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Synthesis, Structural, and Biological Evaluation of new isatin based 1,3,4-thiadiazole linked 1,2,3-triazoles

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KEYWORDS
1,3,4-thiadiazole linked 1,2,3-triazoles; isatin; in vitro anticancer activity.

Abstract
In the present paper, isatin based 1,3,4-thiadiazole linked 1,2,3-triazoles (5a-i) were synthesized and well characterized by using different techniques such as ^{1}H NMR, ^{13}C NMR, ESI-Mass, and element analysis. Further the compounds were also investigated by in vitro anticancer activity using different human cancer cell lines such as MCF-7, A549, Colo-205 and also tested normal cell line HEK 293. Among all compounds, **5e** exhibited potent activity against MCF-7, A549, and Colo-205 cell lines. The compounds **5h** and **5i** displayed good activity against tested cell lines.

1. Introduction

In the world, governments are closely monitoring the cancer problem. Furthermore, the World Health Organization (WHO) published statistical studies on cancer incidence, treatment recommendations, and preventative measures on a regular basis [1]. According to the most recent WHO forecasts [2], the global cancer burden is predicted to rise by more than 18 million new cases annually and reach about 9.6 million fatalities over the next ten years. Medicinal chemistry is the best source for developing novel, cutting-edge chemotherapeutic medications for the treatment of various tumors. Heterocyclic compounds with nitrogen often exhibited a broad spectrum of biological activity. Thus, more researchers focus on the chemistry of sulfur and nitrogen. Imidazo[2,1-b][1,3,4]thiadiazoles are the most significant class of these fused nitrogenized bicyclic heterocyclic compounds; they were first discovered in 1952 [1].These offer a variety of biological qualities and are highly useful intermediates in the pharmaceutical applications [2–9], such as tubulin inhibitor [10], anti–tubercular [11], antimicrobial [12], antitumor [13], anti-inflammatory [14], anticancer [15], anticonvulsant [16], antibacterial [17], and antifungal [18]. The imidazo[2,1-b][1,3,4] thiadiazoles is both a proven therapeutic and an anticancer agent [19, 20].

Conversely, a large variety of pharmaceuticals with a broad spectrum of pharmacological activity, including anticancer [21–26], anti-rheumatoid [27], anti-HIV [28, 29], and antioxidant [30], contain the most common isatin ring system.Numerous heterocyclic moieties with different functional groups have been linked to the isatin ring, resulting in an incredible array of bioactive natural compounds and active pharmaceutical ingredients. [31–33].Most tiny compounds based on isatin have the potential to cause cancer.

Based on the literature data above for both isatin and imidazo[2,1-b][1,3,4]thiadiazoles, were developed and synthesized structurally changed α-bromo-4-substituted acetophenone scaffolds of isatin based 1,3,4-thiadiazole linked 1,2,3-triazoles (**5a-i**) and which are examined for their in vitro activity against tested cell lines.

2. Experimental procedures

2.1 General Methods

All the chemical and reagent that was used was purchased commercially. % C, H, and N was analyzed using a Perkin-Elmer 2400 CHN analyzer for elemental analysis. TLC has been used to examine the reaction process and the quality of the compounds using Merck percolated Silica Gel 60F254 sheets (Germany, Darmstadt), the heptane-ethyl acetate 3:7 elution procedure, and UV light for viewing. ^{1}H and ^{13}C NMR spectra were recorded using DMSO-d^{6} as the solvent and tetramethylsilane as the internal standard on JEOL 400 MHz and 100 MHz, respectively. Using

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Electrospray Ionization–Mass Spectrometry (ESI–MS), the mass spectra were recorded.

2.2. Synthesis of 3-((5-mercapto-1,3,4-thiadiazol-2-yl)imino)-1-methylindolin-2-one (3)

Synthesis of 3-((5-mercapto-1,3,4-thiadiazol-2-yl)imino)-1-methylindolin-2-one (**2**) by 1-methylisatin (**1**) (5 mmol) and 5-amino-1,3,4-thiadiazole-2-thiol (2) (5 mmol) in AcOH under reflux for 4 h. After completion of the reaction, as shown by TLC analysis, the resulting mixture was filtered and washed with ice-cooled water. The resulting precipitate was collected, and the crude product was purified via silica gel chromatography using an eluent (25% ethyl acetate in hexane).

2.2.1. Synthesis of 1-methyl-3-((5-(prop-2-yn-1-ylthio)-1,3,4-thiadiazol-2-yl)imino)indolin-2-one (4)

To a mixture of compound (**3**) (5 mmol) and K_2CO_3 (10 mmol) in DMF (50 mL), propargyl bromide (6.5 mmol) was added at room temperature and stirred for 2h. After completion of the reaction was monitored by TLC analysis, the resulting mixture was concentrated under vacuum to afford a crude product. The resulting precipitate was collected, and the crude product was purified via silica gel chromatography using an eluent (25% ethyl acetate in hexane).

2.3. General synthesis of compounds (5a-i)

A solution of compound (4) (1 mmol), aryl azide (1.3 mmol), and sodium ascorbate (2.5 mmol) in dry THF (10 mL) was combined with $CuSO_4$ (10 mol%), and the reaction mixture was stirred for 6–9 h. at 80 ºC. Following the observation of the reaction's completion through TLC analysis, the reaction mixture was poured out onto ice-cooled water and extracted using ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate, rinsed with water (2 x 20 mL) and brine (1 x 20 mL), filtered, and concentrated under low pressure. With the use of column chromatography (25% EtOAc-hexane), the crude products were refined.

2.3.1. 1-methyl-3-((5-(((1-phenyl-1H-1,2,3-triazol-4-yl)methyl)thio)-1,3,4-thiadiazol-2-yl)imino)indolin-2-one (5a-i)

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.89 (s, 1H), 7.69 – 7.64 (m, 3H), 7.41 (dd, J = 7.5, 1.3 Hz, 1H), 7.32 (dd, J = 7.5, 1.5 Hz, 1H), 7.24 (t, J = 7.5 Hz, 2H), 7.18 (td, J = 7.4, 1.4 Hz, 1H), 7.05 – 6.99 (m, 1H), 4.82 (s, 2H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.02, 166.94, 153.49, 153.40, 143.56, 142.83, 137.08, 133.58, 129.27, 127.60, 125.99, 124.10, 123.77, 121.38, 120.45, 113.08, 35.24, 31.02;MS (ESI) m/z: 433 $[M]^+$; Anal. Calcd. for $C_{20}H_{15}N_7OS_2$: C, 55.41; H, 3.49; N, 22.62; Found: C, 55.47; H, 3.53; N, 22.59.

2.3.2. 3-((5-(((1-(4-methoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)thio)-1,3,4-thiadiazol-2-yl)imino)-1-methylindolin-2-one (5b)

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.86 (s, 1H), 7.66 (dd, J = 7.5, 1.2 Hz, 1H), 7.52 (d, J = 7.5 Hz, 2H), 7.40 (td, J = 7.5, 1.4 Hz, 1H), 7.28 (dd, J = 7.5, 1.5 Hz, 1H), 7.16 (td, J = 7.5, 1.5 Hz, 1H), 6.81 (d, J = 7.5 Hz, 2H), 4.79 (s, 2H), 4.56 (s, 3H), 3.51 (s, 3H);^{13}C NMR(100 MHz, DMSO-d_6): δ 173.96, 166.92, 157.83, 153.48, 153.41, 143.54, 142.83, 133.58, 131.16, 125.97, 124.13, 123.80, 120.46, 114.61, 113.10, 56.10, 35.29, 30.99; MS (ESI) m/z: 464 $[M+H]^+$; Anal. Calcd. for $C_{21}H_{17}N_7O_2S_2$: C, 54.41; H, 3.70; N, 21.15; Found: C, 54.49; H, 3.67; N, 21.11.

2.3.3. 1-methyl-3-((5-(((1-(4-nitrophenyl)-1H-1,2,3-triazol-4-yl)methyl)thio)-1,3,4-thiadiazol-2-yl)imino)indolin-2-one (5c)

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.92 (s, 1H), 8.11 (d, J = 7.5 Hz, 2H), 7.88 (d, J = 7.5 Hz, 2H), 7.66 (dd, J = 7.5, 1.2 Hz, 1H), 7.41 (td, J = 7.5, 1.4 Hz, 1H), 7.29 (dd, J = 7.5, 1.5 Hz, 1H), 7.17 (td, J = 7.5, 1.5 Hz, 1H), 4.59 (s, 2H), 3.50 (s, 3H); ^{13}C NMR(100 MHz, DMSO-d_6): δ 174.07, 166.93, 153.52, 153.45, 146.86, 143.59, 142.80, 140.69, 133.57, 126.02, 124.11, 123.78, 122.47, 120.40, 113.07, 35.24, 31.06; MS (ESI) m/z: 479 $[M+H]^+$; Anal. Calcd. for $C_{20}H_{14}N_8O_3S_2$: C, 50.20; H, 2.95; N, 23.42; Found: C, 50.17; H, 2.98; N, 23.36.

2.3.4. 1-methyl-3-((5-(((1-(3-nitrophenyl)-1H-1,2,3-triazol-4-yl)methyl)thio)-1,3,4-thiadiazol-2-yl)imino)indolin-2-one (5d)

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.90 (s, 1H), 8.54 (s, 1H), 7.91 (dt, J = 7.5, 1.3 Hz, 1H), 7.80 (dt, J = 7.5, 1.4 Hz, 1H), 7.64 (dd, J = 7.5, 1.5 Hz, 1H), 7.47 – 7.38 (m, 2H), 7.34 (dd, J = 7.5, 1.5 Hz, 1H), 7.16 (td, J = 7.4, 1.5 Hz, 1H), 4.63 (s, 2H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6):δ 174.08, 166.89, 153.51, 153.38, 147.64, 143.56, 142.83, 137.68, 133.58, 131.09, 127.95, 125.99, 124.10, 123.77, 121.48, 120.45, 119.90, 113.08, 35.29, 31.05; MS (ESI) m/z: 479 $[M+H]^+$; Anal. Calcd. for $C_{20}H_{14}N_8O_3S_2$: C, 50.20; H, 2.95; N, 23.42; Found: C, 50.26; H, 2.97; N, 23.33.

2.3.5. 3-((5-(((1-(4-chlorophenyl)-1H-1,2,3-triazol-4-yl)methyl)thio)-1,3,4-thiadiazol-2-yl)imino)-1-methylindolin-2-one (5e)

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^{1}H NMR (400 MHz, DMSO-d_6): δ 8.89 (s, 1H), 7.66 (dd, J = 7.5, 1.2 Hz, 1H), 7.59 (d, J = 7.5 Hz, 2H), 7.40 (td, J = 7.5, 1.4 Hz, 1H), 7.31 – 7.26 (m, 3H), 7.17 (td, J = 7.5, 1.5 Hz, 1H), 4.59 (s, 2H), 30.98 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.00, 166.92, 153.48, 153.41, 143.56, 142.83, 136.01, 133.61, 132.65, 129.01, 126.08, 124.14, 123.73, 122.93, 120.46, 113.18, 35.33, 31.18; MS (ESI) m/z: 469 $[M+2]^+$; Anal. Calcd. For $C_{20}H_{14}ClN_7OS_2$: C, 51.33; H, 3.02; N, 20.95; Found: C, 51.29; H, 3.08; N, 20.99.

2.3.6. 3-((5-(((1-(4-chloro-3-nitrophenyl)-1H-1,2,3-triazol-4-yl)methyl)thio)-1,3,4-thiadiazol-2-yl)imino)-1-methylindolin-2-one (5f)

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.96 (s, 1H), 8.41 (s, 1H), 7.74 (dd, J = 7.5, 1.2 Hz, 1H), 7.65 (dd, J = 7.5, 1.2 Hz, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.41 (dd, J = 7.4, 1.3 Hz, 1H), 7.34 (dd, J = 7.5, 1.5 Hz, 1H), 7.17 (td, J = 7.4, 1.5 Hz, 1H), 4.62 (s, 2H), 3.59 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.06, 166.99, 153.51, 153.43, 146.54, 143.57, 142.85, 138.44, 133.59, 129.99, 128.95, 125.97, 124.92, 124.13, 123.78, 123.06, 120.44, 113.19, 35.28, 31.12; MS (ESI) m/z: 514 $[M+2]^+$; Anal. Calcd. For $C_{20}H_{13}ClN_8O_3S_2$: C, 46.83; H, 2.55; N, 21.84; Found: C, 46.87; H, 2.61; N, 21.81.

2.3.7. 3-((5-(((1-(3,5-dimethylphenyl)-1H-1,2,3-triazol-4-yl)methyl)thio)-1,3,4-thiadiazol-2-yl)imino)-1-methylindolin-2-one (5g)

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.85 (s, 1H), 7.66 (dd, J = 7.4, 1.4 Hz, 1H), 7.40 (td, J = 7.5, 1.4 Hz, 1H), 7.34 (s, 2H), 7.28 (dd, J = 7.4, 1.4 Hz, 1H), 7.17 (td, J = 7.5, 1.5 Hz, 1H), 6.82 (s, 1H), 4.58 (s, 2H), 3.48 (s, 3H), 2.43 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.09, 166.97, 153.53, 153.43, 143.56, 142.83, 139.24, 137.96, 133.58, 126.95, 125.99, 125.23, 124.10, 123.77, 120.45, 113.08, 35.49, 31.09, 25.34;MS (ESI) m/z: 462 $[M+H]^+$; Anal. Calcd. For $C_{22}H_{19}N_7O_3S_2$: C, 57.25; H, 4.15; N, 21.24; Found: C, 57.21; H, 4.19; N, 21.20.

2.3.8. 3-((5-(((1-(4-chloro-3,5-dimethoxyphenyl)-1H-1,2,3-triazol-4-yl)methyl)thio)-1,3,4-thiadiazol-2-yl)imino)-1-methylindolin-2-one (5h)

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.89 (s, 1H), 7.65 (dd, J = 7.4, 1.4 Hz, 1H), 7.41 (td, J = 7.5, 1.4 Hz, 1H), 7.32 (dd, J = 7.5, 1.5 Hz, 1H), 7.17 (td, J = 7.5, 1.5 Hz, 1H), 6.94 (s, 2H), 4.61 (s, 2H), 3.79 (s, 6H), 3.45 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.07, 166.94, 153.49, 153.40, 151.38, 143.56, 142.83, 138.28, 133.58, 125.99, 124.10, 123.77, 120.45, 117.66, 113.08, 105.99, 56.78, 35.51, 31.02; MS (ESI) m/z: 527 $[M]^+$; Anal.Calcd.for$C_{22}H_{18}ClN_7O_3S_2$: C, 50.04; H, 3.44; N, 18.57; Found: C, 49.99; H, 3.47; N, 18.61.

2.3.9. 1-methyl-3-((5-(((1-(naphthalen-1-yl)-1H-1,2,3-triazol-4-yl)methyl)thio)-1,3,4-thiadiazol-2-yl)imino)indolin-2-one (5i)

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.91 (s, 1H), 8.56 (d, J = 1.5 Hz, 1H), 7.90 – 7.81 (m, 2H), 7.77 (dt, J = 7.5, 1.4 Hz, 1H), 7.68 (td, J = 7.5, 1.5 Hz, 1H), 7.64 – 7.51 (m, 3H), 7.39 (td, J = 7.4, 1.4 Hz, 1H), 7.30 (dd, J = 7.5, 1.5 Hz, 1H), 7.12 (td, J = 7.4, 1.4 Hz, 1H), 4.58 (s, 2H), 3.49 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 174.02, 166.91, 153.47, 153.39, 143.99, 143.58, 136.80, 134.10, 133.55, 128.31, 127.29, 126.86, 126.40, 125.95, 125.69, 124.22, 124.13, 123.60, 123.36, 120.41, 113.12, 112.84, 35.57, 31.08; MS (ESI) m/z: 483 $[M+H]^+$; Anal. Calcd. For $C_{24}H_{17}N_7OS_2$: C, 59.61; H, 3.54; N, 20.28; Found: C, 59.58; H, 3.59; N, 20.34.

2.4. In vitro cytotoxic bioassay

The cytotoxicity of the ANMTSC ligand and its metal complexes to cultured cancer cells were evaluated by modified 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetraazolium bromide (MTT) colorimetric assay as reported [34, 35]. The assay assesses cell viability by detecting the formazan product formed from the reduction of yellow MTT by mitochondrial succinate dehydrogenase of metabolically active cells [36]. The cultured cancer cells seeded at a density of 5000 cells per well in 96-well plates. After 24 h of incubation, various concentrations of the synthesized compounds were added, respectively to the cells. After incubation for 72 h, MTT reagent (4 µg/mL) was added and the plates were incubated for 4 h at 37 ˚C. additionally, the supernatant was removed by centrifugation and 100 µL of DMSO was added to dissolve the formazan crystals. The MTT plates were shaken well for 5 min, and the absorbance values for tested compounds were determined by Beckmann Coulter Elisa plate at 570 nm. The IC_{50} (concentration that inhibited the survival of cells by 50%) values were determined to represent the cytotoxicity of the compounds

3. Results and discussion

Initially, 1-methylisatin (**1**) condensed with 5-amino-1,3,4-thiadiazole-2-thiol (**2**) in the presence of AcOH under reflux to form 3-((5-mercapto-1,3,4-thiadiazol-2-yl)imino)-1-methylindolin-2-one (**3**). Compound **3** reacts with propargyl bromide in the presence of K_2CO_3

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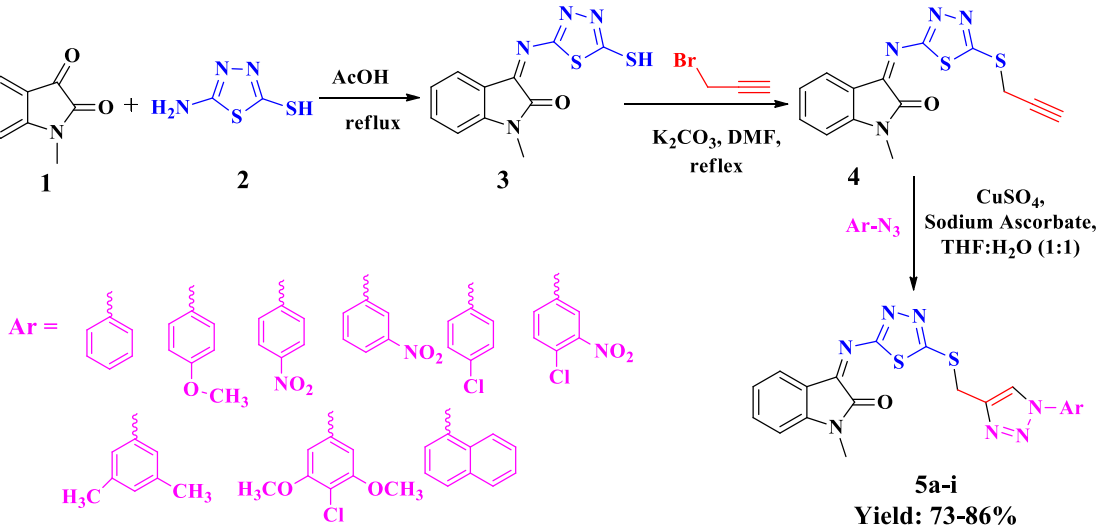
at room temperature to form the key intermediate 1-methyl-3-((5-(prop-2-yn-1-ylthio)-1,3,4-thiadiazol-2-yl)imino)indolin-2-one (**4**). Then, the latter compound **4** with substituted aromatic azides and in the presence of $CuSO_4$ as the catalyst in THF as the solvent to obtain in titled compounds (**5a-i**) in good yields (Scheme 1). The synthesized compounds structures were determined using data from ^1H NMR, ^{13}C NMR, ESI-Mass, and elemental analysis. The ^1H NMR, ^{13}C NMR, ESI-Mass spectra are shown in Fig. 1-12.



Scheme 1: Synthesis of isatin based 1,3,4-thiadiazole linked 1,2,3-triazoles

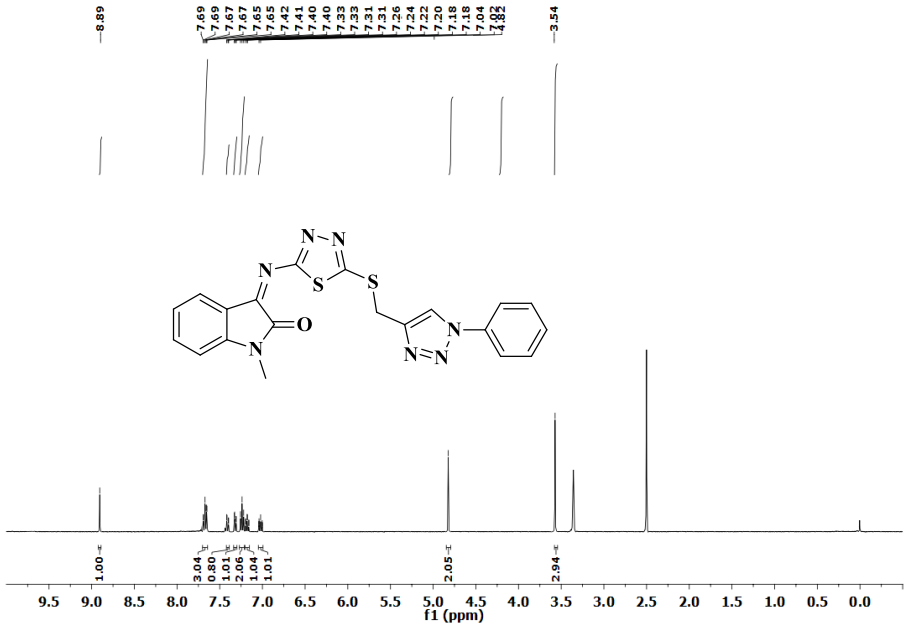


Figure 1: ^1H-NMR of compound **5a** in DMSO-d_6

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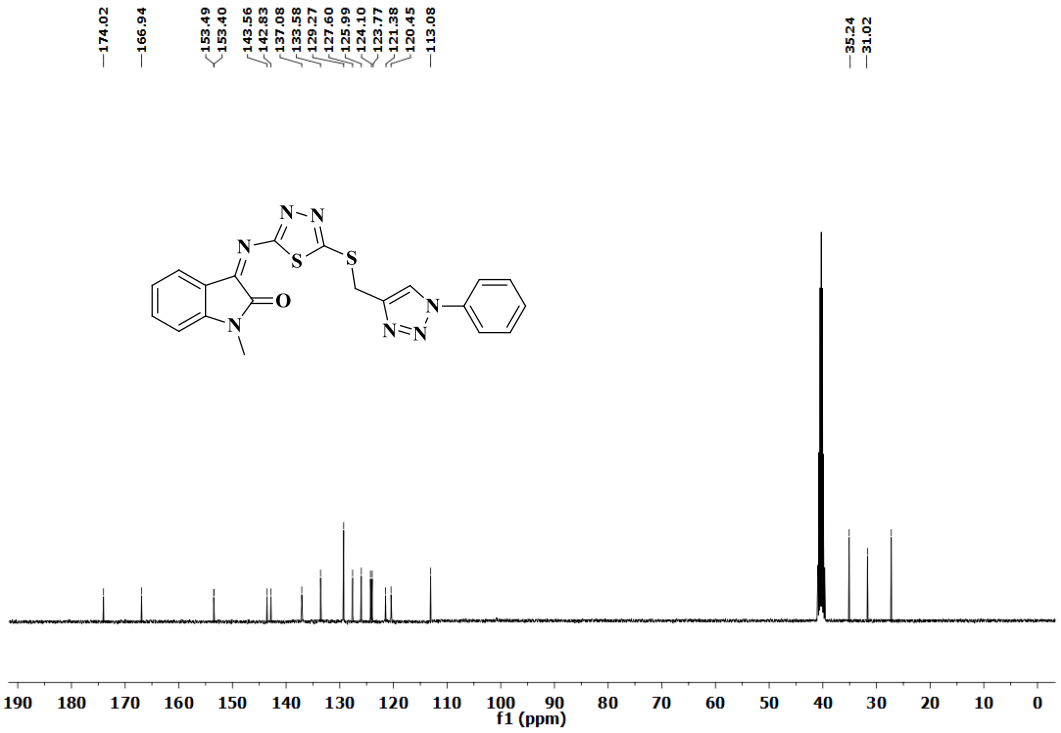

Figure 2: ^{13}C-NMR of compound **5a** in DMSO-d_6

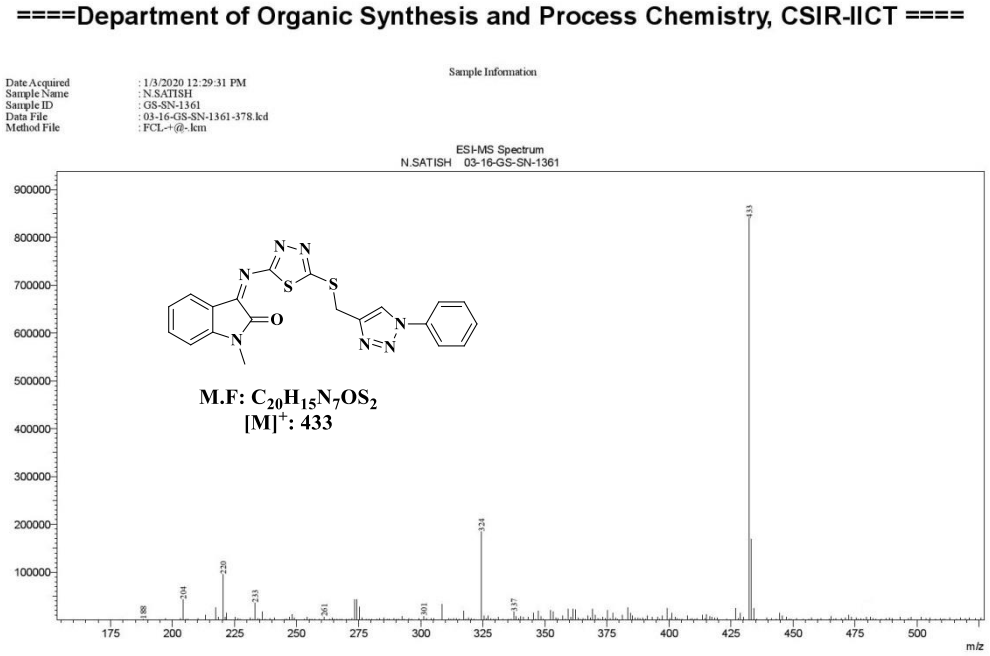

Figure 3: ESI–Mass spectrum of compound **5a**

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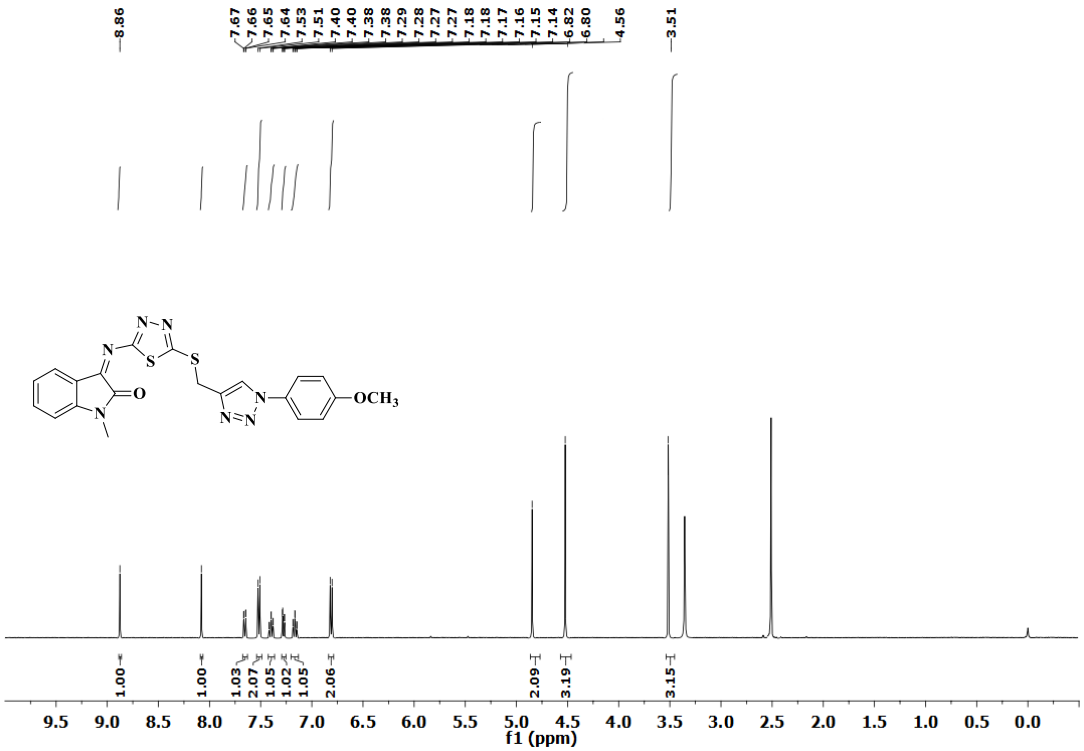

Figure 4: ^{1}H-NMR of compound **5b** in DMSO-d_6

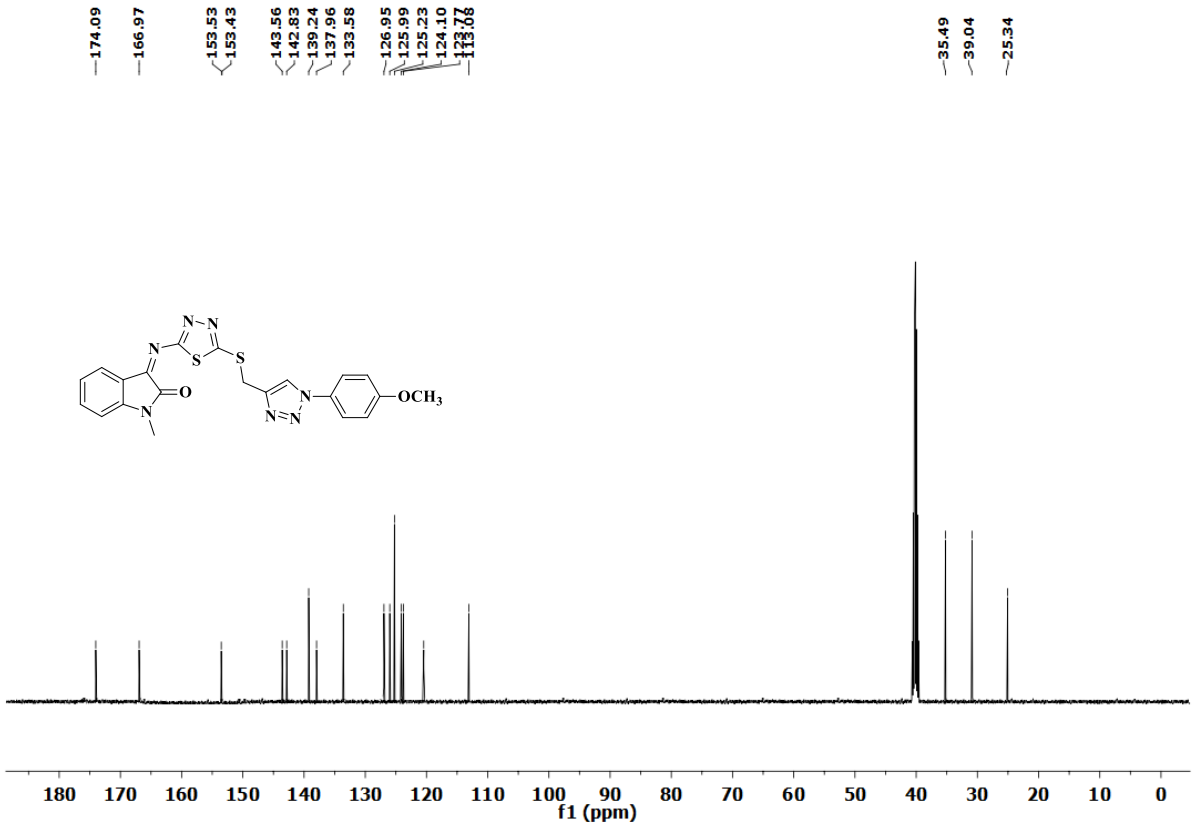

Figure 5: ^{13}C-NMR of compound **5b** in DMSO-d_6

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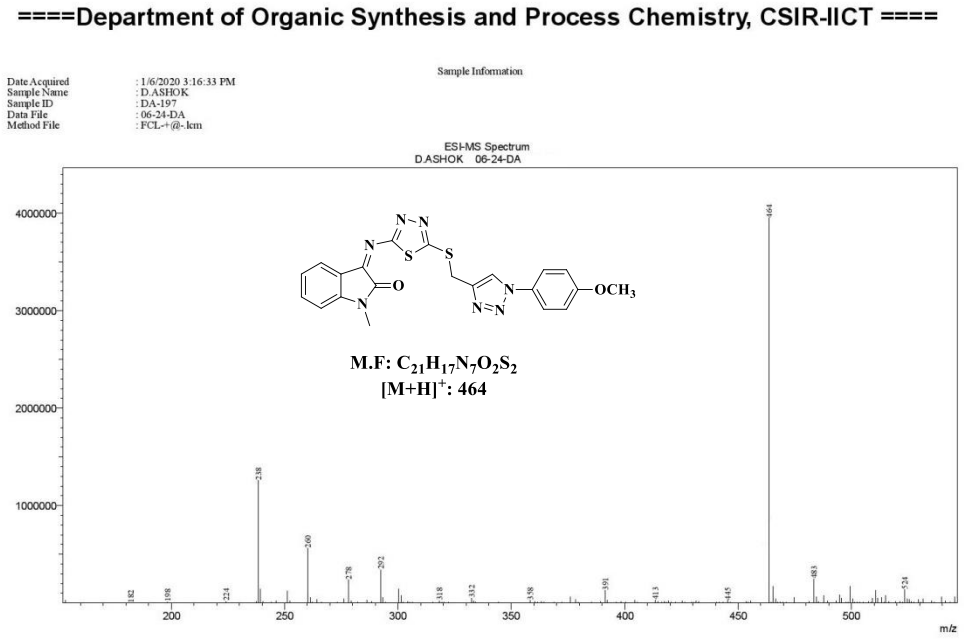

Figure 6: ESI–Mass spectrum of compound **5b**

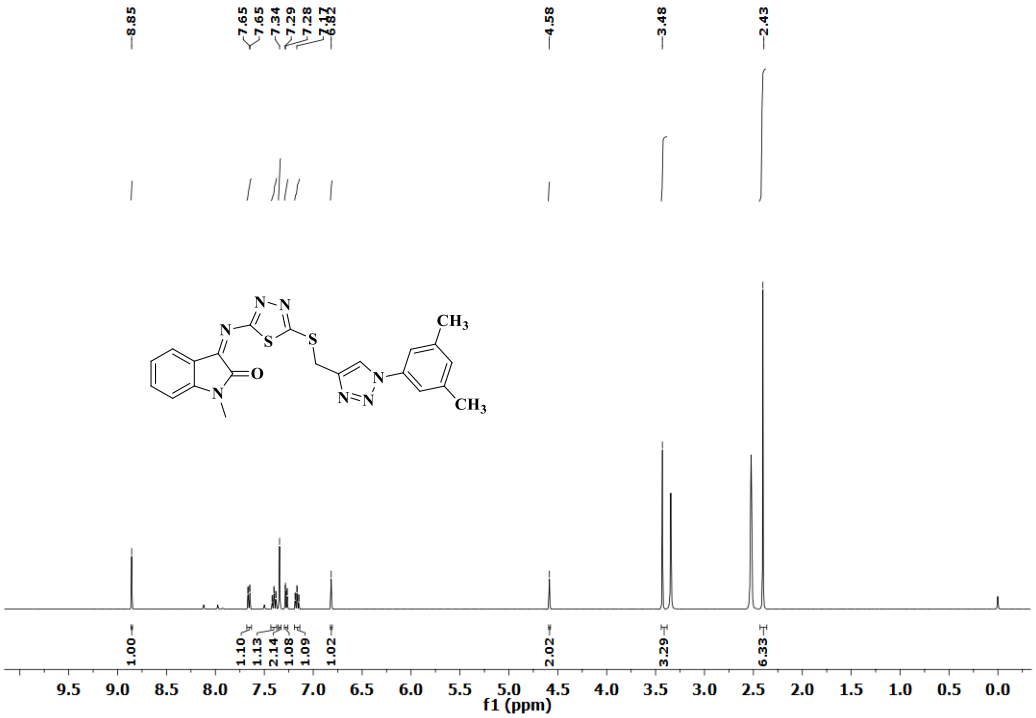

Figure 7: ^{1}H-NMR of compound **5g** in DMSO-d_6

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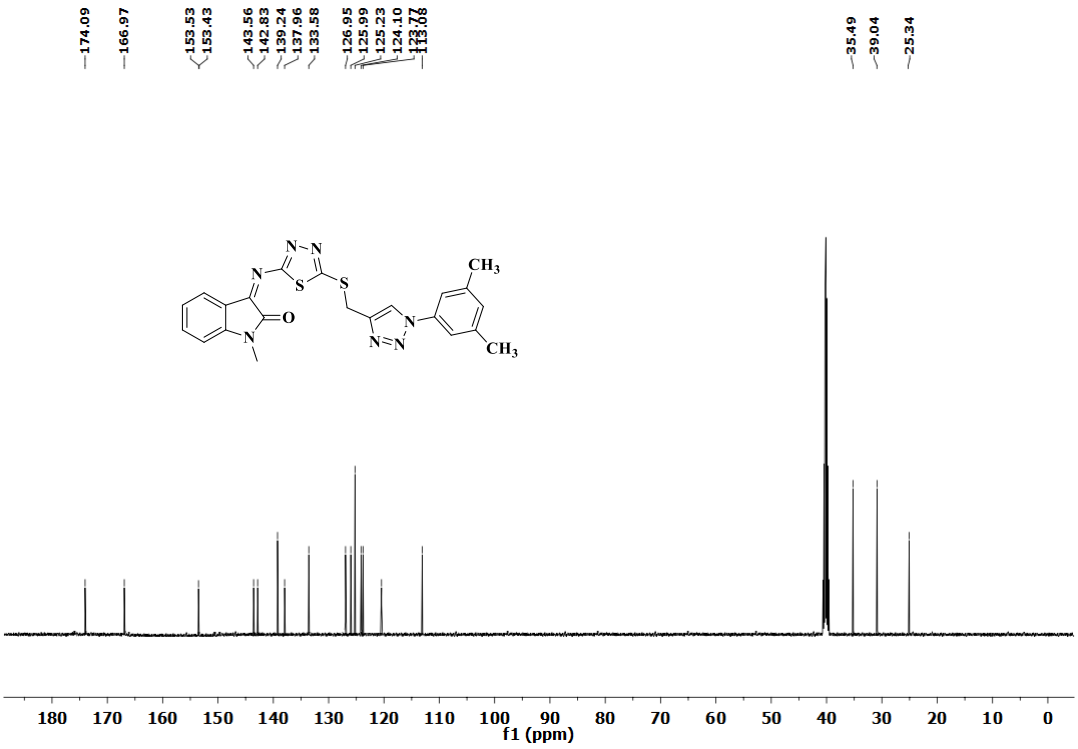

Figure 8: ^{13}C-NMR of compound **5g** in DMSO-d_6

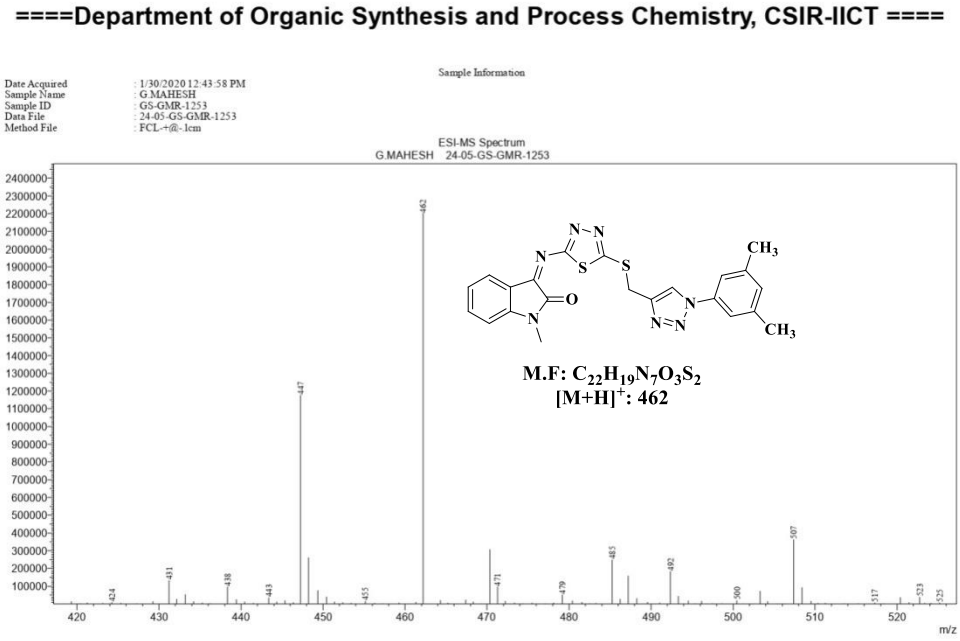

Figure 9: ESI–Mass spectrum of compound **5g**

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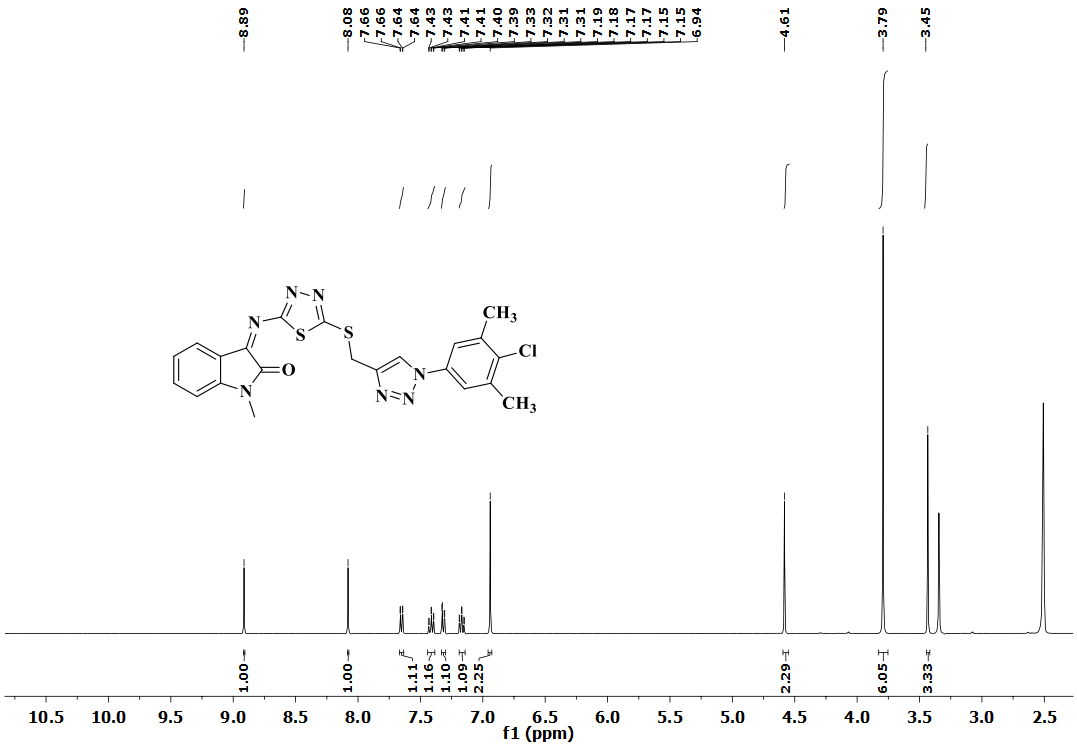

Figure 10: ^{1}H-NMR of compound **5h** in DMSO-d_6

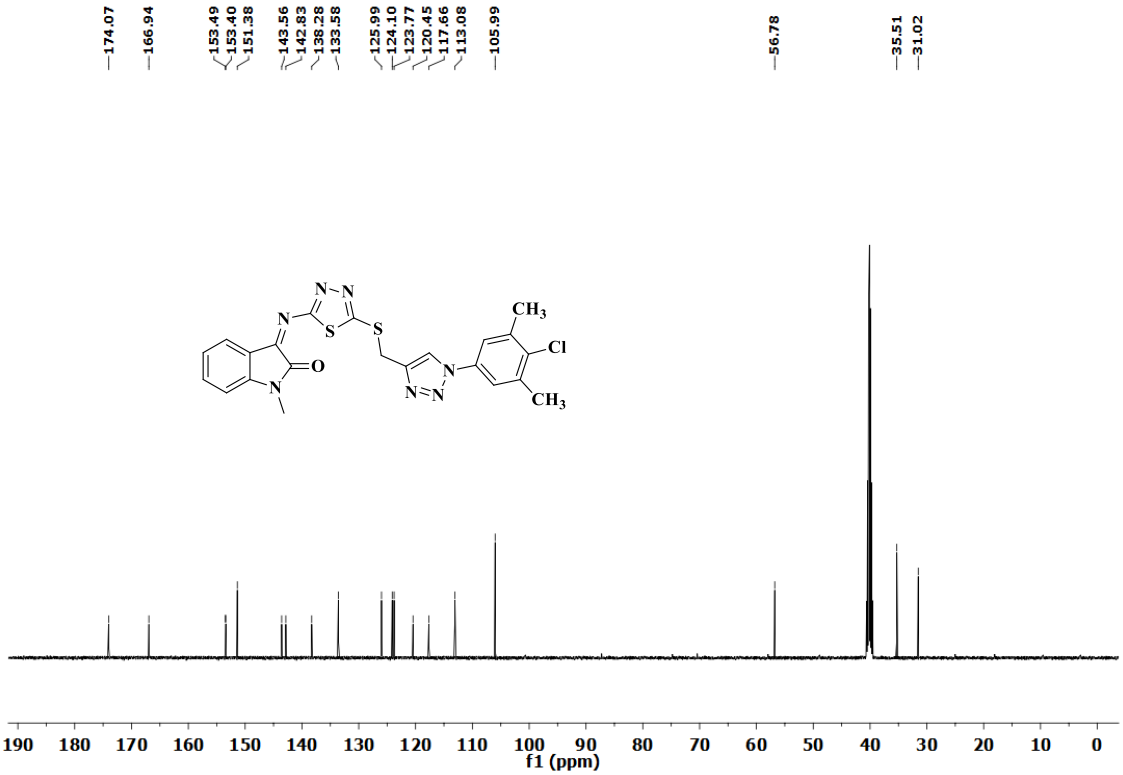

Figure 11: ^{13}C-NMR of compound **5h** in DMSO-d_6

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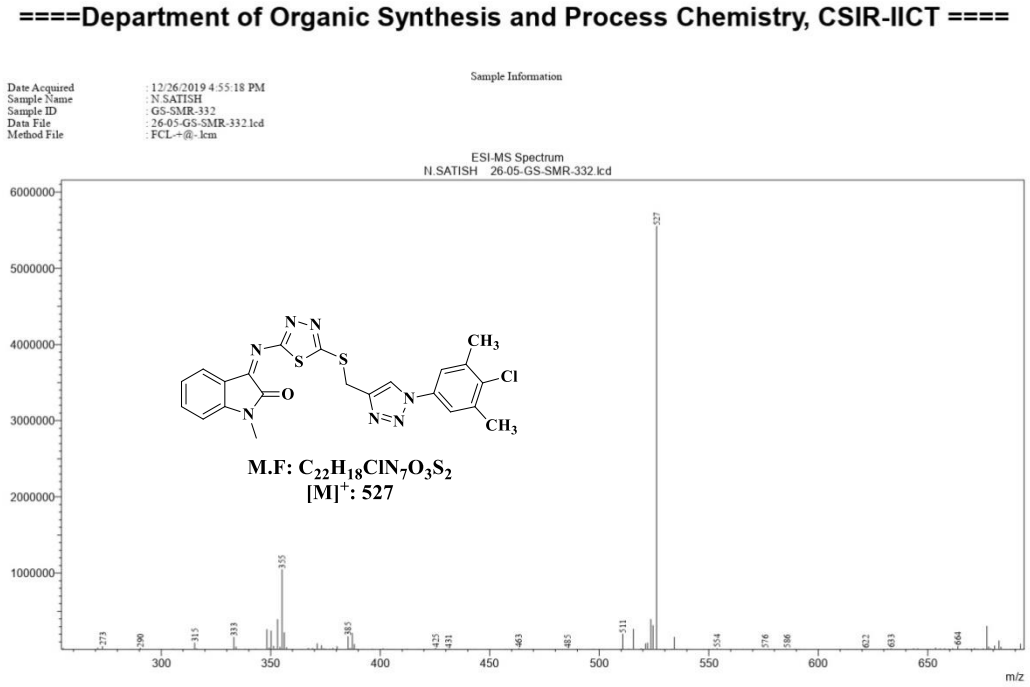

Figure 12: ESI–Mass spectrum of compound **5h**

Anticancer activity

In vitro anticancer activity of the new compounds was investigated by using different cell lines, i.e., MCF-7, A549, Colo-205, and normal cell line HEK-293. Doxorubicin is a reference drug; the findings are listed in **table 1**.

Among all the examined compounds, compound **5e** showed potent activity against MCF-7 with IC_{50} values of 7.31 ± 0.17 µM, A549 with IC_{50} values of 6.89 ± 0.37 µM, and Colo-205 with IC_{50} values of 9.41 ± 0.41µM, respectively. The compounds **5h** and **5i** exhibited good activity against the tested cell lines. The remaining compounds were displayed IC_{50} values ranging from 26.56 ± 1.03 µM to 68.89 ± 1.62 µM, although they exhibited moderate to poor anticancer ability against the tested cell lines. We also further examined the derivatives (**5e**, **5h**, and **5i**) against the normal cancer cell line HEK-293 with IC_{50} values of 86.23 ± 0.99 µM, 79.12 ± 1.08 µM, and 75.74 ± 0.52 µM. The fact that none of the powerful derivatives (**5e**, **5h**, and **5i**) interfered with the normal cell line's viability suggests that they are not harmful.

Table 1: Anticancer activity of isatin based 1,3,4-thiadiazole linked 1,2,3-triazoles (**5a-i**) (IC_{50} in µM).

Compounds Entity	MCF-7	A549	Colo-205	HEK293
5a	38.34 ± 1.08	48.42 ± 1.22	68.89 ± 1.62	ND
5b	48.53 ± 0.56	52.27 ± 0.73	49.79 ± 1.23	ND
5c	53.63 ± 1.13	44.35 ± 1.55	57.86 ± 0.91	ND
5d	33.61 ± 0.96	39.31 ± 0.74	44.35 ± 1.34	ND
5e	**7.31 ± 0.17**	**6.89 ± 0.37**	**9.41 ± 0.41**	**86.23 ± 0.99**
5f	52.16 ± 0.44	38.84 ± 1.03	65.47 ± 1.54	ND
5g	26.56 ± 1.03	31.62 ± 1.15	39.31 ± 0.92	ND
5h	**13.59 ± 0.09**	**10.58 ± 0.28**	**16.43 ± 0.85**	**79.12 ± 1.08**
5i	**19.31 ± 0.31**	**15.71 ± 0.85**	**23.57 ± 1.01**	**75.74 ± 0.52**
Doxorubicin	**3.48 ± 0.14**	**4.21 ± 0.65**	**4.15 ± 1.09**	**ND**

ND: Not determined

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4. Conclusion

A series of novel isatin based 1,3,4-thiadiazole linked 1,2,3-triazoles (5a-i) were synthesized and characterized by various spectroscopic techniques(Elemental analysis, NMR and Mass). Further, all the target compounds screened for their in vitro anticancer activity. The compound **5e** showed potent activity against MCF-7 with IC_{50} values of 7.31 ± 0.17 µM, A549 with IC_{50} values of 6.89 ± 0.37 µM, and Colo-205 with IC_{50} values of 9.41 ± 0.41µM, respectively Whereas, the compounds **5h** and **5i** exhibited significant to moderate activity against these three cell lines.

References

1. World Health Organization. Available online: www.who.int/health-topics/cancer#tab=tab_1. Accessed on 05 September 2022.
2. Matsukawa, T., and Ban, S.,Yakugaku Zasshi, 1952, 72, 610.
3. Avvaru, S.P., Noolvi, M.N., More, U.A., Chakraborty, S., Dash, A,, Aminabhavi, T.M., Narayan, K.P., and Sutariya, V., Med. Chem., 2021, 17, 750.
4. Cascioferro, S., Parrino, B., Petri, G.L., Cusimano, M.G., Schillaci, D., Di Sarno, V., Musella, S., Giovannetti, E., Cirrincione, G., and Diana, P., Eur. J. Med. Chem., 2019, 167, 200.
5. Zinad, D. S., Mahal, A.,and Shareef, O., IOP Conf. Ser: Mater. Sci. Eng. 2020, 770, 012053.
6. Jadhav, V. B., Kulkarni, M. V., Rasal, V. P., Biradar, S. S., and Vinay, M. D., Eur. J. Med. Chem., 2008, 43, 1721.
7. Ramprasad, J., Nayak, N., Dalimba, U., Yogeeswari, P., Sriram, D., Peethambar, S.K., Achur, R., and Kumar, H.S., Eur. J. Med. Chem., 2015, 95, 49.
8. Gadad, A. K., Noolvi, M.N., and Karpoormath, R.V., Bioorg. Med. Chem., 2004, 12, 5651.
9. Alegaon, S.G., Alagawadi, K.R., Sonkusare, P.V., Chaudhary, S.M., Dadwe, D.H., and Shah, A.S., Bioorg. Med. Chem. Lett., 2012, 22, 1917.
10. Narasimha Rao, M.P., Nagaraju, B., Kovvuri, J., Polepalli, S., Alavala, S., Vishnuvardhan, M.V.P.S., Swapna, P., Nimbarte, V.D., Lakshmi, J.K., and Jain, N., Bioorg. Chem., 2018, 76, 420.
11. Patel, H.M., Noolv, M.N., Sethi, N.S., Gadad, A.K., and Cameotra, S.S., Arab. J. Chem., 2017, 10, S996.
12. Tahtaci, H., Karacık, H., Ece, A., Er, M, and Şeker, M.G., Mol. Inform., 2018, 37, 1700083.
13. Luo, Z., Chen, B., He, S.,Shi, Y., Liu, Y., and Li, C., Bioorg. Med. Chem. Lett., 2012, 22, 3191.
14. Reddy, A.G., Sireesha, R., Babu, V.H., Rao, Y.J., Susithra, E., and Rao, M.B., Chemical Data Collections. 2021, 31, 100614.
15. Bhogireddy, D.N., Surapureddi, S.R., Palle, S., and Tadiboina, B.R., Chem. Data Collect., 2022, 39, 100856.
16. Bhoomendra, A.B., Sirajunisa, T., and Ravikiran, A.G.J., Saudi. Chem. Soc., 2016, 20, S463.
17. Foroumadi, A., Emami, S., Hassanzadeh, A., Rajaee, M., Sokhanvar, K., Moshafi, M. H., and Shafiee, A., Bioorg. Med. Chem. Lett., 2005, 15, 4488.
18. Er, M., Ergüven, B., Tahtaci, H., Onaran, A., Karakurt, T., and Ece, A., Med. Chem. Res., 2017, 26, 615.
19. Avvaru, S.P., Noolvi, M.N., More, U.A., Chakraborty, S., Dash, A., Aminabhavi, T.M., Narayan, K.P., and Sutariya, V., Med. Chem., 2021, 17, 750.
20. Noolvi, M. N., Patel, H. M., Singh, N., Gadad, A.K., Cameotra, S.S.,and Badiger, A., Eur. J. Med. Chem., 2011, 46, 4411.
21. Xu, D., and Xu, Z.,Curr. Top. Med. Chem., 2020, 20, 1938.
22. Sachdeva, H., Mathur, J., and Guleria, A., J. Chil. Chem. Soc., 2020, 65, 4900.
23. Devi, N., Kaur, K., Biharee, A., and Jaitak, V., Med. Chem., 2021, 21, 1802.
24. Buvana,, C., Raveendran, A., Suresh, R., and Haribabu, Y., Asian J. Pharm. Res. Develop., 2020,vol. 8, 218.
25. Kaur, K., and Jaitak, V., Med. Chem., 2019, 19, 962.
26. Hatti, I., Sreenivasulu, R., Jadav, S.S., Ahsan, M.J., Raju, R.R., Monatsh. Chem., 2015, 146, 1699.
27. Singh, S., Sharma, N., and Chandra, R., Org. Chem. Front., 2022, 9, 3624.
28. Ragno, R., Coluccia, A., La Regina, G., De Martino, G., Piscitelli, F., Lavecchia, A., Novellino, E., Bergamini, A., Ciaprini, C., Sinistro, A., and Maga, G., J. Med. Chem., 2006, 49, 3172.

29. Chen, Q., Wu,, C., Zhu, J., Li, E., and Xu, Z., Curr. Top. Med. Chem., 2022, 22, 993.
30. Altuntaş, T.G., Baydar, A., Kılıç-Kurt, Z., Acar, C., Yılmaz-Sarıaltın, S., Çoban,, T., J. Res. Pharm., 2020, 24, 350.
31. Gul, W., and Hamann, M.T., Life Sci., 2005, vol. 78, p.442.
32. Brancale, A., and Silvestri,R., Med. Res. Rev., 2007, 27, 209.
33. Singh, P., Kaur, M., and Holzer, W., Eur. J. Med.icinal Chem., 2010, 45, 4968.
34. Skehan, P., Storeng, R., Scudiero, D., Monks, A., McMahon, J., Vistica, D., Warren, J., Bokesch, H., Kenney, S., Boyd, M. J., Natl. Cancer Inst., 1990, 82, 1107.
35. Monks, A., Scudiero, D., Skehan, P., Shoemaker, R., Paull, K., Vistica, D., Hose, C., Langley, J., Cronise, P., Vaigro-wolff, A., et al., J. Natl. Cancer Inst., 1991, 83, 757.
36. Carmichael, J., Degraff, W. G., Gazdar, A. F., Minna, J. D., Mitchell, J. B., Am. Assoc. Cancer Res., 1987, 47, 936.