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Efficient multicomponent synthesis of 1,2,3-triazoles catalyzed by Cu(II) supported on PEI@Fe_3O_4 MNPs in a water/PEG_{300} system

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Abstract: A highly dispersible and magnetically recoverable Cu-PEI@Fe_3O_4 MNPs catalyst was prepared and successfully applied in one-pot three-component coupling of terminal alkynes, sodium azide, and alkyl bromides/chlorides in water to give 1,4-disubstituted 1,2,3-triazoles with good to excellent yields. The catalyst was fully characterized with FT-IR, TGA, TEM, SEM, VSM, EDX, cyclic voltammetry, and ICP-AES spectroscopic techniques. Furthermore, the catalyst was easily recycled by an external magnet and successfully reused six times in the reaction without significant loss of its catalytic activity and copper leaching. The large-scale reaction was also carried out in the absence of any base and reducing agent even with 0.1 mol% of the catalyst in aqueous media, making this protocol a good candidate for practical applications.

Key words: Magnetic nanoparticles, copper catalyst, synthesis, 1,2,3-triazoles

1. Introduction

Recently, magnetic nanoparticles (MNPs) have attracted a great deal of attention in research activities.[1–3] They are readily available, robust, and more importantly can be easily modified by organic and inorganic species, making them resistant against degradation and agglomeration and promising for the immobilization of catalytic centers. Furthermore, they have high surface area and can easily be recovered and reused by an external magnetic field.[4–6] This issue overcome the separation problem of conventional nanocatalysts by filtration or centrifugation; thereby it prevents loss of the catalysts during their separation and recovery.

Huisgen 1,3-dipolar cycloaddition between organic azides and alkynes is well established for the synthesis of 1,2,3-triazoles,[7–10] receiving considerable attention in various fields of chemistry.[11–13]

Cu(I)-catalyzed azide–alkyne cycloaddition, independently reported by Sharpless[14] and Meldal,[15] opened

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This paper is dedicated to the memory of Prof Abbas Shafiee (1937–2016).

the door for the preparation of 1,2,3-triazoles with high regioselectivity and broad substrate scope at room temperature. The noncatalyzed version of the reaction gives the products with poor selectivity and low yield.[7−10] Consequently, many methods based on homogeneous copper catalysts have been reported to date. However, they suffer from the problems of catalyst recycling, product contamination, and use of toxic solvents.[7−10]

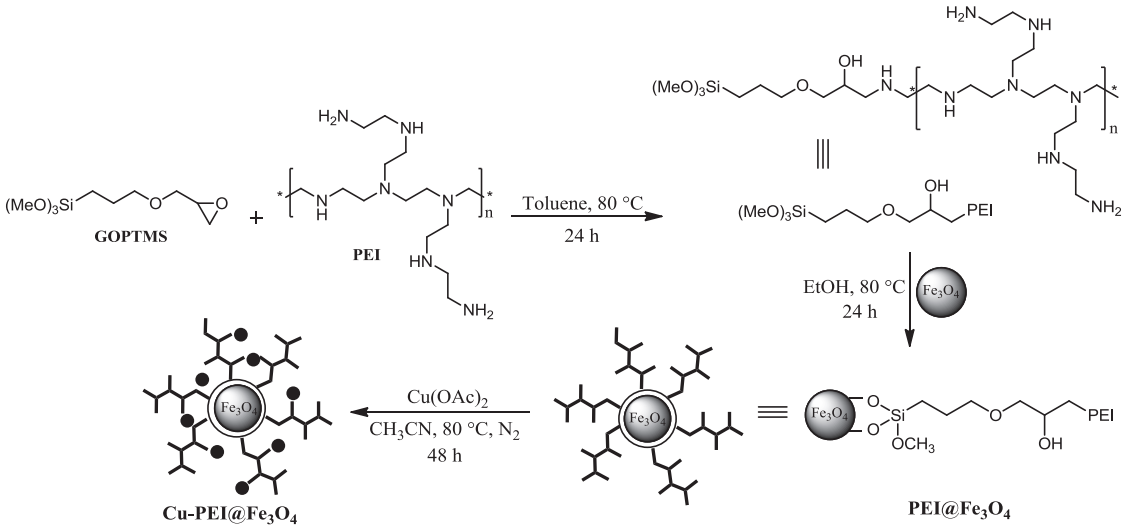
In comparison with homogeneous catalysts, heterogeneous catalysts can bring the advantages of catalyst reusability and easier product separation. Therefore, much effort has been made to immobilize copper complexes on suitable supports including carbon, silica, polymer, alumina, zeolite, dendrimer, and charcoal.[16−21] Although noticeable improvements in terms of reusability, reducing catalyst loading, and working under aerobic conditions were made, most of them still used organic solvents and organic base to improve catalytic efficiency. More importantly they used organic azides directly instead of in situ generated counterparts. Since the organic azides are toxic and their handling is not safe, the development of one-pot Huisgen 1,3-dipolar cycloaddition based on heterogeneous catalysts is highly desirable. To address this issue, some copper-based catalytic systems have been reported. These systems include copper nanoparticles on activated carbon,[22,23] polymeric copper catalyst,[24−27] ionic liquid-supported Cu(I),[28−30] alumina-supported copper nanoparticles,[31] $CuFe_2O_4$,[32] silica-supported Cu(I),[33] nanoferrite–glutathione–copper,[34] nanosilica triazine dendrimer,[35] Cu(II) porphyrin-bridged silsesquioxane PMO,[36] Cu@PMO NCs,[37] magnetic nanoparticle-supported Cu(II) acetate,[38] and silica-immobilized NHC–Cu(I).[39] However, successful examples using this useful strategy are limited and some of them still use organic solvents, base, and reducing agents. We have recently reported that PEI-grafted Fe_3O_4 MNPs (MNPs@PEI) is a very suitable catalyst for one-pot synthesis of 2-amino-3-cyano-4*H*-pyran derivatives in water[40] and also could be used for physical adsorption or covalent attachment of *Thermomyces lanuginosa* lipase (TLL) through different modification.[41] Herein, we supported copper onto magnetic nanoparticle with covalently anchored polyetylimine (PEI) as catalyst for the three-component coupling reaction of sodium azide, alkyl halides, and different alkynes in the absence of any base and reducing agent in H_2O/PEG_{300} as a safe, inexpensive, green, and environmentally benign medium.

2. Results and discussion

The Cu-PEI@Fe_3O_4 MNPs catalyst was prepared as presented in the Scheme. Initially, for grafting of PEI onto Fe_3O_4 MNPs, GOPTMS was added to a solution of PEI in toluene. After 24 h the resulting mixture was allowed for a further 24 h to react with Fe_3O_4 MNPs to give PEI functionalized nanomagnets. The PEI@Fe_3O_4 MNPs material was then used for immobilization of Cu(II) and preparation of the corresponding magnetic nanoparticle-supported copper catalyst (Cu-PEI@Fe_3O_4 MNPs).

The catalyst was characterized by FT-IR, TGA, TEM, VSM, EDX, cyclic voltammetry, and ICP-AES. Anchoring of PEI on the surface of the MNPs was confirmed by FT-IR spectroscopy.. The band at 1457 cm^{-1} could be assigned to the stretching vibration of C–N bonds of PEI macromolecular chains and the bands at around 2924 and 2831 cm^{-1} are attributed to the aliphatic C–H bands. In addition, the characteristic peaks of Fe–O at 584 cm^{-1} and a strong adsorption band at 1110–1000 cm^{-1} of Si–O–Si were also observed. These suggested that PEI moiety was truly attached on the surface of the MNPs (Figure 1).

The XRD spectra of the MNP showed that the position and relative intensity of all the diffraction peaks suitably matched those of standard Fe_3O_4.[40] In addition, characteristic peaks of Fe_3O_4 did not change after coating the surface with PEI and Cu immobilization, showing that the crystalline structures of the MNPs are preserved after the modifications (Figure 2). The average crystalline size of the catalyst calculated by the Debye–Scherrer equation was about 30 nm.



Scheme. Synthesis of Cu-Fe_3O_4-PEI MNPs catalyst.

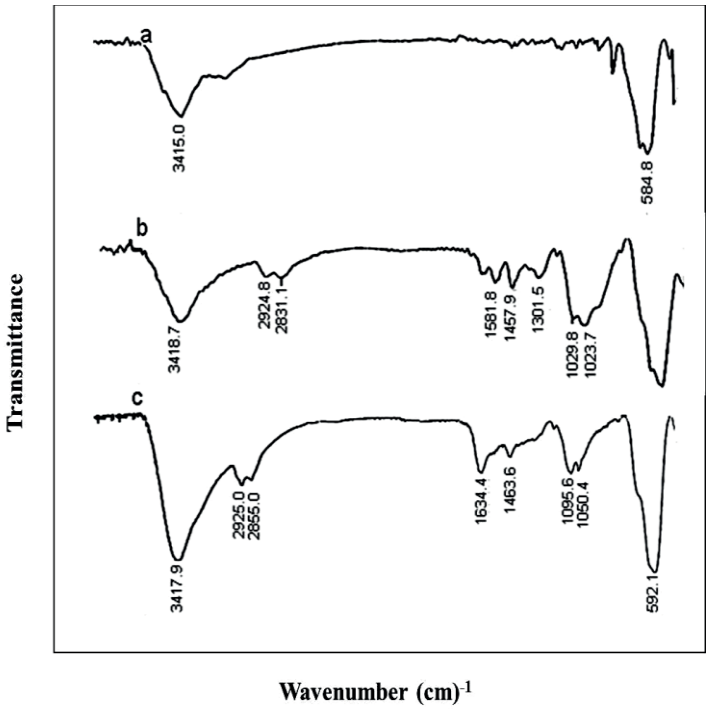


Figure 1. FT-IR spectra of a) Fe_3O_4, b) PEI@Fe_3O_4 MNPs, c) Cu-PEI@Fe_3O_4 MNPs.

The structure of the prepared MNPs was further verified using transmission electron microscopy (TEM) images. PEI@Fe_3O_4 MNPs were spherical with relatively narrow size distribution (Figure 3a). A magnified TEM image of single PEI@Fe_3O_4 MNPs indicated that the diameter of the MNPs is about 20 nm. The structure of the MNPs was maintained after copper supporting (Figure 3b). On the other hand, Figure 3c shows a TEM image of the Cu-PEI@Fe_3O_4 MNPs after recovery from the first cycle of the reaction.

By comparing these two sets of TEM images before and after the first reaction cycle, we can see that the nanoarchitecture of the catalyst survived. The selected area electron diffraction (SAED) pattern taken from

the Cu-PEI@Fe_3O_4 MNPs revealed that copper on the PEI@Fe_3O_4 MNPs was polycrystalline (Figure 3d). All of these observations confirmed the successful preparation and stability of the catalyst.

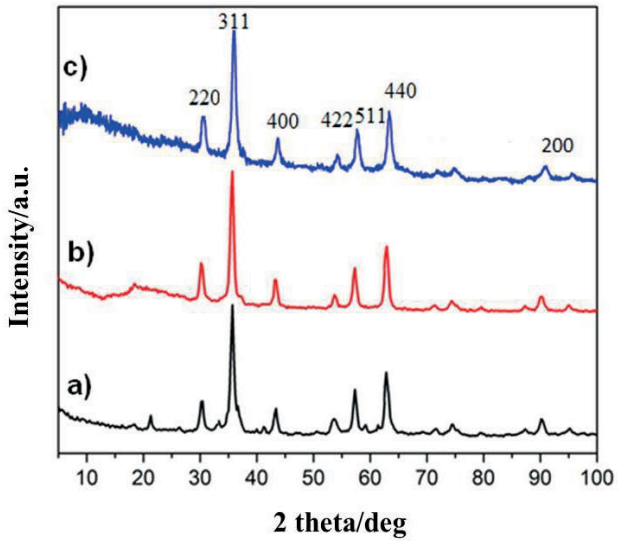


Figure 2. XRD spectra of a) Fe_3O_4, b) PEI@Fe_3O_4 MNPs, and c) Cu-PEI@Fe_3O_4 MNPs.

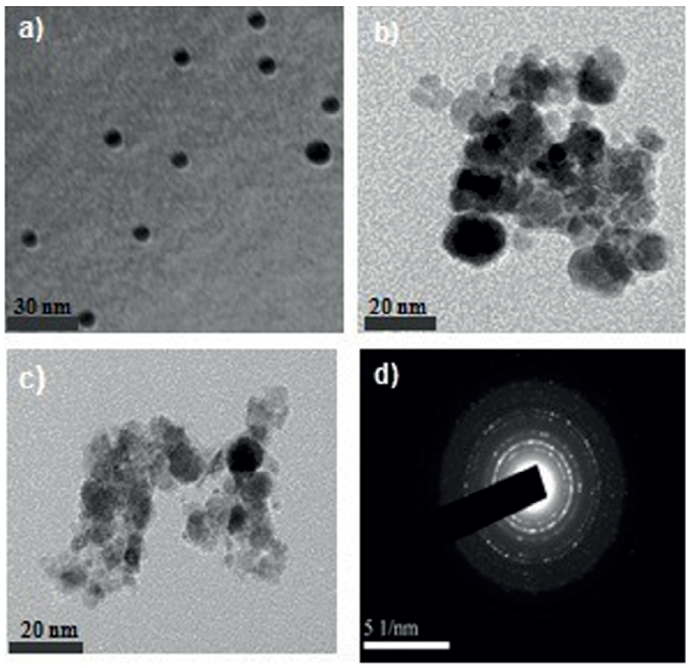


Figure 3. TEM image of a) PEI@Fe_3O_4 MNPs, b) Cu-PEI@Fe_3O_4 MNPs c) recycled Cu-PEI@Fe_3O_4 MNPs, and d) SAED pattern of Cu-PEI@Fe_3O_4 MNPs.

TGA analysis was used to determine the amount of ligand incorporated on Fe_3O_4. There are two weight loss steps in the TGA curve of Cu-PEI@Fe_3O_4 MNPs catalyst. The first weight loss between 60 to 250 °C may be due to removal of surface adsorbed water from the catalyst. The weight loss at temperatures higher than 250 °C could be attributed to the slow decomposition of the higher-molecular-weight species present in the

magnetic nanospheres (EPO and PEI groups). The loading amount of organic moiety anchored on the surface Cu-PEI@Fe_3O_4 MNPs catalyst was found to be about 20% (Figure 4).

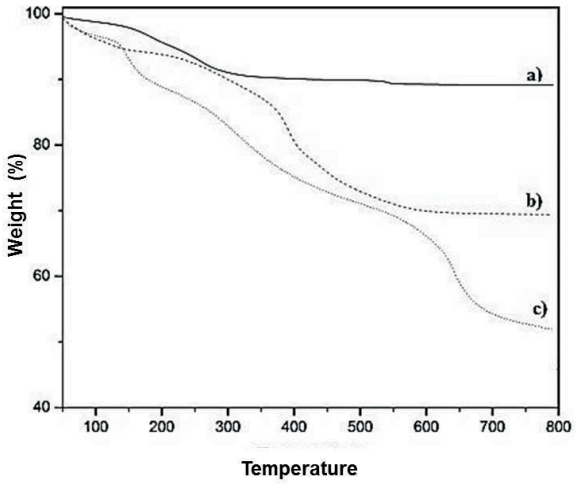


Figure 4. TGA spectra of a) Fe_3O_4 MNPs, b) PEI@Fe_3O_4 MNPs, and c) Cu- PEI@Fe_3O_4 MNPs.

The magnetization curve of the Fe_3O_4 MNPs, PEI@Fe_3O_4 MNPs, and Cu-PEI@Fe_3O_4 MNPs are shown in Figure 5. It can be seen that the magnetic saturation (MS) of the nanoparticles is 35.0, 32.4, and 30.0 emu g^{-1}, respectively. The decrease in mass saturation magnetization can be ascribed to the contribution of the nonmagnetic silica and PEI shell. Although the MS values of the PEI@Fe_3O_4 MNPs decreased, they still could be efficiently separated from the solution with a permanent magnet (Figure 5).

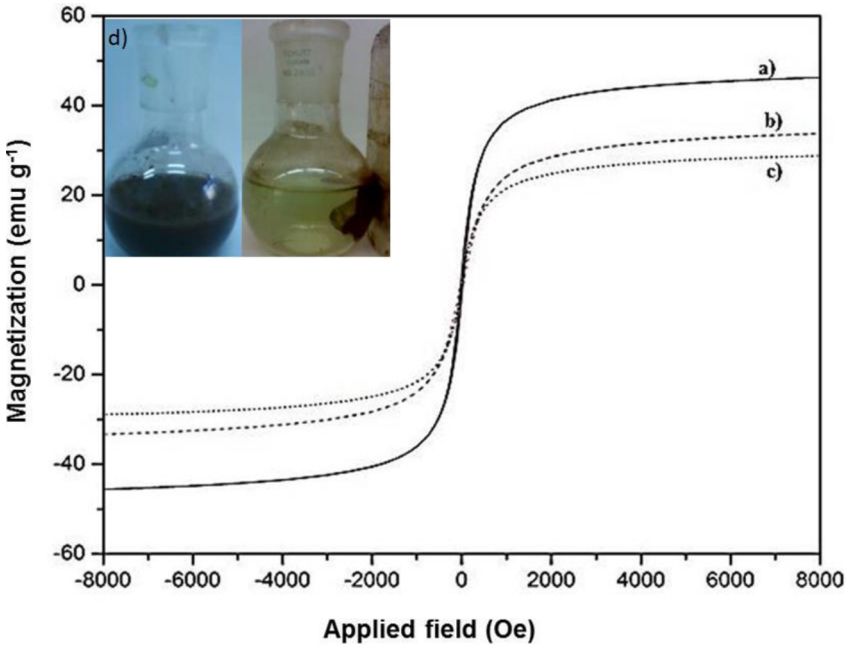


Figure 5. VSM spectra of a) Fe_3O_4 MNPs, b) PEI@Fe_3O_4 MNPs, and c) Cu-PEI@Fe_3O_4 MNPs; d) catalyst ability for easy recovery in the presence of large-scale amount of the reactants (50 mmol).

The loading of copper catalyst was determined using ICP-AES and the results showed loading at 0.22 mmol g^{-1}. After each run, the catalyst was removed by permanent magnet and the solution was concentrated and checked for determination of the leached copper ion by ICP analysis and the isolated catalyst was also applied for the next runs. According to the results obtained by ICP analysis, the amount of leached copper from the catalyst was less than 0.11 ppm for the first run and less than 0.021 ppm for the next runs. Energy-dispersive X-ray (EDX) analysis on various regions with energy bands of 8.05 keV (K lines) and 0.93 keV (L line) confirmed the presence of copper on the support (Figure 6).[23]

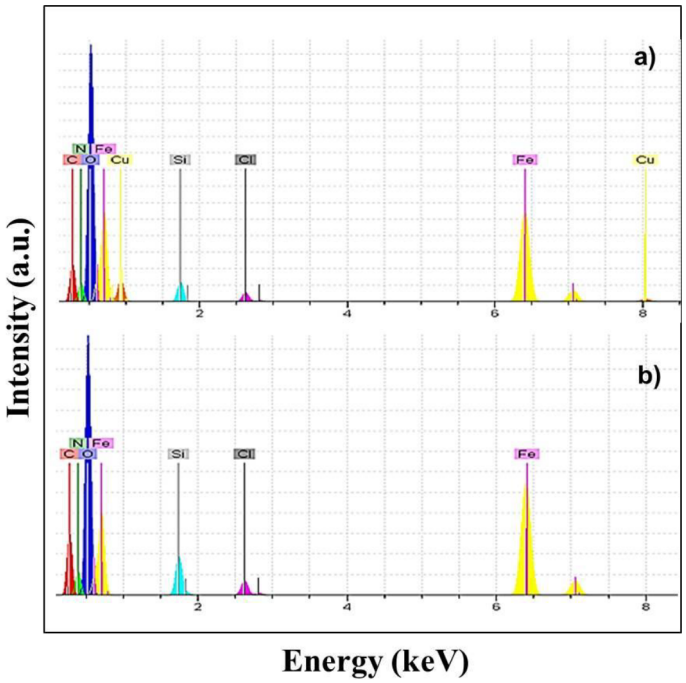


Figure 6. EDX spectra of a) Cu-PEI@Fe_3O_4 MNPs and b) PEI@Fe_3O_4 MNPs.

Anchoring of Cu on the solid surface can be followed by DRUV-vis spectroscopy of the resulting catalysts. The spectrum showed a broad absorption band in the region of 600–900 nm that could be attributed to the d–d transition of Cu(II) ion in the octahedral ligand field generated by oxygen ions. The band at ca. 250 nm may be related to the silica matrix (Figure 7a).

Moreover, the oxidation state of copper supported on PEI@Fe_3O_4 MNPs was confirmed using the electrochemical properties of $Cu(OAc)_2$ and Cu-PEI@Fe_3O_4 MNPs. In this experiment, the cyclic voltammograms of $Cu(OAc)_2$ and Cu-PEI@Fe_3O_4 MNPs in 0.1 M KCl as supporting electrolyte was recorded with the scan rate of 100 mV s^{-1} using a glassy carbon as working electrode. One milligram of Cu-PEI@Fe_3O_4 MNPs was dispersed into water (100 μL) to provide a suspension. Next, 5 μL of suspension was dropped on the cleaned GCE and allowed to dry at room temperature. Cyclic voltammograms of 0.1 μM $Cu(OAc)_2$ were also obtained in supporting electrolyte. The curve of $Cu(OAc)_2$ exhibited one peak (Ec = –0.45 V vs. Ag/AgCl) corresponding to the electron reductions of Cu(II) and formation of Cu(I) species. Furthermore, in accordance with the curve of Cu-PEI@Fe_3O_4 MNPs, the reduction of Cu(II) supported on PEI@Fe_3O_4 MNPs was negatively shifted (Ec = –0.52 V vs. Ag/AgCl) compared with those related to the Cu $(OAc)_2$. These results revealed that $Cu(OAc)_2$ and Cu-PEI@Fe_3O_4 MNPs show partially cathodic shifts (Figure 7b).

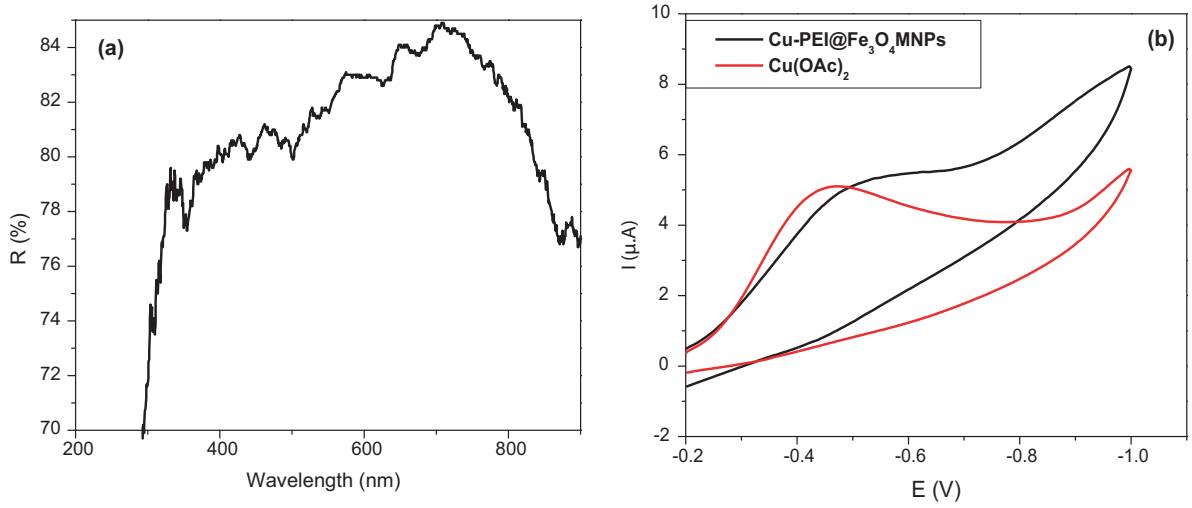


Figure 7. a) DRUV-vis spectra of Cu-PEI@Fe_3O_4 MNPs, b) cyclic voltammograms of Cu-PEI@Fe_3O_4 MNPs, $Cu(OAc)_2$.

Table 1. Optimization study for the three-component coupling of sodium azide, benzyl bromide, and phenyl acetylene under various conditions.

Entry[a]	Catalyst (mol%)	Solvent (additive)	Yield (%)	TON[b]/TOF[c]
1	Cu-PEI@Fe_3O_4 MNPs (0.3)	H_2O	0	0
2[d]	Cu-PEI@Fe_3O_4 MNPs (0.3)	H_2O	70	233/77
3[e]	Cu-PEI@Fe_3O_4 MNPs (0.3)	H_2O	70	233/77
4[f]	Cu-PEI@Fe_3O_4 MNPs (0.3)	H_2O (PEG_{300})	98	326/108
5[f]	Cu-PEI@Fe_3O_4 MNPs (0.3)	H_2O (CTMBr)	30	100/33
6[f]	Cu-PEI@Fe_3O_4 MNPs (0.3)	H_2O (TBAB)	30	100/33
7[f]	Cu-PEI@Fe_3O_4 MNPs (0.3)	H_2O (ADOGEN)	94	313/104
8	Cu-PEI@Fe_3O_4 MNPs (0.1)	H_2O (PEG_{300})	97	970/323
9	Cu-PEI@Fe_3O_4 MNPs (0.3)	1,4-Dioxane	70	233/77
10	Cu-PEI@Fe_3O_4 MNPs (0.3)	CH_3CN	80	266/88
11	Cu-PEI@Fe_3O_4 MNPs (0.3)	DMF	95	316/105
12	No. Cat.	H_2O (PEG_{300})	35	0
13	$Cu(OAc)_2$ (3)	H_2O (PEG_{300})	88	29/9
14[g]	Fe_3O_4 MNPs	H_2O (PEG_{300})	55	-
15[g]	Fe_3O_4@SiO_2 MNPs	H_2O (PEG_{300})	50	-

[a] Reaction conditions: sodium azide (1 mmol), benzyl bromide (1 mmol), and phenyl acetylene (1 mmol), rt, 3 h. [b] TON is mole of the formed 1,4-disubstituted 1,2,3-triazole per mole of the catalyst. [c] TOF is TON per time. [d] The reaction was performed at 70 °C. [e] The reaction was performed at 100 °C. [f] PEG and the other surfactants were added in 20% w/w H_2O. [g] The reaction was carried out in the presence of 5 mg of catalyst.

After full characterization of the prepared catalyst, three-component Huisgen 1,3-dipolar cycloaddition between sodium azide, benzyl bromide, and phenyl acetylene was evaluated as a model reaction in water at 25 °C and in the presence of the catalyst. Only a trace amount of the corresponding triazole **4** was produced at ambient temperature (Table 1, entry 1). Raising the reaction temperature to 70 °C increased the yield to 70% (Table 1, entry 2). Further increasing the reaction temperature not only did not lead to any improvement in catalytic activity but also some by-products were formed (Table 1, entry 3). Interestingly, when the reaction

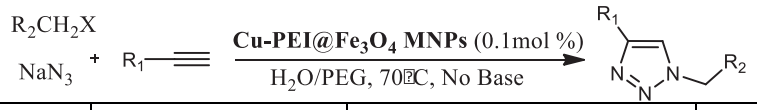
carried out in the presence of water/PEG_{300}, the yield of the product **4** was further increased (Table 1, entry 4). On the other hand, other additives based on tetra alkyl ammonium bromides such as tetra-butyl ammonium bromide (TBAB) and cetyltrimethylammonium bromide (CTMBr) gave poor results and the expected triazole **4** was obtained in 30% yield in both cases (Table 1, entries 5 and 6). It is worth mentioning that the three-component coupling reaction was conducted in water/ADOGEN with high yield of 94% (Table 1, entry 7). Importantly, the catalyst loading could be lowered from 5 to 0.1 mol% Cu without any significant decrease in product yield (Table 1, entry 8). Among the different solvents tested, DMF gave good results but the water/PEG_{300} system was chosen as medium for environmental concerns (Table 1, entries 9–11). It should be pointed out that in the absence of any catalyst the reaction proceeded to give product **4** with much lower yield (35%) and the regioselectivity of the reaction was lost (Table 1, entry 12). These results clearly confirmed that copper is crucial for achieving high activity and selectivity. Our studies on optimization of the reaction conditions revealed that Fe_3O_4 or Fe_3O_4@SiO_2 could also catalyze the reaction but the coupling product was obtained in low yield and regioselectivity (Table 1, entries 14, 15). After optimization of the model reaction, we next investigated the scope of the 3+2 cycloaddition (Table 2). Benzyl bromides/chlorides bearing both electron-donating and electron-withdrawing groups with phenyl acetylene gave the corresponding alkynes in good to excellent yields (Table 2, entries 1–15). These results showed that the nature of substitution did not have a significant impact on the outcome of the reaction. It was found that cyclization of the dibenzyl chloride with phenyl acetylene provided bistriazole in high yield (Table 2, entry 15). Encouraged by these results, we then managed to employ aliphatic alkynes with various types of benzyl bromides/chlorides. The corresponding three-component coupling product was obtained in high yield (Table 2, entries 16–20). However, a longer reaction time (12 h) was required for the formation of triazoles bearing an aliphatic substituent. It is worth mentioning that various bromoalkanes participated in the 3+2 cycloaddition, producing the expected 1,4-disubstituted triazoles with good yields (Table 2, entries 22 and 23). It should be noted that the nitrile functional group is also well tolerated, which could be useful for further functionalization (Table 2, entries 21).

Moreover, this protocol worked well in the case of more complex structures containing coumarin, isatin, and steroid groups and provided the corresponding 1,4-triazoles in good yield (Table 2, entry 23–28). It is also interesting to note that in all tested examples in this protocol, only 1,4-disubstituted triazoles were obtained.

The catalytic activity of the catalyst for the reaction of benzyl halide, phenylacetylene, and sodium azide was compared with that of other previously reported heterogeneous catalysts as depicted in Table 3. Recently, a variety of copper catalysts were prepared via addition of prepared copper particles to different supports. As indicated in Table 3, the Cu-PEI@Fe_3O_4 MNPs showed proper activity with low copper loading in comparison with the other catalysts (Table 3, entries 5 vs. 1–4). In addition, some of them suffer from disadvantages such as the necessity to apply azide derivatives instead of in situ formation of counterparts and the inability of the catalyst to catalyze the reaction of aliphatic or complex substrate as well as large-scale reactions.

Interestingly, when the above-mentioned reaction was conducted in the presence of a large amount of the reactants (50 mmol), the corresponding coupling product was obtained in 90% isolated yield. Since recycling and lifetime of heterogeneous catalysts are two important issues for practical applications, the recycling of Cu-PEI@Fe_3O_4 MNPs was also investigated in the three-component coupling of benzyl bromide, NaN_3, and phenyl acetylene as a model reaction. After completion of the first run, the catalyst was separated by external magnet (Figure 5d) and then washed with ethanol and the recycled catalyst was successfully applied in five successive reaction runs without significant decrease in its catalytic activity (about 90% conversion after the

Table 2. Synthesis of different 1,4-disubstituted 1,2,3-triazoles catalyzed in water.



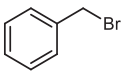
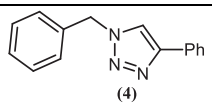
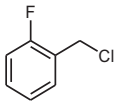
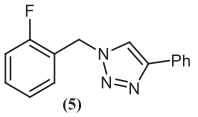
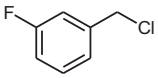
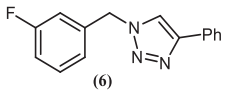
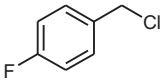
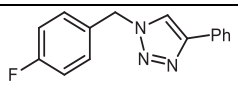
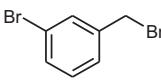
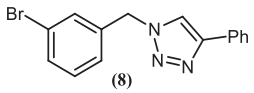
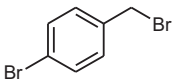
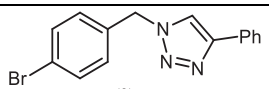
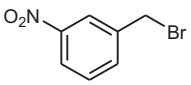
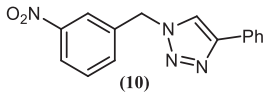
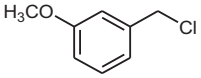
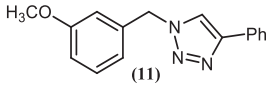
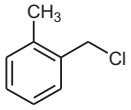
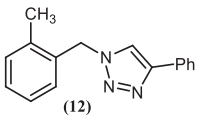
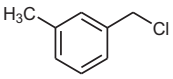
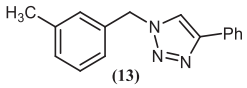
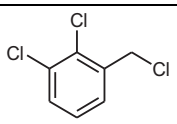
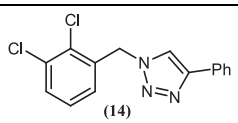
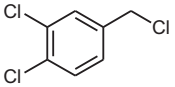
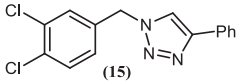
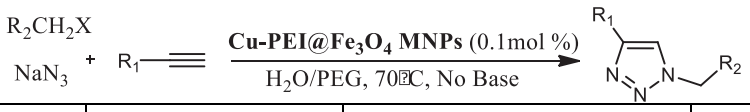
Entry	Organic halide	Alkyne	Triazole	t(h)	Yield (%)	M.P [Ref]
1			 (4)	3	96	112 115 °C[16-21]
2			 (5)	7	90	108-111 °C[43]
3			 (6)	7	88	88-92 °C[43]
4			 (7)	7	93	112-115 °C[43]
5			 (8)	3.5	90	88-92 °C[16-21]
6			 (9)	3.5	93	136-139 °C[16-21]
7			 (10)	3.5	83	148-152 °C[16-21]
8			 (11)	7	88	112-116 °C[16-21]
9			 (12)	7	92	102-105 °C[16-21]
10			 (13)	7	91	96-100 °C[16-21]
11			 (14)	7	90	113-117 °C[16-21]
12			 (15)	7	93	137-141°C[16-21]

Table 2. Continued.



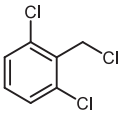
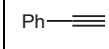
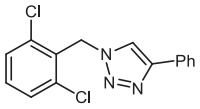
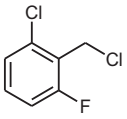
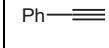
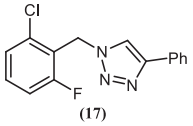
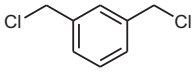
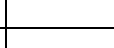
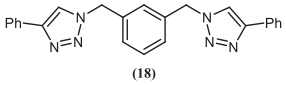
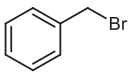
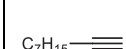
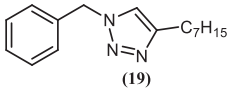
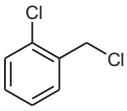
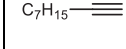
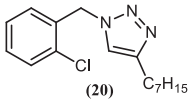
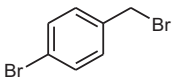
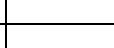
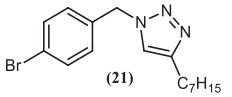
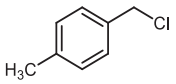
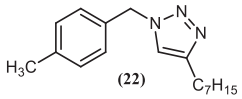
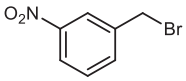
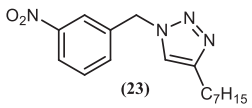
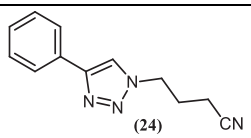
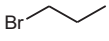
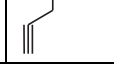
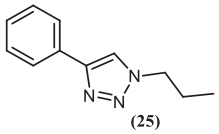
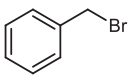
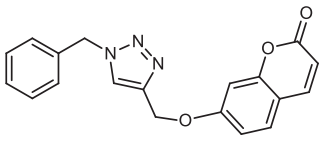
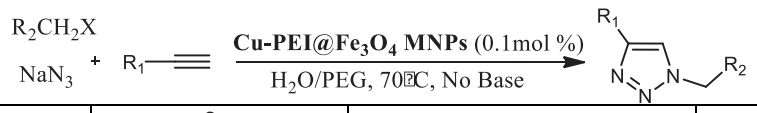
13			 (16)	7	88	150-154°C[16-21]
14			 (17)	7	90	159-162 °C[43]
15			 (18)	7	88	111-114 °C[16-21]
16			 (19)	12	80	70-72 °C[44]
17			 (20)	12	80	58-60 °C[44]
18			 (21)	12	80	76-78 °C[44]
19			 (22)	12	80	62-64 °C[44]
29			 (23)	12	80	99-100 °C[44]
21			 (24)	3	70	85-87 °C
22			 (25)	3	92	57-58 °C[45,46]
23			 (26)	3	90	150-152 °C[47]

Table 2. Continued.



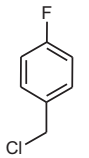
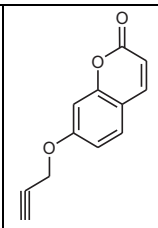
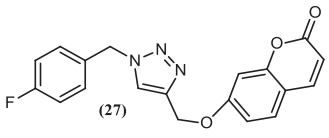
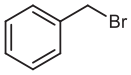
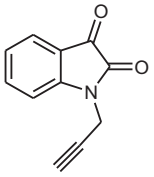
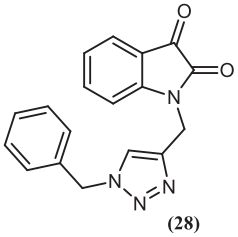
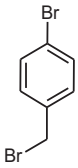
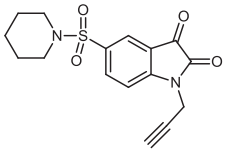
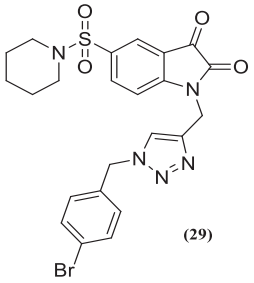
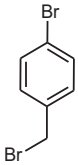
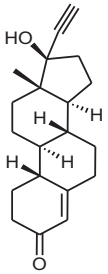
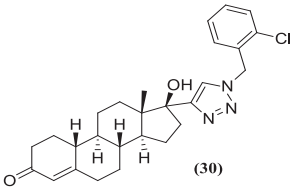
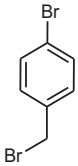
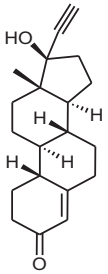
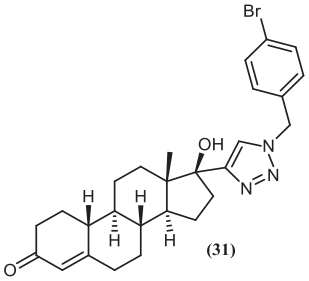
24			 (27)	3	74	130-132 °C
25			 (28)	3	94	112-114 °C[48]
26			 (29)	3	95	207-210 °C
27			 (30)	24	70	101-104 °C
28			 (31)	24	70	108-112 °C

Table 3. The comparison between the prepared catalyst and previously reported heterogeneous catalytic systems.

Entry	Catalyzer	Catalyst amount	Temp. (°C)	Time	Yield (%)	Ref.
1	Cu(0)Fe_3O_4@SiO_2/NH_2cel[a]	0.05 g	60	5 h	97	[49]
2	MNP@PDMA[b]-Cu	0.3 mol %	50	2 h	96	[50]
3	MNPs-CuBr	1.46 mol%	80/MW	20 min	96	[51]
4	Cu_2O/Casein@Fe_3O_4NPs	0.43 mol%,	55	2 h	100	[52]
5	Cu-PEI@Fe_3O_4 MNPs	0.1 mol%	70	3 h	96	

[a]cel: cellulose [b]PDMA: poly(2-dimethylaminoethyl acrylamide)

fifth run). The rapid and efficient recycling method prevents the loss of the catalyst in each run and makes it a promising option for practical applications.

Furthermore, the leaching test after each catalytic run in the model reaction revealed that the amount of the copper leached from the heterogeneous catalyst was negligible as determined by ICP-AES. This result confirmed that there are no contributions from homogeneous catalysis of active species leached into the reaction solution (see Table S1).

3. Conclusion

We developed a recoverable Cu(II)-based heterogeneous catalytic system for one-pot Huisgen 1,3-dipolar cycloaddition in water. The catalyst was prepared by covalent attachment of PEI on the surface of Fe_3O_4 MNPs and subsequent incorporation of Cu(II) on the support. Our studies revealed that several types of alkynes and alkyl bromides/chlorides could participate in the reaction in the presence of a low loading amount of the catalyst under base-free and reducing agent conditions to give 1,4-disubstituted 1,2,3-triazoles in good to excellent yields. Furthermore, this novel catalytic system can be rapidly isolated from the reaction mixture by an external magnet and successfully reused five times in reactions. Besides its efficient and easy recyclability, the use of the catalyst in large-scale reactions makes this system a valuable candidate for practical applications.

4. Experimental

4.1. Synthesis of the catalyst

Fe_3O_4 MNPs were synthesized using co-precipitation.[42] For PEI grafting onto the Fe_3O_4 MNPs (PEI@Fe_3O_4 MNPs), (3-glycidyloxypropyl)-trimethoxysilane (GOPTMS, 1 mmol) was added to a stirred solution of 150 mL of dry toluene containing 3 mmol of PEI. The resultant mixture was allowed to react at 80 °C for 24 h. To this solution, 2.5 g of Fe_3O_4 MNPs and 25 mL of ethanol were added, and the solution was stirred at 80 °C for 24 h. PEI@ Fe_3O_4 MNPs were magnetically isolated by an external magnet and repeatedly washed with methanol and ethanol to obtain the product. Subsequently, it was soxhleted with ethanol for 24 h to remove unreacted substrates and by-products, and dried at 40 °C. For incorporation of copper into the nanocomposite matrix, 300 mg of PEI@Fe_3O_4 MNPs was charged into a round-bottomed flask containing an acetonitrile solution (25 mL) of copper acetate (0.6 mmol) and stirred under nitrogen atmosphere for 48 h. The resultant catalyst was isolated by an external magnet and washed with acetonitrile followed by acetone. The residue was dried in air for 24 h. The copper content in PEI@Fe_3O_4 MNPs was analyzed by the ICP-AES technique (0.22 mmol g^{-1}).

4.2. General process for the synthesis of different 1,4-disubstituted 1,2,3-triazoles

A mixture of sodium azide (1 mmol), benzyl or alkyl halide (1 mmol), and corresponding acetylene (1 mmol of phenyl acetylene or 2 mmol of alkyl acetylene) and catalyst (5 mg of catalyst equal to 0.1 mol % of copper) was taken in a round bottomed flask containing 1 mL of H_2O and 0.2 mL of PEG_{300} and heated at 70 °C for 3 h under vigorous stirring. After completion of the reaction (monitored by TLC), the catalyst was removed by external magnet, washed with EtOH, and dried under vacuum. The collected solvent was concentrated under vacuum and the product was allowed to crystalize, which did not require any further purification. The obtained products were confirmed and completely characterized by physical and spectral data (see the Supporting Information).

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SUPPORTING INFORMATION

Efficient multicomponent synthesis of 1,2,3-triazoles catalyzed by Cu(II) supported on PEI@Fe_3O_4 MNPs in a water/PEG_{300} system

Contents

1. General methods and materials

All commercially available reagents were used without further purification. All reagents were purchased from Merck and Acros Organics. Column chromatography was carried out on silica gel. TLC was conducted on silica gel 250 micron, F254 plates. ^{1}H NMR spectra were recorded at room temperature on 500 MHz spectrometers, using $CDCl_3$ as the NMR solvent. Chemical shifts are reported in ppm with TMS as an internal standard (TMS: δ 0.0 ppm). ^{13}C NMR spectra are referenced from the solvent central peak (77.23 ppm). Chemical shifts are given in ppm.

2. Experimental procedures

Synthesis of different 1,4-disubstituted 1,2,3-triazoles with Cu-PEI@Fe_3O_4 MNPs as catalyst in water

A mixture of sodium azide (1 mmol), benzyl or alkyl halide (1 mmol), and corresponding acetylene (1 mmol of phenyl acetylene and 2 mmol of alkyl acetylene) and catalyst (5 mg of catalyst equal to 0.1 mol% of copper) was taken in a round bottomed flask containing 1 mL of H_2O and 0.2 mmol PEG 300 and heated at 70 °C for 3 h under vigorous stirring. After completion of the reaction (monitored by TLC), the catalyst was removed by external magnet. The catalyst was washed several times with ether followed by water and dried under vacuum. The resulting reaction mixture was extracted with EtOAc. The collected organic phases were

dried with Na_2SO_4 and the solvent was concentrated under vacuum and the product was allowed to be crystalized with the aid of slow evaporation, which did not require any further purification.

3. Leaching test

The model reaction was used to study the amount of leached copper from the catalyst. After each run, the catalyst was removed by permanent magnet and the solution was concentrated and checked for determination of the leached copper ion by ICP analysis and the isolated catalyst was also applied for the next runs. The results are presented in Table S1.

Table S1. Amount of leached copper in solution after each catalytic run.

Entry	Cu (ppm)	Yield of the reaction after each run
Run 1	0.010	94
Run 2	0.088	90
Run 3	0.088	93
Run 4	0.113	85
Run 5	0.070	90

4. Characterization data

1-benzyl-4-phenyl-1H-1,2,3-triazole (4). Yield: 96%; white solid; mp: 112–115 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.58 (s, 2H, CH_2), 7.27–7.41 (m, 8H, CH Arom), 7.69 (s, 1H, CH triazole), 7.81 (d, 2H, J = 7.2); ^{13}C NMR (500 MHz, $CDCl_3$) δ 53.8, 119.1, 125.2, 127.5, 127.7, 128.3, 128.7, 129, 130.2, 134.2, 147.8. IR (KBr): ν = 3141 (=C–H), 1494, 1469, 1449 (aromatic cycle), 1359, 1224 (C–N). Anal. Calcd for $C_{15}H_{13}N_3$ (235.28): C, 76.57; H, 5.57; N, 17.86. Found: C, 76.61; H, 5.43; N, 17.93.

1-(2-fluorobenzyl)-4-phenyl-1H-1,2,3-triazole (5). Yield: 90%; white solid; mp: 108–111 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.65 (s, 2H, CH_2), 7.13–7.43 (m, 7H, CH Arom), 7.78 (s, 1H, CH triazole), 7.82 (d, 2H, J = 7.3, CH). IR (KBr): ν = 3121 (=C–H), 1494, 1462, 1650 (aromatic cycle), 1356, 1230 (C–N), 1610 (C=C). Anal. Calcd for $C_{15}H_{12}FN_3$ (253.27): C, 71.13; H, 4.78; N, 16.59. Found: C, 71.21; H, 4.73; N, 17.03.

1-(3-fluorobenzyl)-4-phenyl-1H-1,2,3-triazole (6). Yield: 88%; white solid; mp: 88–92 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.57 (s, 2H, CH_2), 7.01–7.09 (m, 3H, CH Arom), 7.33–7.41 (m, 4H, CH Arom), 7.74 (s, 1H, CH triazole), 7.81 (d, 2H, J = 6.6, CH). IR (KBr): ν = 3108 (=C–H), 1591, 1483, 1453 (aromatic cycle), 1342, 1248 (C–N), 1600 (C=C). Anal. Calcd for $C_{15}H_{12}FN_3$ (253.27): C, 71.13; H, 4.78; N, 16.59. Found: C, 71.04; H, 4.93; N, 17.12.

1-(4-fluorobenzyl)-4-phenyl-1H-1,2,3-triazole (7). Yield: 93%; pale yellow solid; mp: 112–115 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.56 (s, 2H, CH_2), 7.09–7.42 (m, 7H, CH Arom), 7.69 (s, 1H, CH triazole), 7.81 (2H, d, J = 7.0, CH). ^{13}C NMR (500 MHz, $CDCl_3$): 53.1, 115.6, 115.7, 118.8, 125.2, 125.8, 127.7, 128.3, 129.4, 129.4, 129.8, 129.9, 163.3. IR (KBr): ν = 3124 (=C–H), 1605,

1513, 1462, 1439 (aromatic cycle), 1351, 1227 (C–N), 1650 (C=C). Anal. Calcd for $C_{15}H_{12}FN_3$ (253.27): C, 71.13; H, 4.78; N, 16.59. Found: C, 71.25; H, 4.96; N, 16.45.

1-(3-bromobenzyl)-4-phenyl-1H-1,2,3-triazole (8). Yield: 90%; pale yellow solid; mp: 88–92 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.55 (s, 2H, CH_2), 7.24–7.51 (m, 7H, CH Arom), 7.70 (s, 1H, CH triazole), 7.82 (d, 2H, *J* = 7.3, CH). IR (KBr): *v* = 3084 (=C–H), 1426 (aromatic cycle), 1345, 1221 (C–N).; Anal. Calcd for $C_{15}H_{12}BrN_3$ (314.18): C, 57.34; H, 3.85; N, 13.37. Found: C, 57.28; H, 3.96; N, 13.45.

1-(4-bromobenzyl)-4-phenyl-1H-1,2,3-triazole (9). Yield: 93%; pale yellow solid; mp: 136–139 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.55 (s, 2H, CH_2), 7.21 (d, 2H, *J* = 8.2), 7.35 (t, 1H, *J* = 7.4), 7.42 (t, 2H, *J* = 7.4), 7.53 (d, 2H, *J* = 8.5), 7.70 (s, 1H, CH triazole), 7.82 (d, 2H, *J* = 7.9). IR (KBr): *v* = 3100 (=C–H), 1462 (aromatic cycle), 1377, 1224 (C–N). Anal. Calcd for $C_{15}H_{12}BrN_3$ (314.18): C, 57.34; H, 3.85; N, 13.37. Found: C, 57.28; H, 3.76; N, 13.45.

1-(3-nitrobenzyl)-4-phenyl-1H-1,2,3-triazole (10). Yield: 83%; pale yellow solid; mp: 148–152 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 6.01 (s, 2H, CH_2), 7.10–7.63 (m, 6H), 7.86 (d, 2H, *J* = 6.5), 7.95 (s, 1H, CH triazole), 8.21 (d, 1H, *J* = 6.8). IR (KBr): *v* = 3088 (=C–H), 1608 (C=C), 1524, 1330 (NO_2), 1462, 1406 (aromatic cycle), 1304, 1204 (C–N). Anal. Calcd for $C_{15}H_{12}N_4O_2$ (280.28): C, 64.28; H, 4.32; N, 19.99. Found: C, 64.39; H, 4.16; N, 19.45.

1-(3-methoxybenzyl)-4-phenyl-1H-1,2,3-triazole (11). Yield: 88%; yellow solid; mp: 112–116 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 3.80 (s, 3H, CH_3), 5.57 (s, 2H, CH_2), 6.80 (s, 1H, CH), 6.91 (d, 2H, *J* = 7.8), 7.30–7.34 (m, 2H), 7.41 (t, 2H, *J* = 7.4), 7.70 (s, 1H, CH triazole), 7.81 (d, 2H, *J* = 7.6). IR (KBr): *v* = 3010 (=C–H), 1485, 1434 (aromatic cycle), 1263 (C–N), 1157 (C–O). Anal. Calcd for $C_{16}H_{15}N_3O$ (265.31): C, 72.43; H, 5.70; N, 15.84. Found: C, 72.36; H, 5.93; N, 15.95.

1-(2-methylbenzyl)-4-phenyl-1H-1,2,3-triazole (12). Yield: 91%; yellow solid; mp: 102–105 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 2.30 (s, 3H, CH_3), 5.59 (s, 2H, CH_2), 7.2–7.4 (m, 8H, CH Arom), 7.56 (s, 1H, CH triazole), 7.80 (d, 2H, J = 7.3).^{13}C NMR (500 MHz, $CDCl_3$): 18.5, 51.9, 118.8, 125.1, 126.2, 127.6, 128.3, 128.7, 128.9, 130.1, 130.6, 132.1, 136.5, 147.5. IR (KBr): v = 3143 (=C–H), 1603 (C=C), 1441 (aromatic cycle), 1346 (C–N). Anal. Calcd for $C_{16}H_{15}N_3$ (249.31): C, 77.08; H, 6.06; N, 16.85. Found: C, 77.27; H, 5.95; N, 16.92.

1-(3-methylbenzyl)-4-phenyl-1H-1,2,3-triazole (13). Yield: 92%; pale yellow solid; mp: 96–100 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 2.35 (s, 3H, CH_3), 5.53 (s, 2H, CH_2), 7.13–7.41 (m, 7H, CH Arom), 7.71 (s, 1H, CH triazole), 7.82 (d, 2H, J = 6.2). IR (KBr): v = 3087 (=C–H), 1614 (C=C), 1460, 1435 (aromatic cycle), 1343, 1216 (C–N). Anal. Calcd for $C_{16}H_{15}N_3$ (249.31): C, 77.08; H, 6.06; N, 16.85. Found: C, 77.30; H, 6.15; N, 16.98.

1-(2,3-dichlorobenzyl)-4-phenyl-1H-1,2,3-triazole (14). Yield: 90%; yellow solid; mp: 113–117 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.75 (s, 2H, CH_2), 7.00 (d, 1H, J = 7.8), 7.20 (t, 1H, J = 7.9), 7.32 (t, 1H, J = 7.8), 7.43 (t, 2H, J = 7.8), 7.5 (d, 1H, J = 7.8), 7.8 (s, 1H, CH triazole), 7.83 (d, 2H, J = 7.7). IR (KBr): v = 3113 (=C–H), 1458, 1421 (aromatic cycle), 1357, 1225 (C–N). Anal. Calcd for $C_{15}H_{11}C_{l2}N_3$ (304.17): C, 59.23; H, 3.65; N, 13.81. Found: C, 59.31; H, 3.45; N, 13.66.

1-(3,4-dichlorobenzyl)-4-phenyl-1H-1,2,3-triazole (15). Yield: 93%; yellow solid; mp: 137–141 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 55.50 (s, 2H, CH_2), 7.26–7.47 (m, 7H), 7.72–7.47 (s, 1H, CH triazole), 7.81–7.83 (d, 2H, J = 7.8). IR (KBr): v = 3088 (=C–H), 1485 (aromatic cycle), 1214 (C–N). Anal. Calcd for $C_{15}H_{11}C_{l2}N_3$ (304.17): C, 59.23; H, 3.65; N, 13.81. Found: C, 59.02; H, 3.51; N, 13.93.

1-(2,6-dichlorobenzyl)-4-phenyl-1H-1,2,3-triazole (16). Yield: 88%; yellow solid; mp: 150–154 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.92 (s, 2H, CH_2), 7.30–7.34 (m, 2H), 7.39–7.44 (m, 3H), 7.72 (s, 1H, CH triazole), 7.81 (d, 2H, J = 7.7). IR (KBr): v = 3128 (=C–H), 1481, 1480 (aromatic cycle), 1216 (C–N). Anal. Calcd for $C_{15}H_{11}Cl_2N_3$ (304.17): C, 59.23; H, 3.65; N, 13.81. Found: C, 59.12; H, 3.79; N, 13.95.

1-(2-chloro-6-fluorobenzyl)-4-phenyl-1H-1,2,3-triazole (17). Yield: 90%; yellow solid; mp: 159–162 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.80 (s, 2H, CH_2), 7.13 (t, 1H, J = 8.8), 7.27–7.43 (m, 5H), 7.80 (s, 1H, CH triazole), 7.81 (d, 2H, J = 7.3). IR (KBr): v = 3128 (=C–H), 1605 (C=C), 1459, 1433 (aromatic cycle), 1245 (C–N). Anal. Calcd for $C_{15}H_{11}ClFN_3$ (304.17): C, 62.62; H, 3.85; N, 14.60. Found: C, 62.77; H, 3.75; N, 11.90.

1,3-bis((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)benzene (18). Yield: 88%; yellow solid; mp: 111–114 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.58 (s, 4H, CH_2), 7.27–7.41 (m, 10H), 7.70 (s, 2H, CH triazole), 7.80 (d, 4H, J = 7.3). MS (EI) (70 eV): *m/z* (%) 392 (9) (M^+), 364 (20), 335 (3), 290 (5), 248 (23), 219 (21), 178 (6), 146 (3), 116 (100), 89 (34), 63 (12). Anal. Calcd for $C_{24}H_{20}N_6$ (392.46): C, 73.45; H, 5.14; N, 21.41. Found: C, 73.22; H, 5.09; N, 21.54.

1-benzyl-4-hexyl-1H-1,2,3-triazole (19). Yield: 86%; yellow solid; mp: 70–72 °C; ^{1}H NMR (300 MHz, $CDCl_3$): 0.80 (t, 3H, J = 7.0, CH_3), 1.17–1.30 (m, 6H), 1.43–1.56 (m, 2H), 2.59–2.64 (t, 2H, J = 7.5), 5.39 (s, 2H, CH_2), 7.00–7.52 (6H, m, CH). ^{13}C NMR (300 MHz, $CDCl_3$) = 13.9, 14.1, 21.1, 22.4, 25.5, 28.8, 29.2, 31.4, 53.8, 120.7, 127.8, 128.1, 128.4, 128.9, 134.9. IR (KBr): v = 3113 (=C–H), 2924 (–C–H), 1459 (aromatic cycle), 1323, 1212 (C–N). Anal. Calcd for $C_{15}H_{21}N_3$ (243.35): C, 74.03; H, 8.70; N, 17.27. Found: C, 74.16; H, 8.51; N, 17.38.

1-(2-chlorobenzyl)-4-hexyl-1H-1,2,3-triazole (20). Yield: 78%; pale yellow solid; mp: 58– 60 °C; ^{1}H NMR (300 MHz, $CDCl_3$): 0.78 (t, 3H, J = 6.8, CH_3), 1.10–1.30 (m, 6H, CH_2), 1.55–1.60 (m, 2H, CH_2), 2.59–2.64 (t, 2H, J = 7.3), 5.52 (s, 2H, CH_2), 7.00 (d, 2H, J = 6.7, CH), 7.10–7.31 (m, 5H, CH). ^{13}C NMR (300 MHz, $CDCl_3$) = 13.9, 22.4, 25.6, 29.3, 31.4, 51.2, 120.9, 127.4, 129.7, 129.9, 132.8, 133.1, 148.6. IR (KBr): v = 3113 (=C–H), 2923 (–C–H), 1469, 1444 (aromatic cycle), 1330, 1215 (C–N). Anal. Calcd for $C_{15}H_{20}ClN_3$ (277.79): C, 64.85; H, 7.26; N, 17.26. Found: C, 64.64; H, 7.31; N, 17.34.

1-(4-bromobenzyl)-4-hexyl-1H-1,2,3-triazole (21). Yield: 76%; yellow solid; mp: 76–78 °C; ^{1}H NMR (300 MHz, $CDCl_3$): 0.77 (t, 3H, J = 7.0, CH_3), 1.15–1.28 (m, 6H, CH_2), 1.51–1.58 (m, 2H), 5.36 (s, 2H, CH_2), 7.03–7.05 (d, 2H, J = 8.2, CH), 7.21 (s, 1H, CH triazole), 7.37–7.39 (d, 2H, J = 8.2, CH). ^{13}C NMR (300 MHz, $CDCl_3$) = 14.1, 22.4, 25.6, 28.8, 29.2, 31.4, 53.1, 120.6, 122.5, 12.4, 132.1, 134.1, 148.9. IR (KBr): v = 3110 (=C–H), 2930 (–C–H), 1655 (C=C), 1463 (aromatic cycle), 1323, 1212 (C–N). Anal. Calcd for $C_{15}H_{20}BrN_3$ (322.24): C, 55.91; H, 6.26; N, 13.04. Found: C, 55.74; H, 6.31; N, 13.00.

4-hexyl-1-(4-methylbenzyl)-1H-1,2,3-triazole) (22). Yield: 83%; yellow solid; mp: 62–64 °C; ^{1}H NMR (300 MHz, $CDCl_3$): 0.81 (t, 3H, J = 6.8, CH_3CH_2), 1.24–134 (m, 6H), 1.54–1.64 (m, 2H), 2.30 (s, 3H, CH_3), 2.63 (t, 2H, J = 7.7), 5.40 (s, 2H, CH_2), 7.12 (d, 4H, J = 7), 7.16 (s, 1H, CH triazole). ^{13}C NMR (300 MHz, $CDCl_3$) = 14.1, 21.1, 22.5, 25.6, 25.8, 29.3, 31.5, 35.6, 120.4, 126.9, 127.9, 128.9, 129.6, 132.0, 138.3, 148.7. IR (KBr): v = 3116 (=C–H), 2930 (–C–H), 1466 (aromatic cycle), 1215 (C–N). Anal. Calcd for $C_{16}H_{23}N_3$ (257.37): C, 74.67; H, 9.01; N, 16.33. Found: C, 74.58; H, 9.22; N, 16.18.

4-hexyl-1-(2-nitrobenzyl)-1H-1,2,3-triazole (23). Yield: 86%; yellow solid; mp: 99–100 °C; ^{1}H NMR (300 MHz, $CDCl_3$): 0.80 (t, 3H, J = 6.2, CH_3), 1.23–1.32 (m, 6H, CH_2CH_2), 1.66–1.56 (m, 2H), 1.97 (t, 2H, J = 7.4), 5.85 (s, 2H, CH_2), 6.90 (d, 1H, J = 7.6), 7.48 (s, 1H, CH triazole), 7.56–7.46 (m, 2H), 8.00 (d, 2H, J = 7.9). ^{13}C NMR (300 MHz, $CDCl_3$) = 13.9, 22.8, 25.6, 27.7, 28.6, 29.2, 48.2, 121.7, 125.4, 128.2, 129.3, 129.8, 129.8, 134.2, 147.1. IR (KBr): v = 3116 (=C–H), 2927 (–C–H), 1608, 1524 (NO_2), 1466 (aromatic cycle), 1348 (C–N). Anal. Calcd for $C_{15}H_{20}N_4O_2$ (288.34): C, 62.48; H, 6.99; N, 19.43. Found: C, 62.36; H, 6.72; N, 19.48.

4-(4-phenyl-1H-1,2,3-triazol-1-yl)butanenitrile (24). Yield: 86%; yellow solid; mp: 85–87 °C; ^{1}H NMR (300 MHz, $CDCl_3$): 2.24–2.37 (m, 4H), 4.45 (t, 2H, J = 8.1), 7.73–7.82 (m, 6H, CH Arom).^{13}C NMR (300 MHz, $CDCl_3$) = 14.5, 25.8, 48.3, 118.4, 120.3, 125.6, 128.3, 128.9, 130.2, 147.8. IR (KBr): v = 3124 (=C–H), 2924 (–C–H), 2247 (cyanide), 1458, 1448 (aromatic cycle), 1354, 1222 (C–N). Anal. Calcd for $C_{12}H_{22}N_4$ (288.34): C, 67.90; H, 5.70; N, 26.40. Found: C, 67.96; H, 5.52; N, 26.49.

4-phenyl-1-propyl-1H-1,2,3-triazole (25). Yield: 92%; yellow solid; mp: 57–58 °C; ^{1}H NMR (300 MHz, $CDCl_3$): 1.00 (t, 3H, J = 7.3, CH_3CH_2), 2.01 (m, 2H), 4.37 (t, 2H, J = 7.0), 7.2–7.83 (m, 6H, CH Arom). ^{13}C NMR (300 MHz, $CDCl_3$) = 11.1, 23.7, 51.9, 119.4, 125.6, 128.1, 128.8, 130.6, 147.6. IR (KBr): v = 3131 (=C–H), 2923 (–C–H), 1463 (aromatic cycle), 1330, 1217 (C–N). Anal. Calcd for $C_{11}H_{13}N_3$ (187.24): C, 70.56; H, 7.00; N, 22.44. Found: C, 70.69; H, 7.08; N, 22.29.

7-((1-benzyl-1H-1,2,3-triazol-4-yl)methoxy)-2H-chromen-2-one (26). Yield: 94%; yellow solid; mp: 150–152 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.52 (s, 2H, OCH_2), 5.56 (s, 2H, CH_2), 6.26 (d, 1H, J = 9.4), 6.91–6.93 (m, 2H), 7.27–7.39 (m, 5H), 7.60 (s, 1H, CH triazole), 7.63 (m,

2H). IR (KBr): v = 3066 (=C–H), 1711 (C=O), 1491, 1402 (aromatic cycle), 1346, 1275 (C–N). Anal. Calcd for $C_{19}H_{15}N_3O_3$ (333.34): C, 68.64; H, 4.54; N, 12.61. Found: C, 67.63; H, 4.69; N, 12.49.

7-((1-(4-fluorobenzyl)-1H-1,2,3-triazol-4-yl)methoxy)-2H-chromen-2-one (27). Yield: 95%; yellow solid; mp: 130–132 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.24 (s, 2H, OCH_2), 5.55 (s, 2H, CH_2), 6.28 (d, 1H, J = 8.5), 6.90 (m, 2H), 7.01–7.39 (m, 4H), 7.64 (m, 2H), 7.76 (d, 1H, J = 8.5). ^{13}C NMR (300 MHz, $CDCl_3$) = 53.8, 62.2, 102.1, 112.7, 113.0, 113.5, 116.1, 116.2, 128.8, 130.0, 130.1, 143.2, 155.7, 160.9, 161.2, 161.9, 163.9. IR (KBr): v = 3102 (=C–H), 1705 (C=O), 1614 (C=C), 1348, 1280 (C–N), 1128 (C–O). Anal. Calcd for $C_{19}H_{11}FN_3O_3$ (351.33): C, 64.95; H, 4.02; N, 11.96. Found: C, 64.73; H, 4.09; N, 11.68.

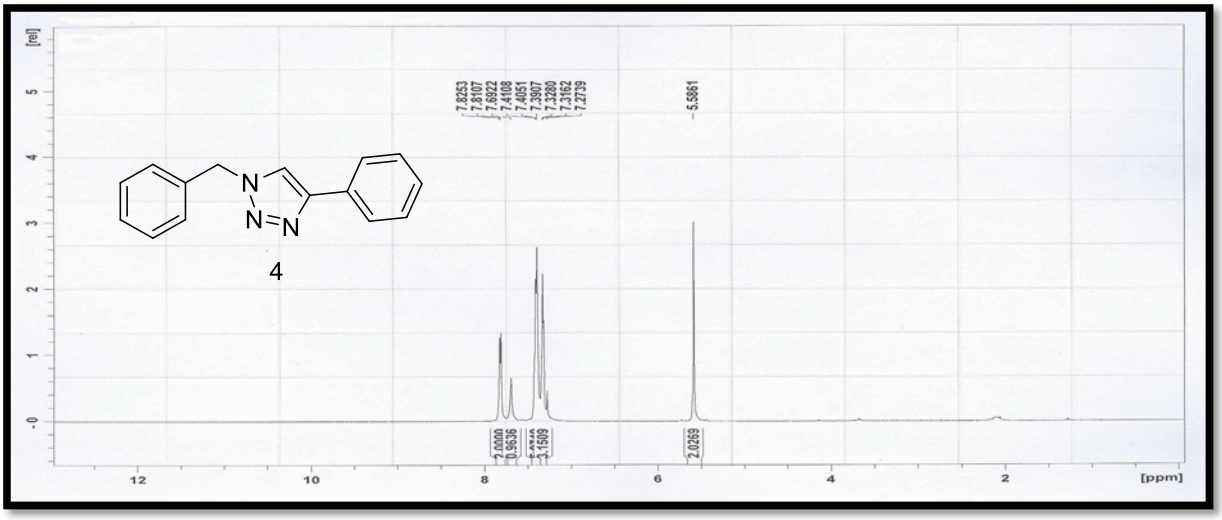
1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)indoline-2,3-dione (28). Yield: 70%; orange solid; mp: 112–114 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 5.00 (s, 2H, CH_2-C triazole), 5.50 (s, 2H, CH_2-N triazole), 7.12 (d, 2H, J = 7.0), 7.28–7.37 (m, 5H), 7.54–7.58 (m, 3H). Anal. Calcd for $C_{18}H_{14}N_4O_2$ (318.33): C, 67.91; H, 4.43; N, 17.60. Found: C, 67.99; H, 4.51; N, 17.52.

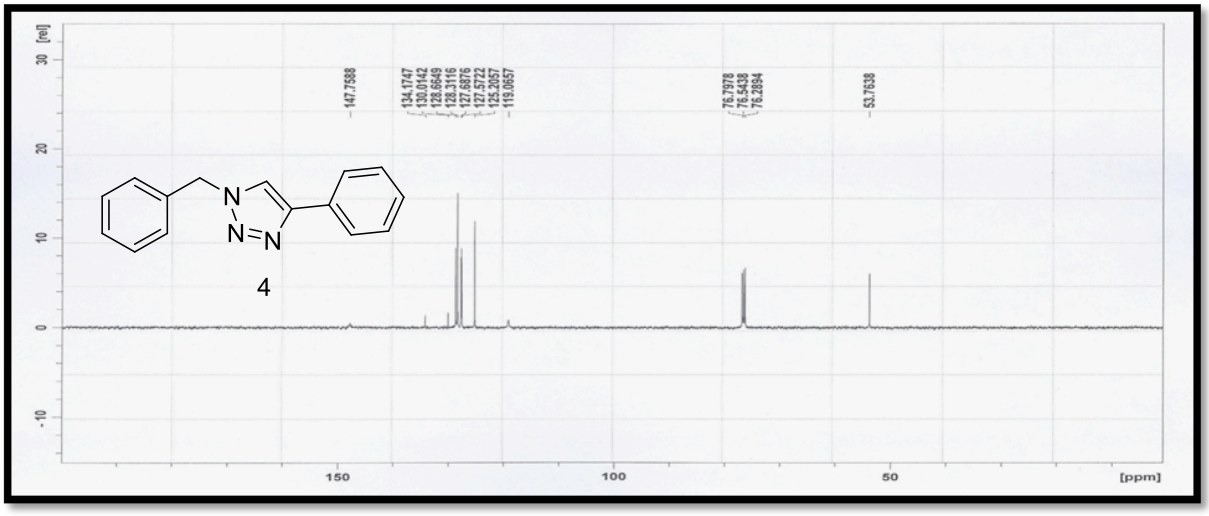
1-((1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl)-5-(piperidin-1-ylsulfonyl)indoline-2,3-dione (29). Yield: 50%; orange solid; mp: 207–210 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 0.89–1.66 (m, 6H), 3.10 (m, 4H), 5.10 (s, 2H), 5.46 (s, 2H), 7.16–8.00 (m, 8H). ^{13}C NMR (300 MHz, $CDCl_3$) = 23.4, 25.1, 29.6, 35.5, 46.9, 53.7, 111.9, 117.2, 123.0, 124.5, 129.9, 132.4, 132.9, 137.7, 141.6, 152.8, 157.4, 181.6. IR (KBr): v = 3128 (=C–H), 1750, 1612 (C=O), 1474, 1448 (aromatic cycle), 1362 (S=O), 1333, 1277 (C–N), 1155 (C–O). Anal. Calcd for $C_{23}H_{22}N_5O_4S$ (544.42): C, 67.91; H, 4.43; N, 17.60. Found: C, 67.99; H, 4.51; N, 17.52.

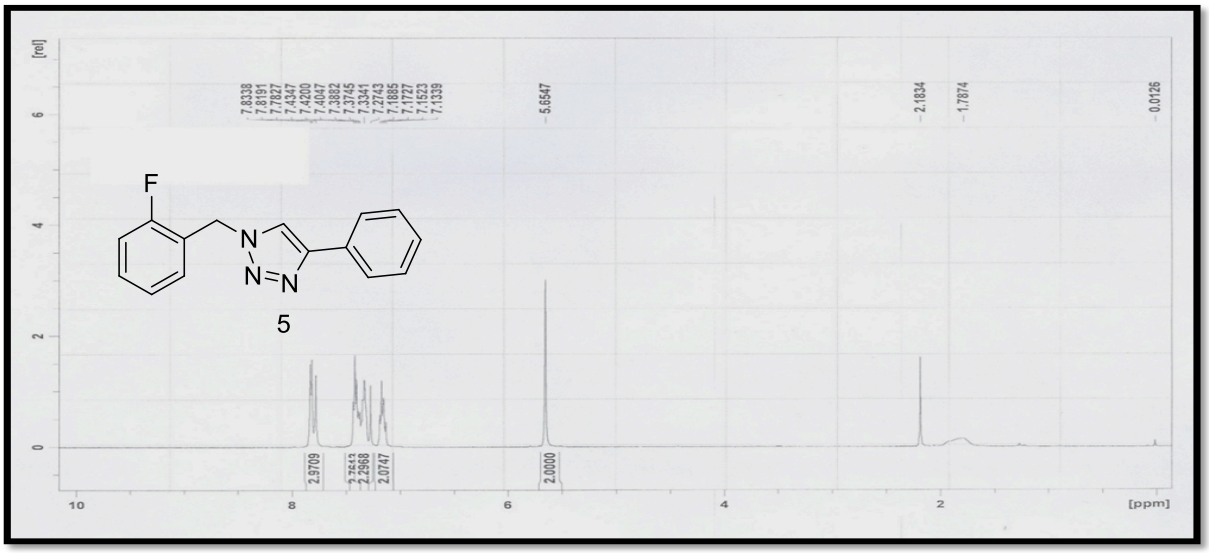
(8R,9S,10R,13S,14S,17S)-17-(1-(2-chlorobenzyl)-1H-1,2,3-triazol-4-yl)-17-hydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3(2H)-one (30). Yield: 70%; orange solid; mp: 101–104 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 0.51–2.97 (m, 23H), 5.70 (s, 2H, CH_2), 5.81 (s, 1H, OH), 7.16–7.145 (m, 5H). ^{13}C NMR (300 MHz, $CDCl_3$) = 26.2, 29.4, 30.5, 32.4, 35.3, 36.2, 37.6, 40.8, 42.3, 46.9, 48.0, 48.7, 53.2, 82.0, 121.2, 122.6, 124.2, 129.4, 132.0, 133.5, 154.1, 167.0, 200.0. IR (KBr): v = 3411 (O–H), 3063 (=C–H), 1661 (C=O), 1449 (aromatic cycle), 1359, 1260 (C–N), 1132 (C–O). Anal. Calcd for $C_{27}H_{32}ClN_3O_2$ (466.01): C, 69.59; H, 6.92; N, 9.02. Found: C, 69.72; H, 6.99; N, 9.15.

(8R,9S,10R,13S,14S,17S)-17-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)-17-hydroxy-13-methyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3(2H)-one (31). Yield: 70%; yellow solid; mp: 108–112 °C; ^{1}H NMR (500 MHz, $CDCl_3$): 0.48–2.47 (m, 23H), 5.45 (s, 2H, CH_2), 5.46 (s, 1H, OH), 5.78 (s, 1H), 7.12 (d, 2H, J = 8.2), 7.30 (s, 1H, CH triazole), 7.48 (d, 2H, J = 8.2). ^{13}C NMR (300 MHz, $CDCl_3$) = 26.5, 29.6, 30.7, 32.6, 35.4, 36.4, 37.8, 41.1, 42.5, 47.1, 48.2, 49.0, 51.5, 82.1, 121.4, 124.5, 127.5, 129.9, 130.2, 153.6, 166.6, 199.9. IR (KBr): v = 3444 (O–H), 3139 (=C–H), 1661 (C=O), 1488, 1452 (aromatic cycle), 1261 (C–N), 1131 (C–O). Anal. Calcd for $C_{27}H_{32}BrN_3O_2$ (510.47): C, 63.53; H, 6.32; N, 8.23 Found: C, 69.45; H, 6.29; N, 8.37.

5. Copy of ^{1}H NMR & ^{13}C NMR spectra of the synthesized compounds:



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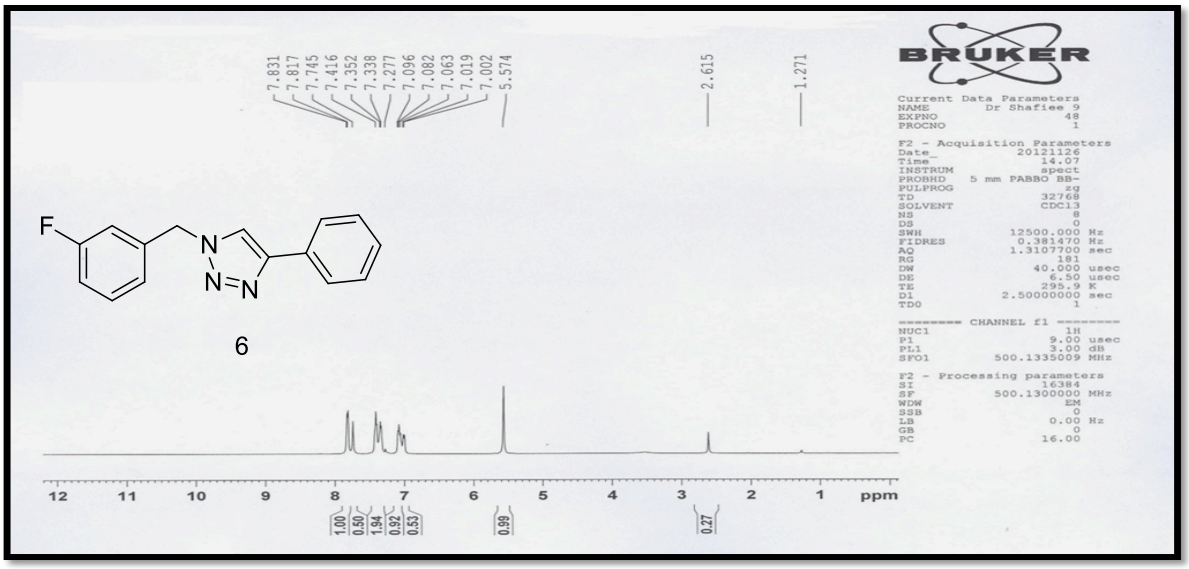
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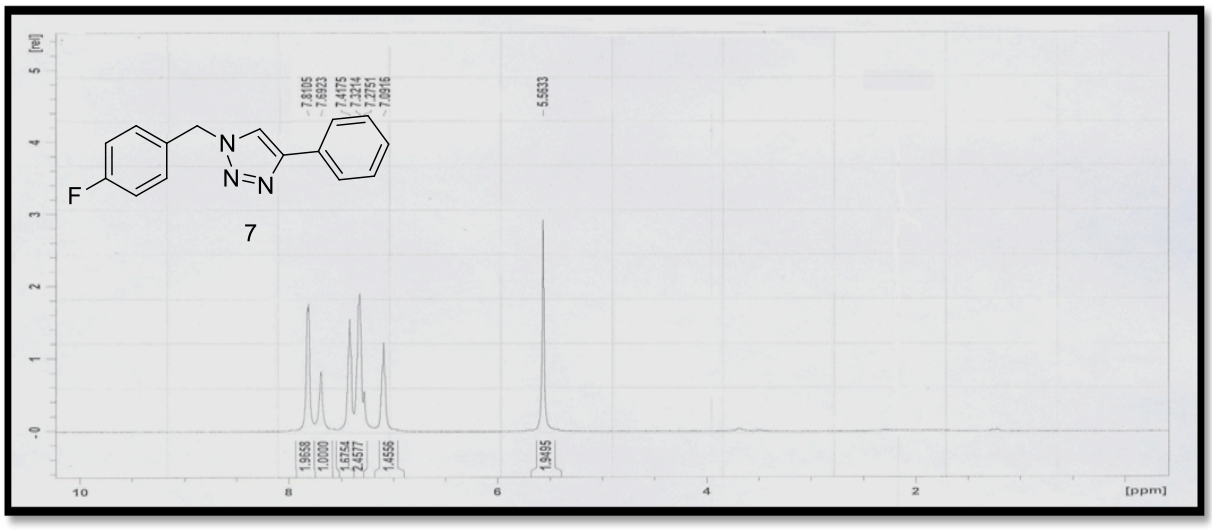
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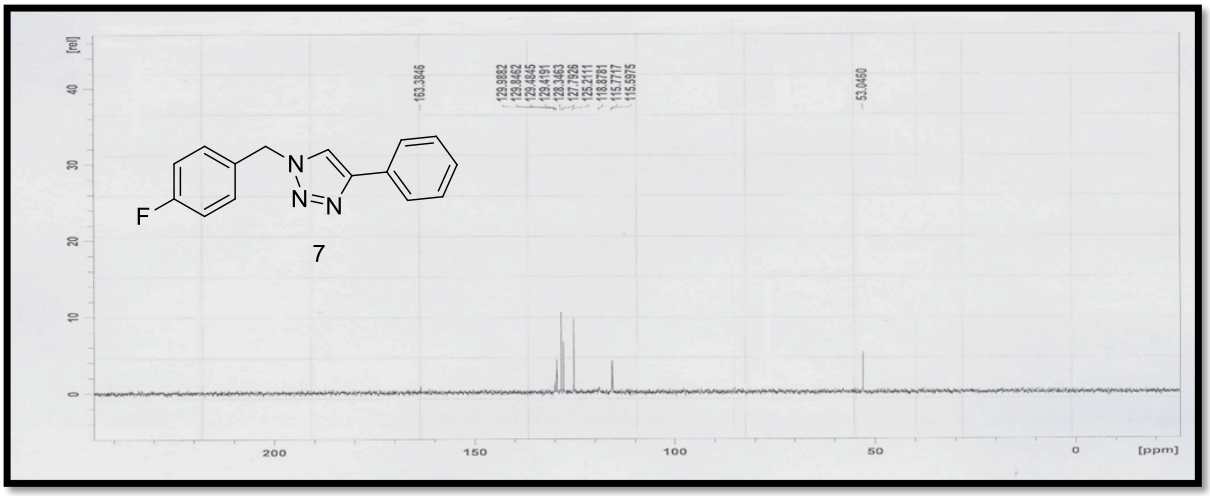
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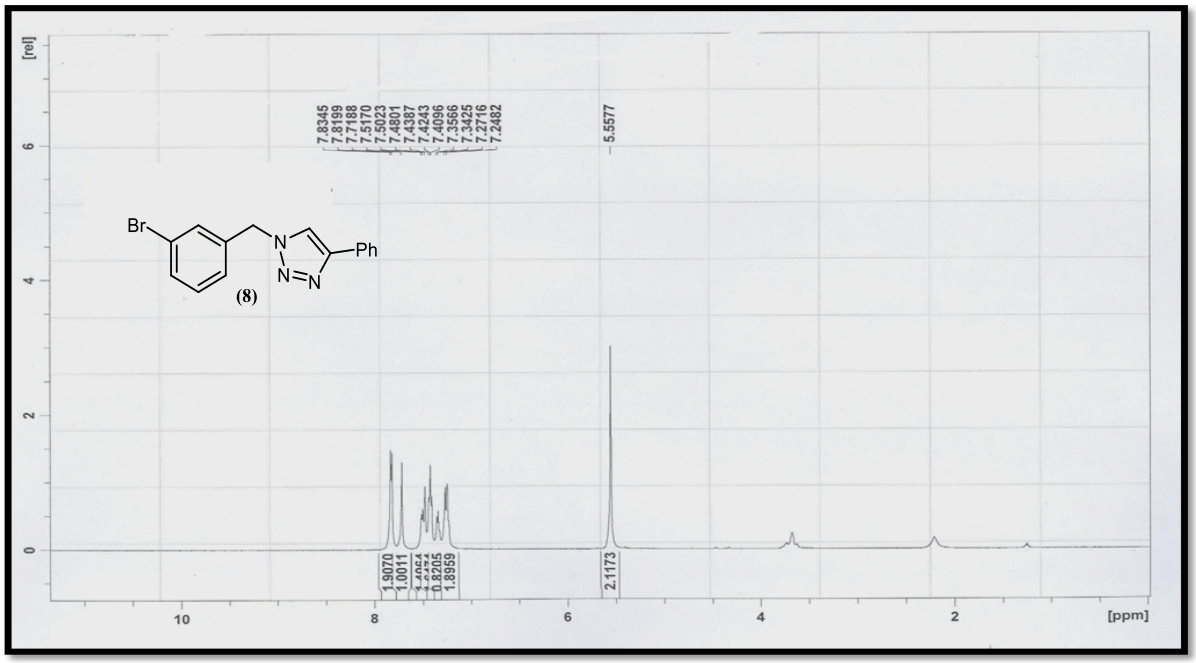
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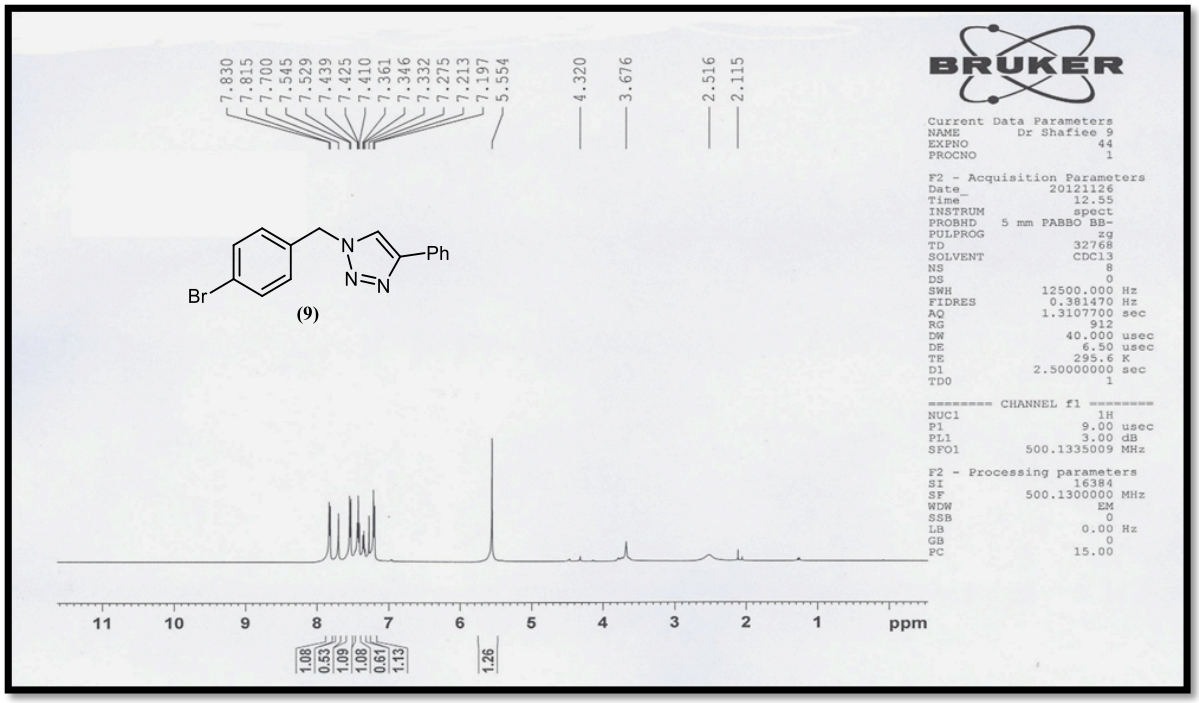
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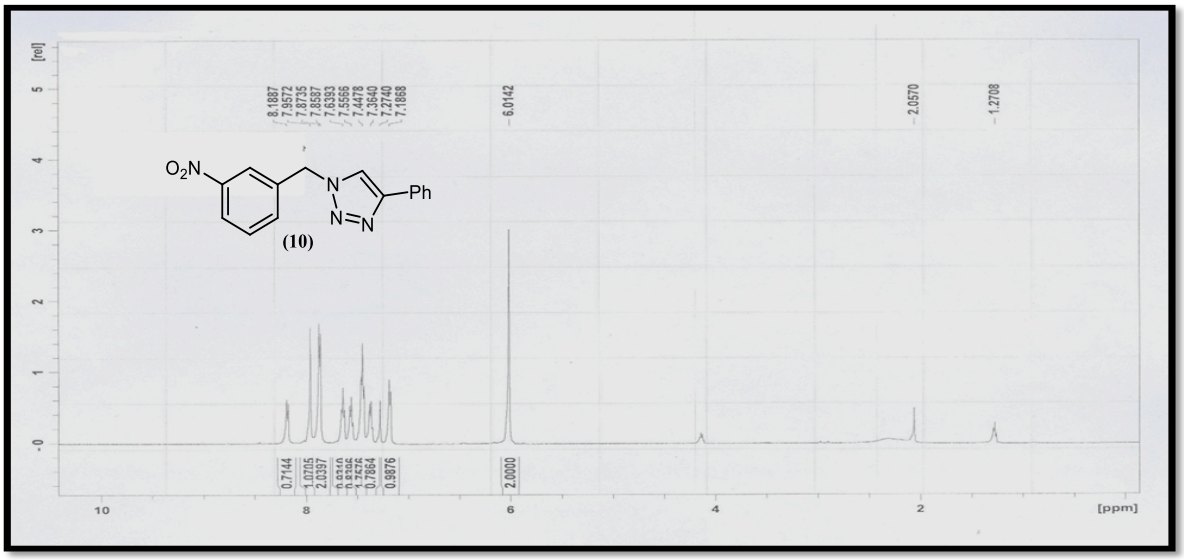
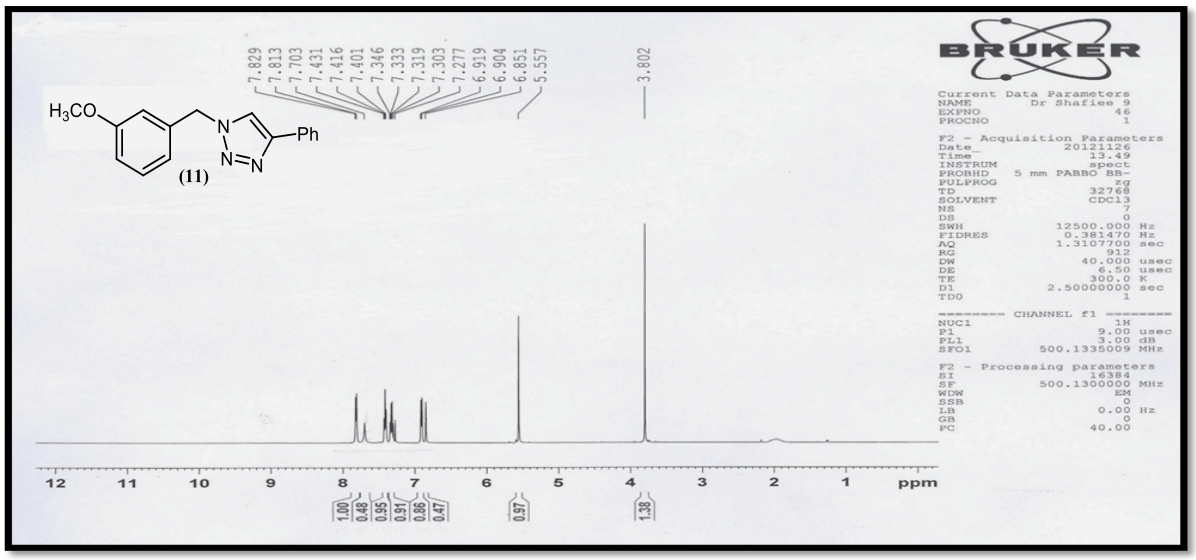
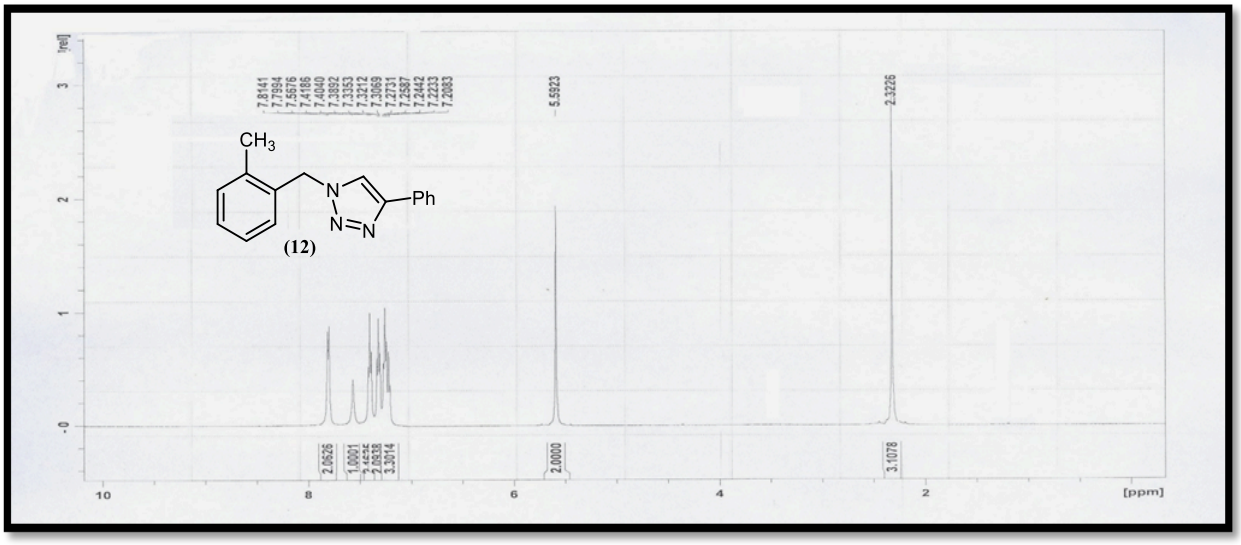
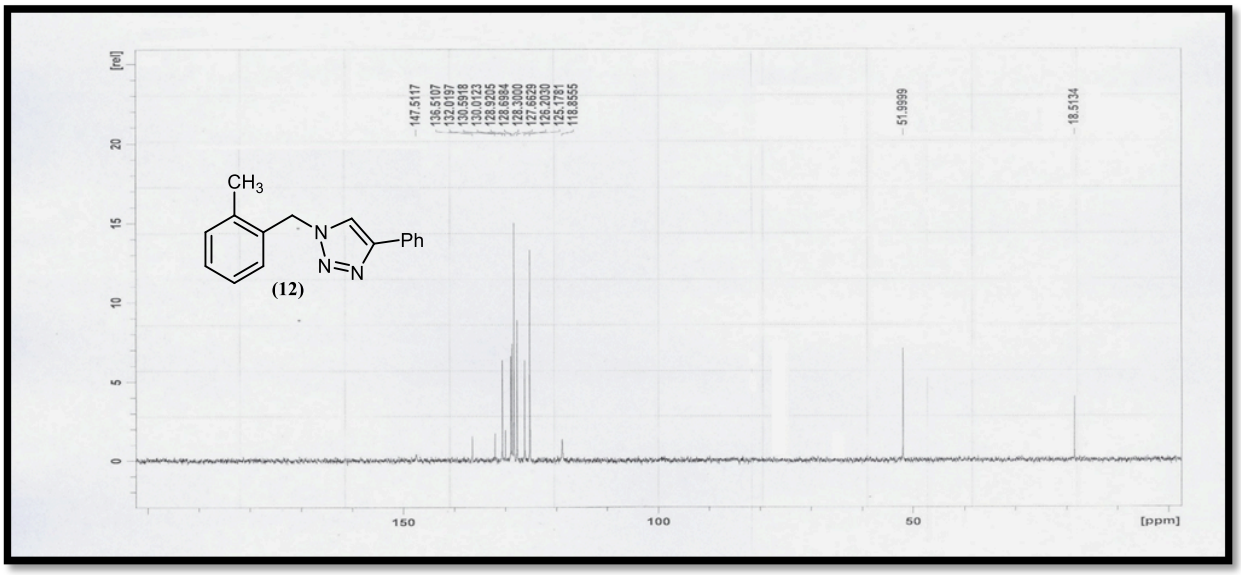
7.197
5.554
4.320
3.676
2.516
2.115
Br
N
N=N
Ph
(9)
BRUKER
Current Data Parameters
NAME Dr Shafiee 9
EXPNO 44
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121126
Time 12.55
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 8
DS 0
SWH 12500.000 Hz
FIDRES 0.381470 Hz
AQ 1.3107700 sec
RG 912
DW 40.000 usec
DE 6.50 usec
TE 295.6 K
D1 2.50000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 9.00 usec
PL1 3.00 dB
SFO1 500.1335009 MHz
F2 - Processing parameters
SI 16384
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 15.00
11
10
9
8
7
6
5
4
3
2
1
ppm
1.08
0.53
1.09
1.08
0.61
1.13
1.26

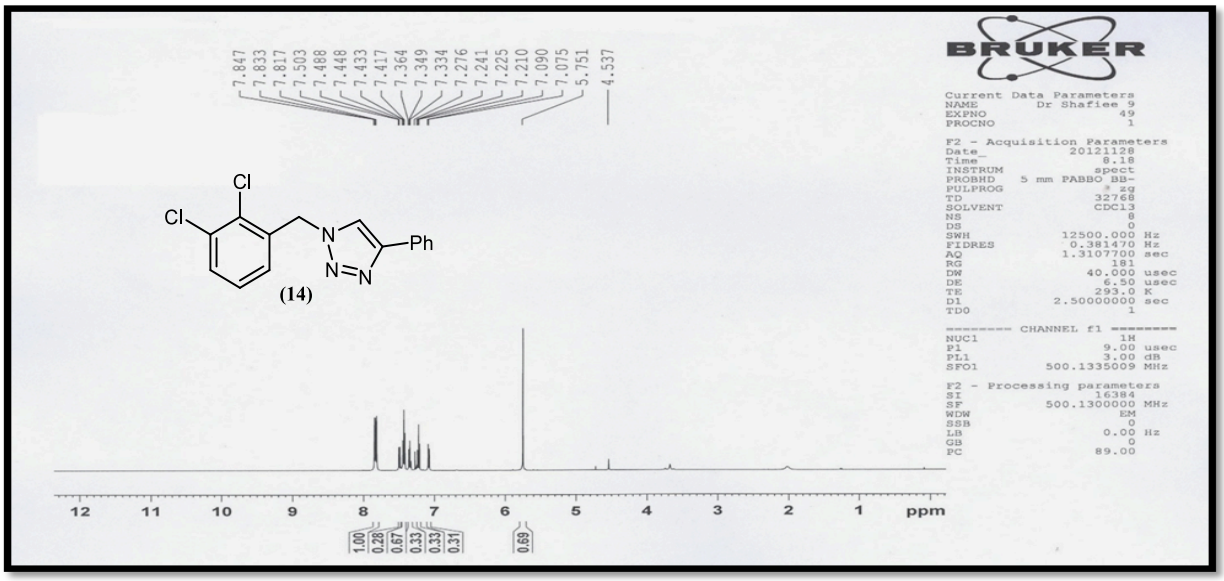

8.1887
7.9572
7.8735
7.8587
7.6393
7.5566
7.4478
7.3640
7.2740
7.1868
6.0142
2.0570
1.2708
O2N
N
N=N
Ph
(10)
0.7144
1.0705
2.0397
1.7526
0.7864
0.9876
2.0000
[ppm]

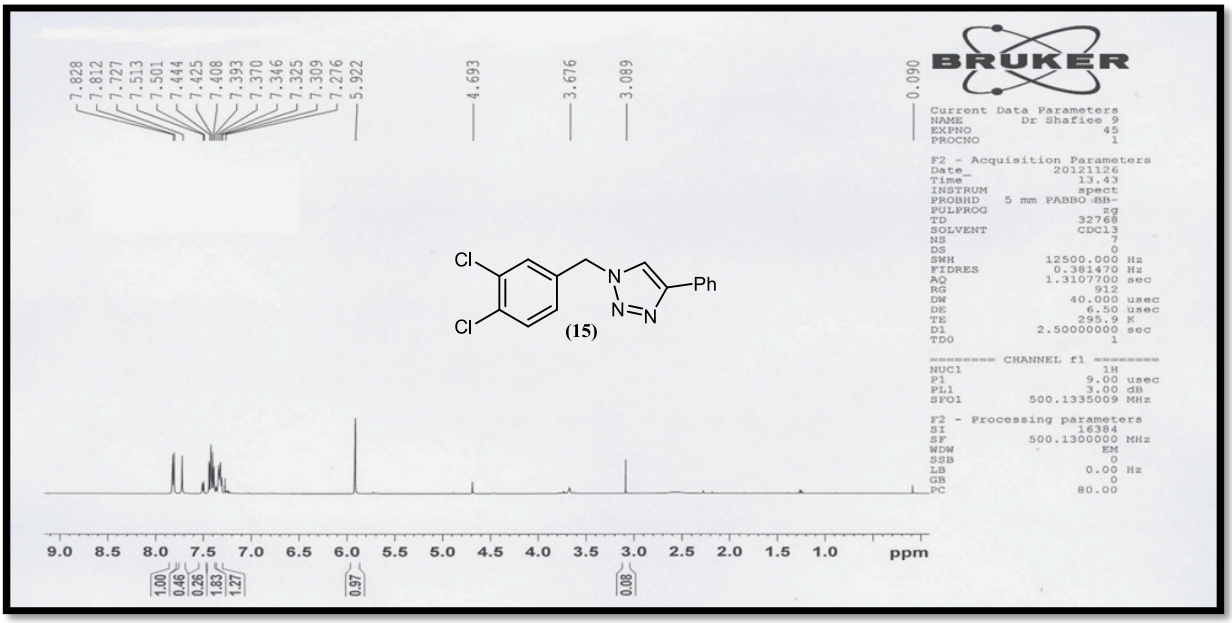

7.829
7.813
7.703
7.431
7.416
7.401
7.346
7.333
7.319
7.303
7.277
6.919
6.904
6.851
5.557
3.802
H3CO
N
N=N
Ph
(11)
1.00
0.48
0.95
0.91
0.86
0.47
0.97
1.38
ppm
BRUKER
Current Data Parameters
NAME Dr Shafiee 9
EXPNO 46
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121126
Time 13.49
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 7
DS 0
SWH 12500.000 Hz
FIDRES 0.381470 Hz
AQ 1.3107700 sec
RG 912
DW 40.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.50000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 9.00 usec
PL1 3.00 dB
SFO1 500.1335009 MHz
F2 - Processing parameters
SI 16384
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 40.00

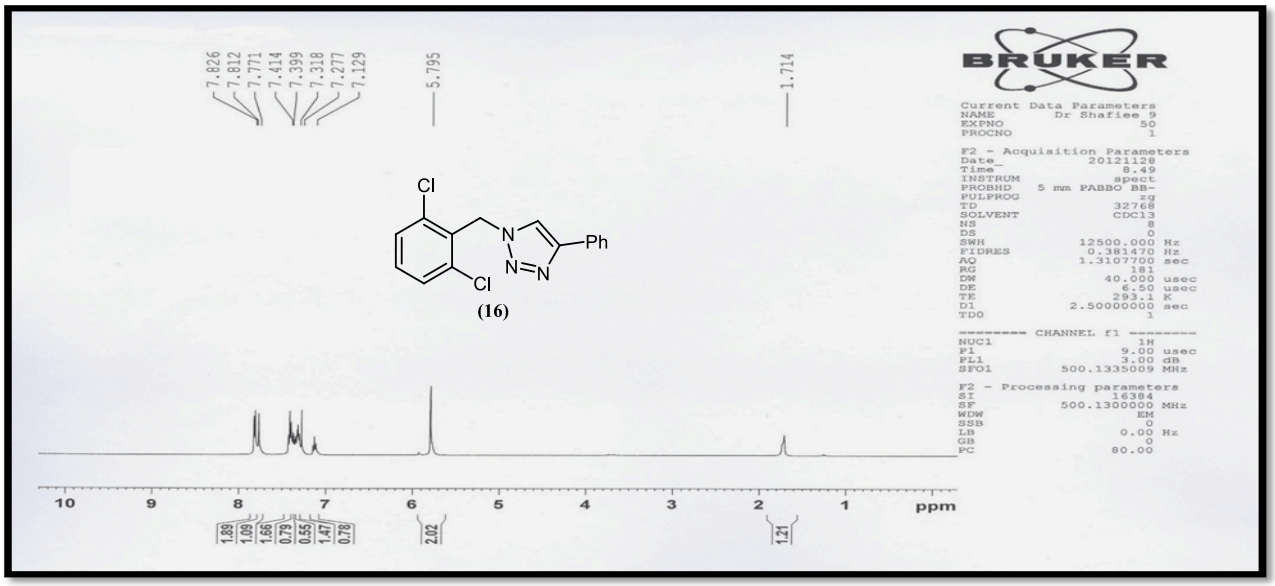

7.8141
7.7994
7.5676
7.4186
7.4040
7.3892
7.3353
7.3212
7.3069
7.2731
7.2587
7.2442
7.2233
7.2083
5.5923
2.3226
CH3
N
N
N
Ph
(12)
2.0626
1.0001
2.4252
2.0000
3.1078
3.3014
[rel]
[ppm]

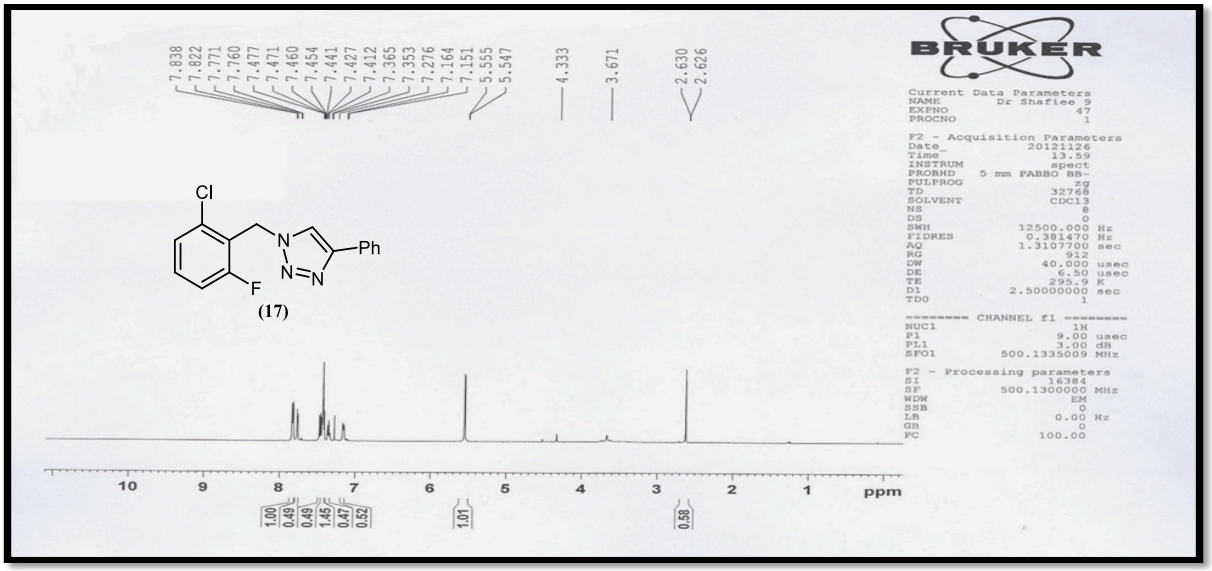

147.5117
136.5107
132.0197
130.5918
130.0123
128.9225
128.8984
128.3000
127.6629
126.4320
125.7261
118.8555
51.9999
18.5134
CH3
N
N
N
Ph
(12)
[rel]
[ppm]

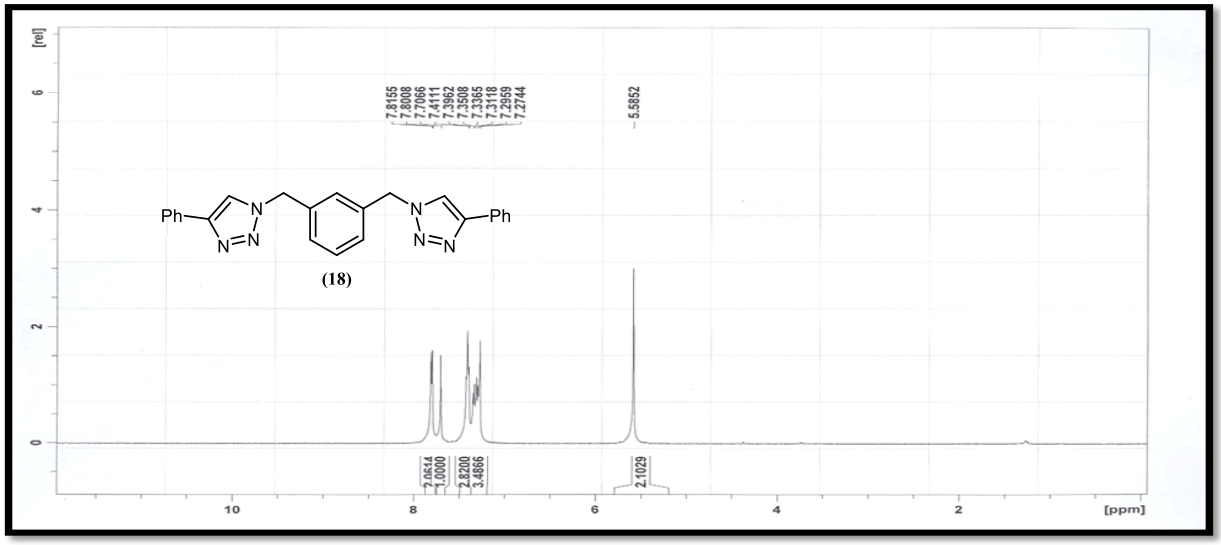

[rel]
7.8303
7.6978
7.4089
7.3244
7.2827
7.1903
7.1292
5.5322
2.3552
2.0585
1.2758
H3C
N
N=N
Ph
(13)
2.0248
1.0152
4.5459
3.0452
2.0000
3.0270
10
8
6
4
2
[ppm]

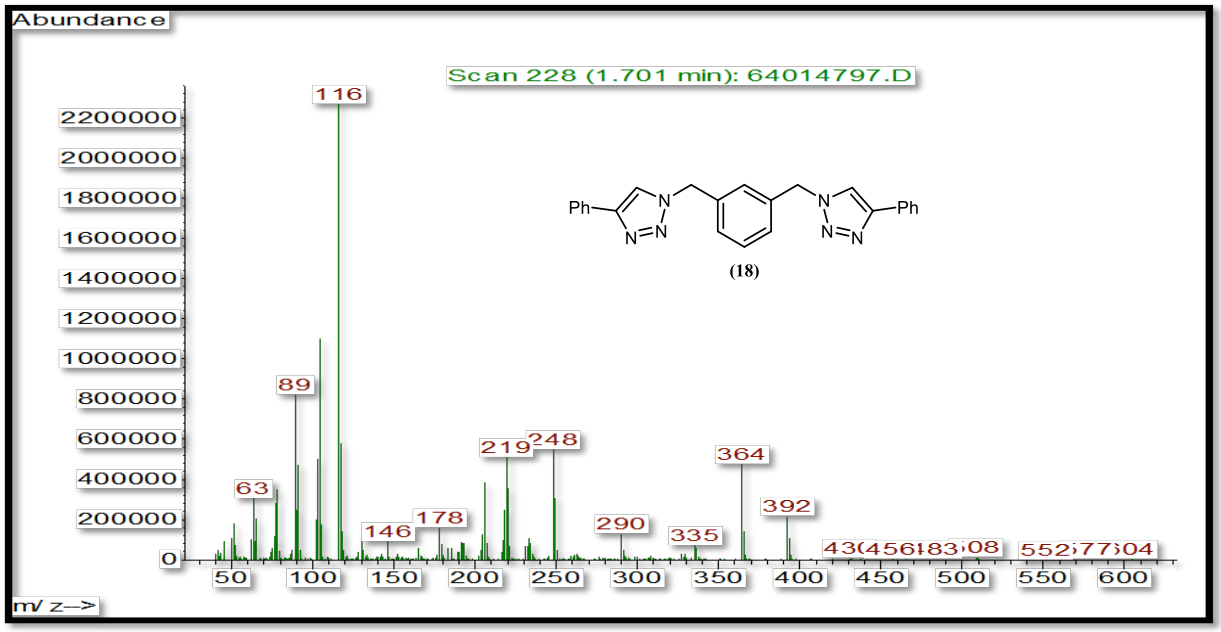

7.847
7.833
7.817
7.503
7.488
7.448
7.433
7.417
7.364
7.349
7.334
7.276
7.241
7.225
7.210
7.090
7.075
5.751
4.537
Cl
Cl
N
N=N
Ph
(14)
BRUKER
Current Data Parameters
NAME Dr Shafiee 9
EXPNO 49
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121128
Time 8.18
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 8
DS 0
SWH 12500.000 Hz
FIDRES 0.381470 Hz
AQ 1.3107700 sec
RG 181
DW 40.000 usec
DE 6.50 usec
TE 293.0 K
D1 2.50000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 9.00 usec
PL1 3.00 dB
SFO1 500.1335009 MHz
F2 - Processing parameters
SI 16384
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 89.00
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.00
0.28
0.67
0.33
0.33
0.31
0.69

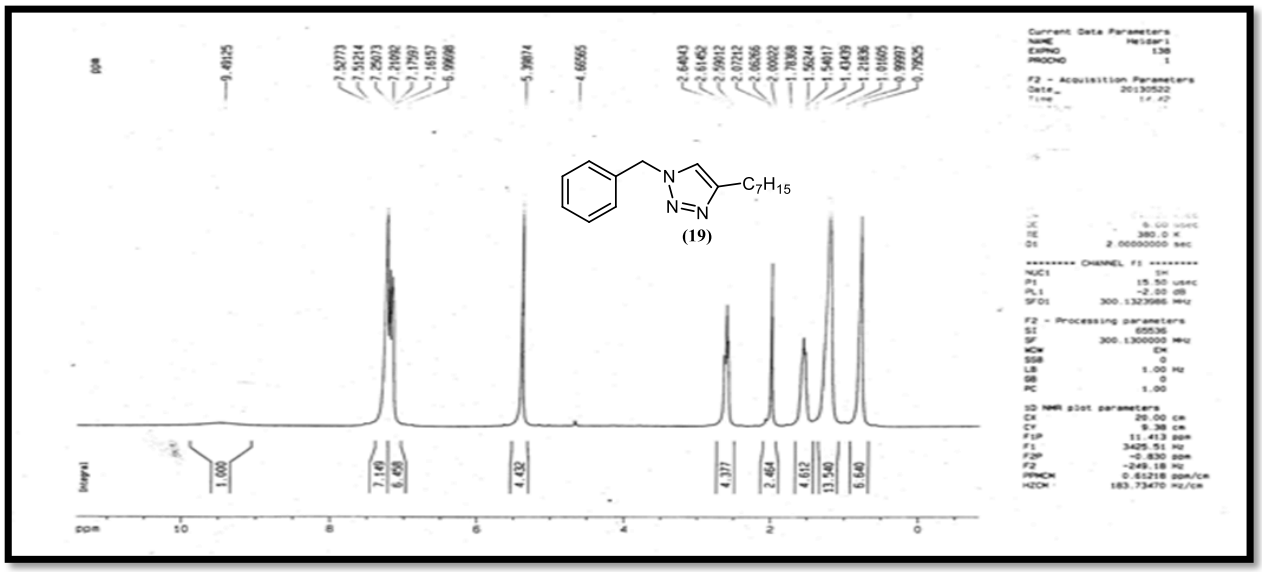

7.828
7.812
7.727
7.513
7.501
7.444
7.425
7.408
7.393
7.370
7.346
7.325
7.309
7.276
5.922
4.693
3.676
3.089
0.090
Cl
Cl
N
N=N
Ph
(15)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.00
0.46
0.26
1.83
1.27
0.97
0.08
BRUKER
Current Data Parameters
NAME Dr Shafiee 9
EXPNO 45
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121126
Time 13.43
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 7
DS 0
SWH 12500.000 Hz
FIDRES 0.381470 Hz
AQ 1.3107700 sec
RG 912
DW 40.000 usec
DE 6.50 usec
TE 295.9 K
D1 2.50000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 9.00 usec
PL1 3.00 dB
SFO1 500.1335009 MHz
F2 - Processing parameters
SI 16384
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 80.00

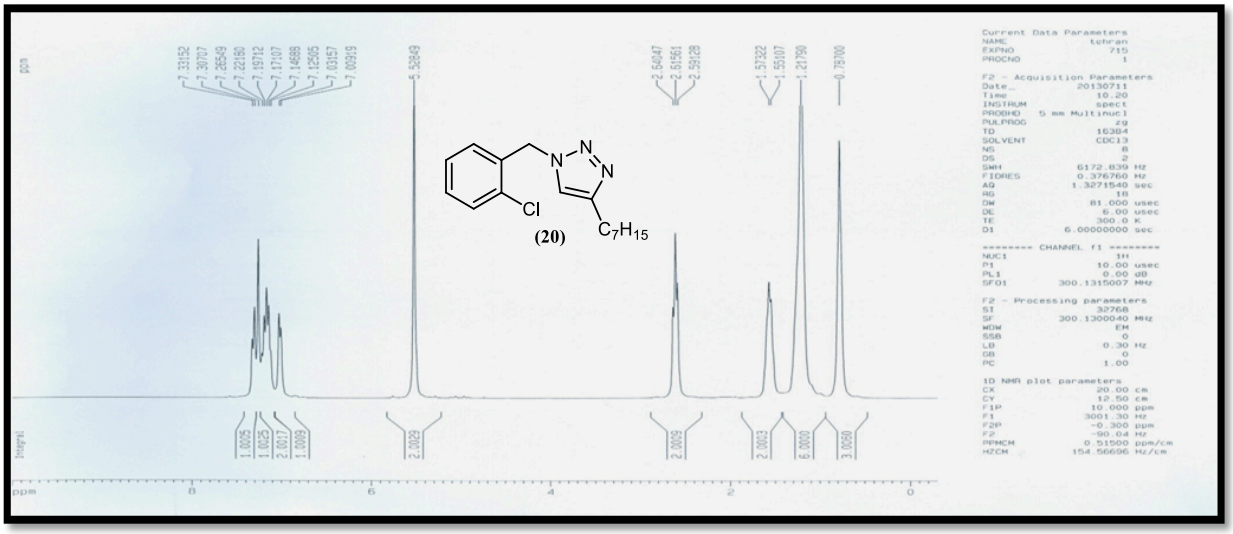

7.826
7.812
7.771
7.414
7.399
7.318
7.277
7.129
5.795
1.714
Cl
Cl
N
N=N
Ph
(16)
10 9 8 7 6 5 4 3 2 1 ppm
1.89
1.09
1.66
0.73
0.55
1.47
0.78
2.02
1.21
BRUKER
Current Data Parameters
NAME Dr Shafiee 9
EXPNO 50
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121128
Time 8.49
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 8
DS 0
SWH 12500.000 Hz
FIDRES 0.381470 Hz
AQ 1.3107700 sec
RG 181
DW 40.000 usec
DE 6.50 usec
TE 293.1 K
D1 2.50000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 9.00 usec
PL1 3.00 dB
SFO1 500.1335009 MHz
F2 - Processing parameters
SI 16384
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 80.00

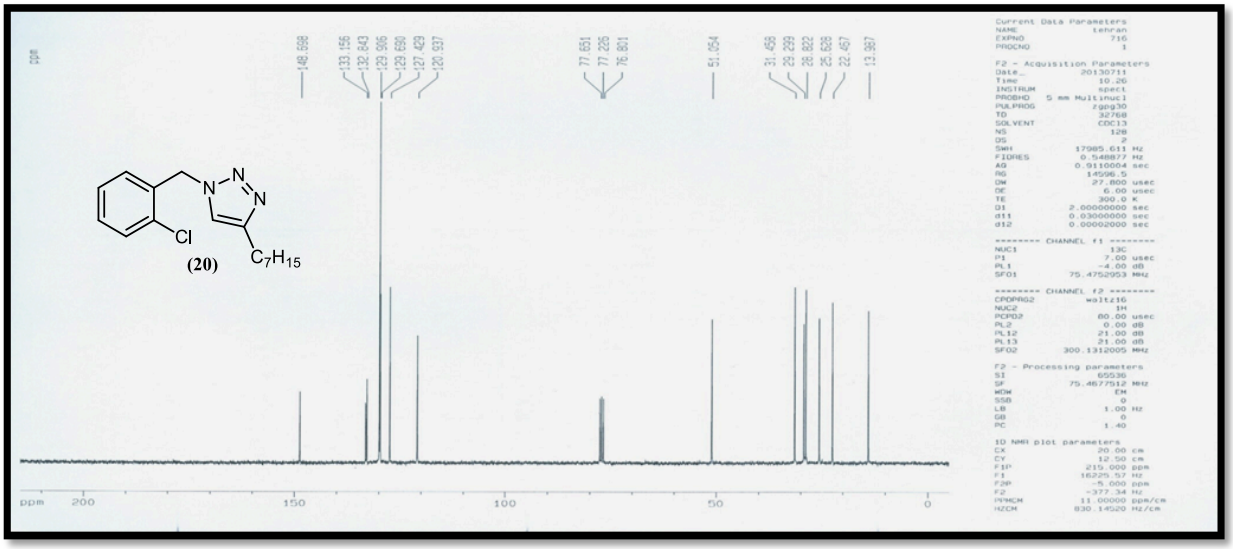

7.838
7.822
7.771
7.760
7.477
7.471
7.460
7.454
7.441
7.427
7.412
7.365
7.353
7.276
7.164
7.151
5.555
5.547
4.333
3.671
2.630
2.626
Cl
F
Ph
N
N=N
(17)
BRUKER
Current Data Parameters
NAME Dr Shafiee 9
EXPNO 47
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121126
Time 13.59
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 8
DS 0
SWH 12500.000 Hz
FIDRES 0.381470 Hz
AQ 1.3107700 sec
RG 912
DW 40.000 usec
DE 6.50 usec
TE 295.9 K
D1 2.50000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 9.00 usec
PL1 3.00 dB
SFO1 500.1335009 MHz
F2 - Processing parameters
SI 16384
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 100.00
10 9 8 7 6 5 4 3 2 1 ppm
1.00 0.49 0.49 1.45 0.47 0.52 1.01 0.58

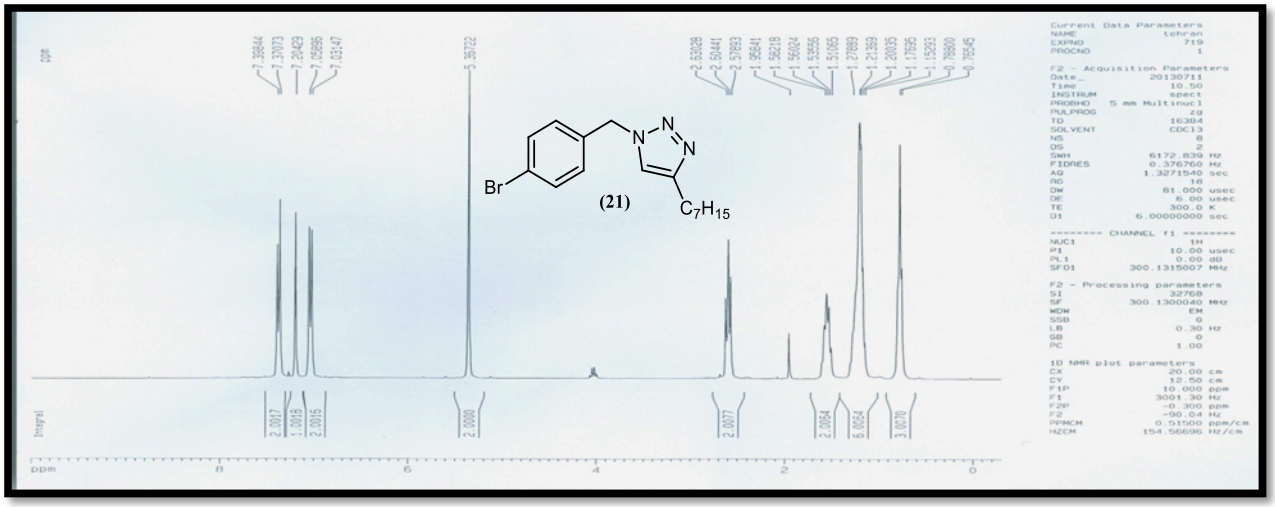

[rel]
7.8155
7.8008
7.7066
7.4111
7.3962
7.3508
7.3365
7.3118
7.2959
7.2744
5.5852
Ph
N
N=N
Ph
(18)
2.0644
1.0000
2.8200
3.4866
2.1029
10 8 6 4 2 [ppm]

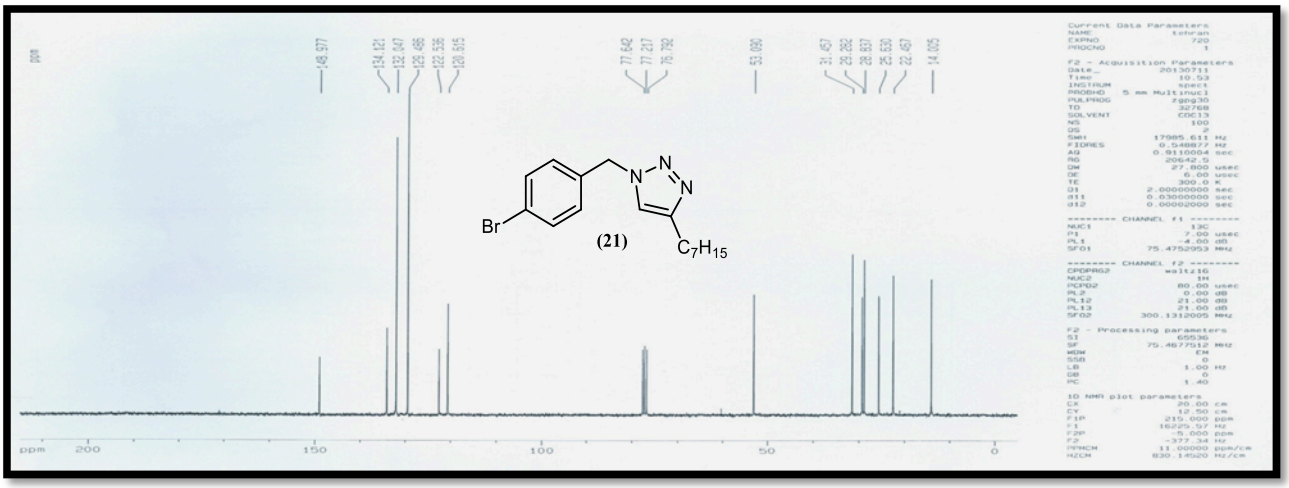

Abundance
Scan 228 (1.701 min): 64014797.D
116
89
63
219
248
364
392
146
178
290
335
43(456)83)08
552)77)04
2200000
2000000
1800000
1600000
1400000
1200000
1000000
800000
600000
400000
200000
0
50
100
150
200
250
300
350
400
450
500
550
600
m/ z-->
Ph
Ph
(18)

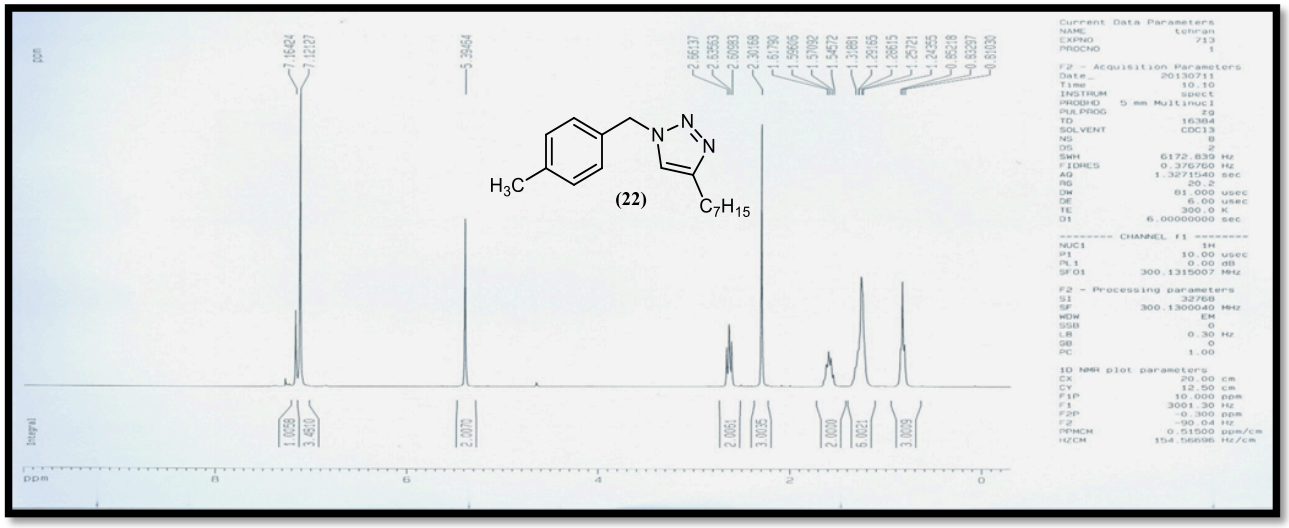

C7H15
(19)

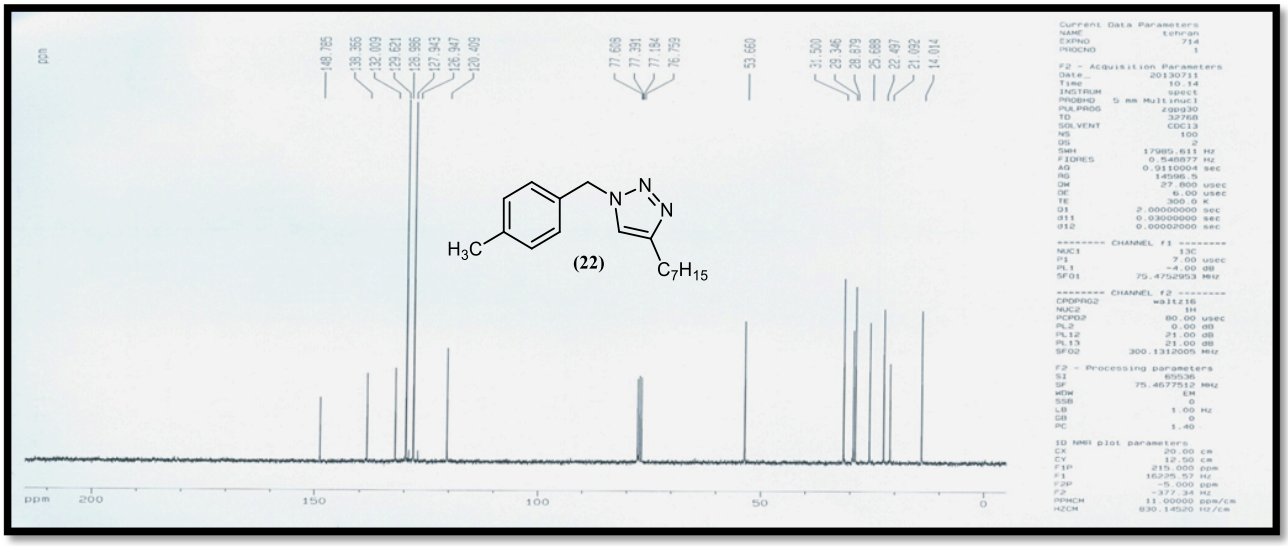

(20)

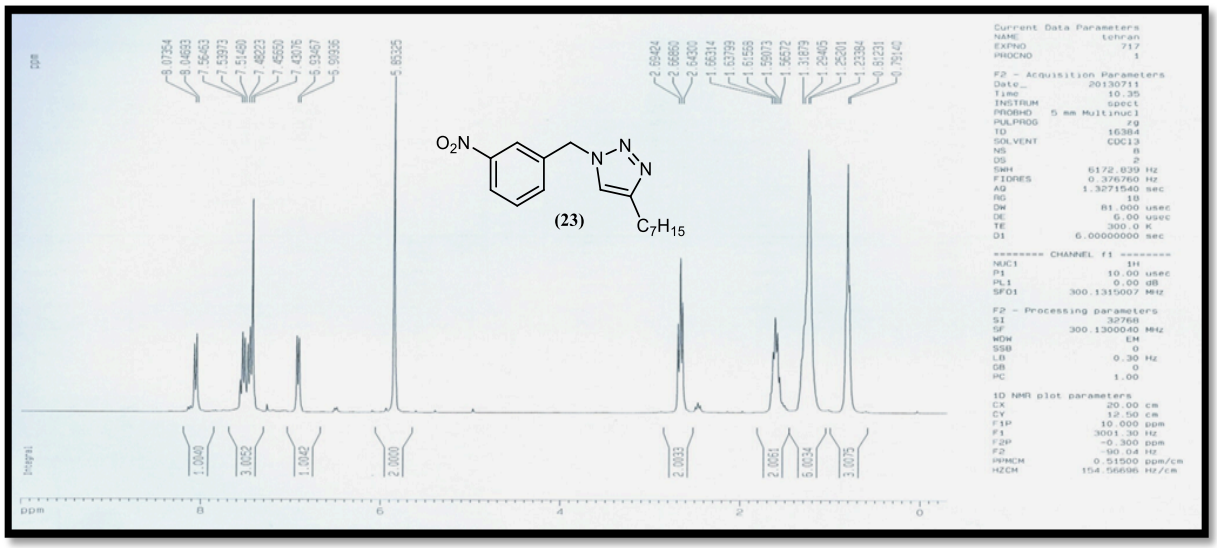

(20)

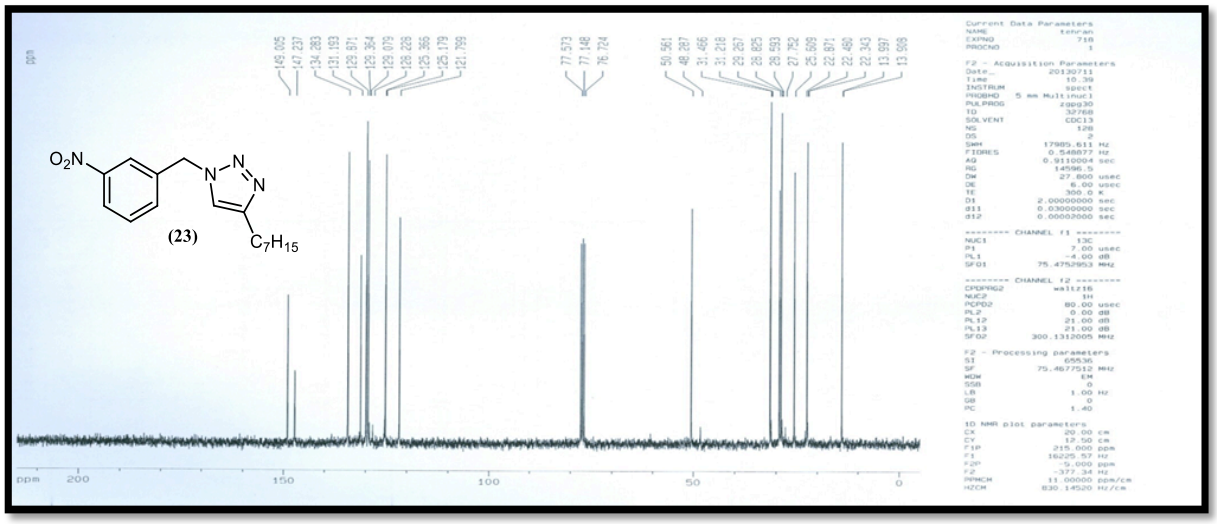

Br
(21)
C_7H_{15}

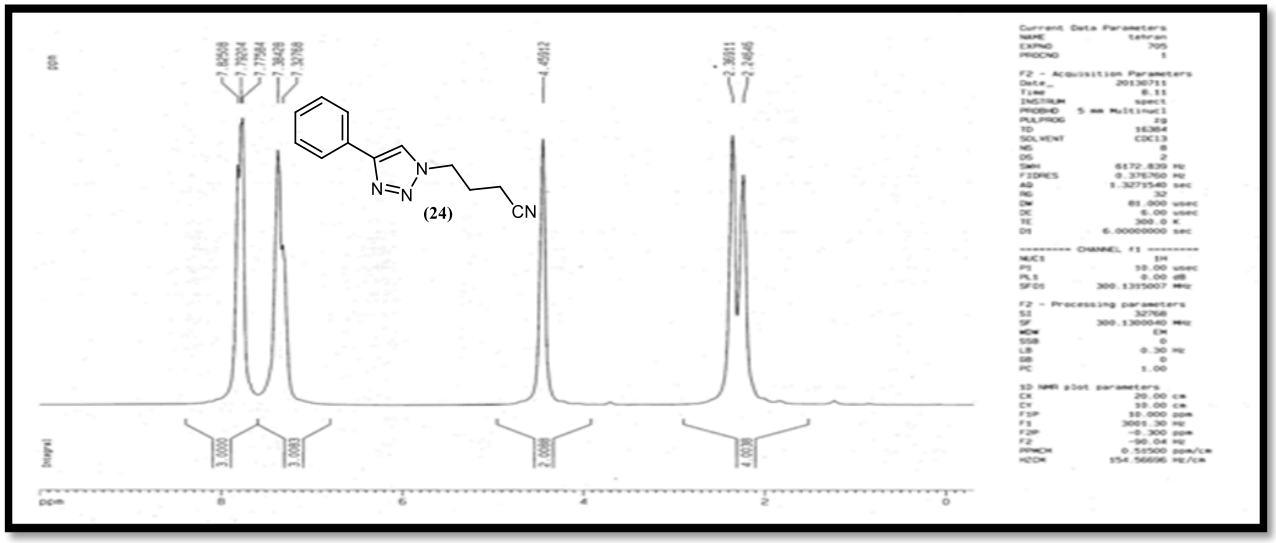

Br
(21)
C_7H_{15}

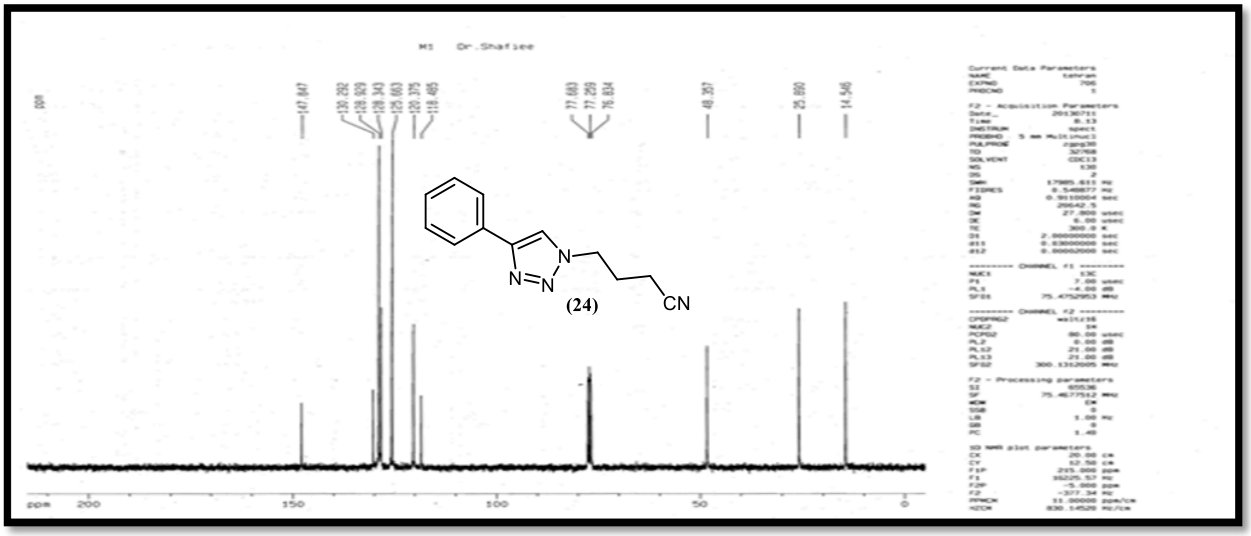

(22)

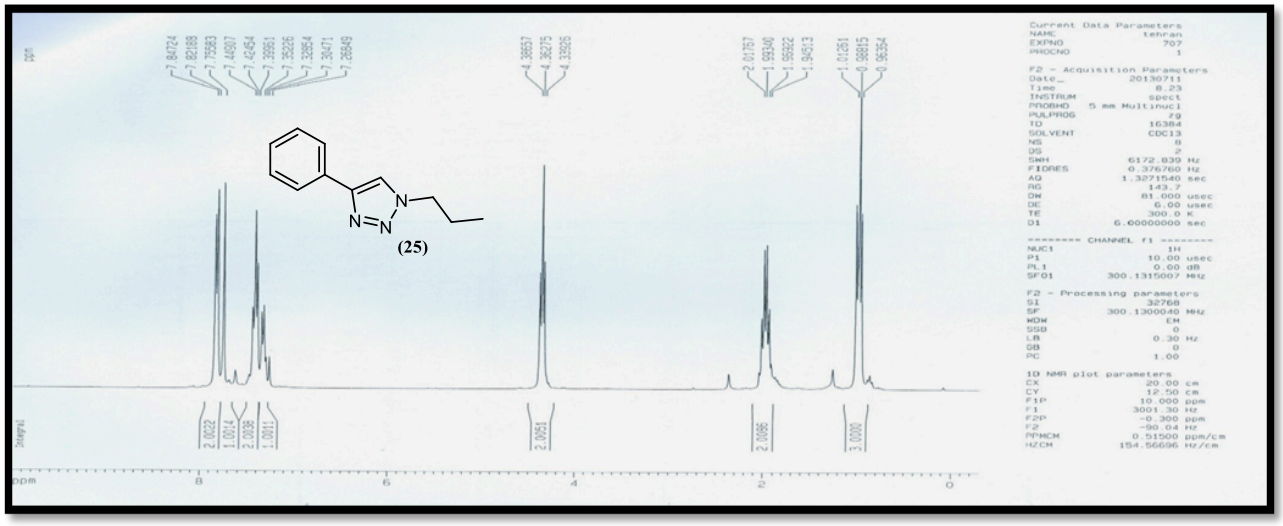

(22)

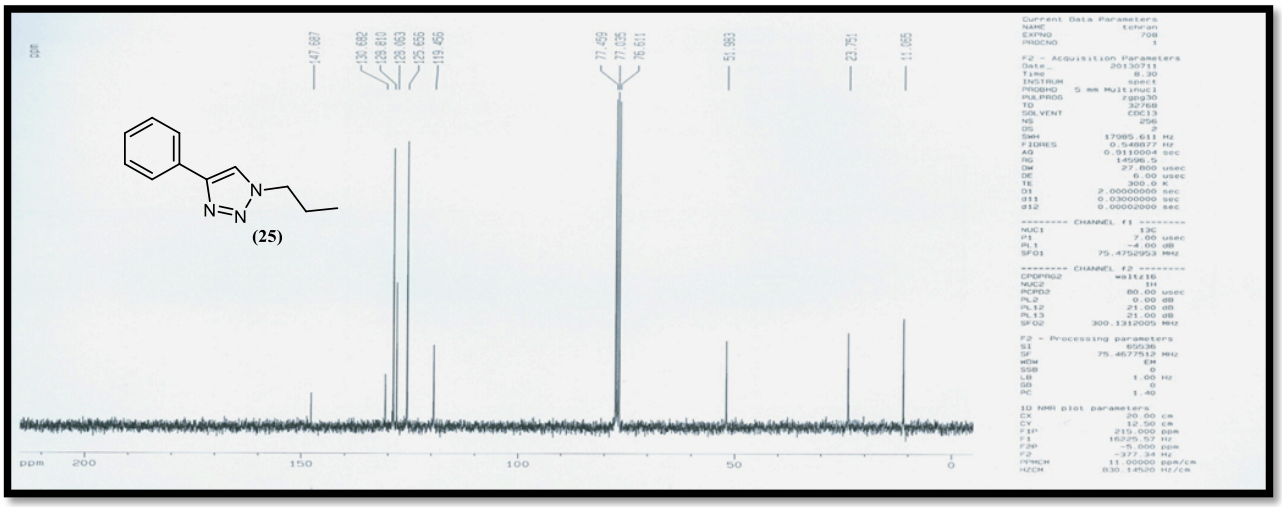

(23)

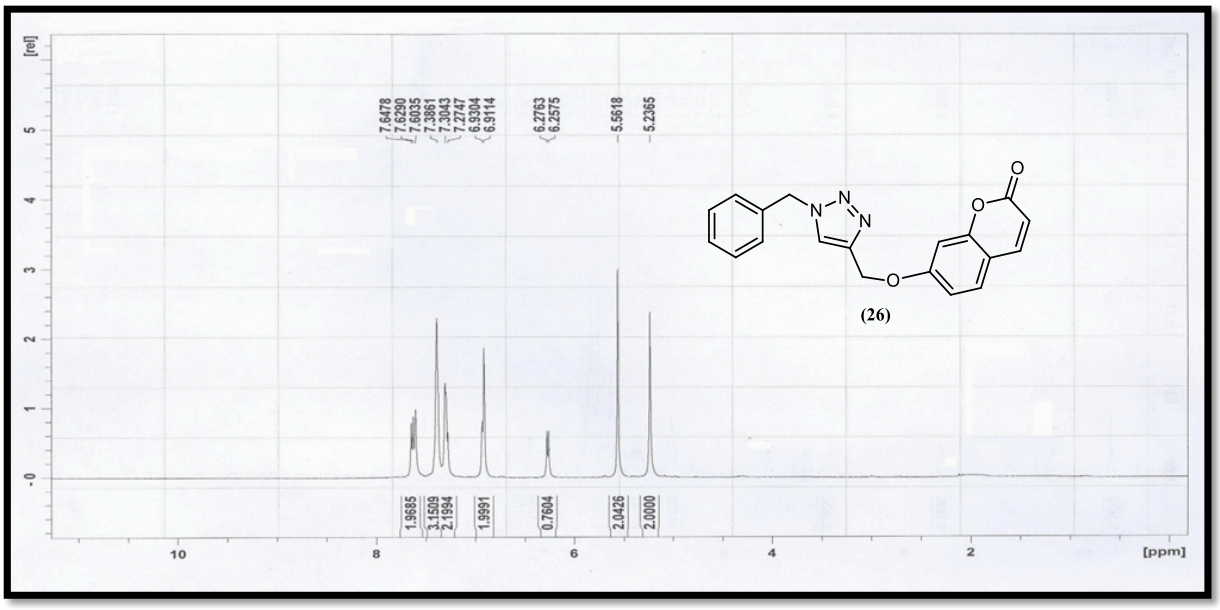

(23)


(24)
CN

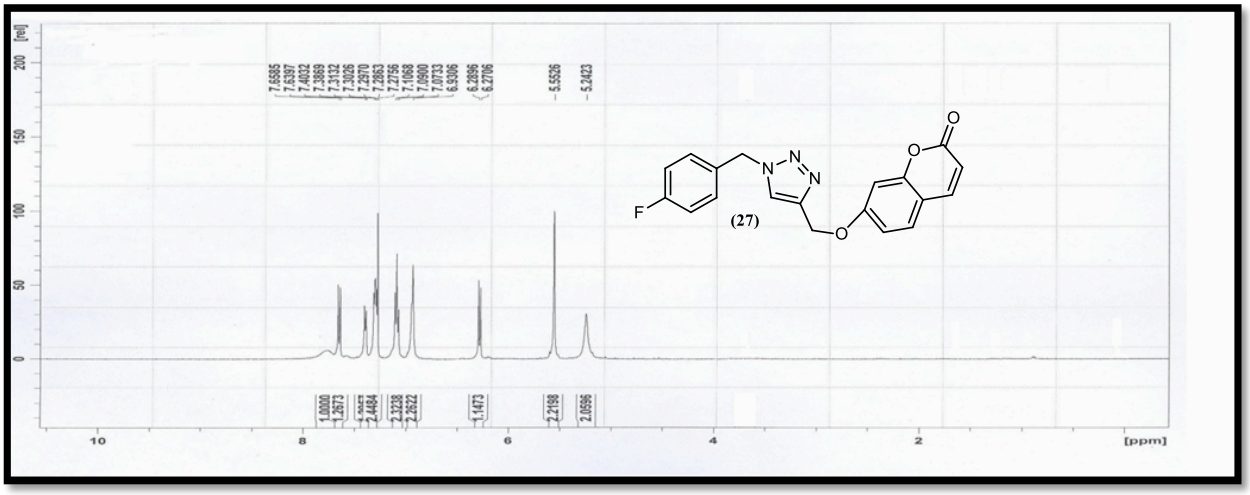

(24)
CN


(25)

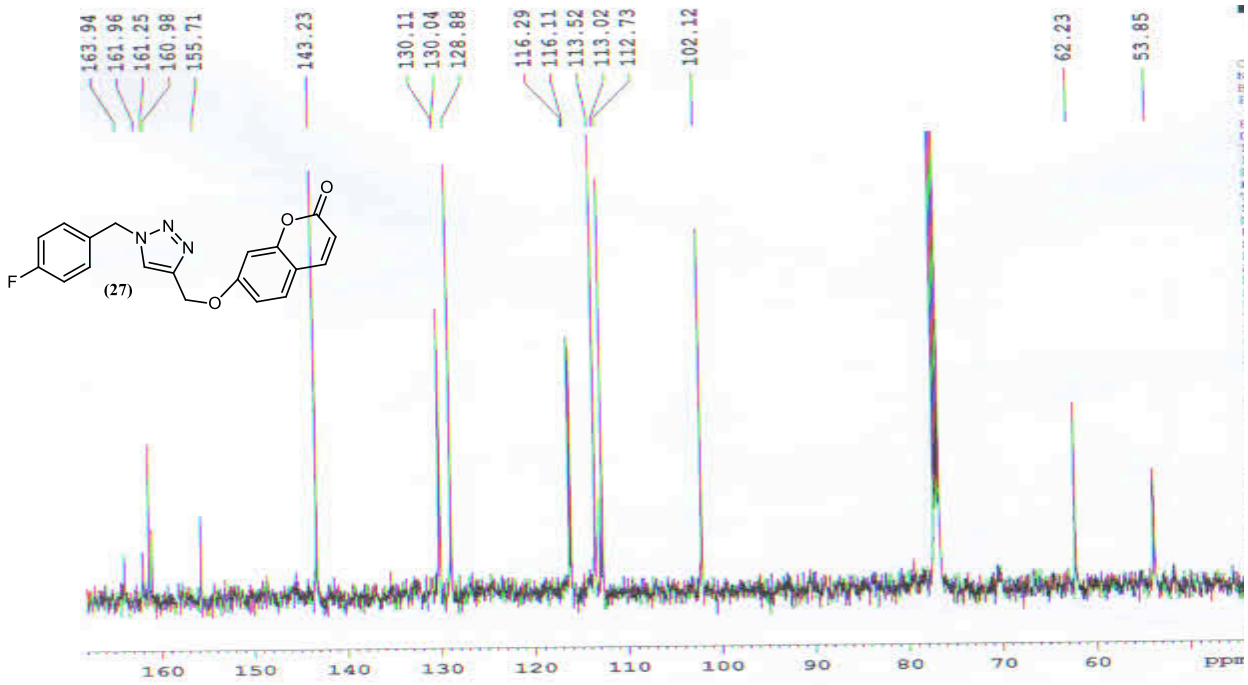

(25)

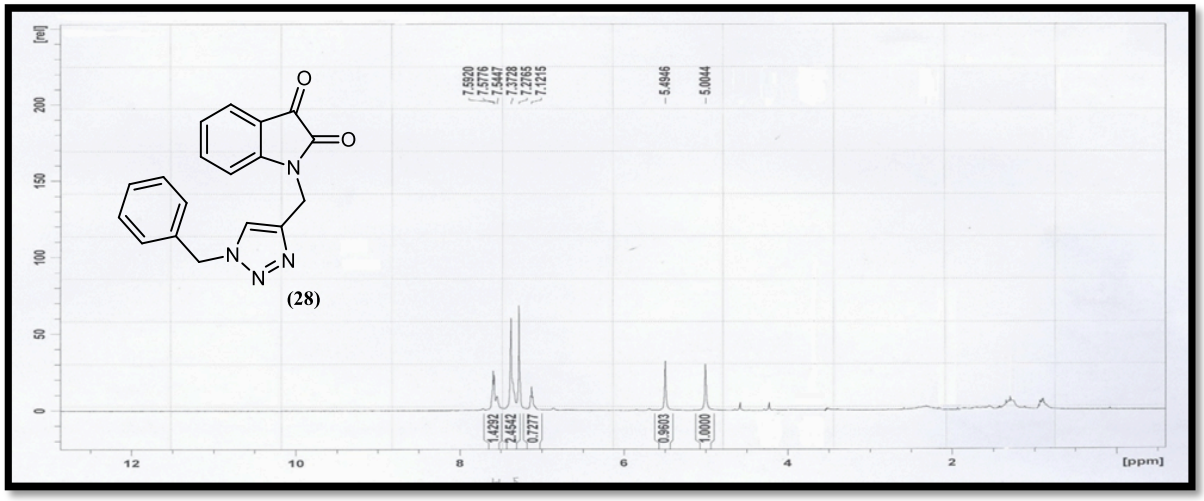

[rel]
7.6478
7.6290
7.6035
7.3861
7.3043
7.2747
6.9304
6.9114
6.2763
6.2575
5.5618
5.2365
1.9685
3.1509
2.1994
1.9991
0.7604
2.0426
2.0000
10
8
6
4
2
[ppm]
O
N
N
N
O
O

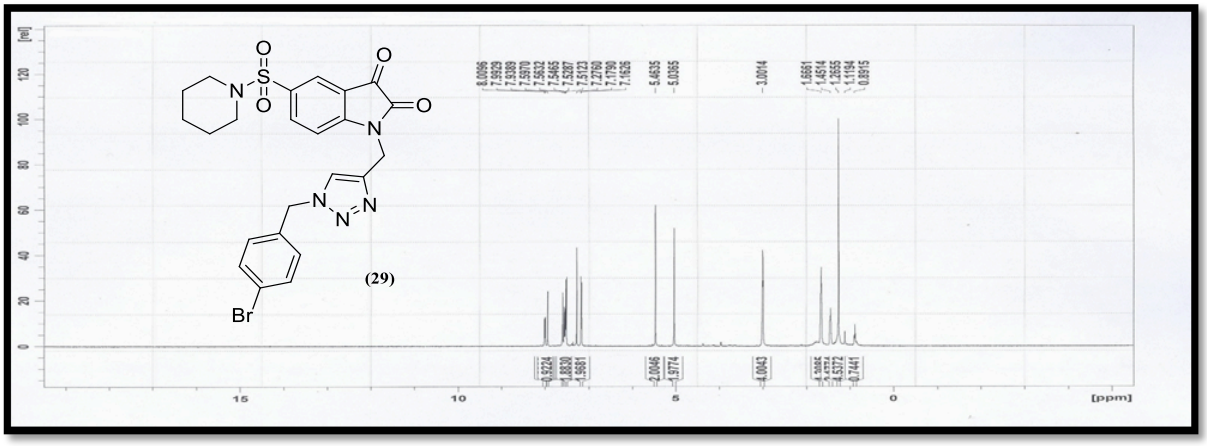
(26)

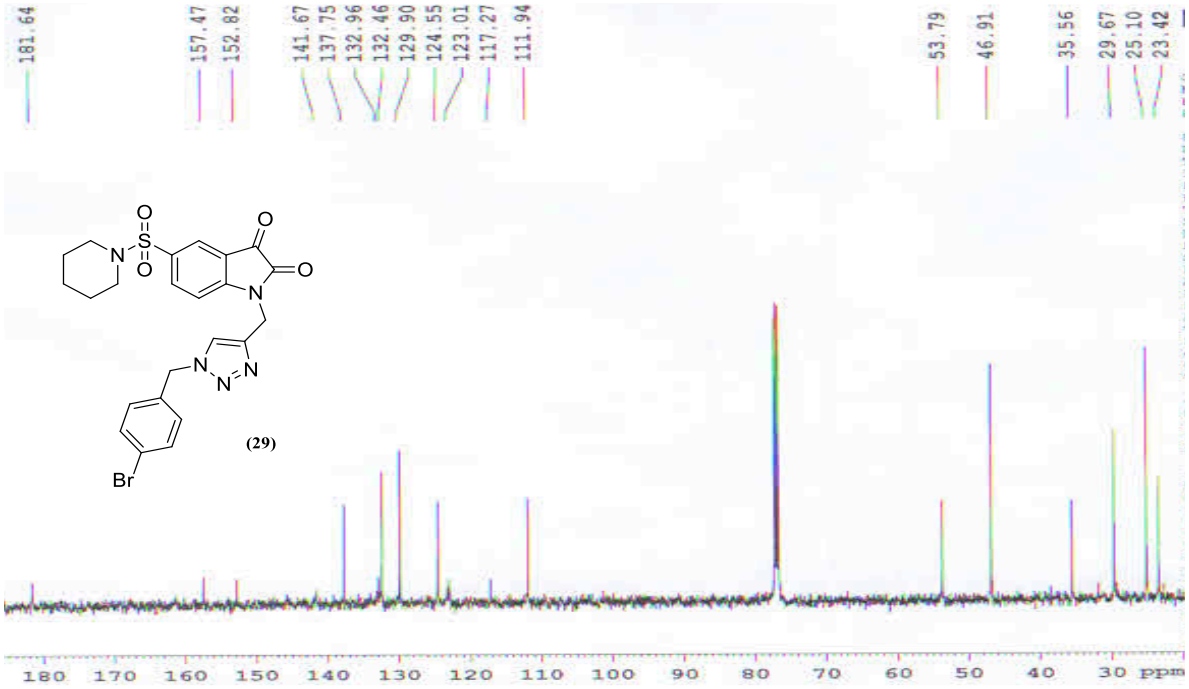

[rel]
7.6585
7.6397
7.4032
7.3869
7.3132
7.3026
7.2970
7.2863
7.2756
7.1068
7.0900
7.0733
6.9306
6.2896
6.2706
5.5526
5.2423
1.0000
1.2673
2.4484
2.3238
2.2922
1.1473
2.2198
2.0596
10
8
6
4
2
[ppm]
F
O
N
N
N
O
O

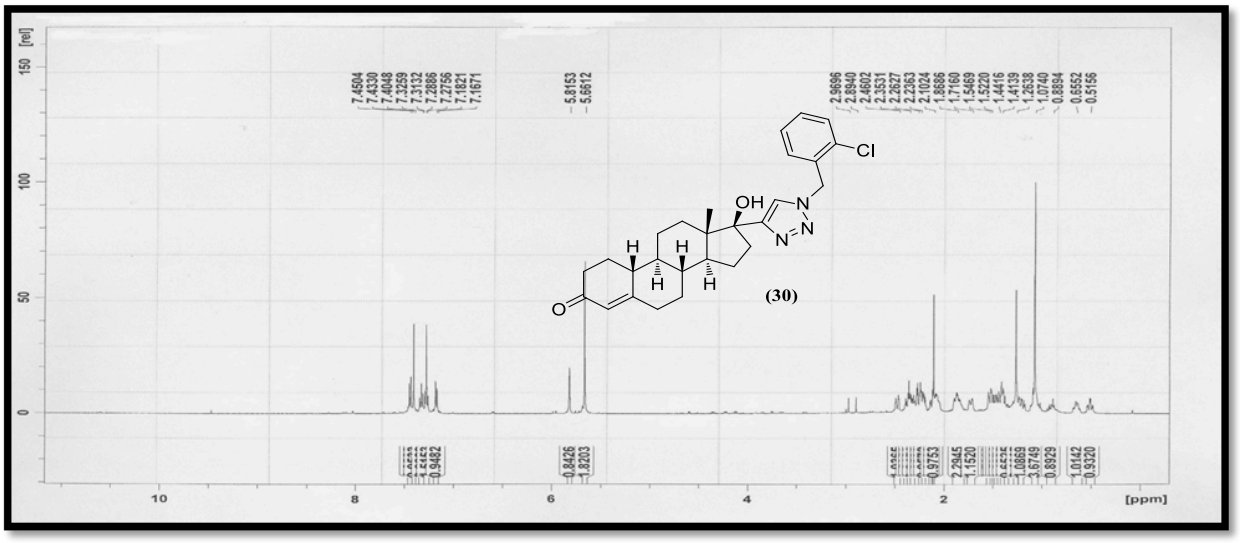
(27)


163.94
161.96
161.25
160.98
155.71
143.23
130.11
130.04
128.88
116.29
116.11
113.52
113.02
112.73
102.12
62.23
53.85
F
O
O
O
N
N
N
O
(27)
160
150
140
130
120
110
100
90
80
70
60
ppm


O
O
N
N
N
N
(28)
7.5920
7.5776
7.5447
7.3728
7.2765
7.1215
5.4946
5.0044
1.4282
2.4542
0.7277
0.9603
1.0000
[ml]
200
150
100
50
0
12
10
8
6
4
2
[ppm]


(29)
Br
[ppm]


181.64
157.47
152.82
141.67
137.75
132.96
132.46
129.90
124.55
123.01
117.27
111.94
53.79
46.91
35.56
29.67
25.10
23.42
(29)
Br
ppm


7.4604
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2.9696
2.8940
2.4602
2.3531
2.2627
2.2363
2.1024
1.8686
1.7160
1.5469
1.5220
1.4416
1.4139
1.2638
1.0740
0.8894
0.6552
0.5156
0.8426
1.8203
0.9753
2.2945
1.1520
1.0869
3.6749
0.8929
1.0142
0.9320
Cl
OH
N
N
N
H
H
H
H
O
(30)
[rel]
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100
50
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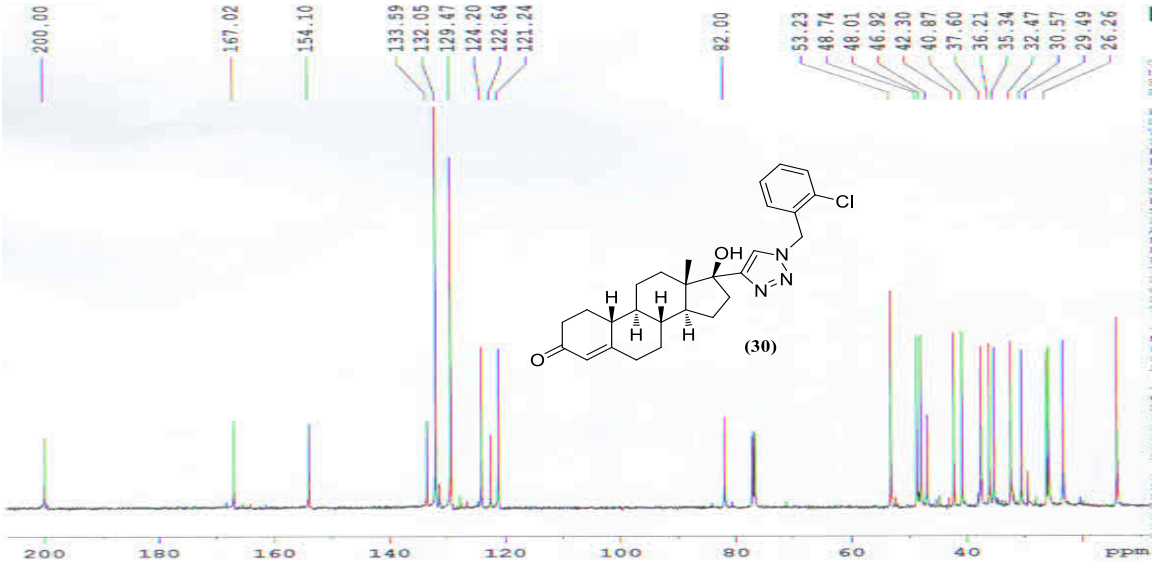
8
6
4
2
[ppm]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154.10
133.59
132.05
129.47
124.20
122.64
121.24
82.00
53.23
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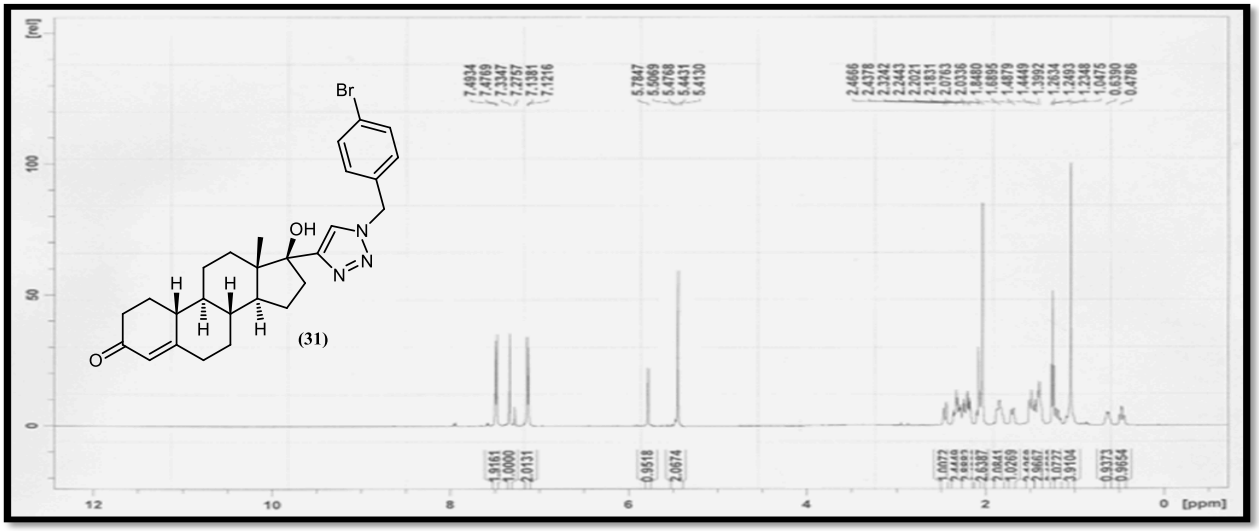
48.01
46.92
42.30
40.87
37.60
36.21
35.34
32.47
30.57
29.49
26.26
Cl
OH
N
N
N
H
H
H
H
O
(30)
200
180
160
140
120
100
80
60
40
ppm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N
N
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H
H
H
O
(31)
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7.3347
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7.1216
5.7847
5.5069
5.4768
5.4431
5.4130
2.4666
2.4378
2.3242
2.2443
2.2021
2.1831
2.0763
2.0336
1.8480
1.6895
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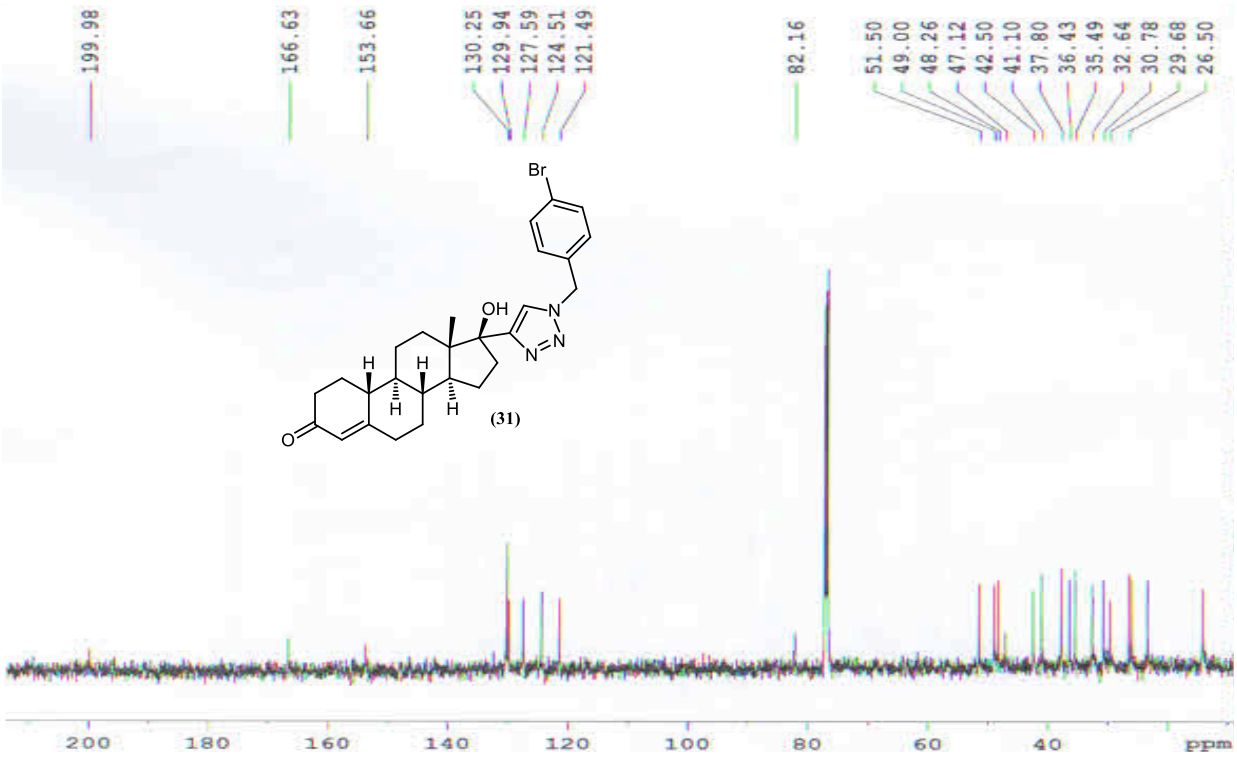
[ppm]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127.59
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121.49
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49.00
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42.50
41.10
37.80
36.43
35.49
32.64
30.78
29.68
26.50
Br
OH
N
N
N
H
H
H
H
O
(31)
ppm