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$[(C_3H_7)_3N\text{-}SO_3H]Cl$: An Efficient Ionic Liquid Catalyst for the Synthesis of Oxoindolin Hydrazine Carbothioamide Derivatives and their Antimicrobial Evaluation

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Abstract

In the present study, we disclose a efficient synthesis of oxoindolin hydrazine carbothioamide derivatives catalyzed by Brønsted acidic $[(C_3H_7)_3N\text{-}SO_3H]Cl$ ionic liquid. The synthesized BAIL represents an efficient catalyst for the reaction of isatin and thiosemicarbazide for the synthesis of oxoindolin hydrazine carbothioamide by a one-pot synthesis in an aqueous solution at ambient conditions. The significant features of the protocol includes use of green solvent, simple operational and work-up procedures, high yield, shorter reaction times and recyclability of ionic liquid catalyst, etc. Moreover, the synthesized oxoindolin hydrazine carbothioamides were screened for antimicrobial activity against pathogenic bacteria *E. coli* and *S. aureus*. The compound, **3j** show the most remarkable anti-microbial activity as compared to commercial drugs.

Keywords: Anti-microbial activity; Aqueous medium; Ionic liquid; Recyclable catalyst; oxoindolinhydrazinecarbothio-amide.

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Introduction

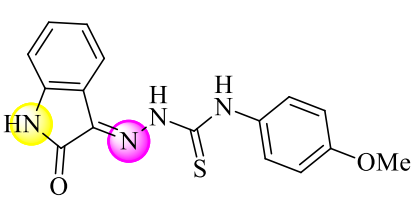
Using organic synthesis chemists have synthesized a diverse range of simple as well as complex organic molecules for various applications [1]. However, chemists have realized that chemical processes generate a significant amount of toxic waste in the environment. Thus, the concept green chemistry has gained considerable importance in order to tackle environmental issues [2, 3]. It has been identified that different toxic reagents, volatile and non-volatile solvents posed serious environmental pollution around the globe [4]. Water is identified as a safe, non-toxic and green solvent for variety of chemical reactions of laboratory and commercial scale synthesis [5]. Moreover, water possesses strong hydrogen bond-forming ability; high dielectric constant and surface tension are important factor for enhancing rate and yield of chemical reactions [6].

Recently, ionic liquids (ILs) have become interesting topic among organic chemists due to environmentally friendly nature and effective reaction media for diverse class of organic as well as biochemical transformations [7]. Also, it holds important properties like negligible vapor pressure, good affinity with a wide range of chemicals, non-flammability and high thermal stability makes them ultimate replacement for volatile organic solvents [8]. Owing to significant properties, ionic liquids (ILs) have been explored as solvent in chemical reactions and solvent extraction, catalysis, and adsorbent for toxic gases. Among ILs, Bronsted acidic ILs have received wide interest because of potent catalytic properties proved in variety of chemical transformations such as esterification, Michael addition, Knovenagel condensation, Friedel Craft's alkylation, etc [9]. Most importantly, Bronsted acidic ILs eliminates drawbacks associate with Bronsted acids such as reaction with metallic vessel, release of hydrogen gas after reaction with metals and corrosion [10].

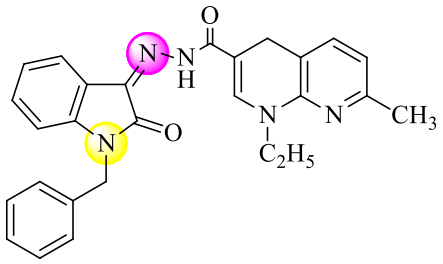
The search for new oxygen-based Schiff bases have been attracting increasing interest because of their utility in pharmaceutical and medicinal field. When thiosemicarbazide is fused with an isatins, it forms a Schiff base known as thiosemicarbazone [11]. These compounds have been extensively studied for their wide-ranging biological applications over the past 50 years. oxoindolin condensed with hydrazinecarbothioamide exhibits significant biological activities such as cytotoxicity [12], EGR-1 inhibitor [13], antitumor [14], antioxidant [15], anti-inflammatory and antinociceptive activities [16], etc.

Some of the oxoindolin and hydrazinecarbothioamide based derivatives like isatinthiosemicarbazones [**A**] shows anticancer activity [17], Schiff bases of indoline-2, 3-dione **[B]** exhibits significant antimycobacterial activity [18], trifluoroacyl substituted oxoindolin derivative **[C]** shows antiviral potencies [19], and benzoxazol based hydrazine carbothioamides **[D]** displayed anti-inflammatory activities [20] (**Fig. 1**). Owing to outstanding pharmaceutical applications, synthesis of oxoindolin based hydrazinecarbothioamide derivatives has received wide

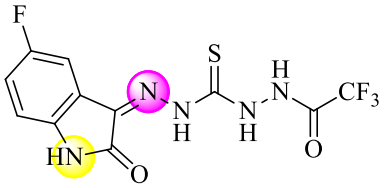
research interest in academic as well as industrial research. In this context, numbers of methods have been developed for the synthesis of oxygen-based hydrazine carbothioamide. Among these, acid catalyzed reaction of isatins with thiosemicarbazide represents straightforward approach for expedient access to oxoindolin hydrazine carbothioamide. Various methodologies have been reported using CH_3COOH [21, 22], H_2SO_4 [23], K10 Clay [24], etc. However, some of the methods show disadvantages of low yield, longer reaction time, and use of expensive catalyst. Therefore, there is considerable scope for the development of greener methodologies for the synthesis of oxoindolin hydrazine carbothioamide. In the present work, we report $[(C_3H_7)_3N\text{-}SO_3H]Cl$ as a novel Bronsted acidic ionic liquid catalyst for expedite synthesis of oxoindolin hydrazine carbothioamide using isatin and thiosemicarbazide in aqueous solvent at ambient condition.



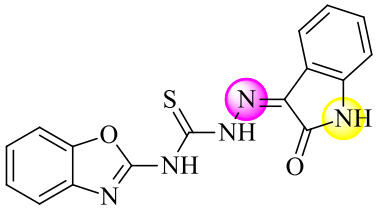
Anticancer activity [**A**]



Antimycobacterial activity [**B**]



Antiviral activity [**C**]



Anti-inflammatory activity [**D**]

Fig. 1 Biologically active oxoindolin fused hydrazine carbothioamides.

Experimental

General

Reagents and chemicals of Sigma Aldrich, Spectrochem, Alfa Aesar and Loba companies were used in its original form. Progress of the reaction and purity of the products were checked by using TLC plates (precoated with silica gel) from petroleum ether: ethyl acetate in the ratio of 8:2 and detected under UV light. All melting points were taken on DBK programmed melting point apparatus (Temp. increment 2 $^oC\ min^{-1}$) and were uncorrected. IR spectra of synthesized compounds were determined by using Brucker IR spectrometer and values are represented in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on Brucker AC 500 and 125 MHz NMR spectrometer at the sophisticated analytical instrumentation facility, Panjab University, Chandigarh. $CDCl_3$ was used as solvent and chemical shifts were measured in δ ppm. Mass spectra was recorded on WS-ERC ESI Q1MS mode.

General procedure for the synthesis of oxoindolin hydrazine carbothioamide

Typically, an isatin (1 mmol) and thiosemicarbazide (1 mmol) were added in a 5 mL of water containing 10 mol % $[(C_3H_7)_3N\text{-}SO_3H]Cl$ IL catalyst and kept for stirring till end of the reaction. The resultant precipitate was separated by simple filtration and further purified by recrystallization in ethanol afforded pure oxoindolin hydrazine carbothioamide. The identification of the product was carried out by IR, ^1H and ^{13}C NMR and Mass analysis.

Antimicrobial Assay

Antibacterial activity of synthesized compounds (**3a-n**) was carried out by agar well diffusion method [27]. The bacterial culture of *Bacillus cereus* (NCIM 2703) and *Escherichia coli* (NCIM 2832) (10^6 cfu/mL) was spread on the sterile agar plates with a glass spreader [28]. Subsequently, using borer 6 mm diameter wells were made into the agar medium and filled with 100 µL, 150 µL, 200 µL from 10mg/500 µL stock, 100 µL of DMSO was kept as control and allowed to diffuse at refrigerator for 15 min. To examine antibacterial effects, plates were placed in the incubator at 37 ^oC for 24 h. After incubation, the antibacterial activity was examined in the terms of zone of inhibition measured in mm. The antibacterial experiment was run three times of each bacterial species.

Results and discussion

In preliminary experiment, $[(C_3H_7)_3N\text{-}SO_3H]Cl$ IL catalyst was synthesized from Tripropylamine and chlorosulfonic acid. In a typical procedure, Tripropylamine (**1**) was reacted with chlorosulfonic acid (**2**) in dry DCM under ice cold condition as per reported method [25]. After attaining room temperature, resultant acidic ionic liquid named $[(C_3H_7)_3N\text{-}SO_3H]Cl$(**3**) was separated and washed with diethyl ether several times and finally dried under vacuum.

Characterization of $[(C_3H_7)_3N\text{-}SO_3H]Cl$ IL

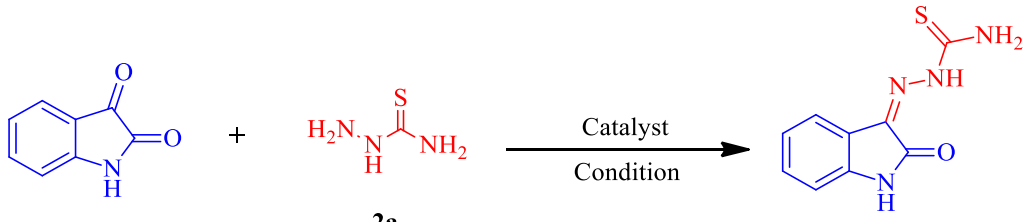
The synthesized Bronsted acidic $[(C_3H_7)_3N\text{-}SO_3H]Cl$ ionic liquid catalyst was characterized by using FT-IR, ^1H and ^{13}C NMR, D_2O exchange and mass analyses as reported in our previous research work.

Catalytic activity of $[(C_3H_7)_3N\text{-}SO_3H]Cl$ IL catalyst

After ensuring the structure, catalytic ability of $[(C_3H_7)_3N\text{-}SO_3H]Cl$ was tested in the synthesis of oxoindolin hydrazine carbothioamide using isatin and thiosemicarbazide as model reacting substrates. We began our experimentation by selecting model reaction of isatin (**1a**) and thiosemicarbazide (**2a**) to establish optimized reaction condition for the synthesis of 5'-(Z)-2-(2-oxoindolin-3-ylidene)hydrazinecarbothioamide **(3a)** and results are tabulated in **Table 1**.

Initially, using catalyst free condition the model reaction was performed in water at ambient temperature, which resulted a moderate yield of **3a** (Table 1, entry 1). Next, 5 mol % of $[(C_3H_7)_3N\text{-}SO_3H]Cl$ catalyst was used at room temperature condition (Table 1, entry 2) produced **3a** in 62 % yield and structure was confirmed by IR, ^1H and ^{13}C NMR and mass technique. In order to improve the yield of **3a**, the model reaction was performed in the presence of 05 mol % of BAIL catalyst in several solvents such as H_2O, H_2O:C_2H_5OH (1:1 *v/v*), C_2H_5OH, CH_2Cl_2 and CH_3CN at room temperature (Table 1, entries 3-7). From the obtained results, it is realized that the use of an aqueous medium was the best solvent condition for this reaction. In addition to these optimization studies, a few more experiments were performed by changing the amount of $[(C_3H_7)_3N\text{-}SO_3H]Cl$ to 10 mol % in water and ethanolic medium (Table 1, entries 8-9). A screening study of solvents and catalysts demonstrated that 10 mol % of $[(C_3H_7)_3N\text{-}SO_3H]Cl$ catalyst gave excellent yield of **3a** in aqueous solvent (Table 1, entry 8). A further increase in catalyst amount (15 mol %) did not show significant change in the yield of **3a** (Table 1, entry 10).

Table 1 Scrutiny of different parameters in the synthesis of 3a[a].



1a **2a** **3a**

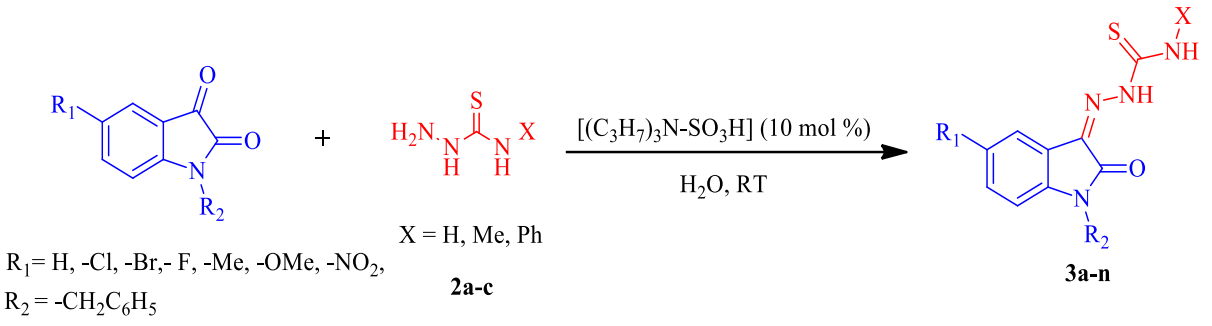
Entry	Solvent	Catalyst (mol %)	Time (min)	Yield[b] (%)
1	H_2O	—	130	55
2	—	$[(C_3H_7)_3N\text{-}SO_3H]Cl$(05)	95	62
3	H_2O	$[(C_3H_7)_3N\text{-}SO_3H]Cl$(05)	15	80
4	H_2O:C_2H_5OH (1:1 v/v)	$[(C_3H_7)_3N\text{-}SO_3H]Cl$(05)	15	76
5	C_2H_5OH	$[(C_3H_7)_3N\text{-}SO_3H]Cl$(05)	20	76
6	CH_2Cl_2	$[(C_3H_7)_3N\text{-}SO_3H]Cl$(05)	80	56
7	CH_3CN	$[(C_3H_7)_3N\text{-}SO_3H]Cl$(05)	95	45
8	**H_2O**	**$[(C_3H_7)_3N\text{-}SO_3H]Cl$(10)**	**10**	**92**
9	C_2H_5OH	$[(C_3H_7)_3N\text{-}SO_3H]Cl$(10)	16	85
10	H_2O	$[(C_3H_7)_3N\text{-}SO_3H]Cl$(15)	10	93

[a]Reaction conditions: Isatin (1mmol), thiosemicarbazide (1 mmol), $[(C_3H_7)_3N\text{-}SO_3H]Cl$ IL catalyst in 5 mL solvent at room temperature.
[b]isolated yield.

Having optimized reaction conditions in hand, the generality of the protocol was determined by reacting structurally diverse isatins with thiosemicarbazides under optimized reaction conditions. As shown in Table 2, reaction of substituted isatin with thiosemicarbazide catalyzed by 10 mol% $[(C_3H_7)_3N\text{-}SO_3H]Cl$ afforded excellent yield of desired oxoindolin hydrazine carbothioamides (Table 2, entries **3a-n**).

Importantly, the functional groups present on the aromatic rings of isatin such as hydroxyl, methoxy, methyl, chloro, bromo, and nitro were unaffected and appeared in the corresponding oxoindolin hydrazine carbothioamide. Pure compounds were by recrystallization from ethanol. The structures of desired oxoindolin hydrazine carbothioamide were examined by IR, ^{1}H and ^{13}C NMR and mass analysis.

Table 2 $[(C_3H_7)_3N\text{-}SO_3H]Cl$ Ionic liquid catalyzed synthesis of oxoindolin hydrazine carbothioamide using isatins[a]



R_1= H, -Cl, -Br,- F, -Me, -OMe, $-NO_2$,
$R_2 = -CH_2C_6H_5$

1

X = H, Me, Ph

2a-c

3a-n

Entry	R_1	X	Product	Time (min)	Yield[b] (%)
1	H	**H**	**3a**	20	94
2	5-Br	**Me**	**3b**	19	91
3	5-Br	**Ph**	**3c**	24	87
4	5-I	**H**	**3d**	22	90
5	5-NO_2	**H**	**3e**	30	87
6	5-OMe	**H**	**3f**	18	92
7	5-F	**H**	**3g**	28	86
8	1-CH_2Ph	**H**	**3h**	20	88
9	1-CH_2Ph	**Me**	**3i**	40	90
10	1-CH_2Ph	**Ph**	**3j**	24	85
11	1-CH_2Ph, 5-Cl	**Me**	**3k**	38	84
12	1-CH_2Ph, 5-Br	**Ph**	**3l**	35	85
13	1-CH_2Ph, 5-Cl	**Me**	**3m**	38	84
14	1-CH_2Ph, 5-Br	**Ph**	**3n**	35	85[c]

[a]Reaction conditions: Isatin (1mmol), thiosemicarbazide (1 mmol), 10 mol % $[(C_3H_7)_3N\text{-}SO_3H]Cl$ in 5 mL water at room temperature. [b]Isolated yield. [c]Novel compound.

Antimicrobial activity

The antimicrobial activity of synthesized compounds (**3a-n**) was evaluated by observing zone of inhibition around selected strains *B. cereus* and *E. coli* by agar well diffusion method. Among these synthesized compounds, **3j** showed strong antimicrobial activity whereas **3b**, **3c**, **3e**, **3f**, **3h**, **3i**, and **3n** showed moderate antimicrobial effect against strain (Fig. 2). We also found that **3a**, **3d**, **3g**, **3k**, **3l** and **3m** showed less antimicrobial activity (Table 3). They conclude that all synthesized compounds have antimicrobial activity but **3j** and **3b**, **3c**, **3e**, **3f**, **3h**, **3i**, **3n** having strong antimicrobial activity against selected strains.

Table 3: Antimicrobial evaluation of oxoindolin hydrazine carbothioamide.

S. No.	Compound	Zone of inhibition (mm)							
		Escherichia coli				*Bacillus cereus*			
		Control 100 (µl)	100 (µl)	150 (µl)	200 (µl)	Control 100 (µl)	100 (µl)	150 (µl)	200 (µl)
1	**3a**	-	ND	12	ND	-	ND	14	18
2	**3b**	-	12	15	18	-	ND	14	18
3	**3c**	-	12	12	15	-	11	12	18
4	**3d**	-	ND	ND	ND	-	10	11	12
5	**3e**	-	15	15	23	-	17	18	24
6	**3f**	-	14	15	23	-	12	13	15
7	**3g**	-	ND	14	17	-	10	11	15
8	**3h**	-	16	17	19	-	15	18	22
9	**3i**	-	13	14	22	-	14	16	23
10	**3j**	-	15	25	30	-	16	17	30
11	**3k**	-	ND	13	14	-	13	14	16
12	**3l**	-	ND	15	23	-	ND	ND	ND
13	**3m**	-	ND	ND	ND	-	10	14	ND
14	**3n**	-	12	15	22	-	13	13	15

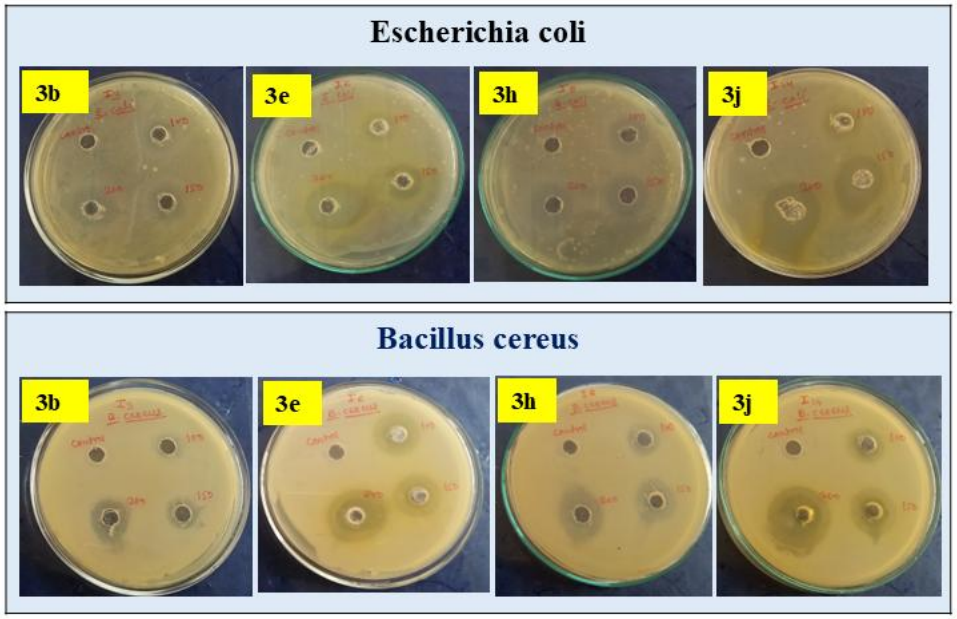


Fig. 2 Zone of inhibhition against gram positive pathogen *E. coli* and gram negative pathogen *B. cereus*

The proposed mechanism for the synthesis of oxoindolin hydrazine carbothioamide **(3a)** from isatin **(1a)** and thiosemicarbazide **(2a)** in the presence of $[(C_3H_7)_3N\text{-}SO_3H]Cl$ catalyst is shown in **Scheme 1**. Initially, the acidic proton from sulfonic acid group increases electron deficient character of the carbonyl group through protonation of oxygen [26]. Here, the electrophilicity of the ketone gets enhanced through the hydrogen bonding with the $-SO_3H$ group of the $[(C_3H_7)_3N\text{-}SO_3H]Cl$ catalytic part which leads to the nucleophilic attack of thiosemicarbazide to produce intermediate **(I)** which upon cyclodehydration gives the corresponding product **3a**.

The catalytic efficacy of $[(C_3H_7)_3N\text{-}SO_3H]Cl$ was compared with previously reported methods for the synthesis of oxoindolin hydrazine carbothioamide (Table 4). The comparative study proves that the present method is superior in comparison with reported methods in terms of reaction time and yield thereby addressing the principles of "Green Chemistry".

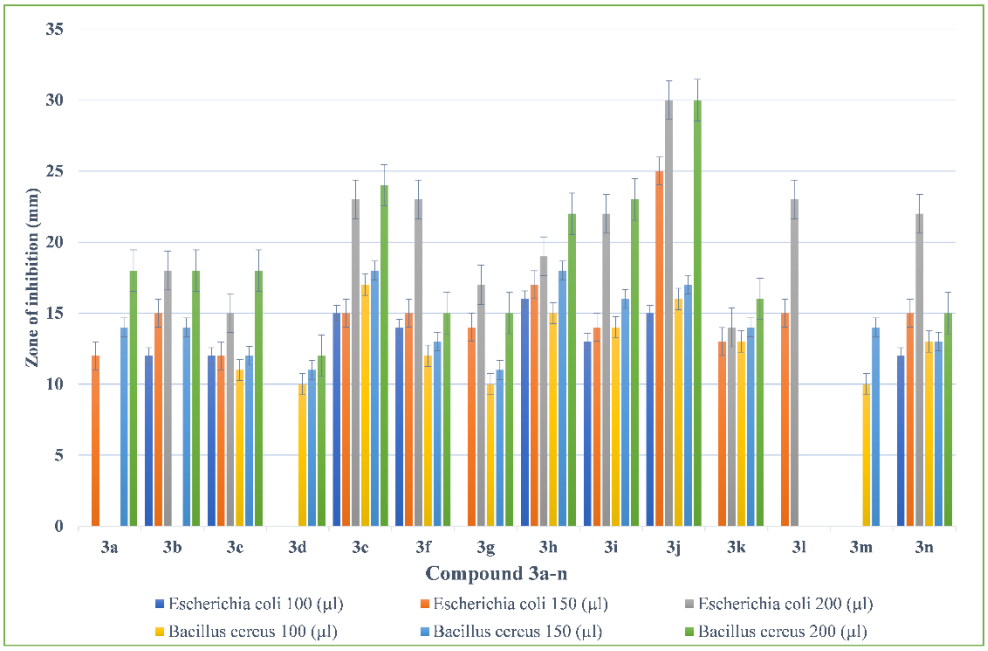
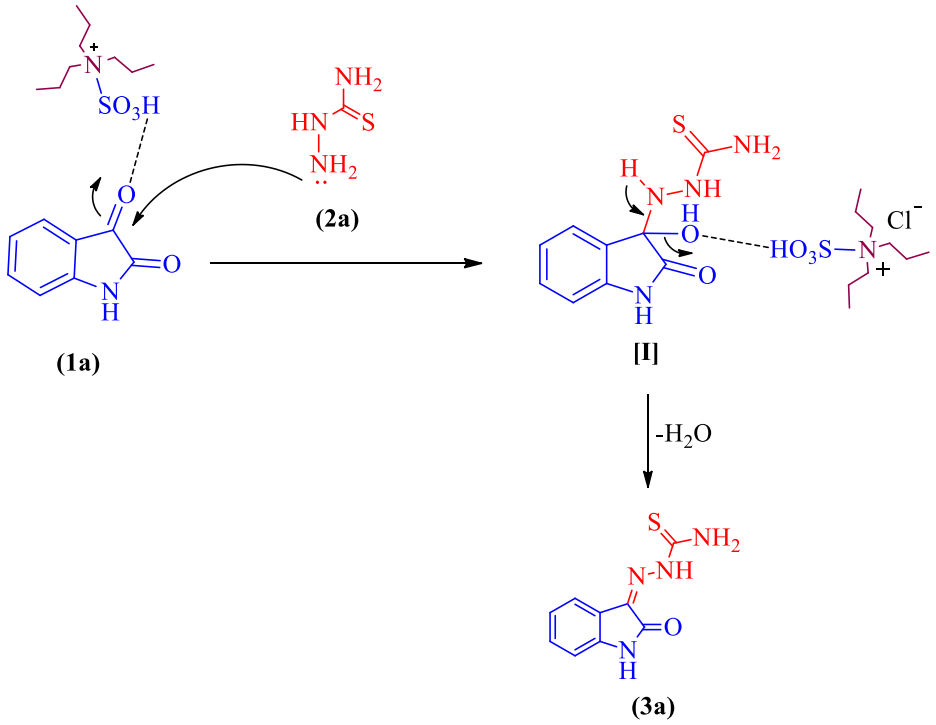


Fig. 3 Antibacterial activity against *E. coli* and *B. cereus*



Scheme 1 Catalytic Role of $[(C_3H_7)_3N\text{-}SO_3H]Cl$ BAIL in the Synthesis of oxoindolin hydrazine carbothioamide.

Table 4 Comparative study of catalytic efficiency of $[(C_3H_7)_3N\text{-}SO_3H]Cl$BAIL with reported methods in the synthesis of oxoindolin hydrazine carbothioamide

Entry	Catalyst	Condition	Time (min)	Yield[a](%)
1	CH_3COOH	EtOH/ reflux	180	86[21]
2	CH_3COOH	EtOH/ MW	5-20	74[22]
3	Conc. H_2SO_4	EtOH/ 70 °C	240	81[23]
4	K10 Clay	EtOH/ MW	20	82[24]
5	**$[(C_3H_7)_3N\text{-}SO_3H]Cl$ IL**	**H_2O/ RT**	**20**	**92**

Conclusion

In conclusion, we have reported a one-pot synthesis of oxoindolin hydrazine carbothioamide derivatives through the fusion of isatins with thiosemicarbazides by $[(C_3H_7)_3N\text{-}SO_3H]Cl$ as a highly efficient, recyclable, biodegradable and inexpensive catalyst in aqueous medium. Readily available precursors, wide substrate scope and product yields, aerobic reaction conditions, and operational simplicity are the notable advantages of this present approach. Additionally, antimicrobial investigation demonstrated that, the compound **3j** has remarkable biological potential against Gram-positive (*E. coli*) and Gram-negative (*B. cereus*) bacterial strains. So, it can manage human pathogens by inhibiting the growth of diverse microbial species in the future.

Supporting Information

The FT-IR, ^{1}H and ^{13}C NMR and GC-MS spectra for all products are appended at the end of this manuscript as supporting information.

Declaration of Competing Interest

There is no conflict of interest to declare.

Acknowledgment

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Supporting Information

$[(C_3H_7)_3N\text{-}SO_3H]Cl$: An efficient ionic liquid catalyst for the synthesis of oxoindolin

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2-(1-benzyl-2-oxoindolin-3-ylidene)hydrazine carbothioamide **3h** (Table 2, entry **8**):
Yellow solid; mp: 264-65 °C; IR (KBr): 515, 629, 699, 748, 825, 1092, 1138, 1188, 1211, 1292, 1362, 1482, 1599, 1680, 1783, 1825, 3065, 3160, 3255, 3332, 3451; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.97 (2H, d-d, -CH_2), 7.01-7.03 (1H, d, *J*=8.0 Hz, Ar-H), 7.11-7.14 (1H, t, *J*=7.5 Hz, Ar-H), 7.25-7.28 (1H, t, *J*=7.0, 7.5 Hz, Ar-H), 7.31-7.34 (3H, t, *J*=7.0, 7.5 Hz, Ar-H), 7.36-7.38 (2H, t, *J*=7.0 Hz, Ar-H), 7.71-7.72 (1H, d, *J*=7.0 Hz, Ar-H), 12.41 (1H, s, -NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 42.43, 110.21, 119.40, 120.69, 122.90, 127.31, 127.48, 128.58, 130.79, 130.91, 135.59, 142.42, 160.70, 178.63; MS (ES+): m/z= 311 [M+1].

2-(1-benzyl-2-oxoindolin-3-ylidene)-N-methylhydrazinecarbothioamide **3i** (Table 2, entry **9**):
Pale yellow solid; mp: 222-26 °C; IR (KBr): 596, 629, 705, 753, 1050, 1140, 1209, 1350, 1476, 1540, 1611, 1692, 1785, 2265, 2928, 3040, 3235, 3343;^{13}C NMR (125 MHz, $CDCl_3$): δ 30.92, 31.34, 43.54, 110.04, 111.00, 119.69, 120.54, 123.16, 125.42, 127.43, 127.48, 128.03, 128.96, 129.06, 130.60, 131.05, 135.04, 138.29, 142.84, 161.09, 178.93, 206.95; MS (ES+): m/z= 325 [M+1].
2-(1-benzyl-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide **3j** (Table 2, entry **10**):
Yellow solid; mp: 150-52 °C; IR (KBr): 650, 695, 748, 1029, 1164, 1354, 1473, 1537, 1605, 1691, 2854, 2924, 3024, 3232, 3289, ; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.93-4.97 (2H, d-d, -CH_2), 6.81-6.83 (1H, d, *J*= 8 Hz, Ar-H), 7.09-7.12 (1H, m, *J*= 7.5 Hz, Ar-H), 7.27-7.35 (9H, m, Ar-H), 7.41-7.44 (2H, t, *J*= 8 Hz, Ar-H), 7.63-7.65 (1H, d, *J*= 7.5 Hz, Ar-H), 7.73-7.75 (2H, t, *J*=8.5 Hz, Ar-H), 9.51 (1H, s, -NH), 13.0 (1H, s, -NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 43.62, 110.16, 120.78, 123.29, 124.02, 126.41, 127.50, 128.08, 128.93, 129.00, 131.38, 137.60; MS (ES+): m/z= 387.
2-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)-N-methylhydrazinecarbothioamide **3k** (Table 2, entry **11**):
Dark yellow solid; mp: 240 °C; IR (KBr): 648, 694, 1043, 1149, 1203, 1268, 1337, 1483, 1546, 1691, 1742, 1822, 2930, 3023, 3267; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.10 (3H, s, -Me), 4.98 (2H, d-d, -CH_2), 7.03-7.05 (1H, d, *J*= 8.0 Hz, Ar-H), 7.26-2.29 (1H, t, *J*=7.0, Ar-H), 7.31-7.37 (4H, m, Ar-H), 7.39-7.41 (1H, d-d, *J*= 8.5 Hz, Ar-H), 7.76 (1H, s, Ar-H), 9.41-9.44 (1H, s, -NH), 12.35 (1H, s, -NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 31.23, 42.51, 111.77, 120.08, 121.35, 127.16, 127.29, 127.54, 128.60, 129.11, 129.96, 135.36, 140.95, 160.45, 177.50; MS (ES+): m/z= 359 [M+1].
2-(1-benzyl-5-bromo-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide **3l** (Table 2, entry **12**):
Yellow solid; IR (KBr): 568, 631, 711, 1029, 1070, 1167, 1338, 1471, 1517, 1603, 1698, 1747, 2925, 3041, 3248, 3287; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.95 (2H, d-d, -CH_2), 6.68-6.70 (1H, d, *J* = 8.0 Hz, Ar-H), 7.28-7.30 (3H, m, Ar-H), 7.33-7.36 (3H, m, Ar-H), 7.39-7.44 (3H, m, Ar-H), 7.73-7.74 (2H, d, *J* = 8.0 Hz, Ar-H), 7.76 (1H, s, Ar-H), 9.47 (1H, s, -NH), 12.93 (1H, s, -NH); ^{13}C NMR (125 MHz, $CDCl_3$): δ 43.72, 111.64, 116.18, 121.31, 123.64, 123.98, 126.55, 127.44, 128.24, 128.97, 129.09, 129.30, 133.66, 134.55, 137.42, 141.65, 160.77, 175.76;MS (ES+): m/z= 465.
Compound **3h,** Table 2

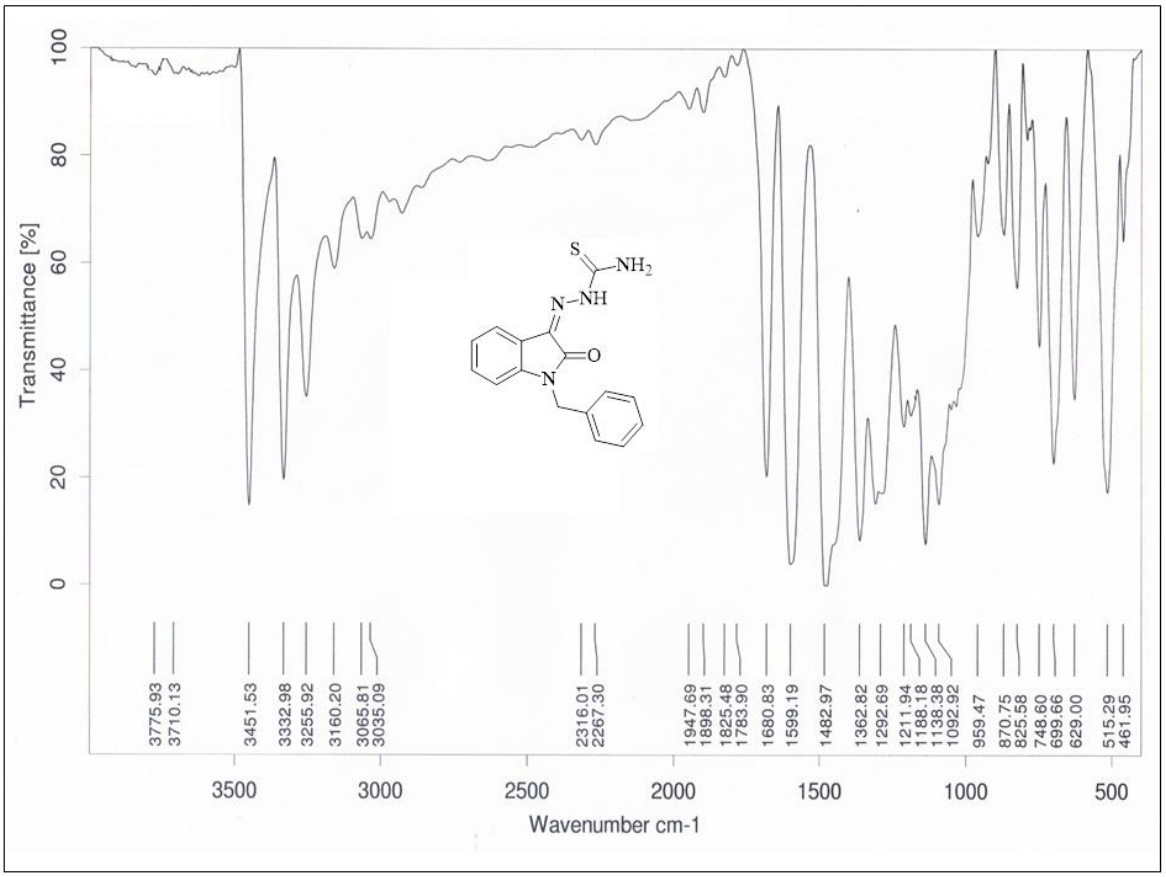

Fig. 1: FT-IR analysis of 2-(1-benzyl-2-oxoindolin-3-ylidene)hydrazine carbothioamide

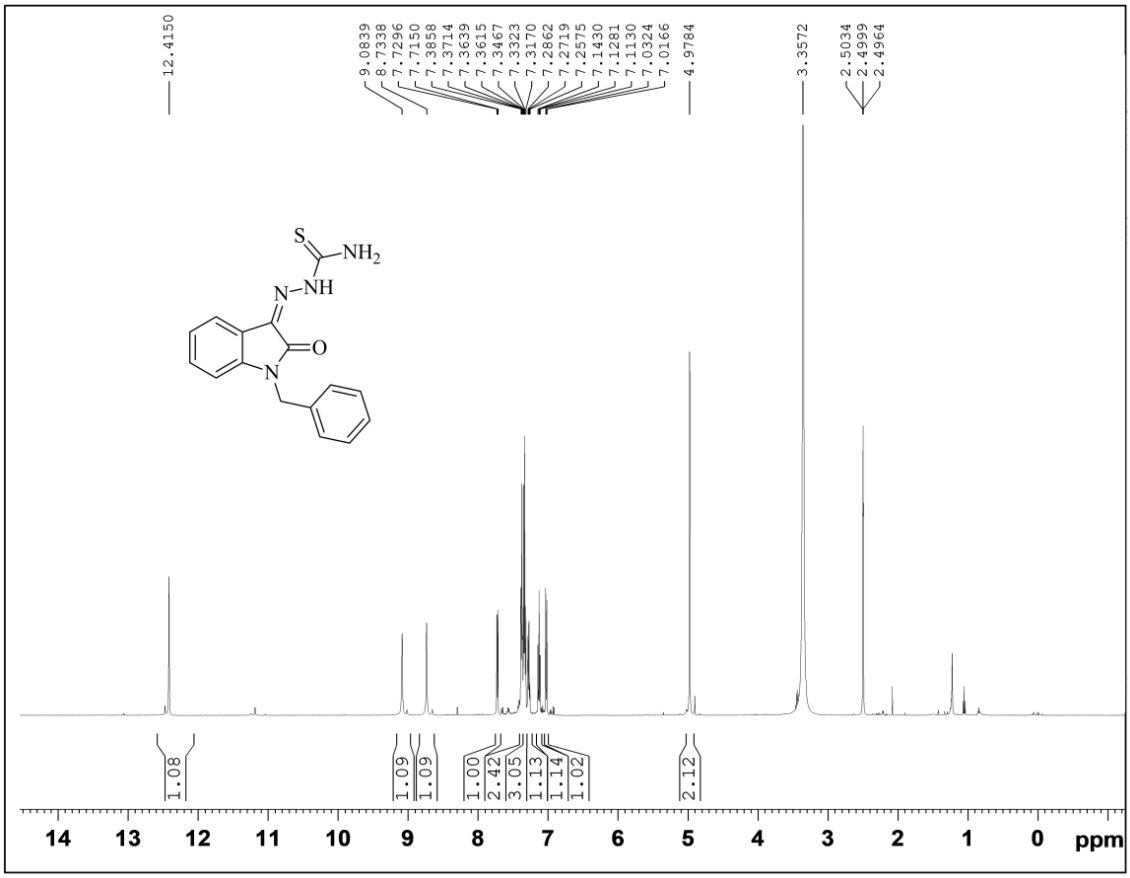

Fig. 2 ^{1}H NMR of 2-(1-benzyl-2-oxoindolin-3-ylidene)hydrazine carbothioamide

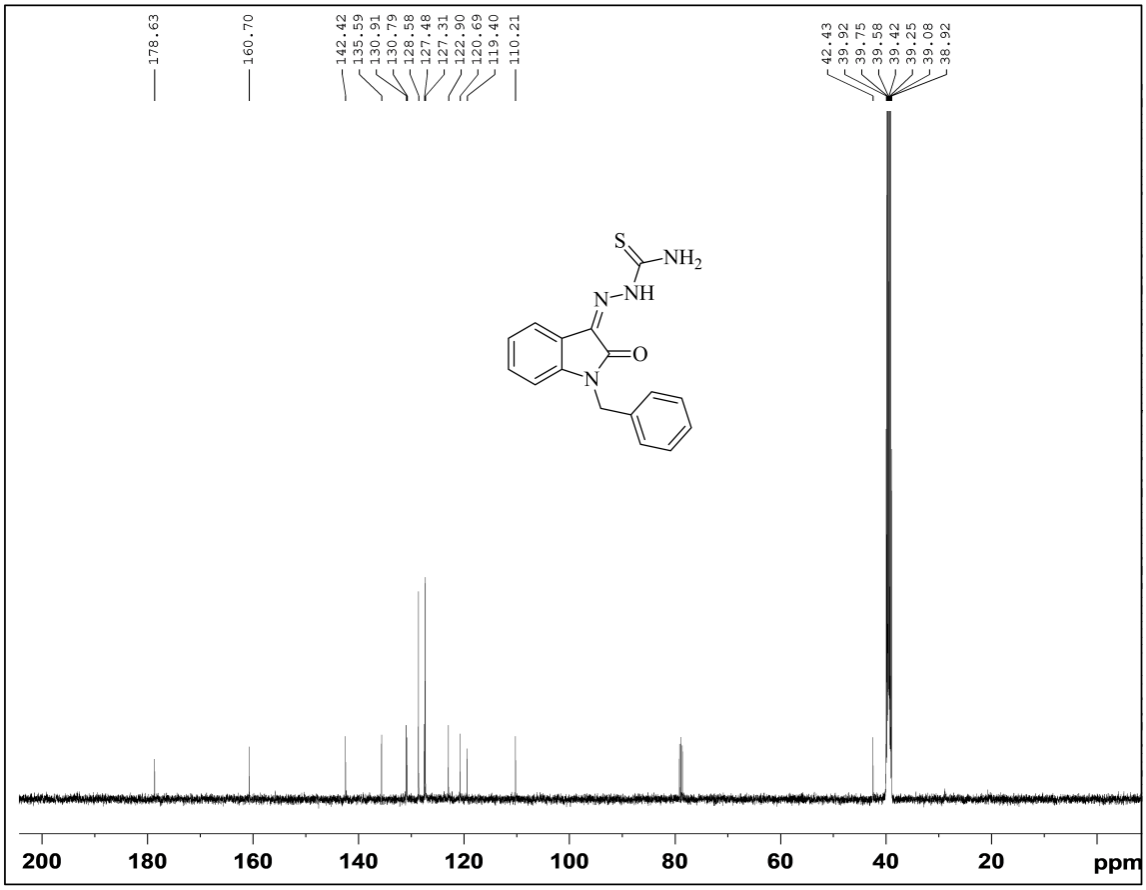

Fig. 3 Fig. 2 ^{13}C NMR of 2-(1-benzyl-2-oxoindolin-3-ylidene)hydrazine carbothioamide

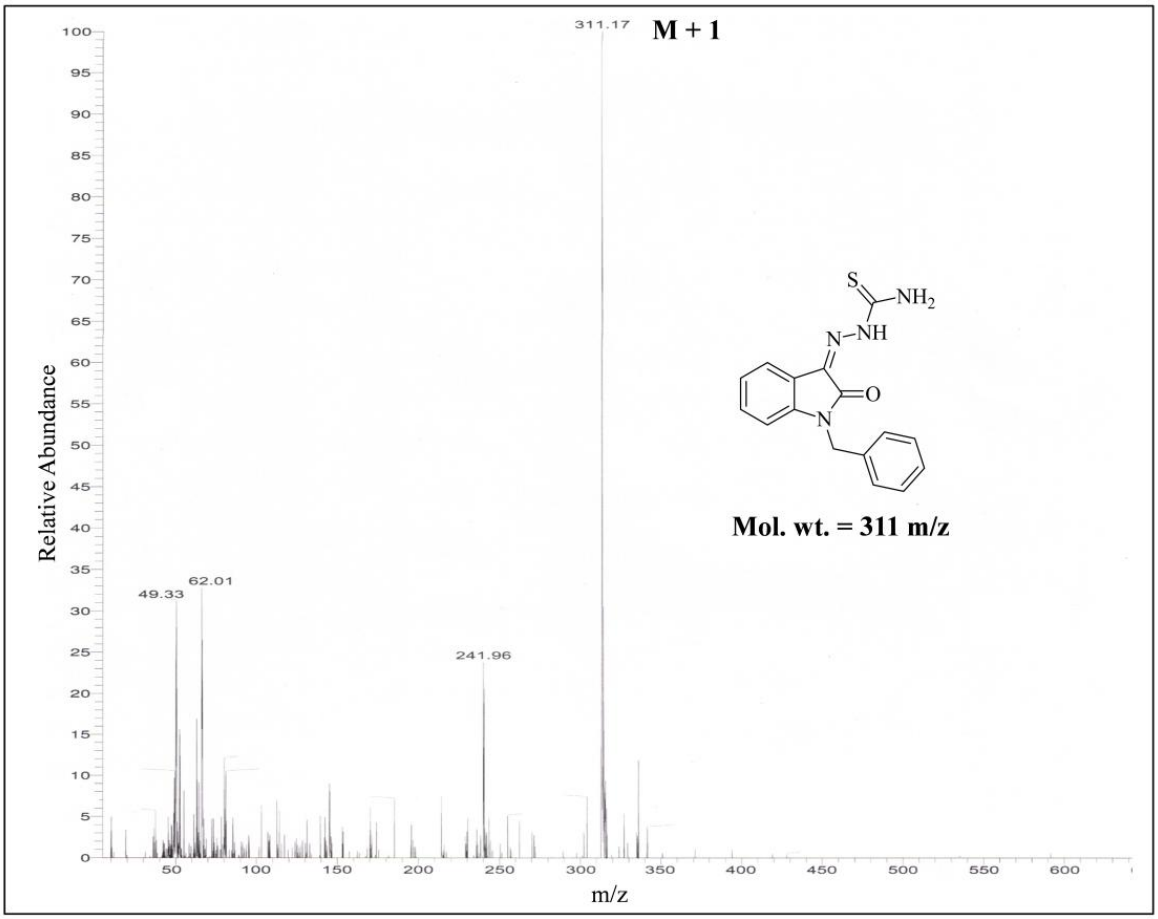

Fig. 4 ^{13}C Mass analysis of 2-(1-benzyl-2-oxoindolin-3-ylidene)hydrazine carbothioamide

Compound **3i,** Table 2

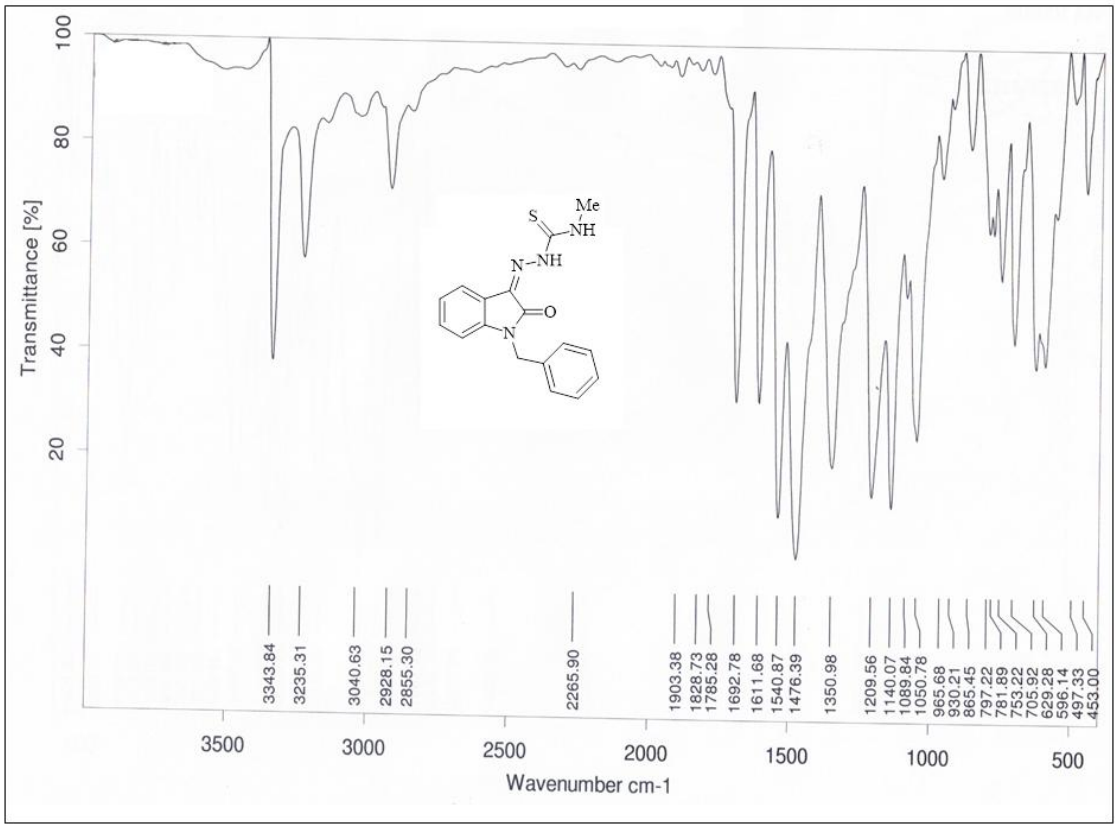

Fig. 5 FT-IR analysis of 2-(1-benzyl-2-oxoindolin-3-ylidene)-N-methyl hydrazine carbothioamide

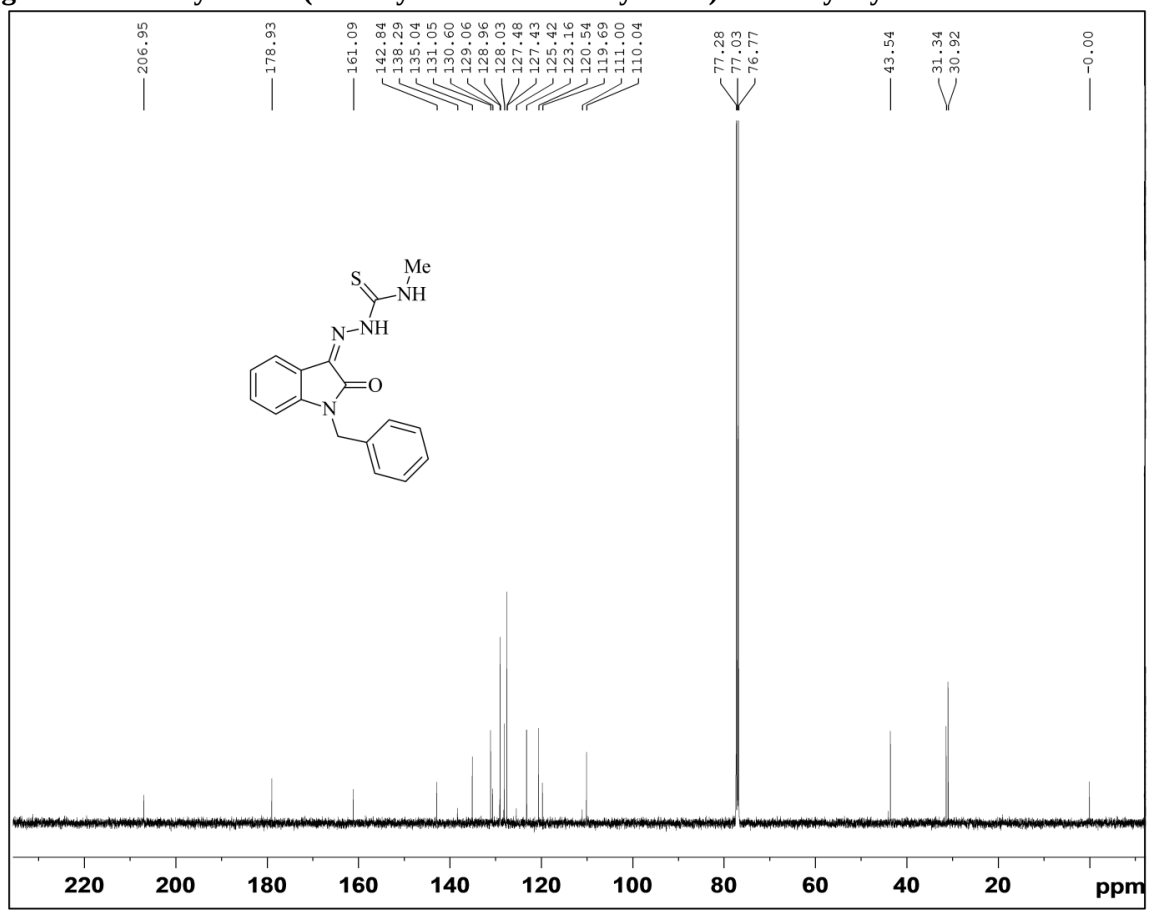

Fig. 6 ^{13}C NMR of 2-(1-benzyl-2-oxoindolin-3-ylidene)-N-methylhydrazinecarbothioamide

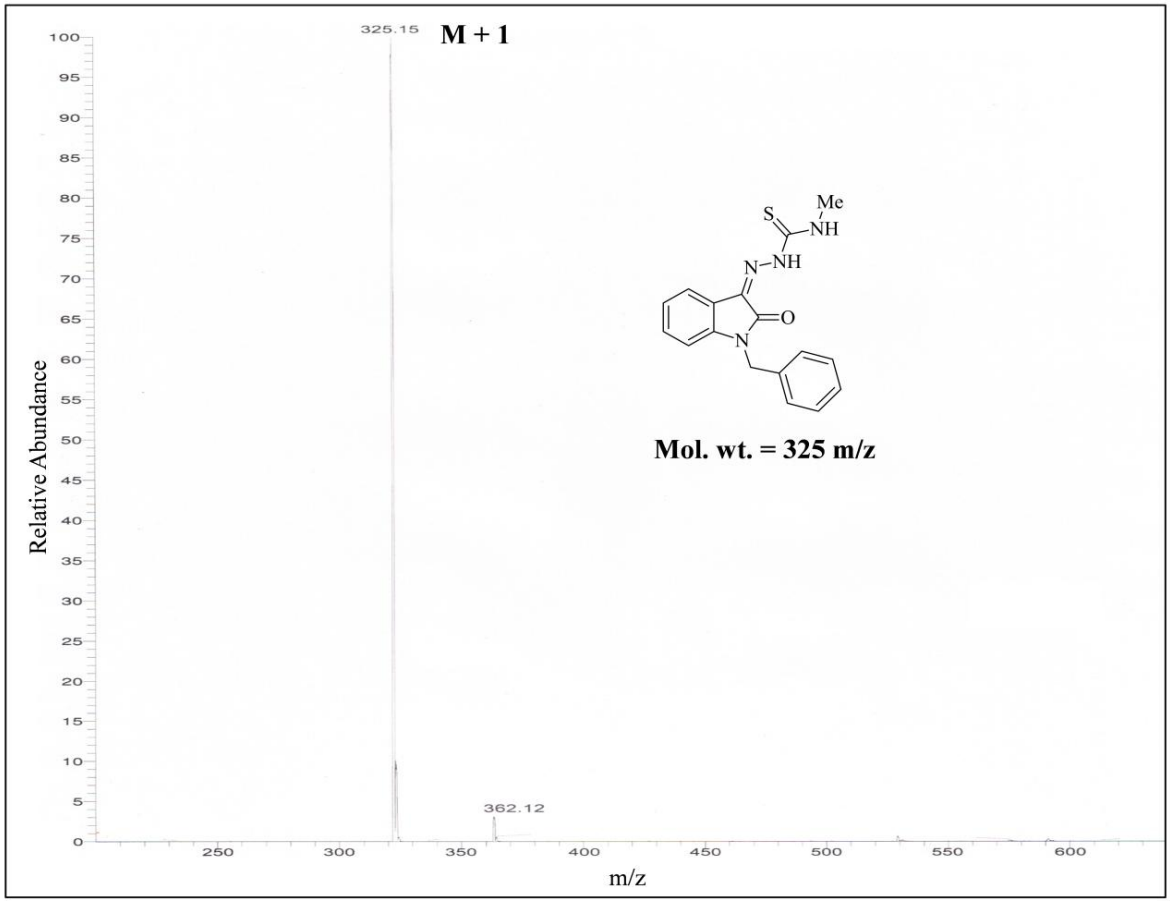

Fig. 7 Mass of 2-(1-benzyl-2-oxoindolin-3-ylidene)-N-methylhydrazinecarbothioamide

Compound **3j,** Table 2

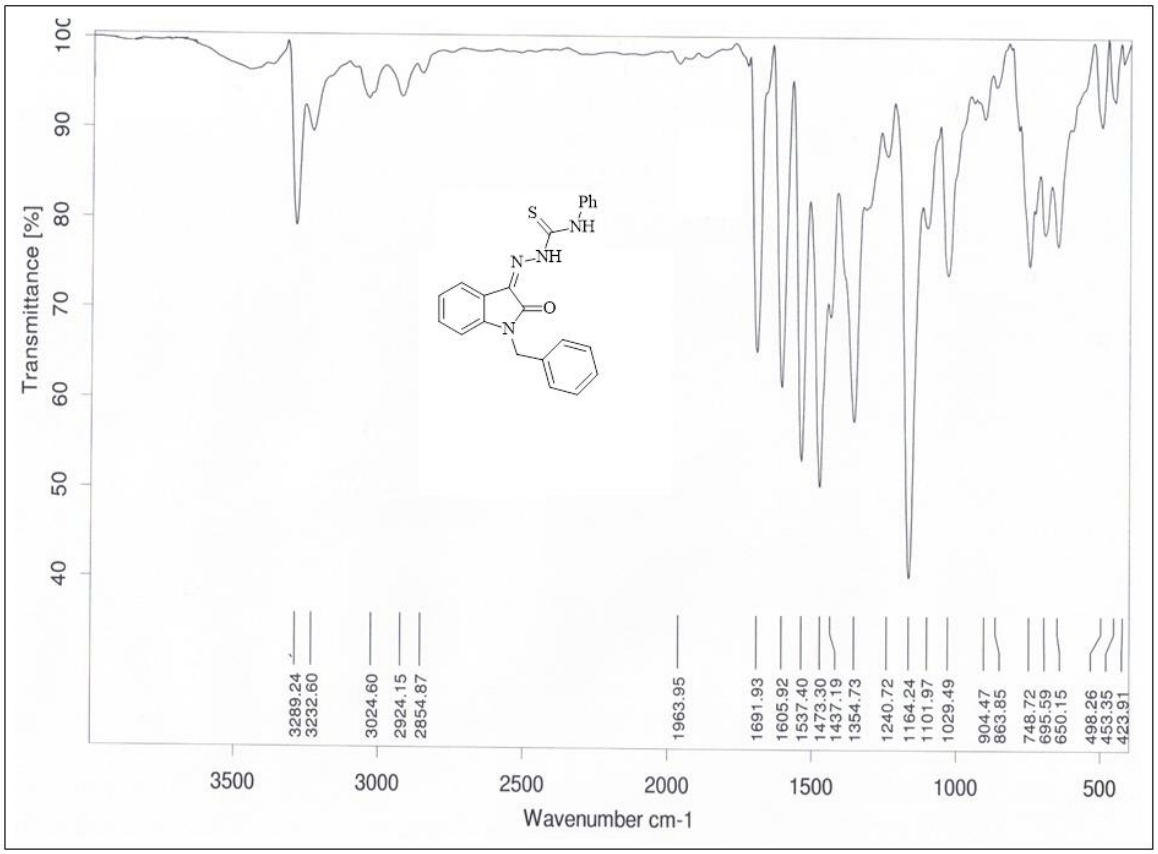

Fig. 8 FT-IR of 2-(1-benzyl-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide

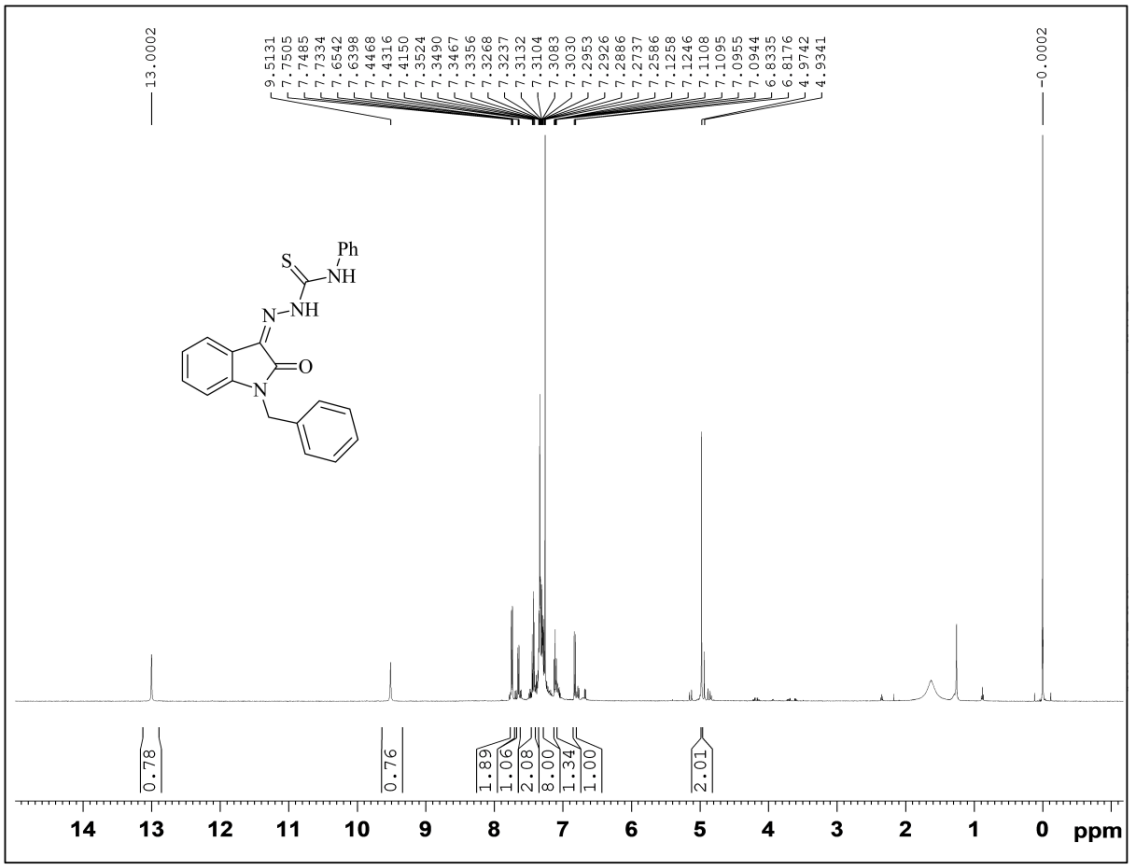

Fig. 9 ^{1}H NMR of 2-(1-benzyl-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide

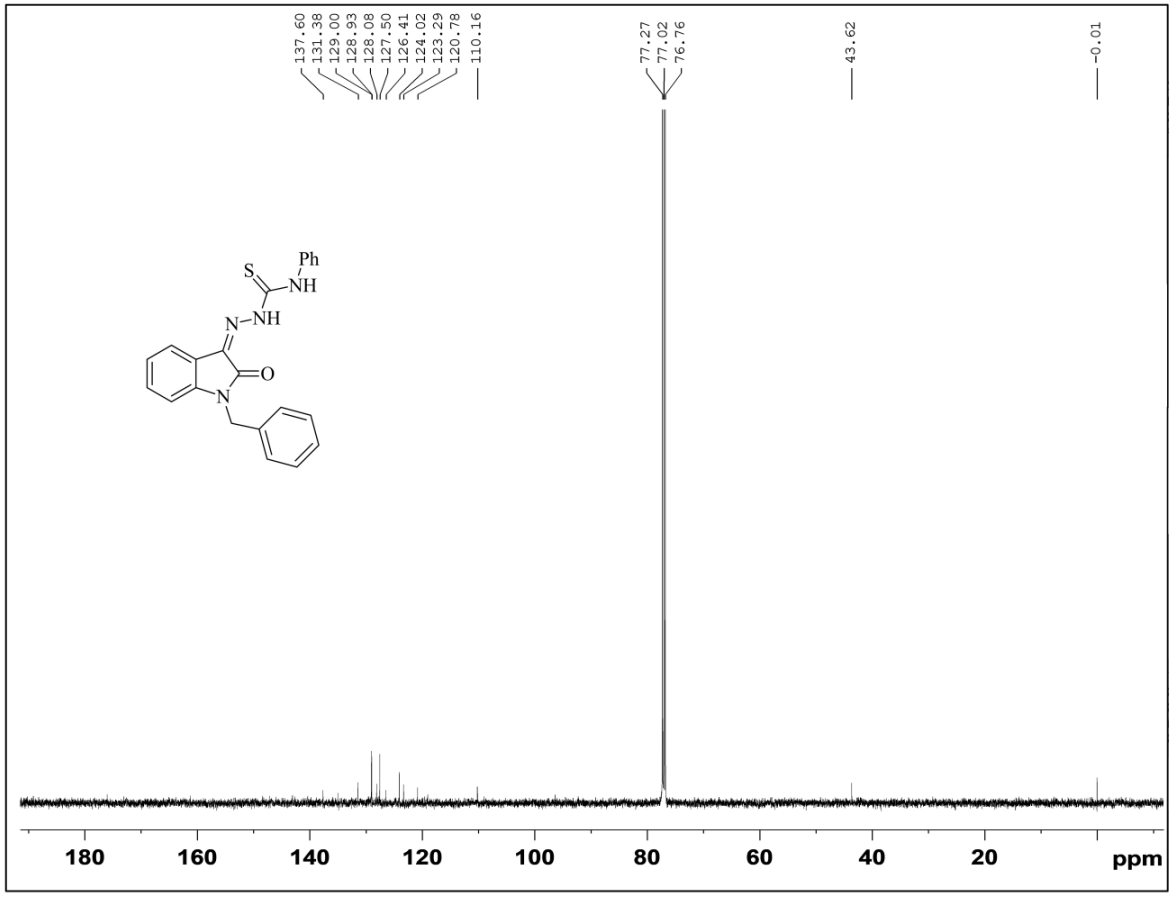

Fig. 10 ^{13}C NMR of 2-(1-benzyl-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide

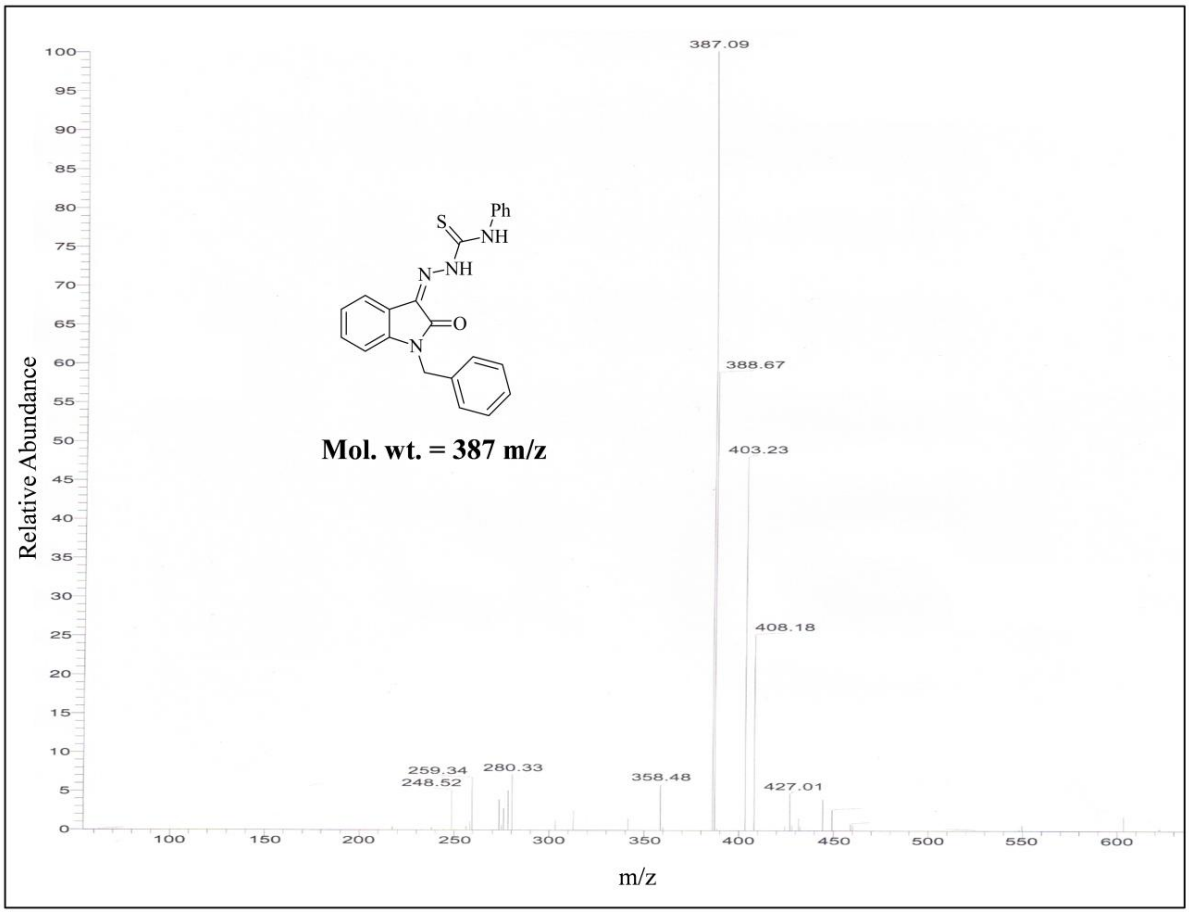

Fig. 11 Mass of 2-(1-benzyl-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide

Compound **3k,** Table 2

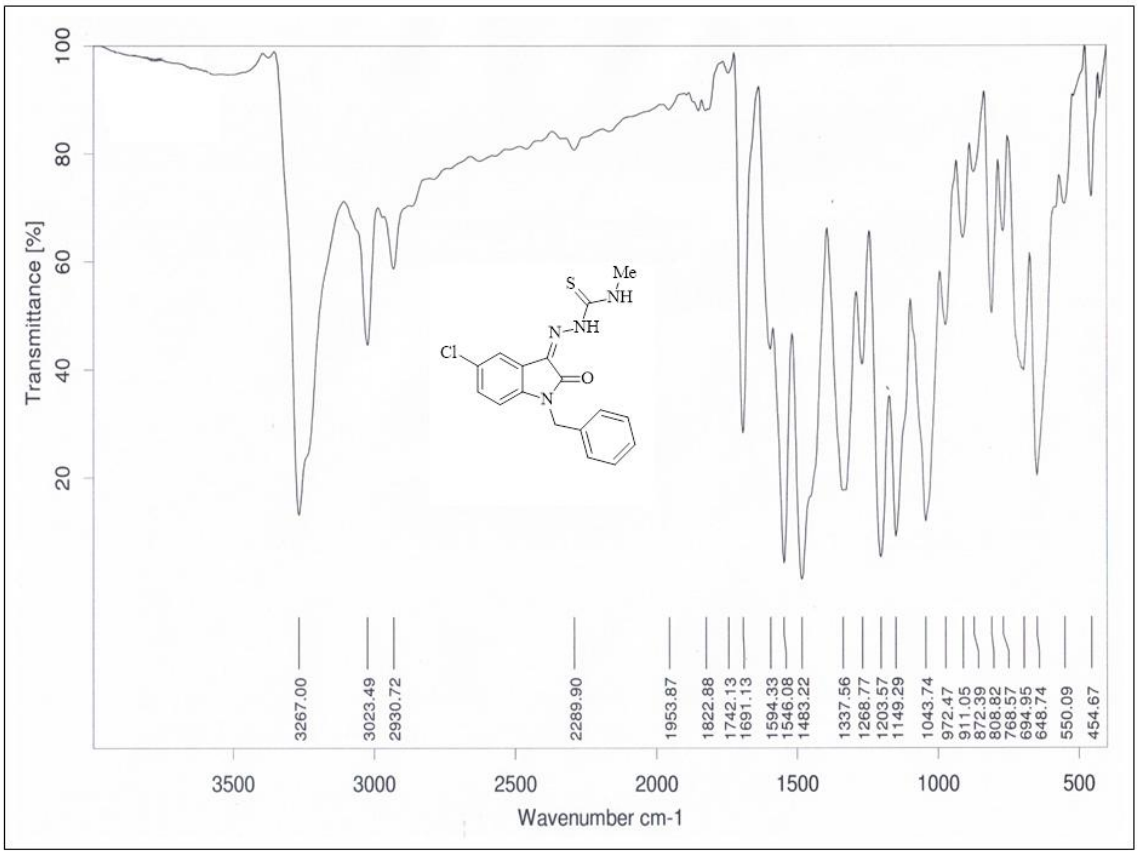

Fig. 12 FT-IR of 2-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)-N-methylhydrazinecarbothioamide

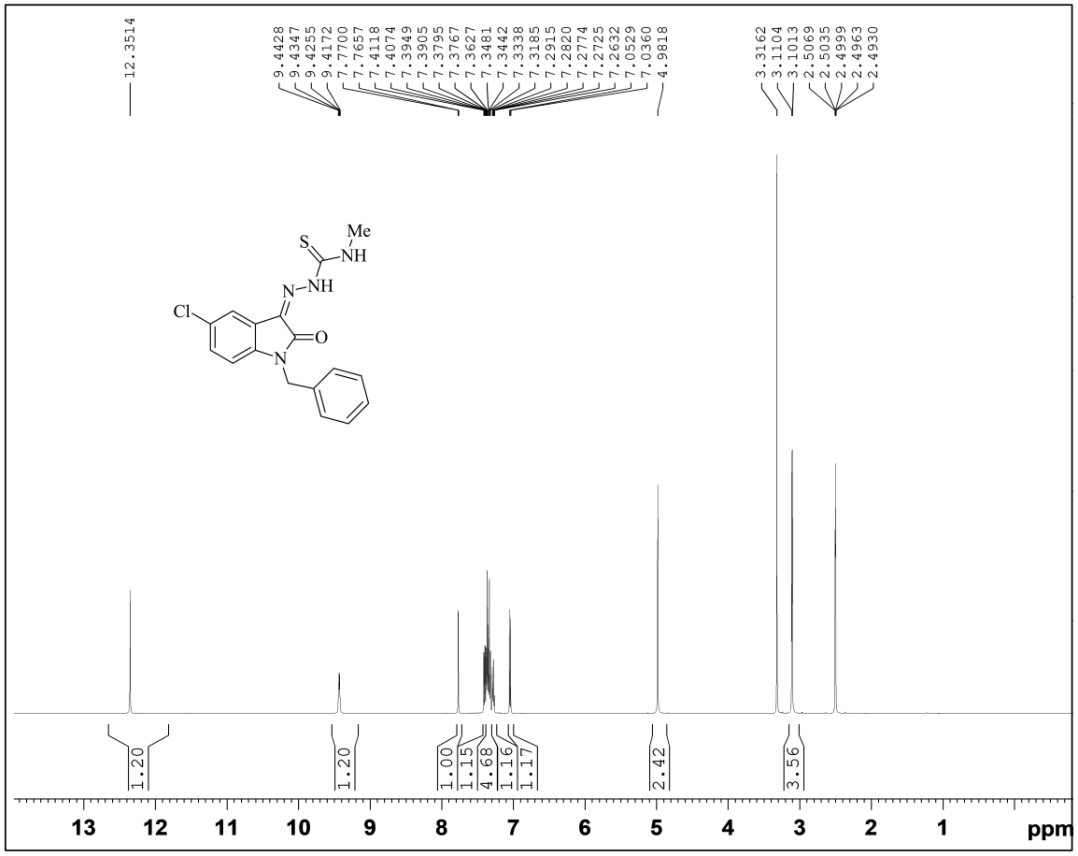

Fig. 13 ^{1}H NMR of 2-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)-N-methylhydrazinecarbothioamide

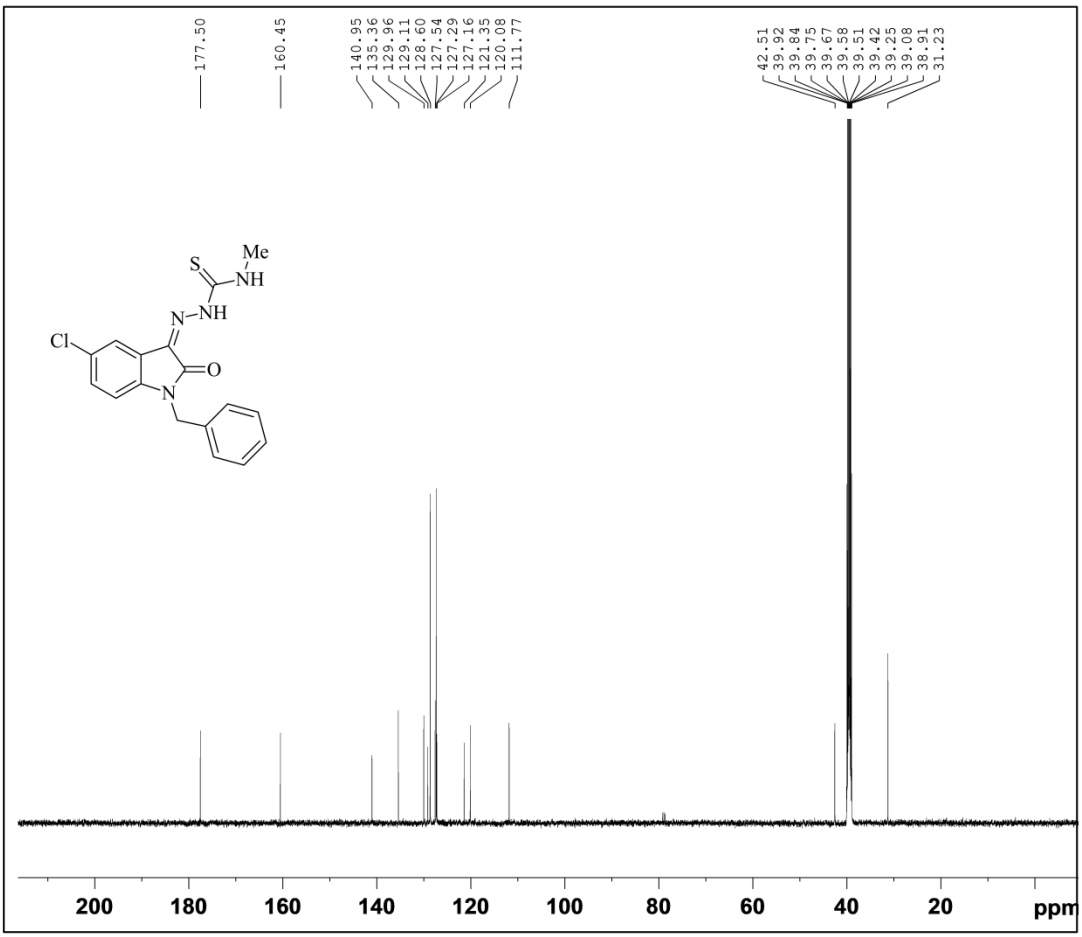

Fig. 14 ^{13}C NMR of 2-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)-N-methylhydrazinecarbothioamide

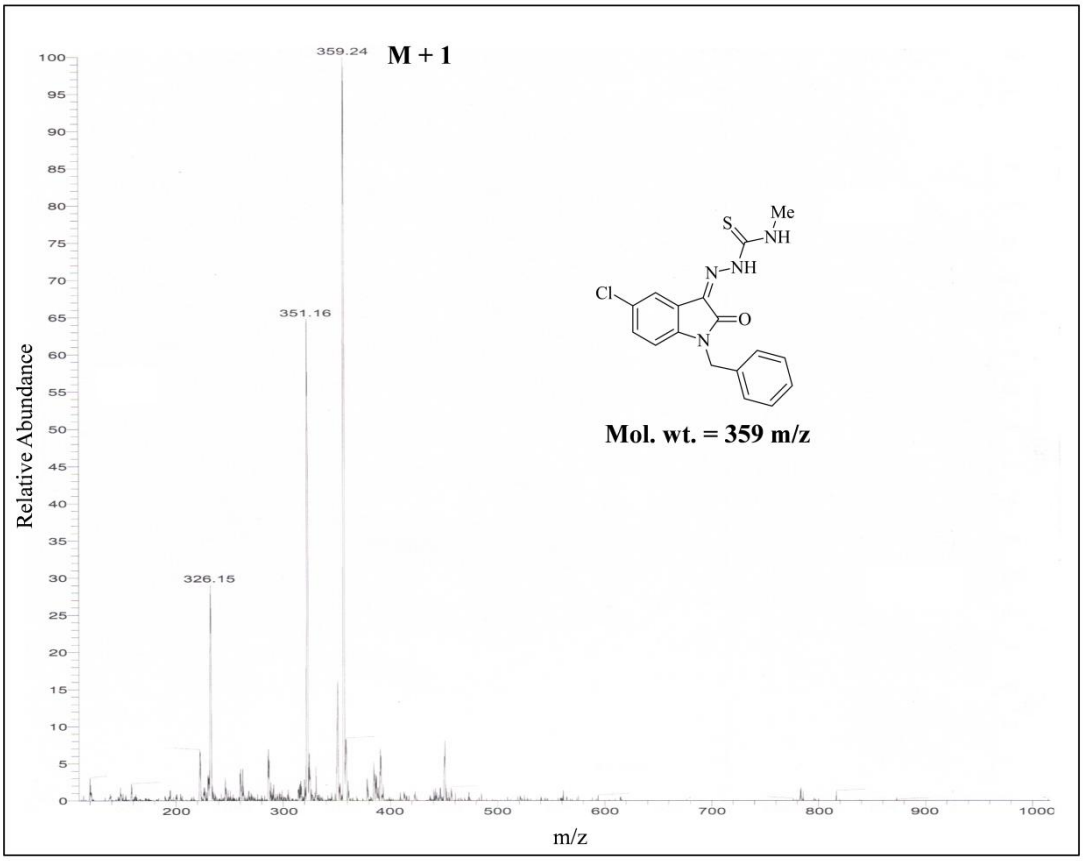

Fig. 15 Mass of 2-(1-benzyl-5-chloro-2-oxoindolin-3-ylidene)-N-methylhydrazinecarbothioamide

Compound **3l**, Table 2

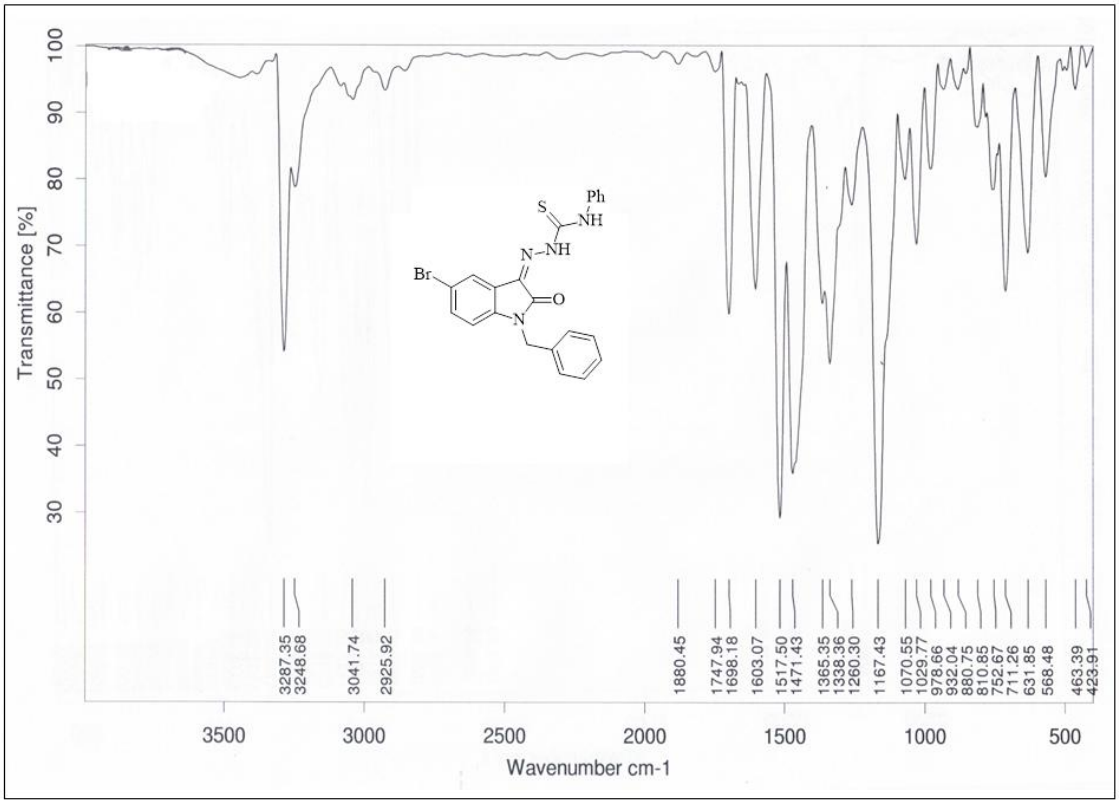

Fig. 16 FT-IR of 2-(1-benzyl-5-bromo-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide

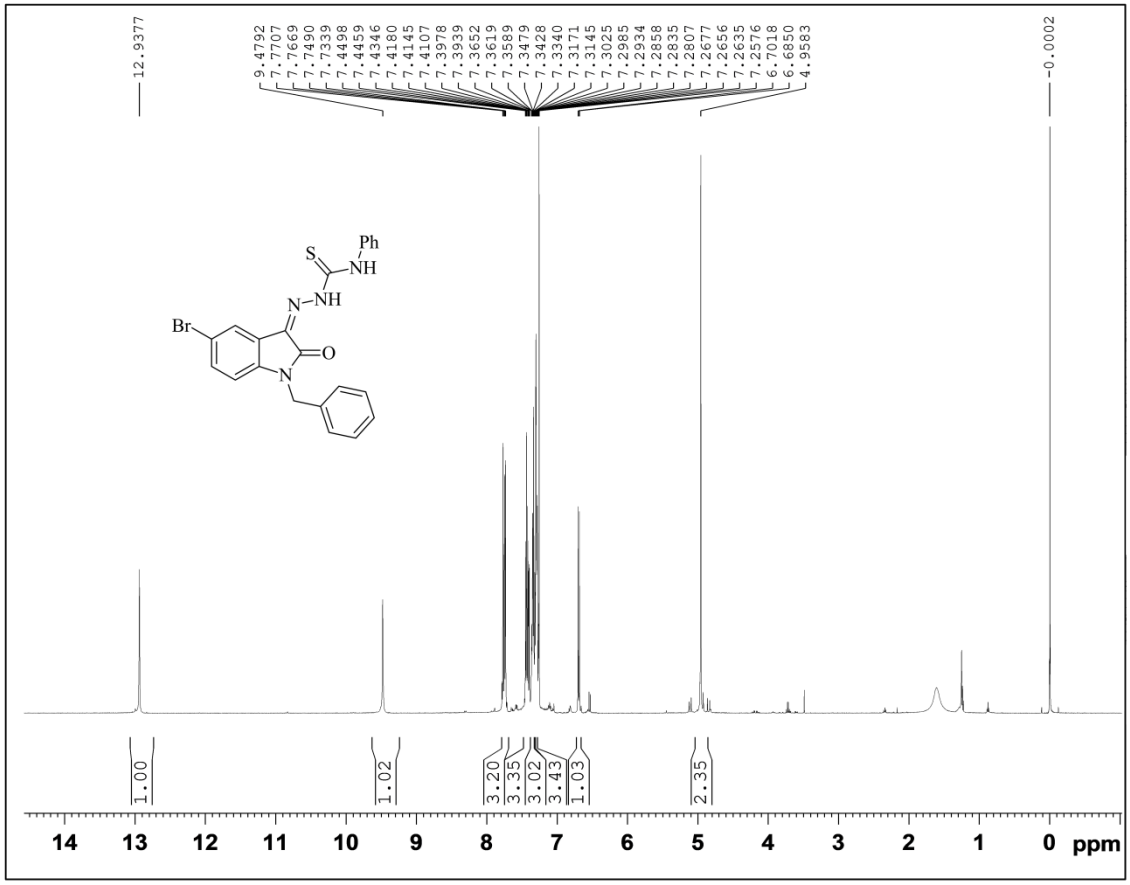

Fig. 17 ^{1}H NMR of 2-(1-benzyl-5-bromo-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide

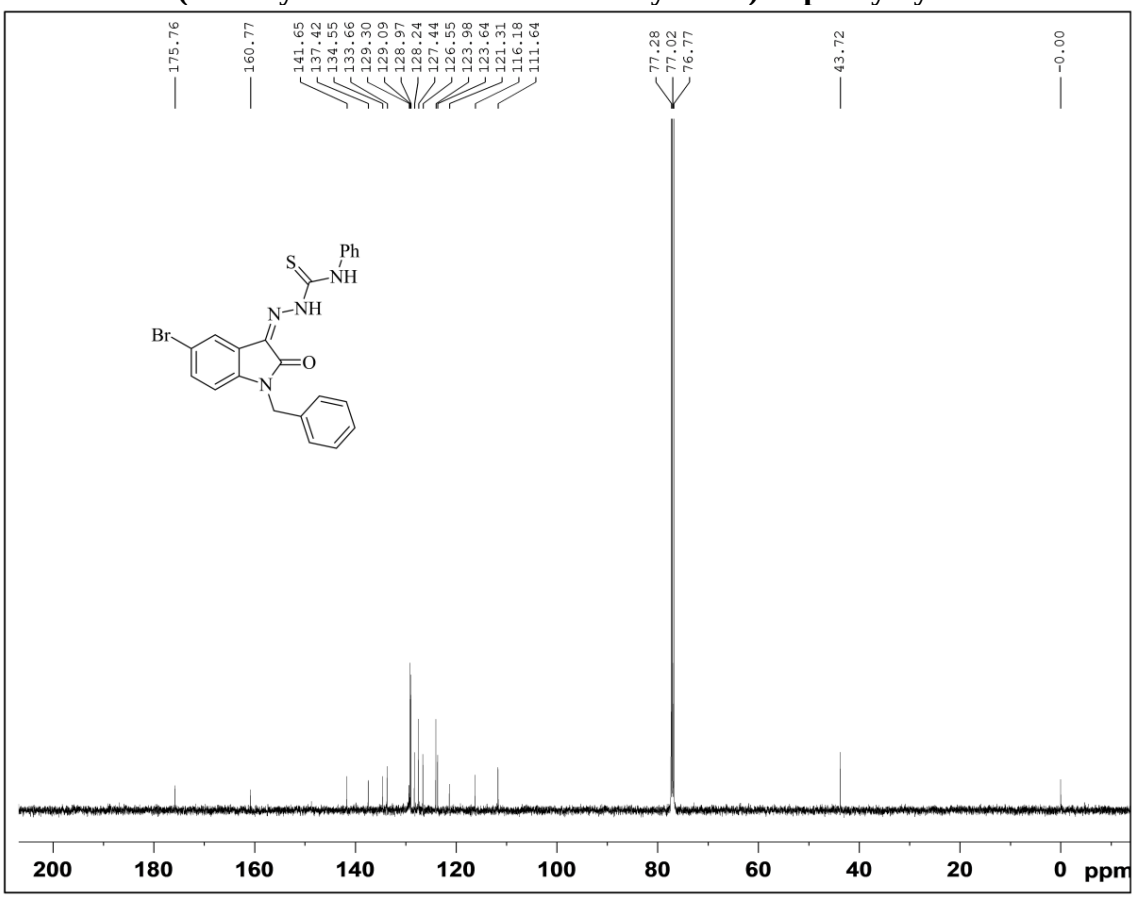

Fig. 18 ^{13}C NMR of 2-(1-benzyl-5-bromo-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide

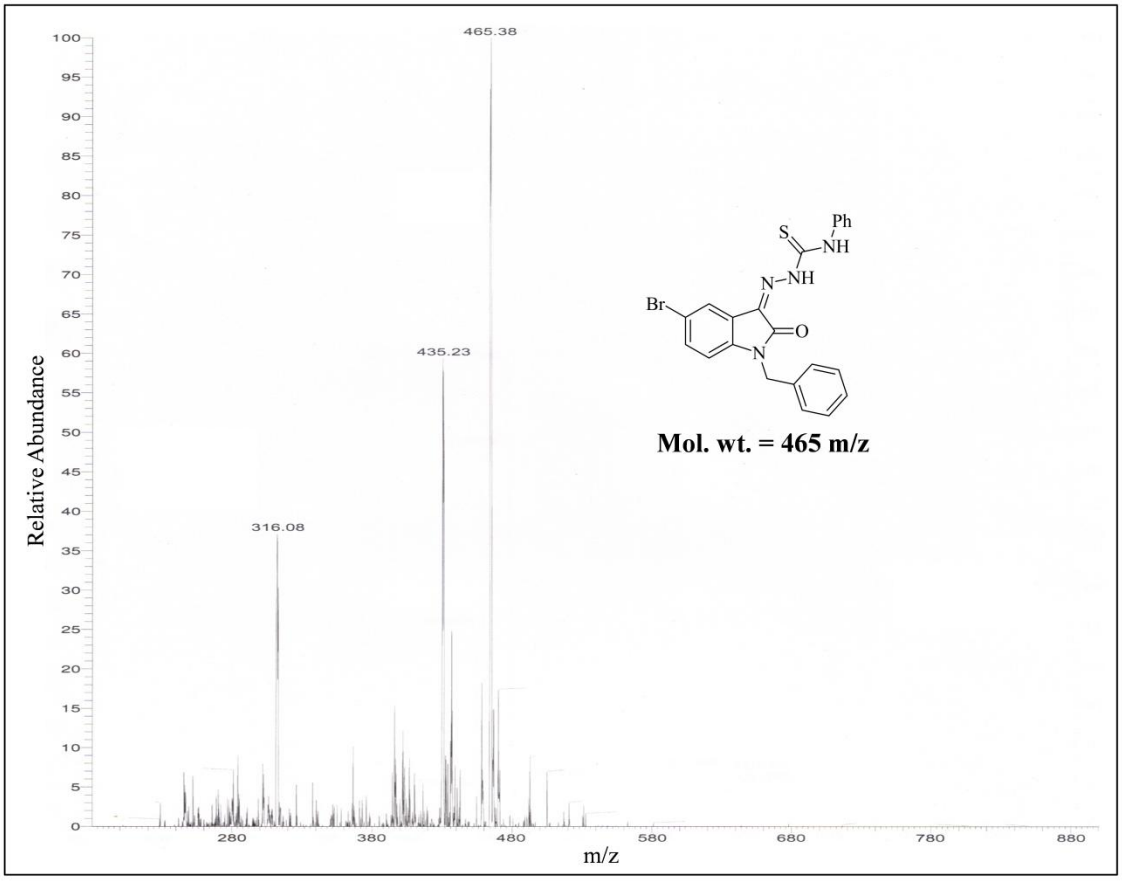

Fig. 19 Mass of 2-(1-benzyl-5-bromo-2-oxoindolin-3-ylidene)-N-phenylhydrazinecarbothioamide