanism for the synthesis of tetrahydrotetrazolo[1,5-*a*]quinazolines **5a–f** in the presence of $Fe_3O_4@SiO_2@$propyl–ANDSA

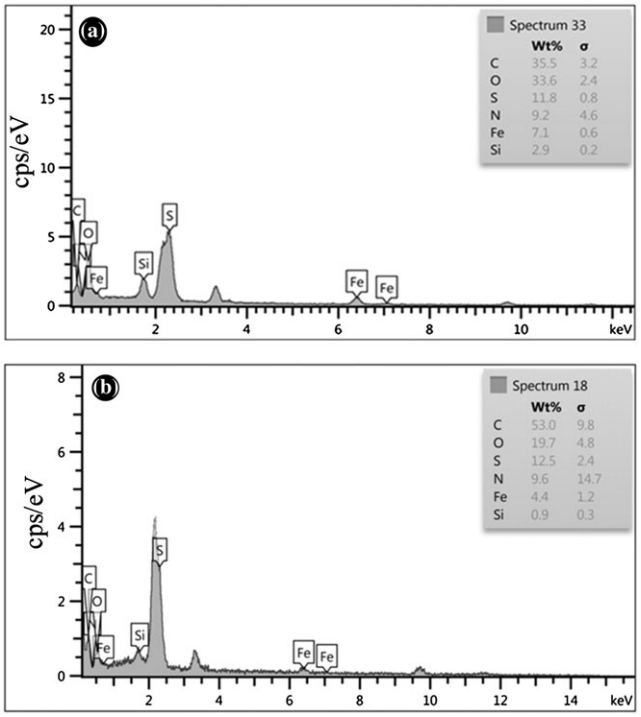


FIGURE 2 EDX spectra of $Fe_3O_4@SiO_2@$propyl–ANDSA before (a) and after (b) the reaction

2.4.9 | 3-Methoxy-7-(3,4,5-trimethoxyphenyl)-5,6,7,12-tetrahydrobenzo[h]tetrazolo[5,1-b] quinazoline

White solid, **6e**, mp: 262-263 °C. ^{1}HNMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.86 (ddd, J = 15.6, 8.8, 6.4 Hz, CH, 1H), 2.18 (ddd, J = 16.0, 7.6, 6.8 Hz, CH, 1H), 2.67 (ddd, J = 15.2, 8.8, 6.4 Hz, CH, 1H), 2.75 (ddd, J = 15.2, 8.8, 6.4 Hz, CH, 1H), 3.65–3.78 (m, OCH_3, 12H), 6.36 (s, CH, 1H), 6.65 (s, CH, 1H), 6.84 (d, J = 2.8 Hz, 1H), 6.88 (dd, J = 2.8, 2.4 Hz, 1H), 7.65 (d, J = 8.8 Hz, 1H), 10.38 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 23.52, 27.79, 55.16, 55.89, 59.92, 61.68, 103.36, 104.85, 111.20, 113.77, 121.10, 123.41, 127.07, 134.92, 137.59, 138.04, 153.16, 159.26 ppm; Mass (m/z): 421, Anal. Calcd for $C_{22}H_{23}N_5O_4$: C, 62.70; H, 5.50; N, 16.62. Found: C, 62.26; H, 5.11; N, 16.64.

2.4.10 | 3-Methoxy-7-(2-chlorophenyl)-5,6,7,12-tetrahydrobenzo[h]tetrazolo[5,1-b] quinazoline

White solid, **6f**, mp: 272-274 °C. ^{1}HNMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.71 (ddd, J = 16.0, 10.0, 6.8 Hz, CH, 1H), 2.13 (ddd, J = 16.0, 11.6, 4.4 Hz, CH, 1H), 2.62 (ddd, J = 15.2, 15.0, 7.2 Hz, CH, 1H), 2.76 (ddd, J = 16.0, 10.4, 6.8 Hz, CH, 1H), 3.77 (s, OCH_3, 3H), 6.80 (s, CH aromatic, 1H), 6.82 (d, J = 2.4 Hz, CH aromatic, 1H), 6.87 (dd, J = 2.8, 2.4 Hz, CH aromatic, 2H), 7.40 (s, CH aromatic, 1H), 7.41 (d, J = 2.8 Hz, CH aromatic, 1H), 7.49 (s, CH aromatic, 1H), 7.65 (d, J = 8.4 Hz, CH aromatic, 2H), 10.50 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 23.26, 27.55, 55.16, 111.22, 113.75, 120.95, 121.01, 123.38, 127.94, 127.98, 128.04, 130.30, 130.35, 130.70, 132.33, 137.88, 159.29 ppm; Mass (m/z): 365, Anal. Calcd for $C_{19}H_{16}ClN_5O$: C, 62.38; H, 4.41; N, 19.14. Found: C, 62.15; H, 4.23; N, 19.15.

2.4.11 | 3-Methoxy-7-(4-methoxyphenyl)-5,6,7,12-tetrahydrobenzo[h]tetrazolo[5,1-b] quinazoline

White solid, **6g**, mp: 243-245 °C. ^{1}HNMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.8 (ddd, J = 16.0, 10.0, 6.4 Hz,

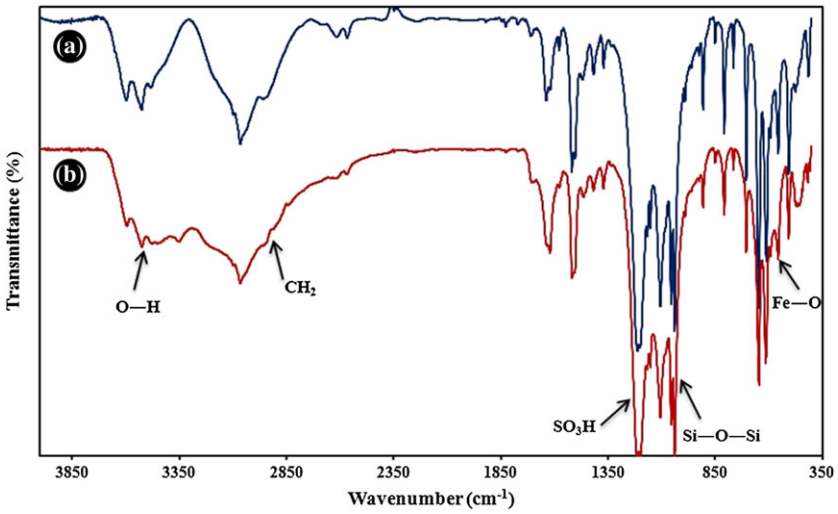


FIGURE 3 FT- IR spectra of Fe_3O_4@SiO_2@propyl–ANDSA before (a) and after (b) the reaction

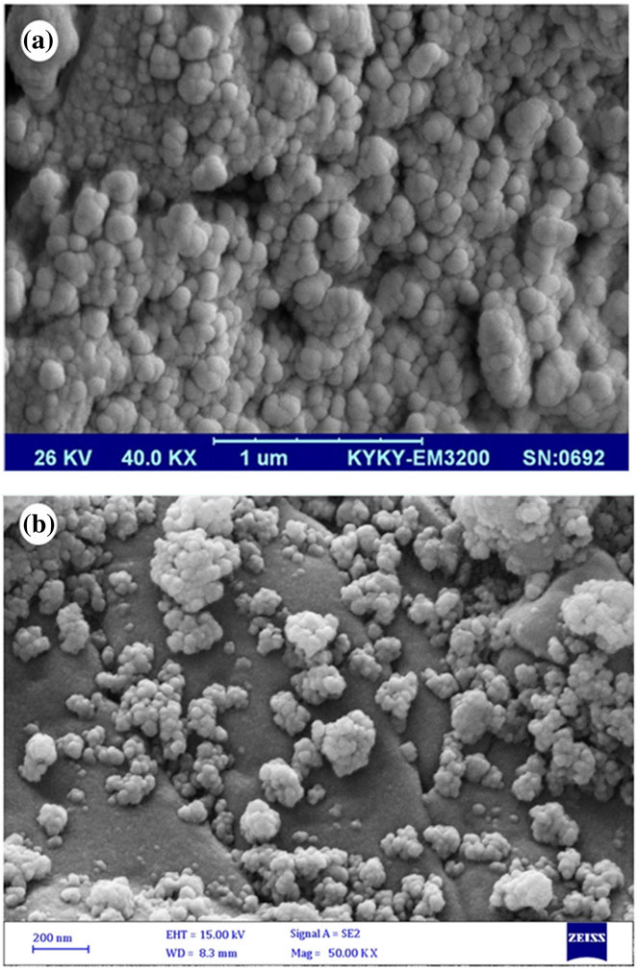


FIGURE 4 SEM images of Fe_3O_4@SiO_2@propyl–ANDSA before (a) and after (b) the reaction

CH, 1H), 2.13 (ddd, J = 16.0, 13.6, 6.8 Hz, CH, 1H), 2.64 (ddd, J = 16.0, 15.2, 7.2 Hz, CH, 1H), 2.74 (ddd, J = 16.0, 10.4, 6.8 Hz, CH, 1H), 3.74 (s, OCH_3, 3H), 3.77 (s, OCH_3, 3H), 6.39 (s, CH, 1H), 6.87 (dd, J = 2.4, 2.0 Hz, CH aromatic, 1H), 6.94 (d, J = 8.4 Hz, CH aromatic, 2H), 7.26 (d, J = 8.4 Hz, CH aromatic, 2H), 7.64 (d, J = 8.4 Hz, CH aromatic, 1H), 10.37 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm) 23.66, 27.69, 55.11, 55.16, 60.93, 103.76, 111.17, 113.76, 114.24, 121.10, 123.35, 128.83, 131.34, 137.89,159.44 ppm; Mass (m/z): 365, Anal. Calcd for $C_{20}H_{19}N_5O_2$: C, 62.47; H, 5.30; N, 19.38. Found: C, 62.08; H, 5.21; N, 19.12.

2.4.12 | 3-Methoxy-7-(3-chlorophenyl)-5,6,7,12-tetrahydrobenzo[h]tetrazolo[5,1-b] quinazoline

White solid, **6h,** mp: 258-259 °C. ^{1}HNMR (400 MHz, DMSO-d_6): δ_H (ppm) 1.79 (ddd, J = 16.4, 10.4, 6.4 Hz, CH, 1H), 2.17 (ddd, J = 16.8, 14.8, 7.2 Hz, CH, 1H), 2.64 (ddd, J = 16.0, 15.2, 6.8 Hz, CH, 1H), 2.75 (ddd, J = 16.0, 10.4, 6.4 Hz, CH, 1H), 3.77 (s, OCH_3, 3H), 6.51 (s, CH, 1H), 6.83 (d, J = 2.4 Hz, CH aromatic, 1H), 6.88 (dd, J = 2.8, 2.4 Hz, CH aromatic, 1H), 7.28 (ddd, J = 5.6, 4.0, 2.4 Hz, CH aromatic, 1H), 7.34 (s, CH aromatic, 1H), 7.45 (m, CH aromatic, 1H), 7.6 (d, J = 8.4 Hz, CH aromatic, 1H), 2.48 (s, NH, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ_c (ppm): 23.45, 27.61, 55.17, 60.73, 102.78, 111.23, 113.78, 120.90, 120.97, 123.52, 126.19, 127.43, 128.86, 131.04, 133.49, 137.93, 141.61, 150.34, 150.43, 159.34 ppm; Mass (m/z): 365, Anal. Calcd for $C_{19}H_{16}ClN_5O$: C, 62.38; H, 4.41; N, 19.14. Found: C, 62.25; H, 4.24; N, 19.12.

3 | RESULTS AND DISCUSSION

As a part of our continuing effort toward the synthesis of tetrazolopyrimidine derivatives[15] and other organic compounds, and in continuation of our interest in the

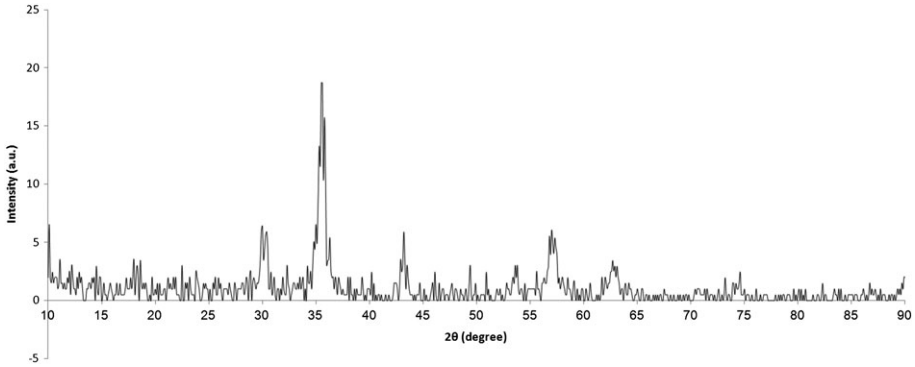


FIGURE 5 XRD pattern of Fe_3O_4@SiO_2@propyl–ANDSA after the reaction

application of nano catalysts in organic reactions,[16] herein, we describe the synthesis of tetrahydrotetrazolo[1,5-*a*]quinazolines and tetrahydrobenzo[*h*]tetrazolo[5,1-*b*]quinazolines through the condensation reaction of substituted aldehydes, 5-aminotetrazole, and dimedone or 6-methoxy-3,4-dihyronaphtalen-1(2*H*)-one in the presence of Fe_3O_4@SiO_2@Propyl–ANDSA (Scheme 1).

Initially, MNPs@SiO_2 was synthesized through a modified method of Stöber,[13] and subsequently, it was functionalized with 7-aminonaphthalene-1,3-disulfonic acid to obtain Fe_3O_4@SiO_2@Propyl–ANDSA. Then, the effect of Fe_3O_4@SiO_2@Propyl–ANDSA as catalyst was investigated in the synthesis of 9-(4-chlorophenyl)-6,6-dimethyl-5,6,7,9-tetrahydrotetrazolo[1,5-a]quinazolin-8(4*H*)-one **5a**. First, the reaction progress was examined in the absence of catalyst and it was observed that the reaction could not proceed without the catalyst even after a prolonged reaction time (Table 1, entry 1). According to Table 1, it was determined that 0.2 g of catalyst is optimal to this reaction, meanwhile less than 0.2 g of the catalyst leads to the low reaction yield (Table 1, entries 3–5). In addition, the yield of product did not increase by increasing the catalyst to more than 0.2 g (Table 1, entries 7–8). Furthermore, different temperatures were tested in this reaction (Table 1, entries 10–13) and it was found that 100 ℃ is the optimal temperature for this reaction (Table 1, entry 6). Then, the effect of different solvents was investigated (Table 1, entries 15–17) and it was concluded that H_2O/EtOH (1:1) is the best choice. In addition, the reaction in the presence MNPs@SiO_2 was less progress compared with MNPs@SiO_2-Pr-ANDSA (Table 1, entry 9). Thus the best result was achieved in the presence of Fe_3O_4@SiO_2@Propyl–ANDSA (0.2 g) in H_2O/EtOH (1:1) as solvent (Table 1, entry 6). All products were fully charectrized on the basis of their spectroscopic data: ^{1}H NMR, ^{13}C NMR, MS and (C, H, N) elemental analysis.

These results encouraged us to investigate the scope and generality of this protocol for various aromatic aldehydes under optimized conditions. As shown in Table 2, both electron-rich and electron-deficient aldehydes gave tetrahydrotetrazolo[1,5-*a*]quinazolines and tetrahydrobenzo[*h*]tetrazolo[5,1-*b*]quinazolines with satisfactory yields.

Literature surveys revealed that various catalysts such as I_2 and *p*-TSA have been employed in this reaction as demonstrated in Table 3. It is obvious from the results that the products were obtained in high yields within shorter reaction times in the current work in comparison with other reported procedures. Therefore, the use of Fe_3O_4@SiO_2@Propyl–ANDSA can significantly improve the product yields and decrease reaction time.

In the next step, the recyclability of Fe_3O_4@SiO_2@Propyl–ANDSA was evaluated in the model reaction. The reusability was tested up to seven consecutive cycles for the synthesis of 6,6-dimethyl-9-aryl-5,6,7,9-tetrahydrotetrazolo[1,5-*a*]quinazoline-8(4*H*)-one **5a** under the optimized reaction conditions and no significant decrease in activity was observed (94, 93, 93, 91, 90, 88, and 86, respectively) and the amount of catalyst that has been used in each cycle was 0.2 g. After completion of the reaction, the catalyst was recovered by washing with EtOH and H_2O and then dried at 50–60 °C in an oven to be used for seven continuous runs.

The proposed mechanism in the presence of Fe_3O_4@SiO_2@Propyl–ANDSA is shown in Scheme 2. It is likely that this catalyst released H^+, which can act as electrophilic species. The initiation step begins with the protonation of aldehydes which in Knoevenagel condensation with dimedone results in the formation of benzylidene compound. Next, Michael addition of 5-aminotetrazole to this intermediate followed by next cyclization results in the final ring system.

The catalyst was analyzed by different methods such as scanning electron microscopy (SEM), transmission electron microscopy (TEM), FT-IR spectroscopy, energy-dispersive X-ray spectroscopy (EDX), thermogravimetric analysis (TGA) and vibrating sample magnetometry

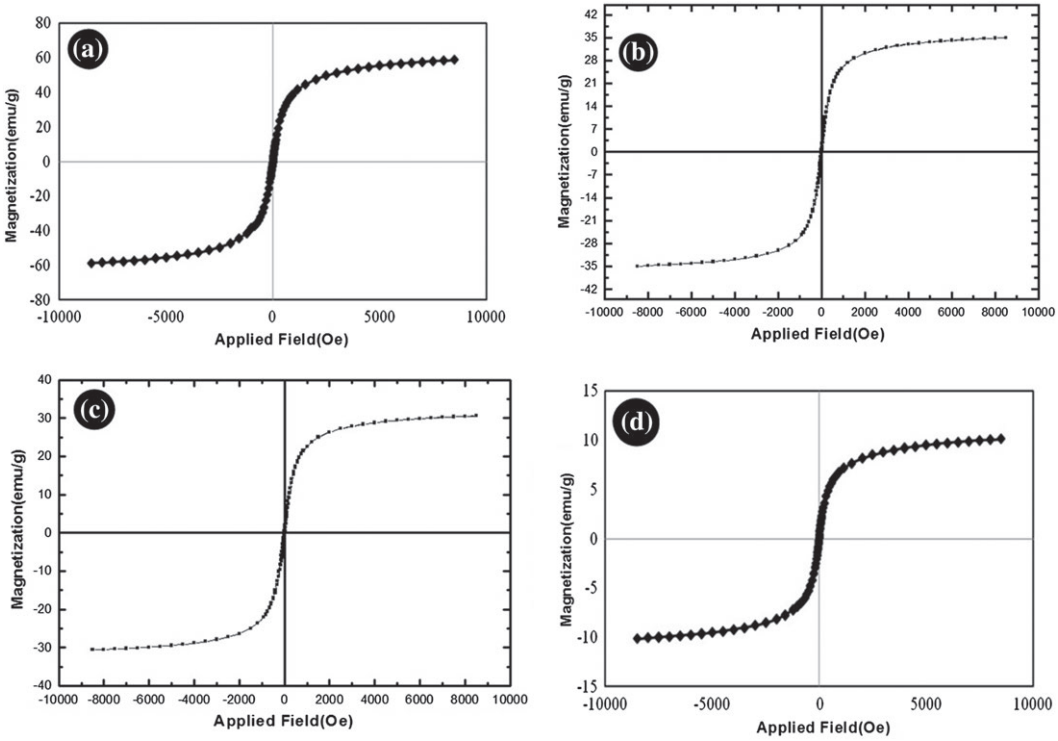


FIGURE 6 Magnetization curves of (a) Fe_3O_4, (b) Fe_3O_4@SiO_2, (c) Fe_3O_4@SiO_2@propyl, and (d) Fe_3O_4@SiO_2@propyl–ANDSA

(VSM) confirming the successful synthesis of Fe_3O_4@SiO_2@Propyl–ANDSA.[12] In addition, the catalyst was characterized after the reaction to compare with its structure before reaction. Fe_3O_4@SiO_2@Propyl–ANDSA was collected after the reaction and subjected to different analyses. The EDX spectra of the catalyst before and after reaction are shown in Figure 2. The EDX spectra of catalyst before and after reaction were almost identical which indicated that there was no obvious change for the catalyst composition after the reaction. In both spectra, the peaks related to O, Si, and Fe elements are present and the characteristic peaks of S and N in Figure 4 indicate that the iron oxide nanoparticles have been successfully coated with ANDSA.

The FT-IR spectra of the catalyst before and after reaction are shown in Figure 3. For FT-IR spectrum, the major bands attributed to Fe—O and O—H stretching vibrations, the presence of sulfonyl moieties, and the characteristic peaks of silica framework were all observed which indicated that the structure of catalyst did not change after the reaction.

Figure 4 displays the SEM images of the catalyst before and after the reaction revealing the maintenance of the morphology of nearly spherical nanoparticles with nanometric dimensions after the reaction.

Figure 5 shows the X-ray diffraction pattern of the catalyst after the reaction. The positions and relative intensities of all characteristic diffractions at 2θ values of 20°, 25.5°, 27.5°, 29°, 30.5° and 32° implies that the original structure of Fe_3O_4@SiO_2@Propyl–ANDSA was successfully preserved after the organic reaction.

The magnetic properties of four major steps in the synthesis of the catalyst were provided via VSM. The magnetization curves of Fe_3O_4, Fe_3O_4@SiO_2, Fe_3O_4@SiO_2@Propyl, and Fe_3O_4@SiO_2@Propyl–ANDSA are shown in Figure 6. The saturation magnetization value of catalyst was found to be 10 emu g^{-1} (Figure 6 d), which is lower than the obtained values for Fe_3O_4, Fe_3O_4@SiO_2, and Fe_3O_4@SiO_2@Propyl.

4 | CONCLUSION

In conclusion, we have developed an efficient and environmental friendly procedure for the synthesis of novel tetrazolo quinazoline derivatives from the reaction of various aldehydes, 5-aminotetrazole, and dimedone or 6-methoxy-3,4-dihyronaphtalen-1(2*H*)-one. The method provided several advantages including excellent product yields, short reaction times, easy purification, recyclability of the catalyst, and simple procedure. The application of Fe_3O_4@SiO_2@Propyl–ANDSA as the catalyst showed efficient catalytic activity for the synthesis of quinazolines due to the presence of two-SO_3H groups of the catalyst which provided efficient acidic sites and excellent catalytic activities.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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