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Synthesis, characterization and evaluation of antioxidant and anticancer activities of novel benzisoxazole-substituted-allyl derivatives

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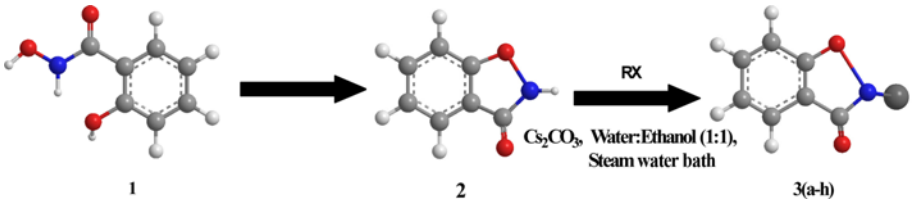
Abstract−A novel series of various *2-allylbenzo[d]isoxazol-3(2H)-ones* were synthesized using *benzo[d]isoxazol-3(2H)-one* treated with different allyl bromides/chlorides in the presence of water-mediated cesium carbonate as a new catalyst **3(a-h)**. The structures of the newly synthesized Benzisoxazole-substituted-allyl derivatives were characterized by spectroscopic methods and mass spectrometry. These synthesized compounds were evaluated for their in *vitro* antioxidant and anticancer activity. Compounds **3b**, **d**, **f**, **h** were identified as the best hit against HT-29 Human colon cancer cells. Similarly, compounds like **3b**, **d**, **f**, **h** showed significant antioxidant activity compared to the standard drug butylated hydroxy toluene (BHT).



Keywords: *2-Allylbenzo[d]isoxazol-3(2H)-ones*, Antioxidant Activity, Anticancer Activity

INTRODUCTION

The development of anticancer drugs represents one of the most important advances in therapeutics, which has improved the quality of life and advances in many other areas of medicine, such as cancer chemotherapy, organ transplantation, and major surgery [1]. Many reports ascribe interesting biological activities of 1,2-benzisoxazoles and their derivatives. The chemistry of substituted 1,2-benisoxazoles occupies an extremely important role in the pharmaceutical and medicinal fields [2-4]. 1,2-benzisoxazoles substituted compounds are widely used as anticonvulsant [5], anti-psychotic [6,7] anti-cancer [8,9] anti-microbial [10], anti-thrombotic [11], uricosuric [12], anti-inflammatory [13], tuberculostatic [14], sedative [15], analgesic [16] and neuroleptic [17].

Recently, organic solvents have been the most common and perhaps the only choices of solvents among researchers. This scenario has substantially changed during the last decade or so due to the intensive research towards environmentally benign substitutes for volatile and toxic organic solvents like halogenated hydrocarbons, aromatic hydrocarbons, dimethyl formamide, and dimethyl sulfoxide [18]. Now researchers have to deal with the challenge of reducing the environmental impact of the process without losing their efficacy by using the so-called green solvents. The green solvents are free from toxic materials, dissolve a great range of organic compounds, are inexpensive and of course can be recyclable. An extensive literature survey illustrated that the use of green solvents in the synthesis of organic drug molecules will be more efficient in future aspects. In view of the diverse type of biological activity it was thought worthwhile to prepare the title compound with the anticipation that allyl substituent at second positions may prove to be biologically active and to evaluate them for antioxidant and anticancer activities. The present work reports the synthesis of various *2-allyl benzo[d]isoxazol-3(2H)-ones* using green solvent water in ethanol and screening of their anticancer and antioxidant activities.

MATERIALS AND METHODS

Analytical grade solvents and commercially available reagents were used for the synthesis of 1,2-benzisoxazole derivatives. Column chromatography was carried out over silica-gel (60-120 mesh), purchased from Sigma Aldrich Private Ltd. Melting points were determined in open capillaries in electrical melting point apparatus. The completion of the reaction and the purity of the compounds were regularly checked by TLC on Silica-gel G plates using iodine vapors as visualizing agents. ^{1}H-NMR, ^{13}C-NMR spectra were recorded on JEOL 500-MHz and 125-MHz Bruker spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard. Chemical shifts are given in δ relative to TMS. IR spectra in KBr disk were

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recorded from 4,000 to 400 cm^{-1} on Avatar 330 FTIR spectrometer equipped with DTGS detector. The mass spectrum was recorded using Agilent 1100 MSD spectrometer in electrospray mode. Elemental analysis (CHNS) was obtained on Vario EL III Elementar. The starting compound *benzo [d] isoxazol-3 (2H)-one* was prepared by previously reported method [19].

1. Preparation of Benzo [d] Isoxazol-3(2H)-one (2)

A mixture of salicylichydroxamic acid (0.02 M) in 10 mL of tetrahydrofuran and thionyl chloride (0.05 M) added in drops and stirring was continued for about 6 hrs. The excess organic solvent was removed, triethylamine (0.06 M) in 15 mL of 1,4-dioxane was added dropwise and the reaction mixture was stirred magnetically for about 6 hrs. After completion of the reaction it was poured into ice-cold water and then stirred well. The solution turned acidic by the addition of dilute hydrochloric acid. The crude product obtained was recrystallized using methanol as a solvent.

2. Preparation of 2-Allylbenzo[d]isoxazol-3(2H)-one (3a)

A mixture of cesium carbonate (0.04 M) in water and ethanol (1 : 1) (20 mL) was added to the reaction blend of (0.02 M) *benzo[d] isoxazol-3[2H]-one [2]*. The resulting solution was treated with (0.04 M) *3-bromoprop-1-ene* and refluxed on the water bath for about 2 hrs. After completion of the reaction, the excess solvent was removed. The reaction mixture was poured into the crushed ice and extracted with diethyl ether. The crude product was recrystallized from hexane: ethyl acetate (5 : 5). Similar procedure was followed for other compounds like *3b-h*, respectively.

2-1. 2-(But-3-enyl)benzo[d]isoxazol-3(2H)-one (3a)

Pale yellow solid, mp 48-50 °C; FTIR (u, KBr) 3087 (Ar-H), 1778 (>C=O) cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.23 (m, 4H, Ar-H), 5.84 (m, 1H, CH), 5.34 (d, 2H, =CH_2), 4.46 (d, 2H, CH_2), 2.26 (m, 2H, CH_2). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 44.68, 109, 110.08, 118.83, 122.58, 123.91, 130.60, 130.99, 142.71, 154.45. ESI-MS (*m/z*) 189.08 (M^+). Anal. Calc. for $C_{11}H_{11}NO_2$; C, 69.83; H, 5.86; N, 7.40. Found: C, 69.80; H, 5.76; N, 7.30.

2-2. 2-(Pen-2-ynyl[d]isoxazol-3(2H)-one (3b)

Yellow solid, mp 58-60 °C; FTIR (u, KBr) 3082 (Ar-H), 1770 (>C=O) cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.34 (m, 4H, Ar-H of benzisoxazole ring), 7.30-7.14 (m, 5H, Ar-H), 6.19, 6.53 (dd, 2H, -CH=CH-), 3.87 (d, 2H, -CH_2), 2.26 (m, 2H, CH_2); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.47, 32.29, 44.27, 61.42, 87.62, 109.27, 109.27, 122.62, 123.81, 130.32, 142.61, 164.2. ESI-MS (*m/z*) 265.11 (M^+). Anal. Calc. for $C_{17}H_{15}NO_2$; C, 76.76; H, 5.70; N, 5.28. Found: C, 75.94; H, 4.67; N, 5.90.

2-3. 2-Cinnamyl-benzo[d]isoxazol-3(2H)-one (3c)

Yellow solid, mp 102-104 °C; FTIR (u KBr) 3067 (Ar-CH), 1782 (>C=O) cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.32-6.91 (m, 4H, Ar-H of benzisoxazole ring), 6.16 (t, 1H, -CH=CH-), 3.22 (d, 2H, -CH_2), 2.24 (m, 2H, -CH_2), 1.71 (t, 6H, -CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 19.6, 21.1, 25.6, 49.0, 116.0, 120.7, 121.5, 123.5, 128.9, 156.1, 164.2. ESI-MS (*m/z*) 251.09 (M^+). Anal. Calc. for $C_{16}H_{13}NO_2$; C, 71.87; H, 6.96; N, 6.46. Found: C, 72.94; H, 5.92; N, 7.19.

2-4. 2-(-3-Methylbut-2-enyl)-benzo[d] isoxazol-3(2H)-one (3d)

White solid, mp 68-70 °C; FTIR (u KBr) 3070 (Ar-H), 1753 (>C=O) cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.20-6.91 (m, 4H, Ar-H of benzisoxazole ring), 5.34 (m, 1H, =CH), 5.30 (d, 2H, -CH_2), 4.46 (d, 2H, -CH_2), 1.71 (s, 6H, -CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 12.4, 13.3, 47.4, 116.0, 120.6, 121.6, 123.4, 128.5, 156.2, 164.3. ESI-MS (*m/z*) 278.99 (M^+). Anal. Calc. for $C_{13}H_{15}BrNO_2$; C, 53.08; H, 4.11; N, 4.76. Found: C, 53.13; H, 3.96; N, 4.67.

2-5. 2-(4-Chlorobut-2-ynyl)-benzo[d]isoxazol-3(2H)-one (3e)

Yellow solid, mp 60-62 °C; FTIR (u KBr) 3067 (Ar-H), 1779 (>C=O) cm^{-1}. ^{1}H-NMR (500 MHz $CDCl_3$) δ 7.10-7.23 (m, 4H, Ar-H of benzisoxazole ring), 4.7 (t, 2H, -CH_2), 4.10 (m, 2H, -CH_2). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 29.81, 32.9, 78.30, 80.37, 109.08, 110.18, 122.96, 124.9, 129.98, 142.62, 153.66, 164.2; ESI-MS (m/z) 215.09 (M^+). Anal. Calc. for $C_{13}H_{13}NO_2$; C, 72.54; H, 6.09; N, 6.51. Found: C, 72.44; H, 6.20; N, 6.41.

2-6. 2-Benzylbenzo[d]isoxazol-3(2H)-one (3f)

White solid, mp 96-98 °C; FTIR (u KBr) 3070 (Ar-H), 1753 (>C=O) cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.34 (m, 4H, Ar-H of benzisoxazole ring), 7.34-6.91 (m, 4H, Ar-H), 5.1 (s, 2H, N-CH_2), 3.24 (d, 2H, -CH_2), 2.02 (m, 2H, -CH_2), 1.18 (s, 3H, -CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 46.1, 108.94, 110.07, 122.57, 124.03, 125.83, 127.68, 128.28, 128.98, 130.85, 134.69, 142.70, 143.99, 154.84. ESI-MS (m/z) 225.08 (M^+). Anal. Calc. for $C_{14}H_{11}NO_2$; C, 75.87; H, 5.97; N, 5.53. Found: C, 75.87; H, 5.97; N, 5.53.

2-7. 2-Allylbenzo[d]isoxazol-3(2H)-one (3g)

Pale yellow solid, mp 48-50 °C; FTIR (u KBr) 3087 (Ar-H), 1778 (>C=O) cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.23 (m, 4H, Ar-H), 5.84 (m, 1H, CH), 5.34 (d, 2H, =CH_2), 4.46 (d, 2H, CH_2), 2.26 (m, 2H, CH_2). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 44.68, 109, 110.08, 118.83, 122.58, 123.91, 130.60, 130.99, 142.71, 154.45. ESI-MS (m/z) 189.08 (M^+). Anal. Calc. for $C_{11}H_{11}NO_2$; C, 69.83; H, 5.86; N, 7.40. Found: C, 69.80; H, 5.76; N, 7.30.

2-8. 2-(6-Phenylbut-2-ynyl)-benzo[d]isoxazol-3(2H)-one (3h)

Pale yellow solid, mp 56-58 °C; FTIR (u KBr) 3087 (Ar-H), 1767 (>C=O) cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.34-6.91 (m, 4H, Ar-H of benzisoxazole ring), 7.06-7.14 (m, 5H, Ar-H), 3.89 (s, 2H, -CH_2), 3.24 (d, 2H, -CH_2), 2.02 (m, 2H, -CH_2), 1.18 (s, 3H, -CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): δ 12.6, 13.9, 19.6, 21.1, 25.6, 49.0, 81.0, 116.0, 120.7, 121.5, 123.5, 128.9, 156.1, 164.2; ESI-MS (*m/z*) 263.09 (M^+). Anal. Calc. for $C_{17}H_{13}NO_2$; C, 78.33; H, 5.88; N, 4.81. Found: C, 78.33; H, 5.88; N, 4.81.

3. Antioxidant Activity

Free radical scavenging activity of the synthesized compounds was determined using standard DPPH method. About 1 mL of 0.1 mM methanolic solution of DPPH was added to 3 mL of the synthesized samples *3(a-h)*, at different concentrations in methanol (10, 20, 50, 75, 100 μg/mL). The samples were kept in the dark for about 30 min, after which the absorbance was measured at 517 nm in UV spectrophotometer (Systronics 2202). In its radical form, DPPH absorbs light at 517 nm, but upon reduction by an antioxidant (or) a radical species its absorption decreases. Lower absorbance of the reaction mixture indicates higher free radical scavenging activity. butylated hydroxy toluene (BHT), which is a good antioxidant, is taken as a standard in this study. The capability to scavenge the DPPH radical was calculated using the following equation:

$$\text{DPPH Scavenging effect (\%)} = [(A_c - A_s)/A_c)\ 100]$$

where A_c is the absorbance of the control reaction and A_s is the absorbance in the presence of sample.

4. Anticancer Activity

The anticancer activity of the synthesized compounds was determined by using standard MTT assay method [20,21]. The cancer

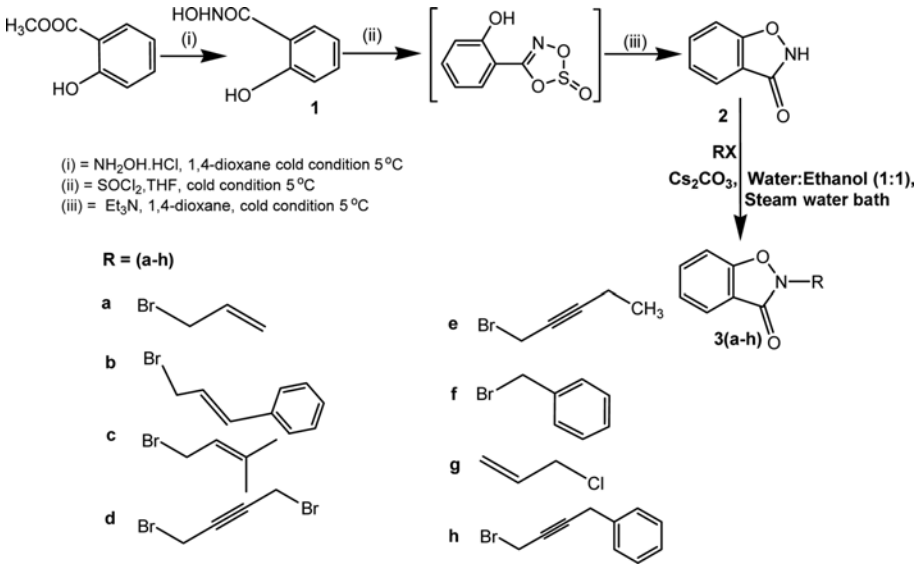
cell lines used for the study were *HT*-29 Human colon cancer cells obtained from Maratha Mandal Medical Hospital. The cell lines were preserved in DMEM (Hi-Media Laboratories Pvt. Ltd, Mumbai, India) supplemented with 10% heat-inactivated FBS (v/v), streptomycin (100 μg/mL) and penicillin (100 μg/mL). The cell line was maintained at 37 °C with 5% carbon dioxide in CO_2 incubator. The MTT cell proliferation assay was used to evaluate the anticancer activity of various 2-allylbenzo[*d*]isoxazol-3(2*H*)-ones derivatives *3(a-h)* using the cell quantification MTT cell viability assay kit (Bioassay Systems). The optical density was measured at 570 nm for each well on the absorbance plate reader. Trypan blue dye exclusion assay was also used to count the number of viable and non-viable HT-29 cancer cells in the culture medium after drug treatment. Treatment with 5-FU at the same concentration served as positive control.

RESULTS AND DISCUSSION

The schematic of the method employed to prepare the final compounds **3a-h** is outlined in reaction Scheme 1.

The key starting compound, N, 2-dihydroxybenzamide (**1**) and benzo[d]isoxazol-3[2H]-one (**2**) was prepared by the procedure reported in the literature [19].

The key intermediate N,2-dihydroxybenzamide (**1**) was prepared by treating methyl salicylate with hydroxylamine hydrochloride and sodium hydroxide in 1,4-dioxane. The reaction mixture was stirred at cold condition to get the key intermediate product as a white solid [Melting point: 168-170 °C; Literature: 170-172 °C]. The FTIR spectrum of the compound (**1**) showed band at 3,288.67 and 3,118.98, 1,618.60 cm^{-1} for -NH and -OH amide carbonyl groups. The start-



Scheme 1.

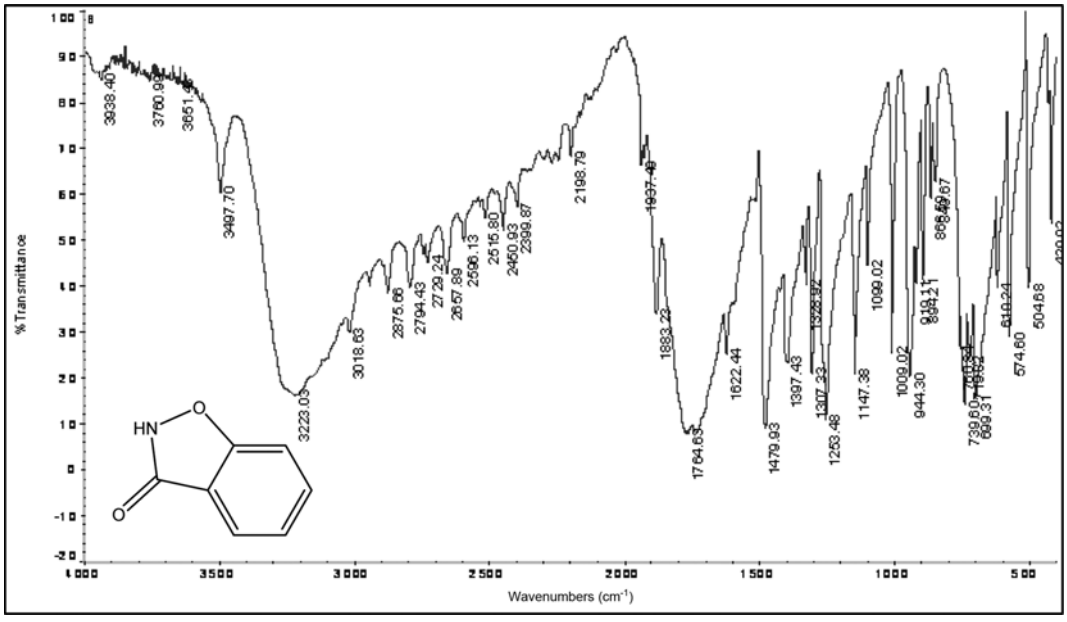


Fig. 1. The spectra of benzo[d]isoxazol-3[2H]-one (2).

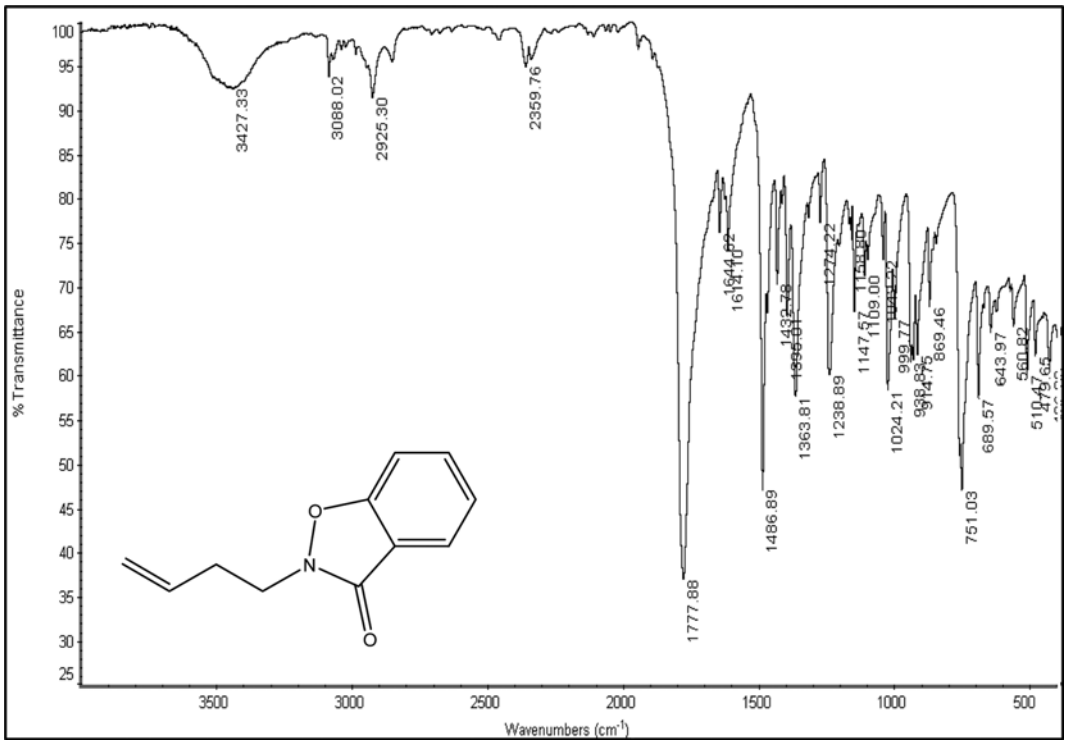


Fig. 2. The spectra of 2-*(but-3-enyl)benzo[d]isoxazol-3(2H)-one* (3a).

ing target compound benzo[d]isoxazol-3[2H]-one (**2**) was prepared by treating the N,2-dihydroxybenzamide (**1**) with thionyl chloride in the presence of tetrahydrofuran and triethylamine in 1,4-dioxane stirred in cold condition not exceeding 5 °C to furnish a white solid. The intermediate target molecule (**2**) was purified by column chromatography using a mixture of hexane and ethyl acetate (90 : 10). [Melting point: 138-140 °C; Literature: 140-142 °C].

The FTIR spectrum of the compound (**2**) showed absorbance at 1,774.95 cm^{-1} for carbonyl group, which clearly indicates the product formation (**2**) in keto form. Absorbance at 3,497.18 cm^{-1} showed the presence of -NH group as shown in Fig. 1.

The ^{1}H-NMR spectra showed multiplet at δ 6.9-7.17 for four aromatic protons, a broad absorbance for -NH proton at δ 9.91 ppm. The spectral data clearly confirms the structure of the compound to be benzo[d]isoxazol-3(2H)-one (**2**). The starting compound (**2**) was treated with various allyl bromides and chlorides in the presence of anhydrous cesium carbonate in a solvent made of ethanol and water. The final product (**3a**) obtained was a yellow solid and the melting point was 50 °C. The FTIR spectrum of the compound (**3a**) showed a sharp intense band at 1,777.88 cm^{-1} for >C=O group and this clearly indicates that the compound (**3a**) is in Keto form as shown in Fig. 2.

The ^{1}H-NMR spectrum in $CDCl_3$ solvent exhibits multiplet at δ 6.9-7.17 ppm for four aromatic protons, multiplet at 5.85-5.88 ppm for one -CH proton, doublet at δ 4.42-4.43 ppm for two O-CH_2 protons, doublet at δ 5.26-5.29 ppm for two -CH_2 terminal protons. Similarly, in the case of ^{13}C-NMR spectrum, 2-(but-3-enyl)benzo[d] isoxazol-3(2H)-one (**3a**) showed carbon peaks at 29.81, 32.9 (aliphatic carbons), 78.30, 80.37, 109.08, 110.18, 124.9, 129.98 (aromatic carbons) 122.96 and 142.62 (allyl carbon), 153.66 (tertiary carbon), 164.2 (carbonyl carbon), clearly indicating corresponding allyl and carbonyl groups confirm the structure of the synthesized compound (**3a**).

Mass fragmenation peaks [M^+ −189.08, 134.02, 107.03, 93.03, 55.05] of (**3a**) represent that the molecule possesses an aromatic and five membered rings. All the spectral data clearly confirms the structure of the title compound *2*-allylbenzo[d]isoxazol-3(2H)-one (**3a**). Similarly, all the other compounds (**3b-3h**) were successfully synthesized in good yields. The structures of all the synthesized compounds were confirmed by spectroscopic methods.

1. Antioxidant Activity

All the newly synthesized compounds *3(a-h)* were screened for their free radical scavenging activity. The free radical scavenging activity of the synthesized compounds was determined by 1,1-diphenyl-2-picryl-hydrazil (DPPH) method [22]. The samples were prepared at different concentrations (10, 20, 50, 75, 100 μg/mL). Butylated hydroxytoluene (BHT) was used as a standard in this study. The

Table 1. Antioxidant activity of the synthesized compounds 3(a-h)

Synthesized compounds	% Inhibition				
	Concentration (μg/mL)				
	10	20	50	75	100
3a	31	45	82	85	90
3b	47	58	86	94	96
3c	39	49	76	87	90
3d	19	31	49	78	83
3e	19	34	51	74	82
3f	44	59	84	92	95
3g	28	37	76	82	85
3h	31	45	82	85	90
BHT	43	59	82	94	96

Table 2. Anticancer activity of allyl benzo[*d*]isoxazol-3(2*H*)-ones 3b, 3d, 3f and 3h against HT-29 cancer cell lines[a]

Synthesized compounds	IC_{50} (μM)
	HT-29
3a	58.50
3b	**16.04**
3c	44.62
3d	**8.86**
3e	46.05
3f	**12.04**
3g	52.26
3h	**28.94**
5-FU	64.42

[a]Values presented are means of three experiments; values in bold are better than that of 5-FU

benzo[*d*]isoxazol-3(2*H*)-one derivative (*3a-h*) showed good free radical scavenging activity at all five different concentrations studied. The results of the antioxidant activity are summarized in Table 1.

2. Anticancer Activity

The anticancer activity of the synthesized compounds was determined by MTT Assay method. Based on the optical density values of the various *2-allylbenzo[d]isoxazol-3(2H)-one* derivative, half maximal (50%) inhibitory concentration (IC) of the target drugs was calculated. The anticancer activity of benzisoxazole substituted allyl derivatives 3(a-h) against HT-29 human colon cancer cell lines (IC_{50} Values) results is represented in Table 2. The results indicated that the aromatic ring substituted allyl derivatives *3(b, d, f, g)* showed potent anticancer activity against HT-29 colon cancer cell line as compared to the standard drug 5-flurouracil.

CONCLUSION

We have synthesized a new series of various 2-allylbenzo[d]isoxazol-3(2H)-ones *3(a-h)* using water and ethanol as a solvent by green synthesis technique. FTIR, ^{1}H-NMR, ^{13}C-NMR and mass spectral data confirmed the structures of the synthesized compounds. All the synthesized compounds were screened for antioxidant and anticancer activity. Some of the synthesized compounds exhibited potent anticancer activity against HT-29 colon cancer cell lines, based on their pharmacophoric unit. The synthesized compounds *3(a-h)* showed significant antioxidant activity with respect to the standard drug BHT.

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Supporting Information

Synthesis, characterization and evaluation of antioxidant and anticancer activities of novel benzisoxazole-substituted-allyl derivatives

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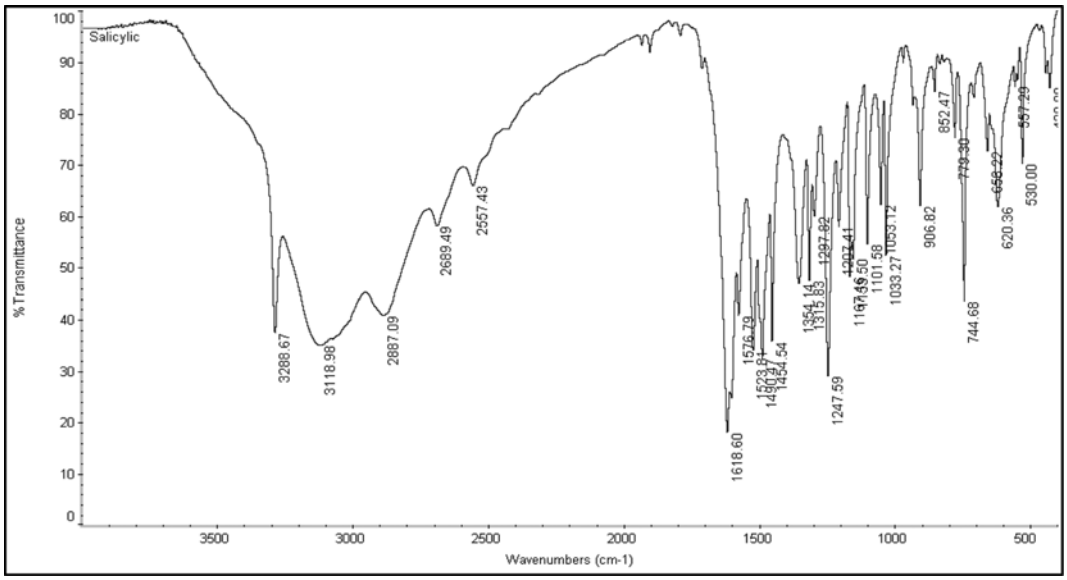

Fig. 1. FTIR spectrum of salicyl hydroxamic acid.

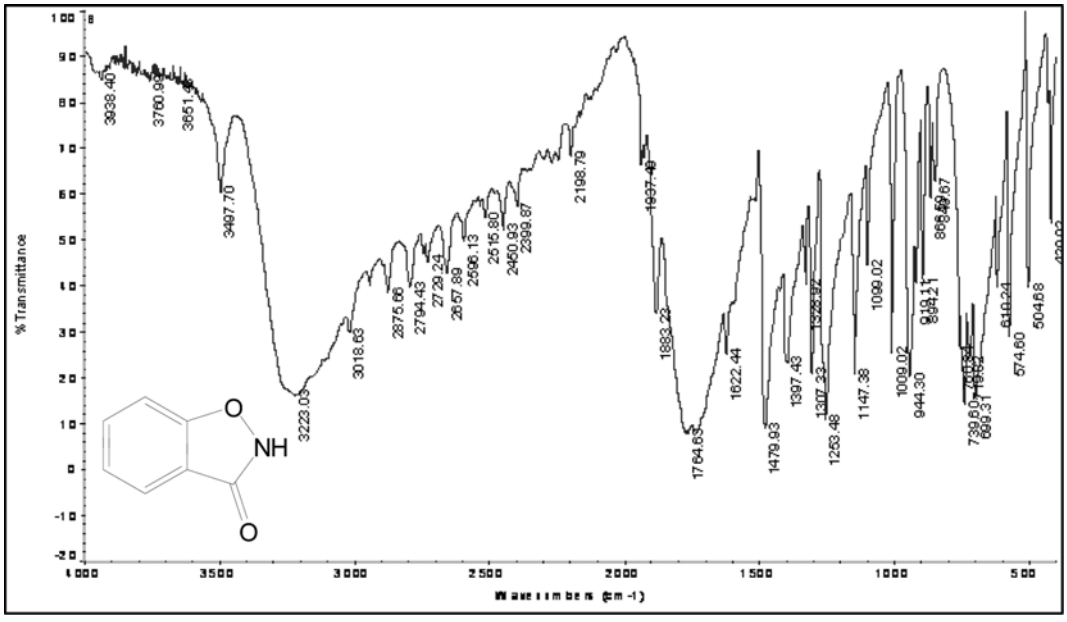

Fig. 2. FTIR spectrum of Benzo [*d*] isoxazol-3(2H)-one.

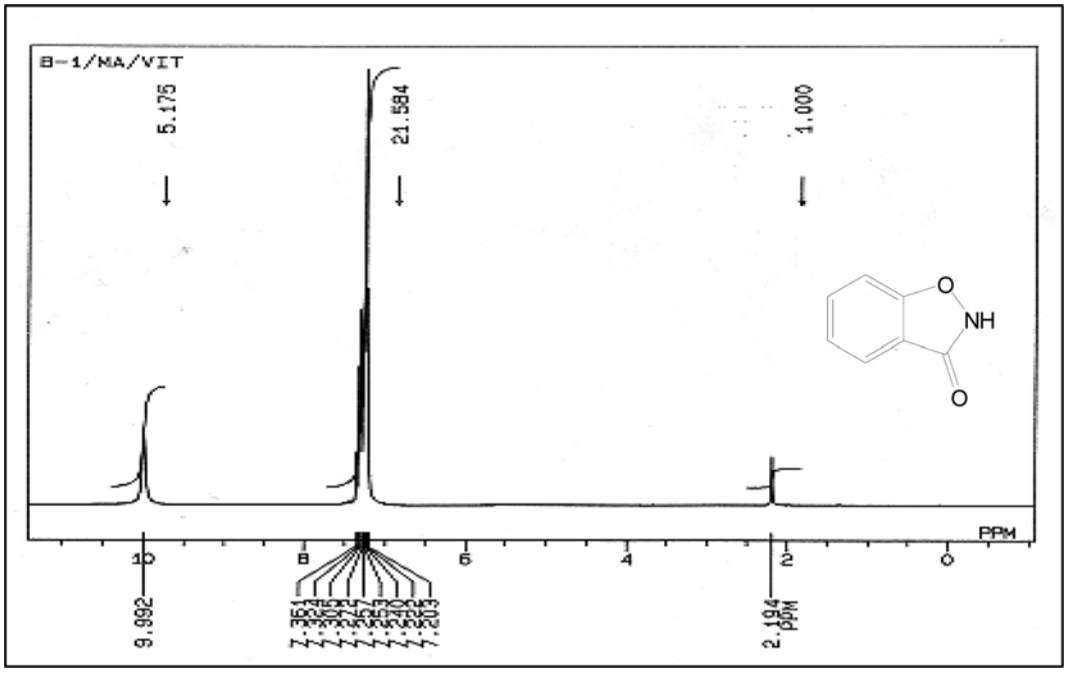

Fig. 3. ^{1}H NMR spectrum of benzo [*d*] isoxazol-3(2H)-one.

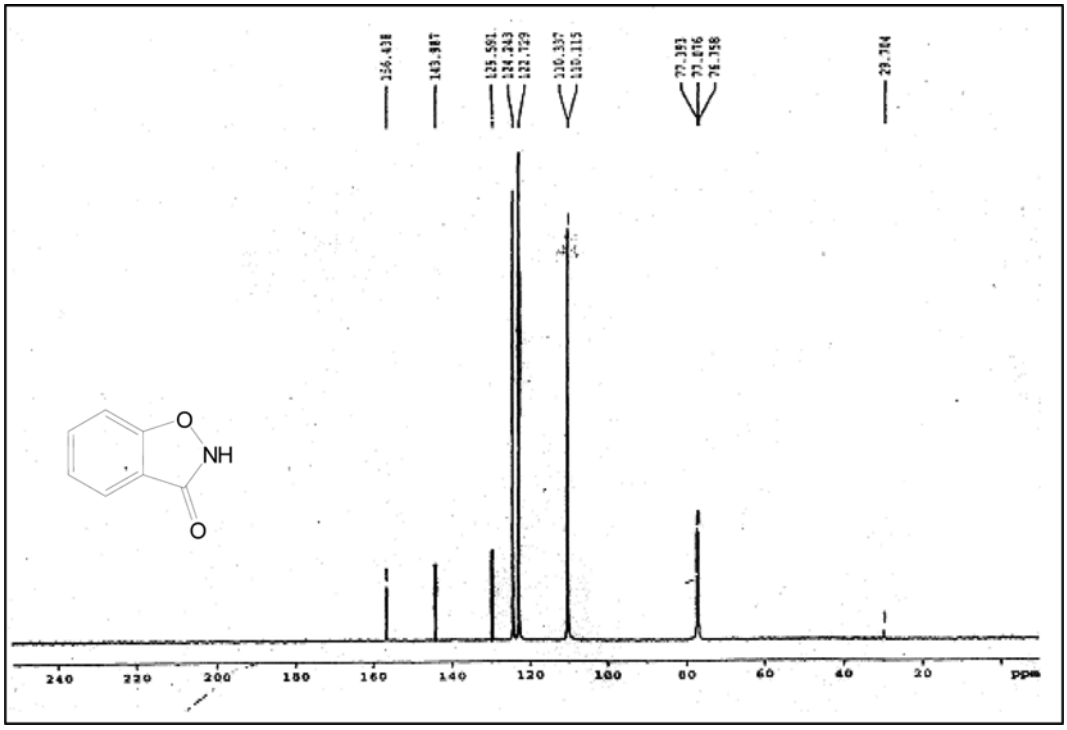

Fig. 4. ^{13}C NMR spectrum of benzo [*d*] isoxazol-3(2H)-one.

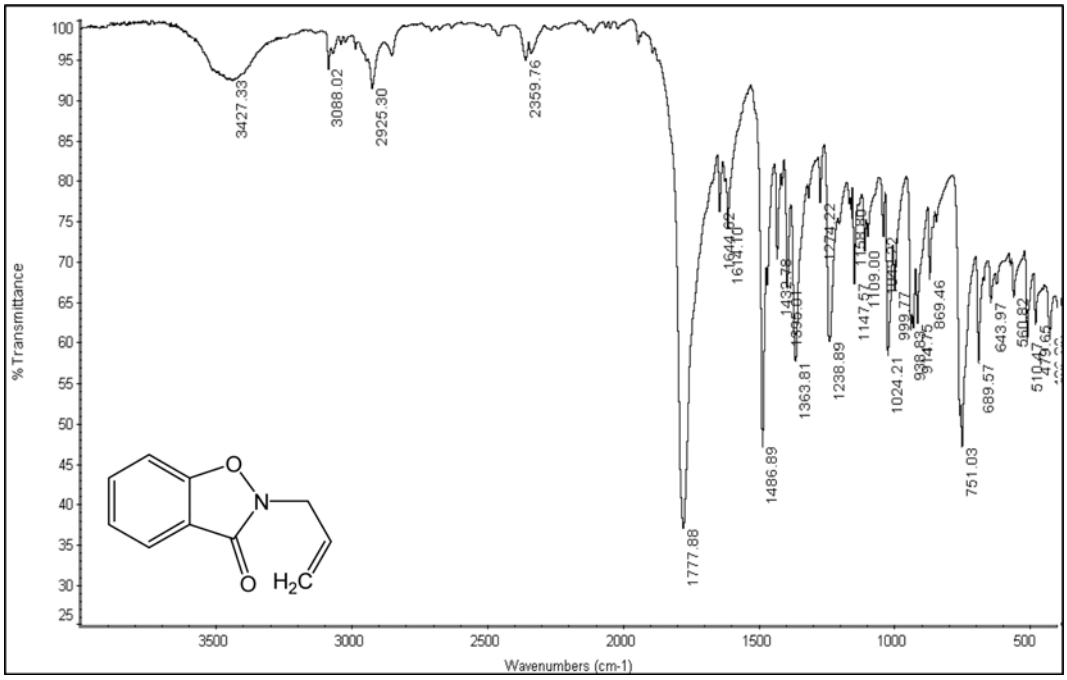

Fig. 5. FTIR spectrum of 2-allylbenzo [*d*] isoxazol-3(*2H*) one.

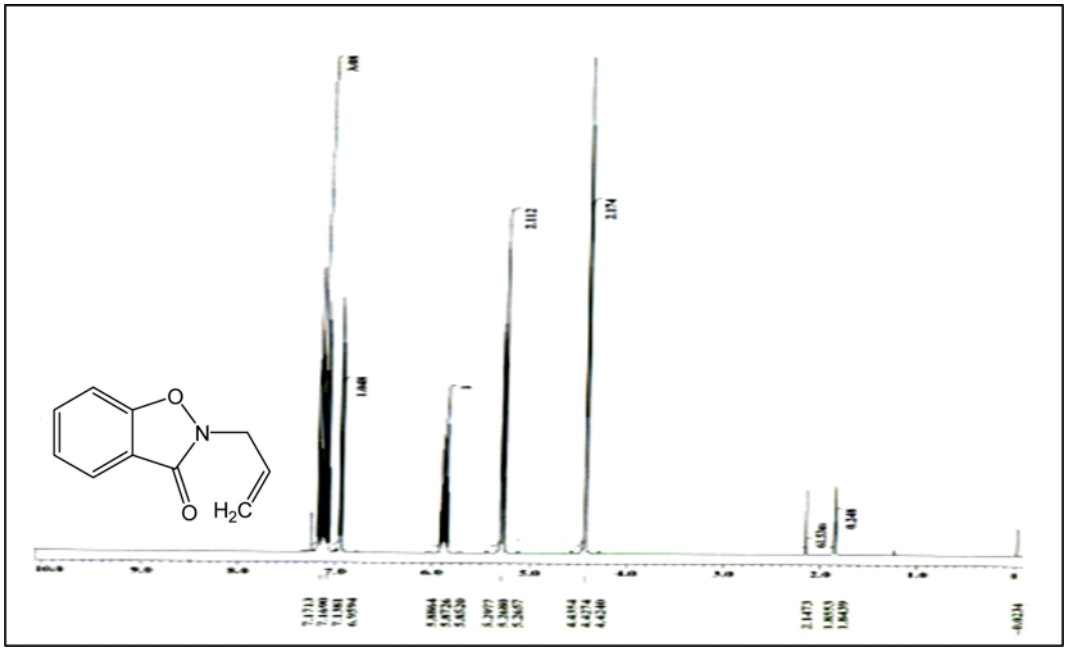

Fig. 6. ^{1}H NMR spectrum of 2-allylbenzo [*d*] isoxazol-3(*2H*) one.

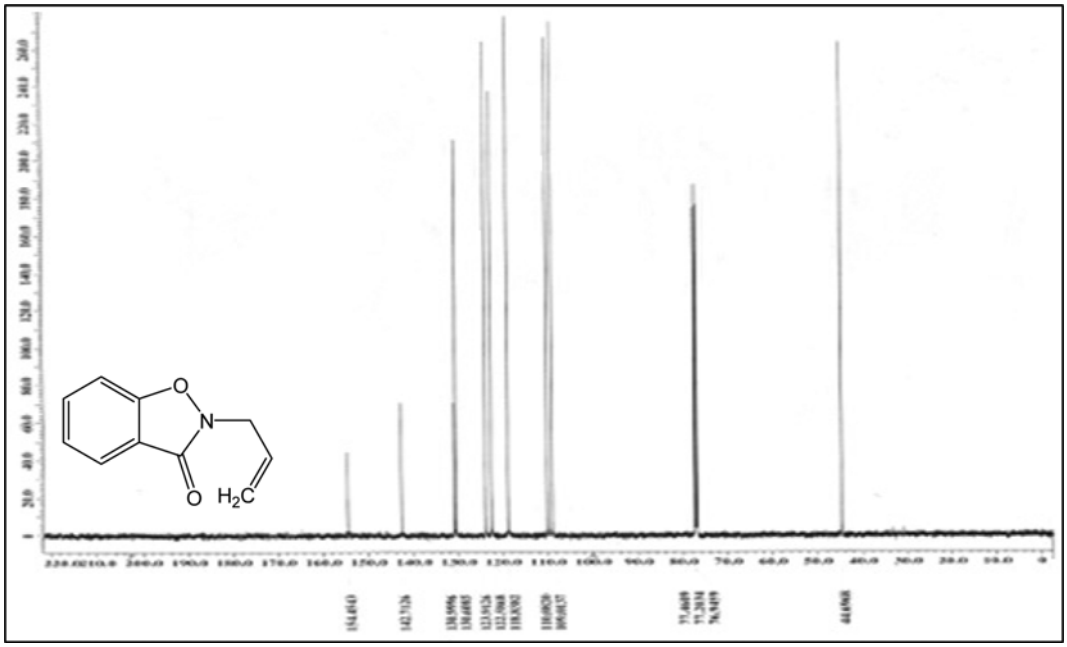

Fig.. 7. ^{13}C NMR spectrum of 2-allylbenzo [*d*] isoxazol-3(*2H*) one.

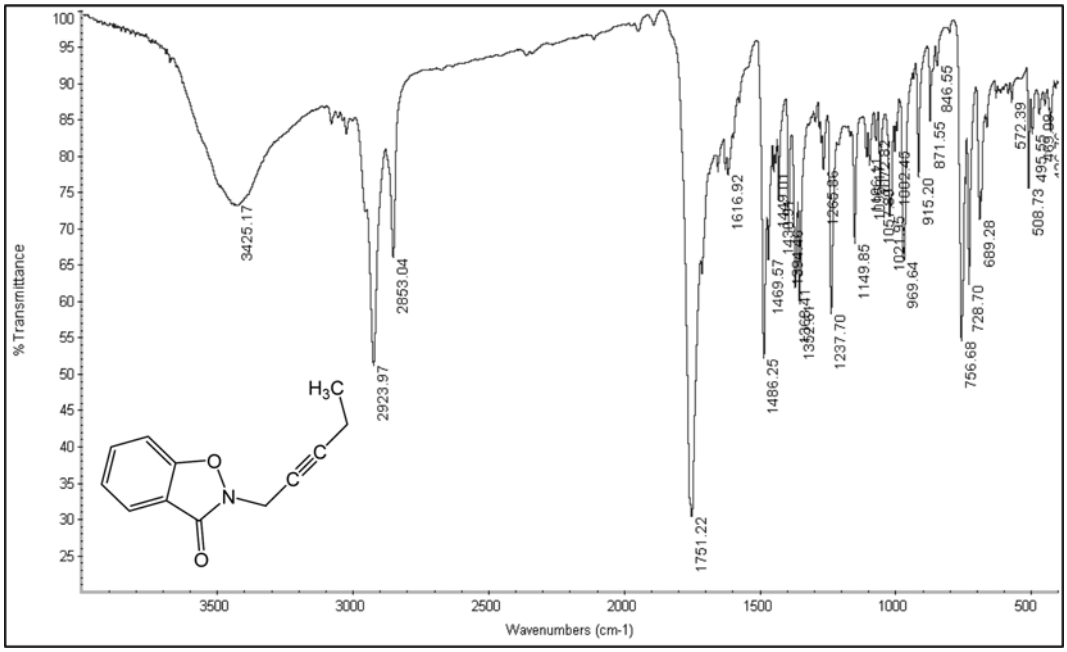

Fig. 8. FTIR spectrum of 2-(pen-2-ynyl) benzo [*d*] isoxazol-3(2H)-one.

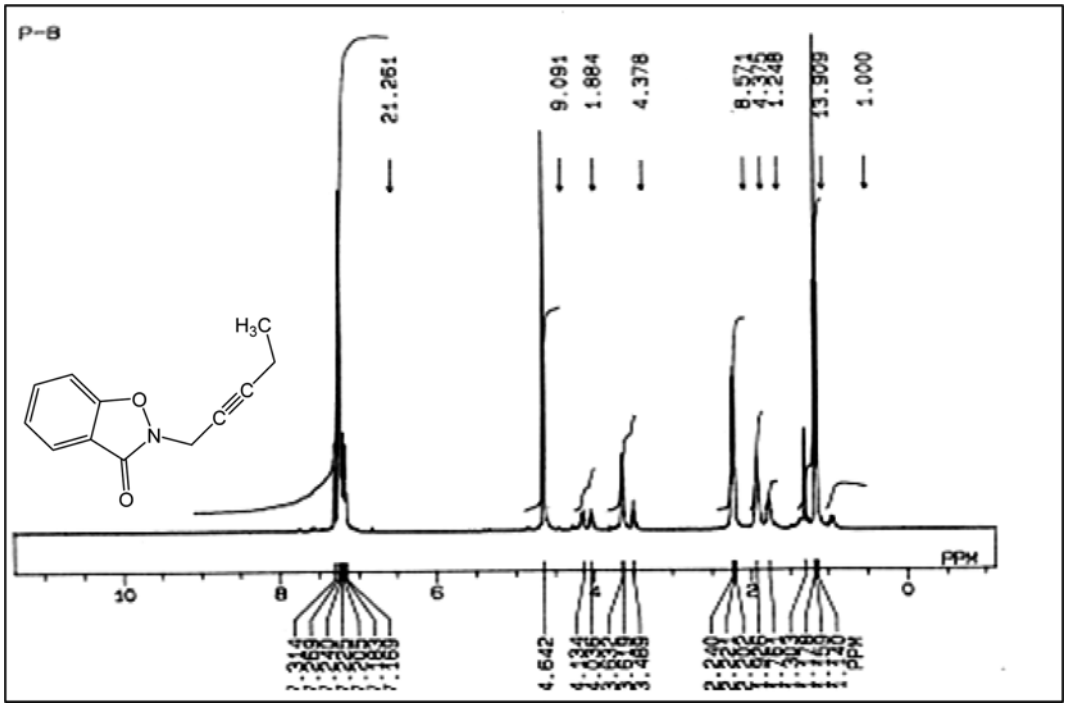

Fig. 9. [1]H NMR spectrum of 2-(pent-2-ynyl) benzo [*d*] isoxazol-3(2H)-one.

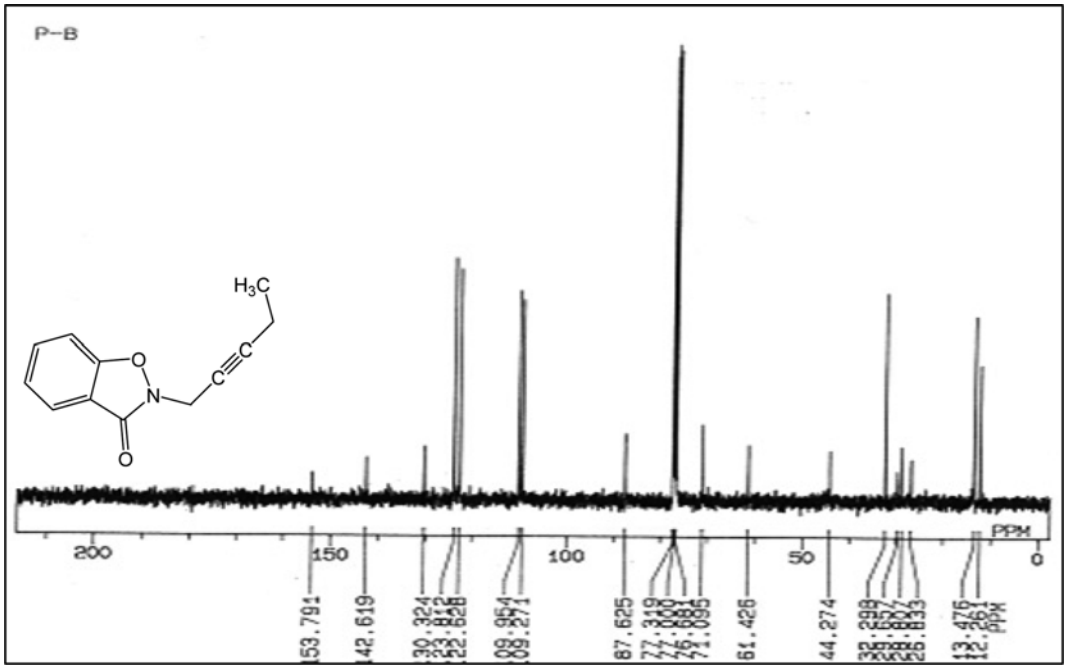

Fig. 10. [13]C NMR spectrum of 2-(pent-2-ynyl) benzo [*d*] isoxazol-3(2H)-one.

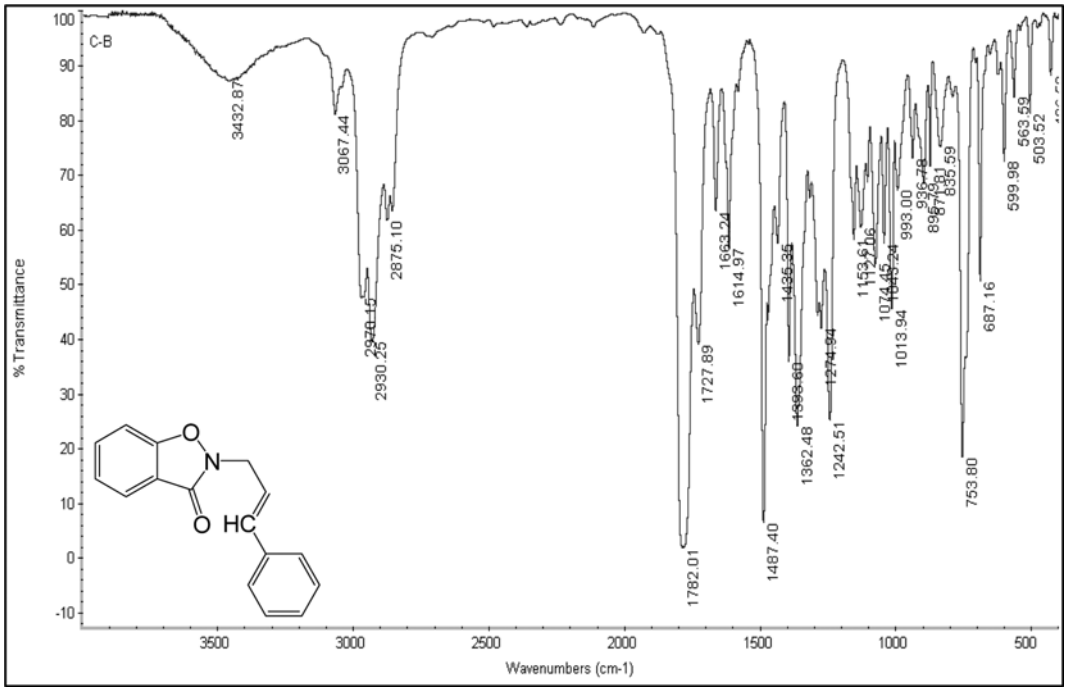

Fig. 11. FTIR spectrum of 2-cinnamyl-benzo [*d*] isoxazol-3(2H)-one.

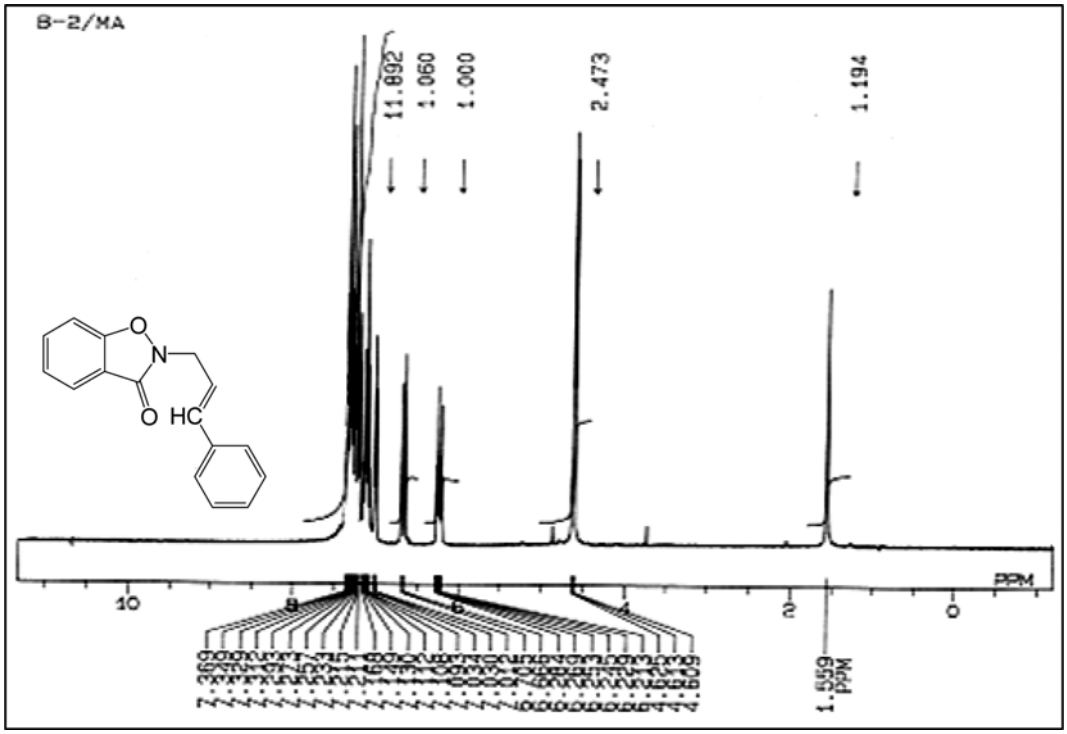

Fig. 12. ^{1}H NMR spectrum of 2-cinnamyl-benzo [*d*] isoxazol-3(2H)-one.

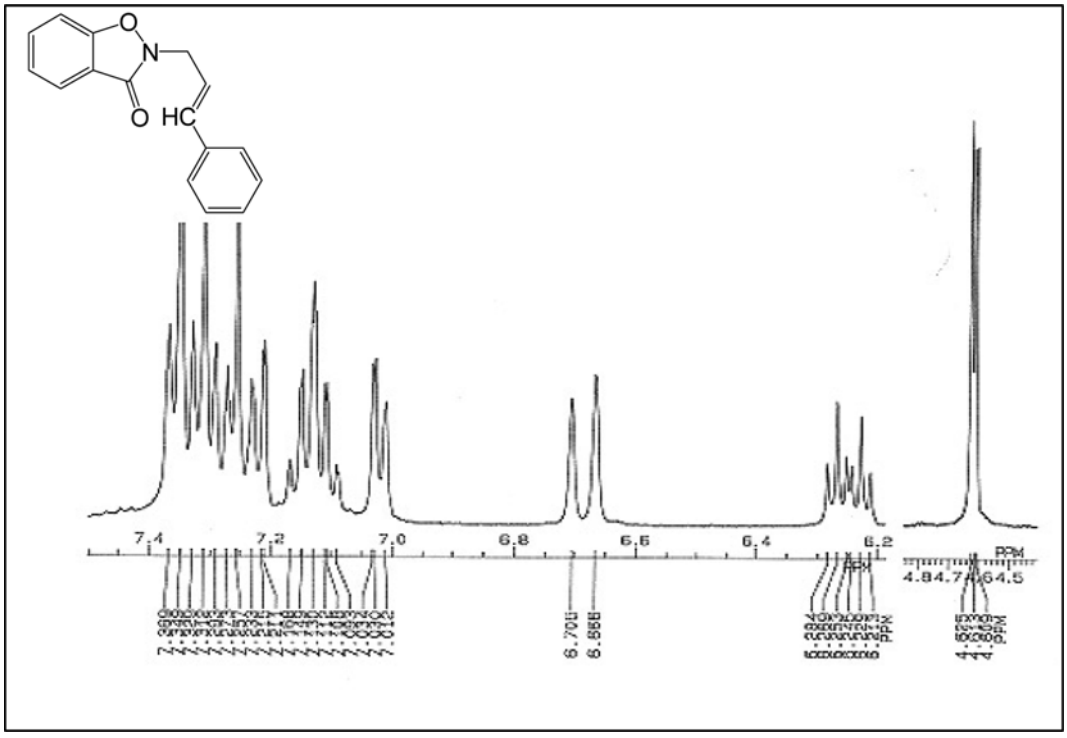

Fig. 13. Enlarged ^{1}H NMR spectrum of 2-cinnamyl-benzo [*d*] isoxazol-3(2H)-one.

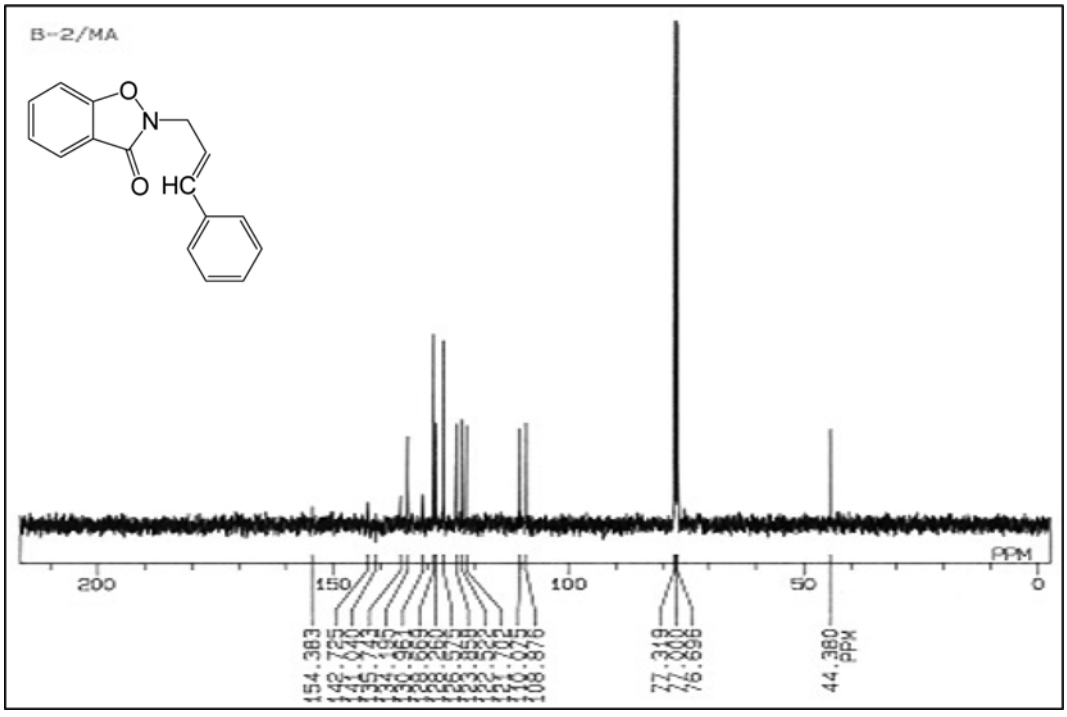

Fig. 14. ^{13}C NMR spectrum of 2-cinnamyl-benzo [*d*] isoxazol-3(2H)-one.

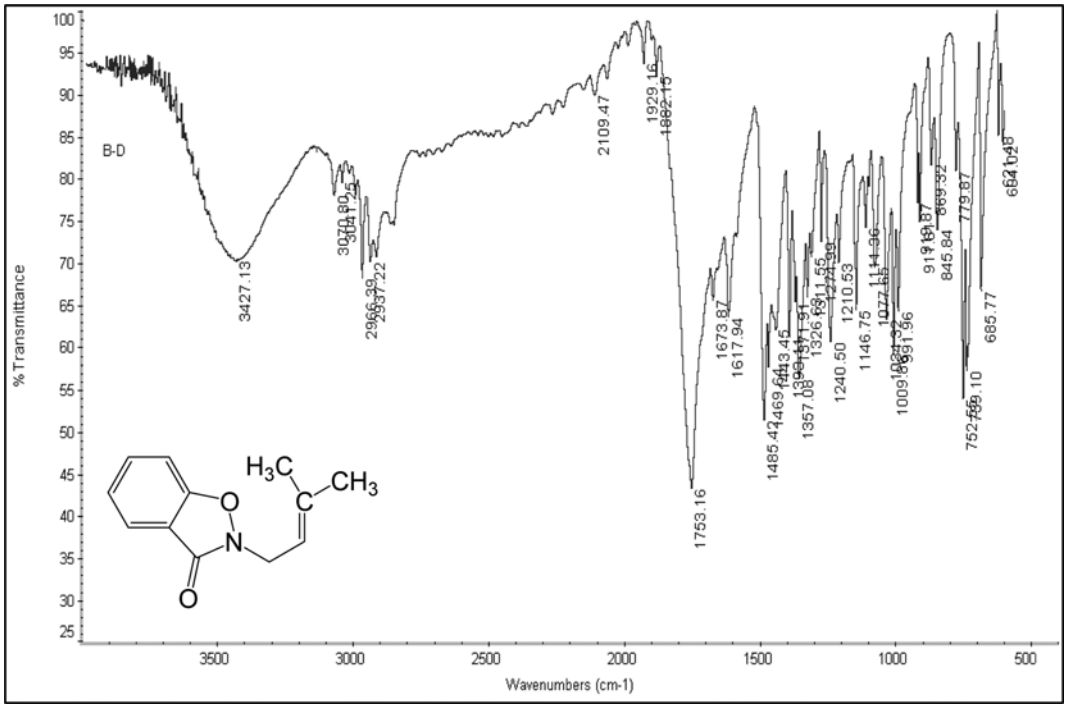

Fig. 15. FTIR spectrum of 2-(-3-methylbut-2-enyl) benzo [*d*] isoxazol-3(2H)-one.

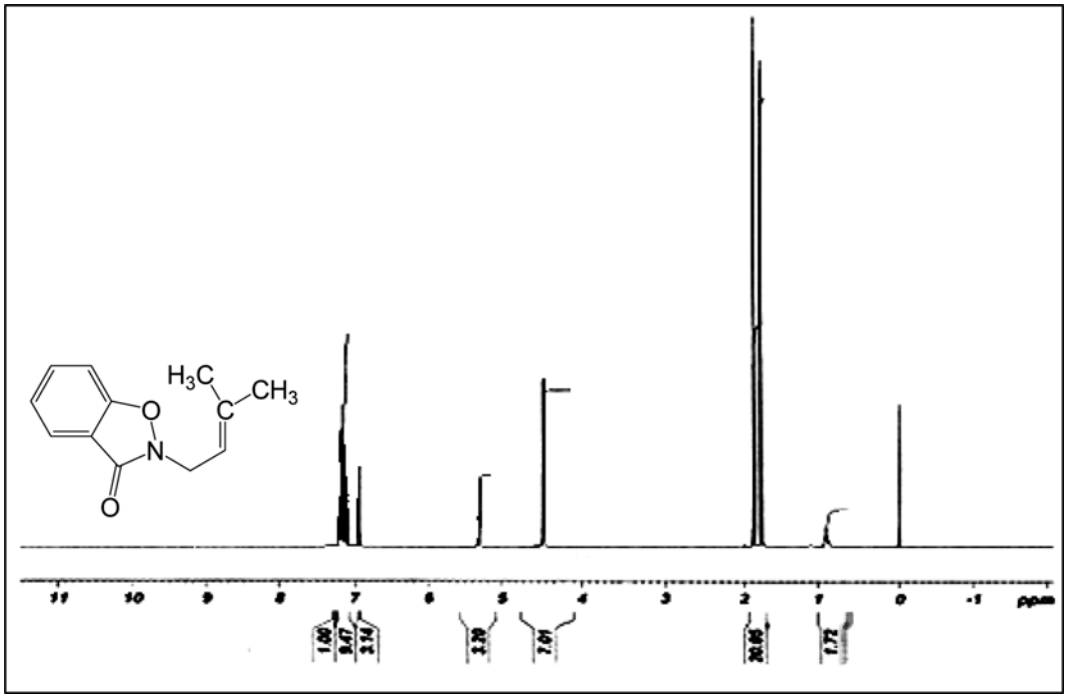

Fig. 16. ^{1}H NMR spectrum of 2-(-3-methylbut-2-enyl) benzo [*d*] isoxazol-3(2H)-one.

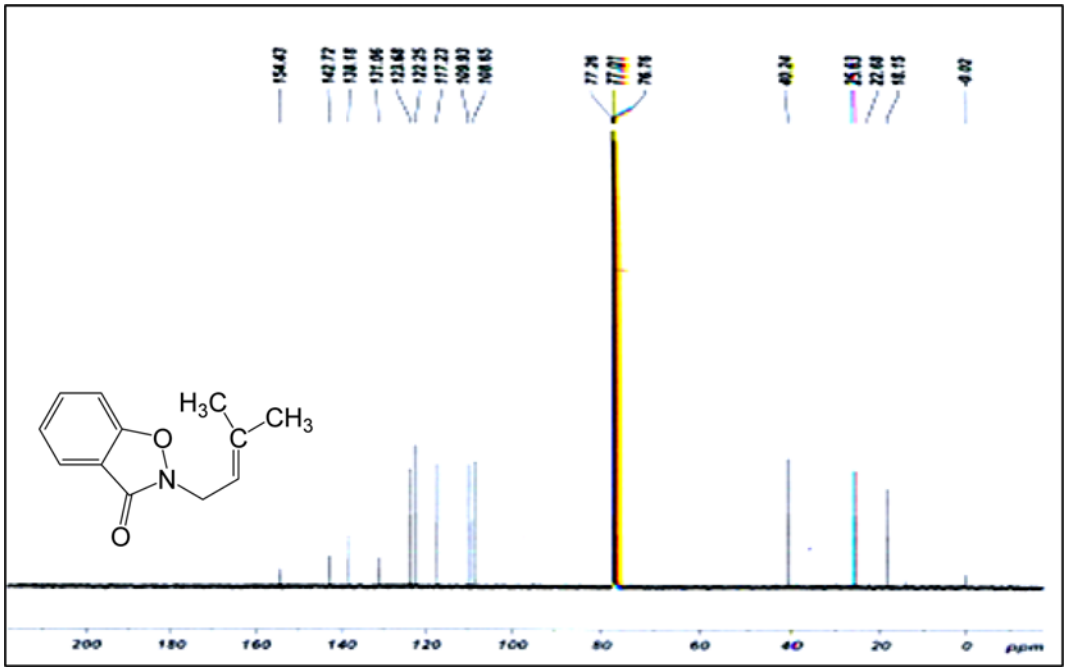

Fig. 17. ^{13}C NMR spectrum of 2-(-3-methylbut-2-enyl) benzo [*d*] isoxazol-3(2H)-one.

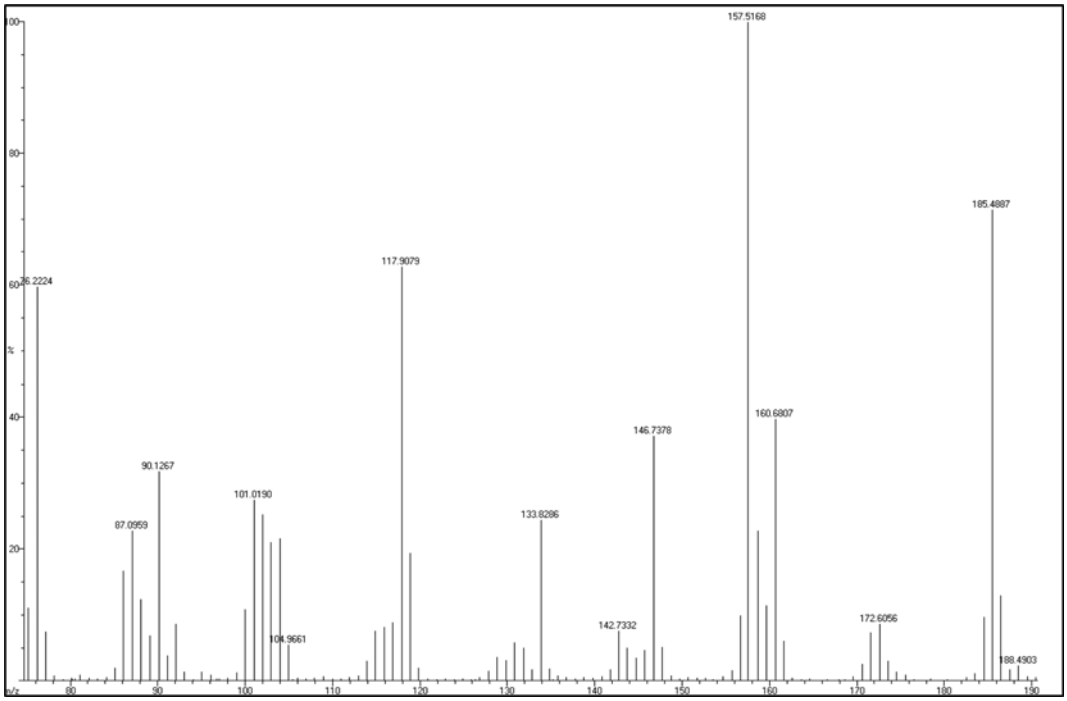

Fig. 18. Mass spectrum of 2-(but-3-enyl)benzo[d]isoxazol-3(2H)-one (3a).

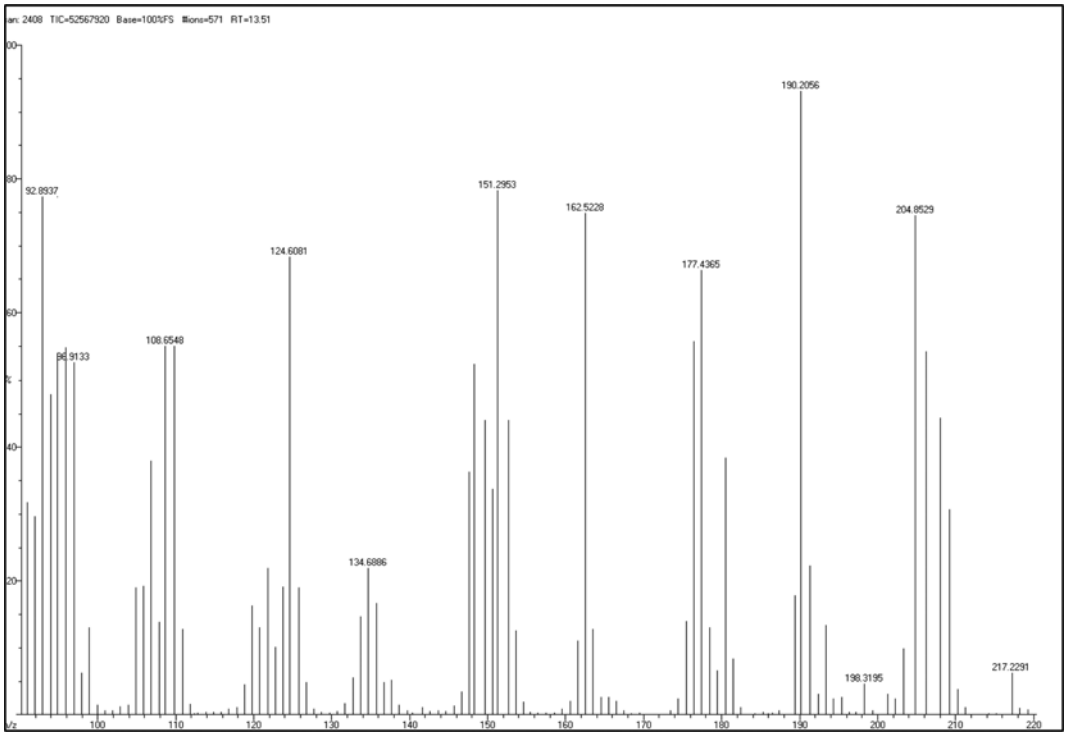

Fig. 19. Mass spectrum of 2-(4-methylpent--3-enyl)benzo[*d*]isoxazol-3(2H)-one.

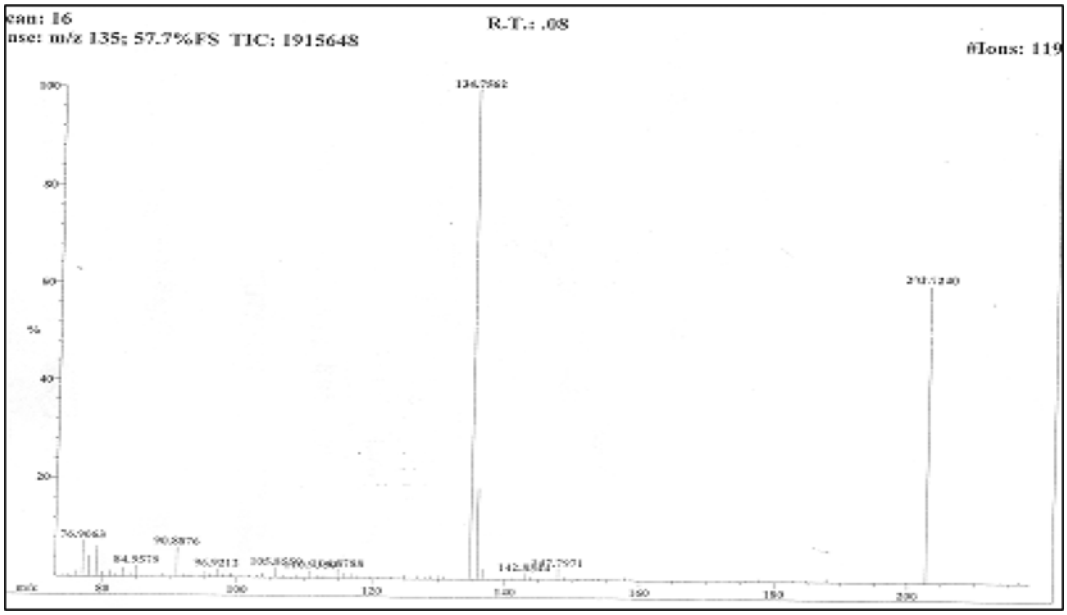

Fig. 20. Mass spectrum of 2-(3-methylbut-2-enyl) benzo[*d*]isoxazol-3(2H)-one.

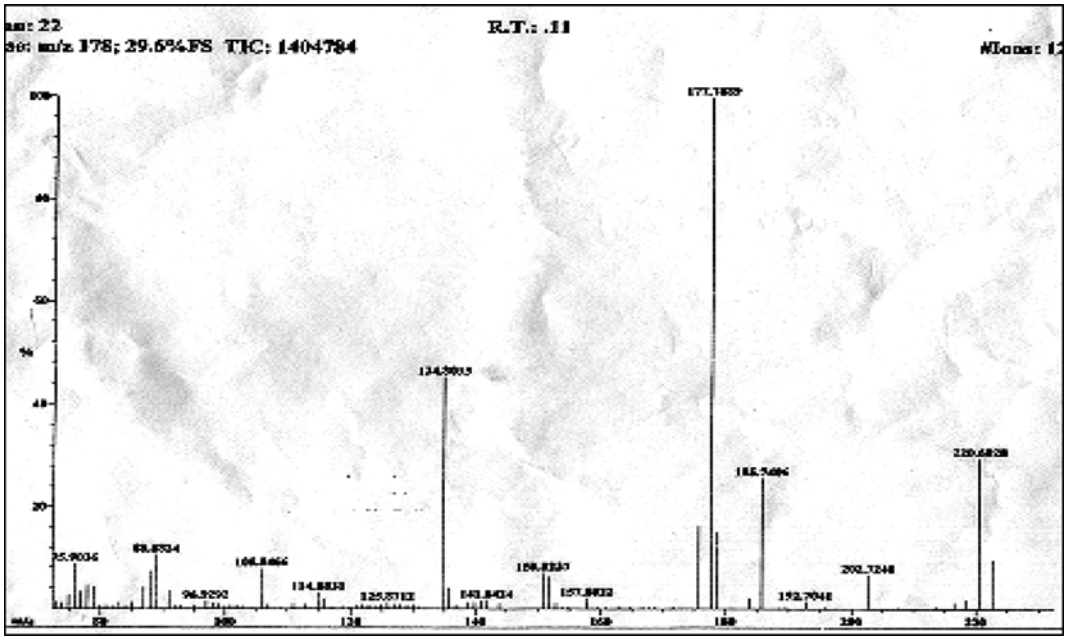

Fig. 21. Mass spectrum of 2-(4-chlorobut-2-ynyl) benzo[*d*]isoxazol-3(2H)-one.