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Data Article

Anti-proliferative activity and characterization data on oxadiazole derivatives

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ABSTRACT

This data in brief article explains the anti-cancer activity and characterization of oxadiazoles [1]. The main objective of this article was to provide general synthetic procedures, spectral discussion and physical data on the new oxadiazole tethered indazole (OTDs). This article discusses the ^{1}H NMR, ^{13}C NMR, mass spectroscopy, HPLC and melting point of the synthetic compounds. MTT assay was used to determine the anti-proliferative activity in hepatocellular cell lines.

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Specifications table

Subject	Chemistry
Specific subject area	Organic Chemistry
Type of data	Figure, Spectra
How data were acquired	^{1}H NMR and ^{13}C NMR spectra were recorded on the Agilent NMR instrument in DMSO-d6/$CDCl_3$ solvent. Mass spectra have been recorded on an Agilent LC-MS.HPLC was recorded Waters (USA) connected to W2998 Photo-Diode Arrary Detector. Cytotoxicity was determined by MTT Assay.
Data format	Raw Analyzed
Parameters for data collection	All reagents and solvents were commercially available in the reagent grade. These were used without further purification. All the final compounds were purified by column chromatography on silica gel (60–120 mesh).
Description of data collection	All the final isolated compounds were characterized by NMR spectroscopy, LC-MS and melting points.
Data source location	Institution: University of Mysore, Manasagangotri, Mysore-570006 City/Town/Region: Mysore Country: India
Data accessibility	Data available with article
Related research article	Dukanya, M. K. Shanmugam, S. Rangappa, P. K. Metri, S. Mohan, Basappa, K. S Rangappa,Exploring the newer oxadiazoles as real inhibitors of human SIRT2 in hepatocellular cancer cells. *Bioorg. Med. Chem. Lett.* ***30****,2020,127330*. doi:10.1016/j.bmcl.2020.127330.

Value of the data

- Indazole tethered oxadiazole (OTD) derivatives have significant anti-cancer activity against hepatocellular carcinoma (HCC) cells.
- The given procedure for the synthesis of Indazole tethered oxadiazoles could be useful for organic chemists to develop novel drugs.
- The given spectroscopic data on the Indazole tethered oxadiazoles could be useful for organic chemists for synthesis of OTDs.

1. Data description

A series of Indazole tethered oxadiazoles (OTDs) (**3a-k**) were synthesized by refluxing N-methyindazole-acid hydrazide with different aromatic carboxylic acids (**2a-k**) in phosphorous oxychloride [1]. The synthetic route and structure of final compounds were given in Fig. 1. All the final compounds (**3a-k**) were characterized by ^{1}H NMR, ^{13}C NMR, LCMS and HPLC for active compounds **3**c, **3d, 3f, 3i**. All the spectra data are provided in this article (Figs. 2–38). The anti-cancer activities of the newly synthesized OTDs are given in Fig. 39. The Crystalographic data for compounds **3a, 3 h** & **3k** have been deposited with the Cambridge Crystalographic Data centre., CCDC No. 1992373, 1992374 and 1992375. Copies of the data can be obtained free of charge upon request to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: 044 (0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

2. Experimental design, materials and methods

2.1. General information

The reagents used for the reaction are commercially available reagent class and were used without further purification. The chemicals were purchased from Sigma-Aldrich, TCI or SD-Fine. The reactions were monitored by thin layer chromatography using pre-coated Merck silica gel 60 F254 plates and analytical TLCs were conducted using ethyl acetate and hexanes as eluent. Then

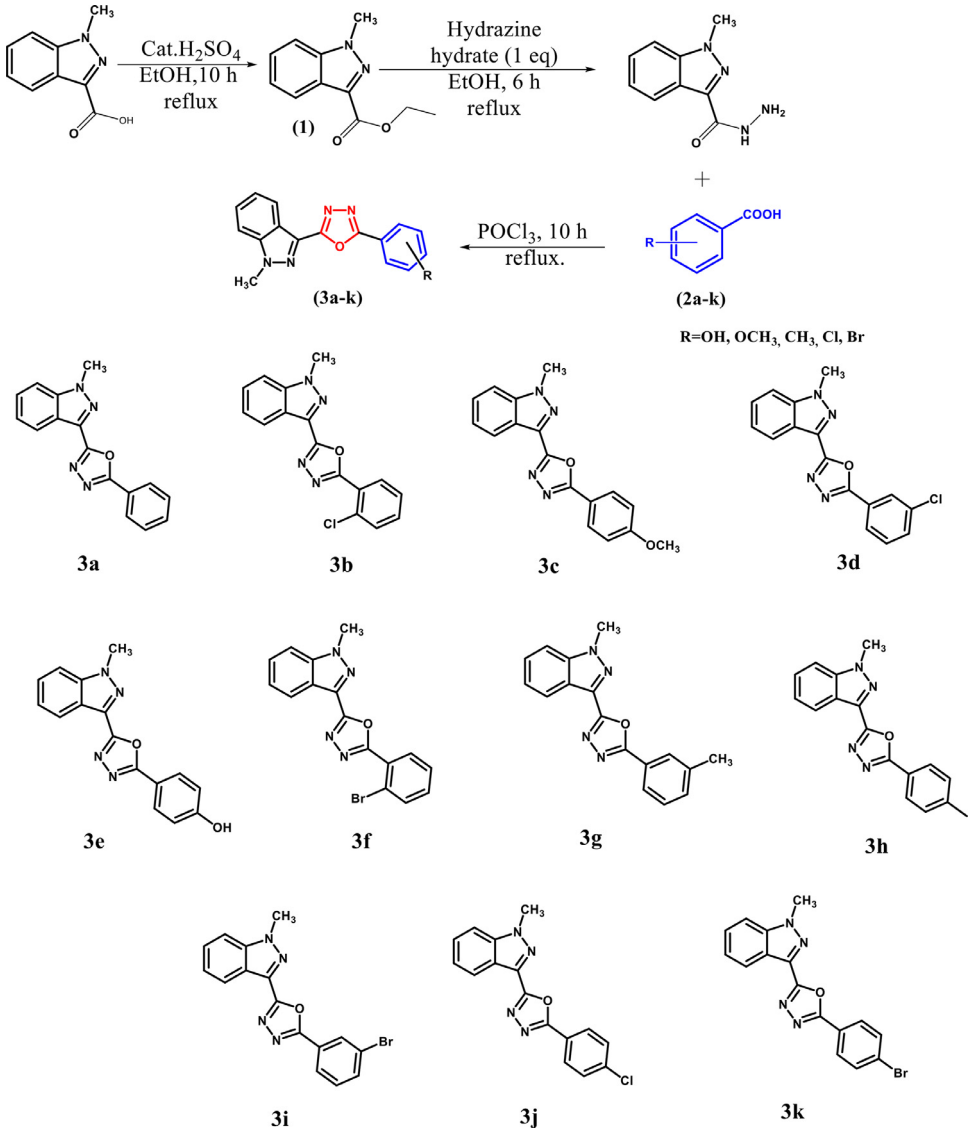


Fig. 1. Synthetic scheme and structure of Oxadiazoles **3a-3k.**

the spots were observed under UV light. The final compounds were purified by silica gel column chomatography using ethyl acetate and hexane as eluent and organic solvents were concentrated under reduced pressure on the rotary evaporator.

The purified samples were dissolved in either $CDCl_3$ or DMSO-d^6 to acquire the NMR spectra using Agilent NMR. ^{1}H NMR and ^{13}C NMR were recorded at 400 and 100 MHz respectively. The ^{1}H NMR Data are expressed in chemical shift (δ, ppm) and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dt = doublet of triplet, dd = doublet of doublets, m = multiplet), coupling constant (*J*, Hz) and integration. The LCMS measurments were performed on Agilent LC-MS using 2 mg/mL of the solutions in HPLC grade acetonitrile or methanol. The HPLC was recorded

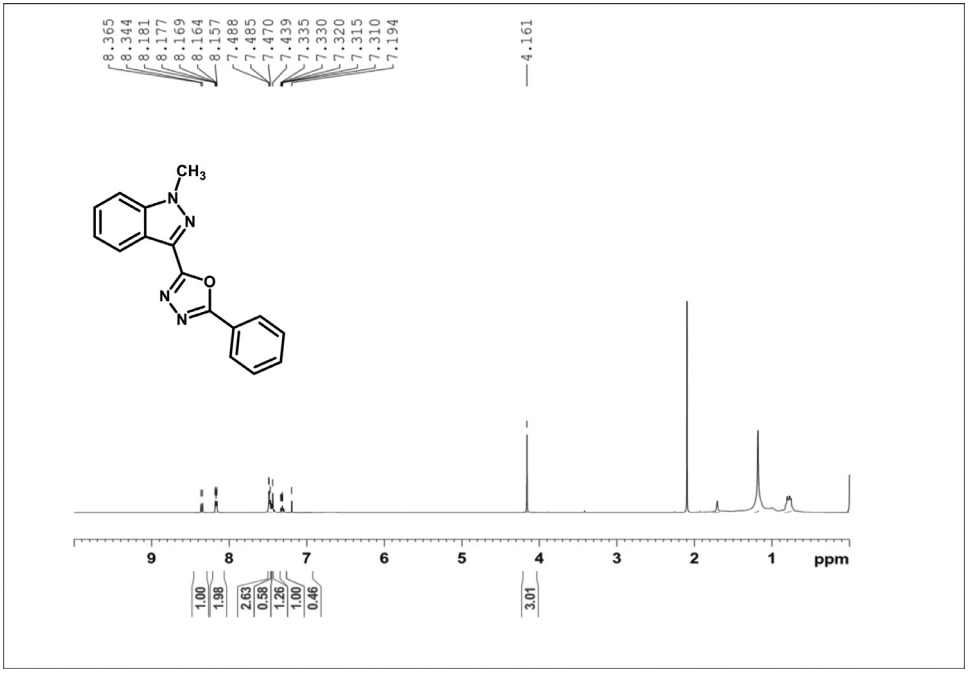


Fig. 2. ^{1}H NMR spectrum of **3a**.

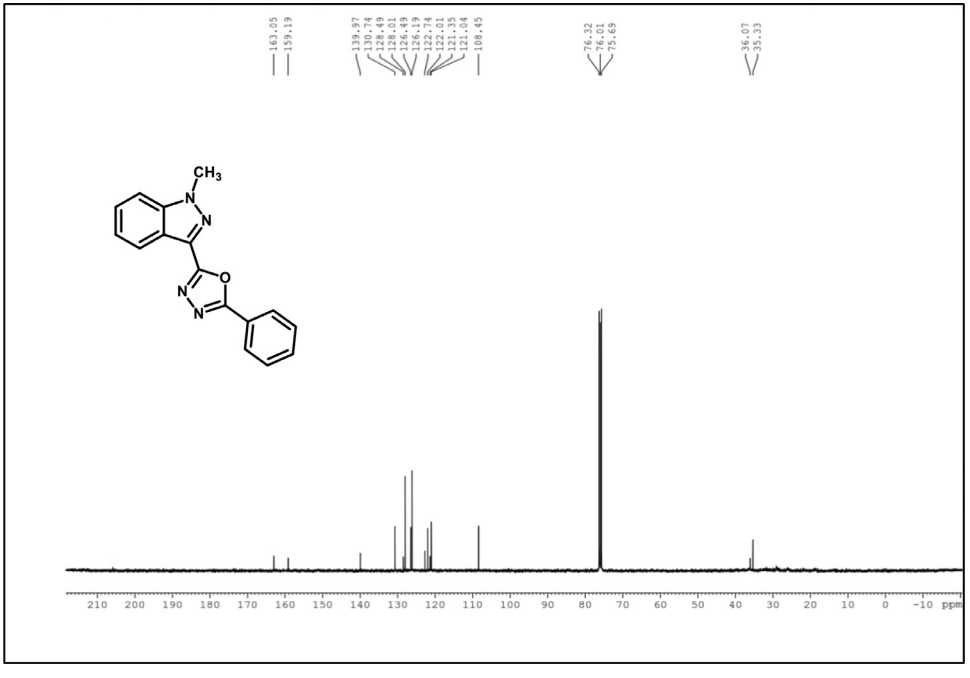


Fig. 3. ^{13}C NMR spectrum of **3a**.

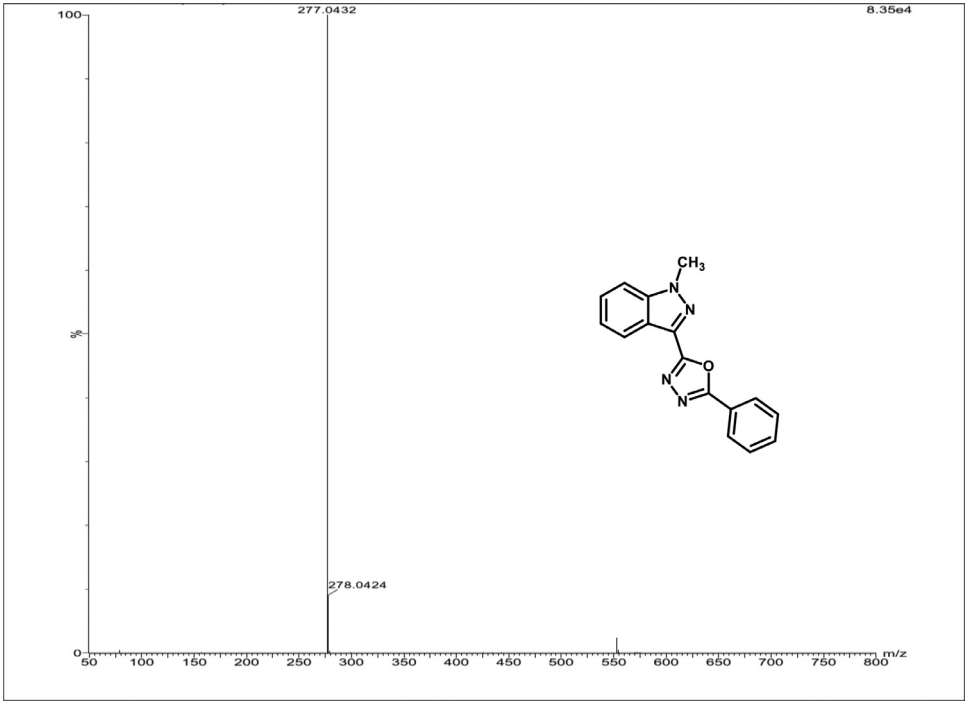


Fig. 4. Mass spectrum of **3a**.

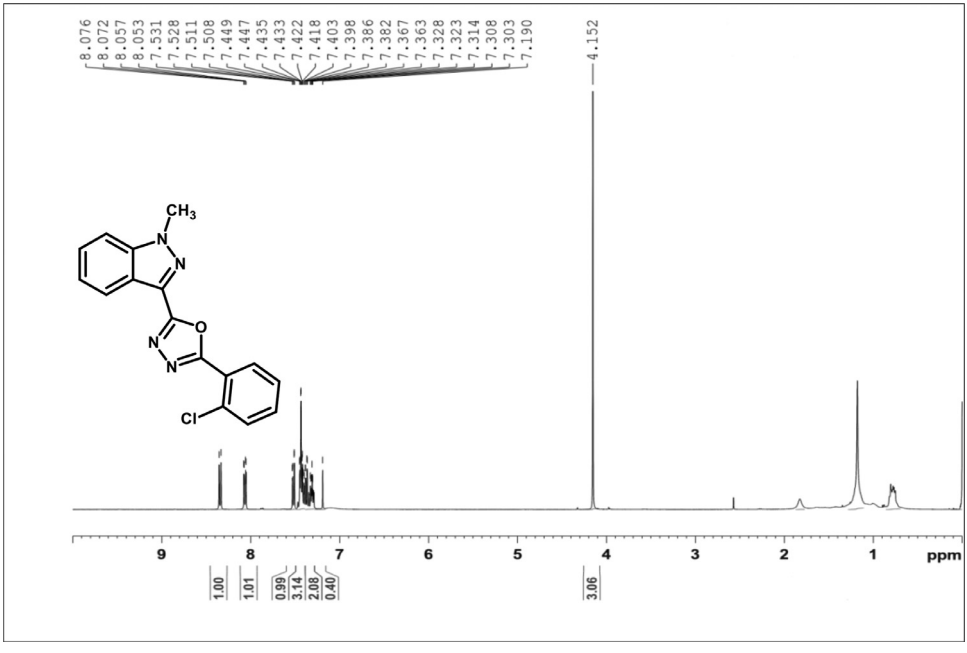


Fig. 5. ^{1}H NMR spectrum of **3b**.

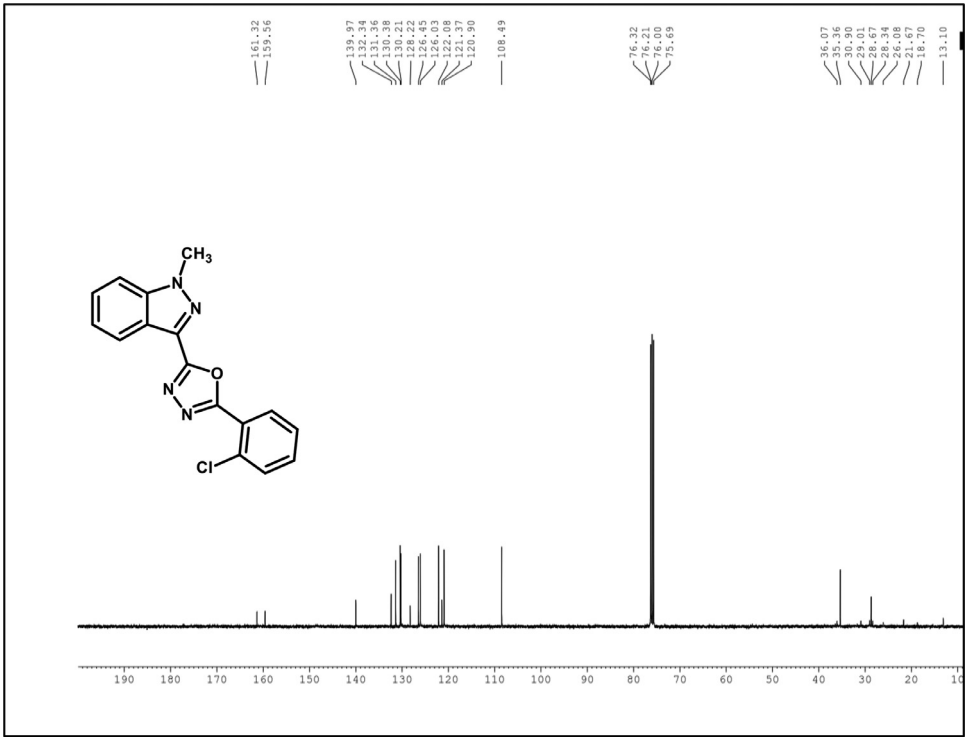


Fig. 6. ^{13}C NMR spectrum of **3b**.

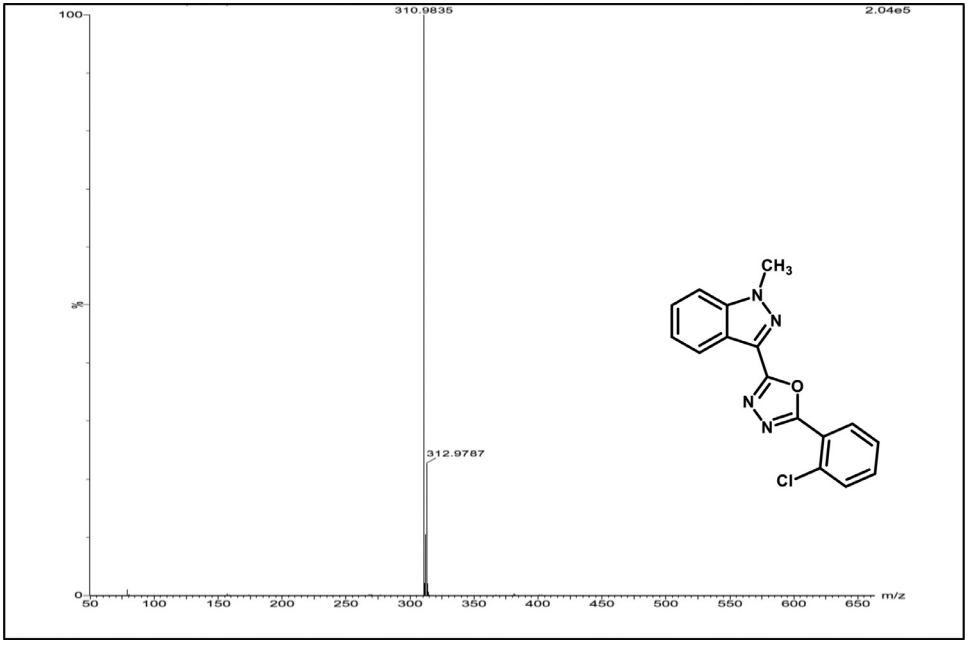


Fig. 7. Mass spectrum of **3b**.

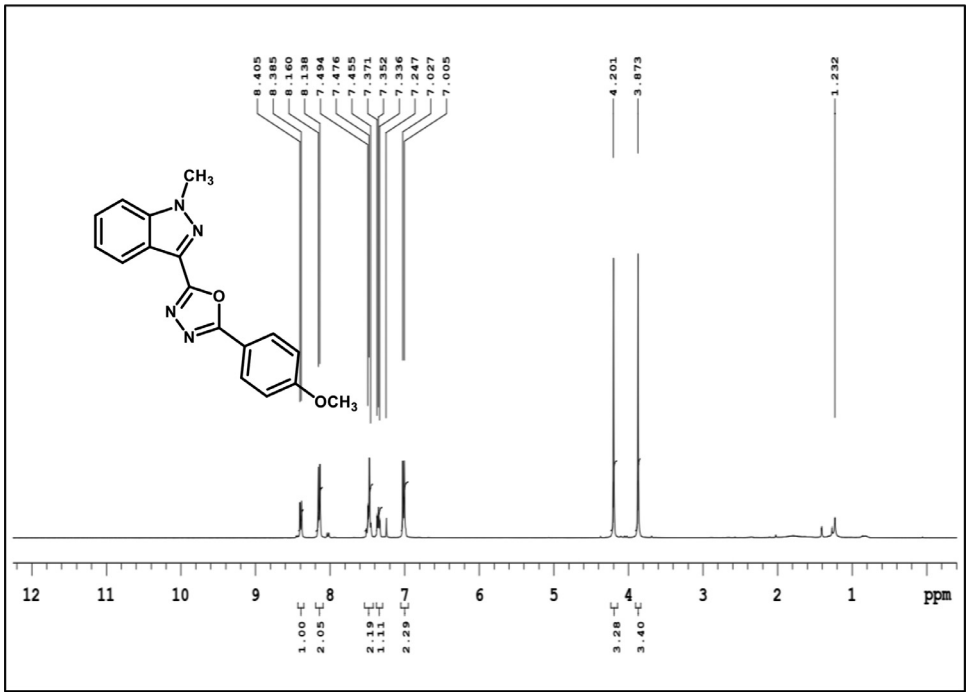


Fig. 8. [1]H NMR spectrum of **3c**.

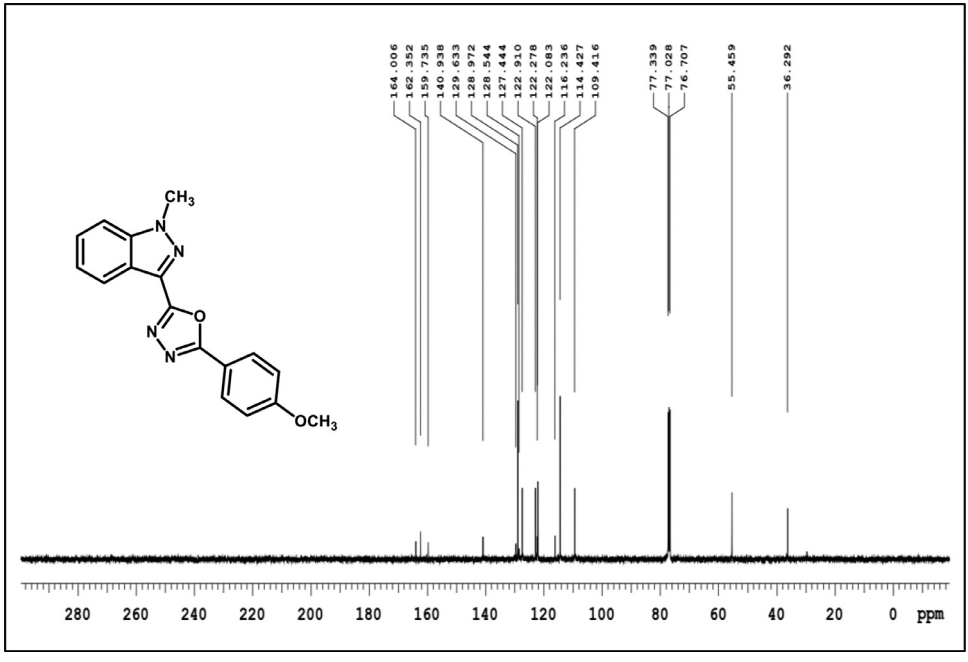


Fig. 9. [13]C NMR spectrum of **3c**.

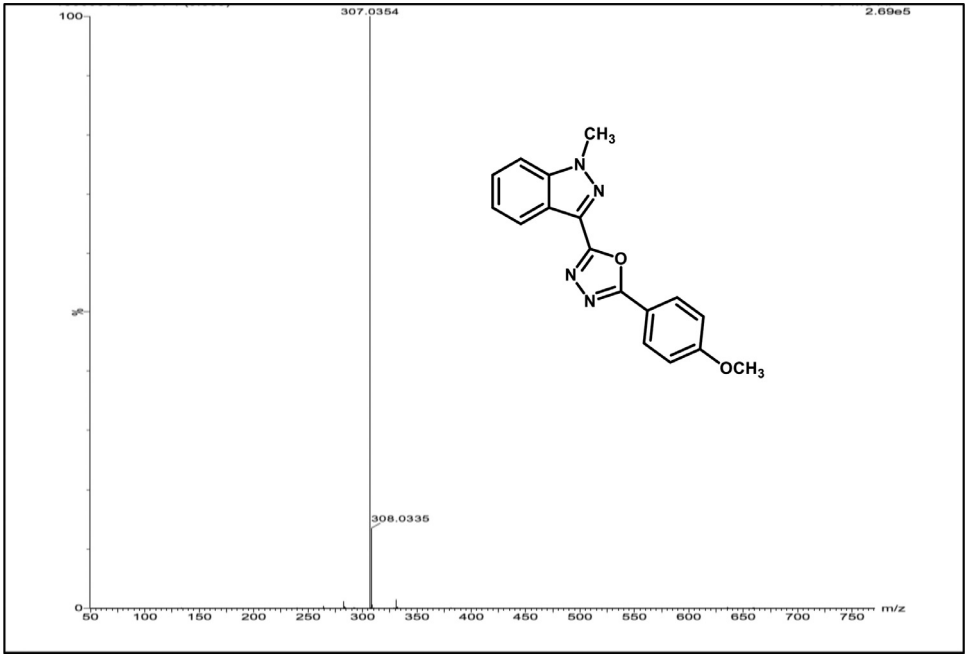
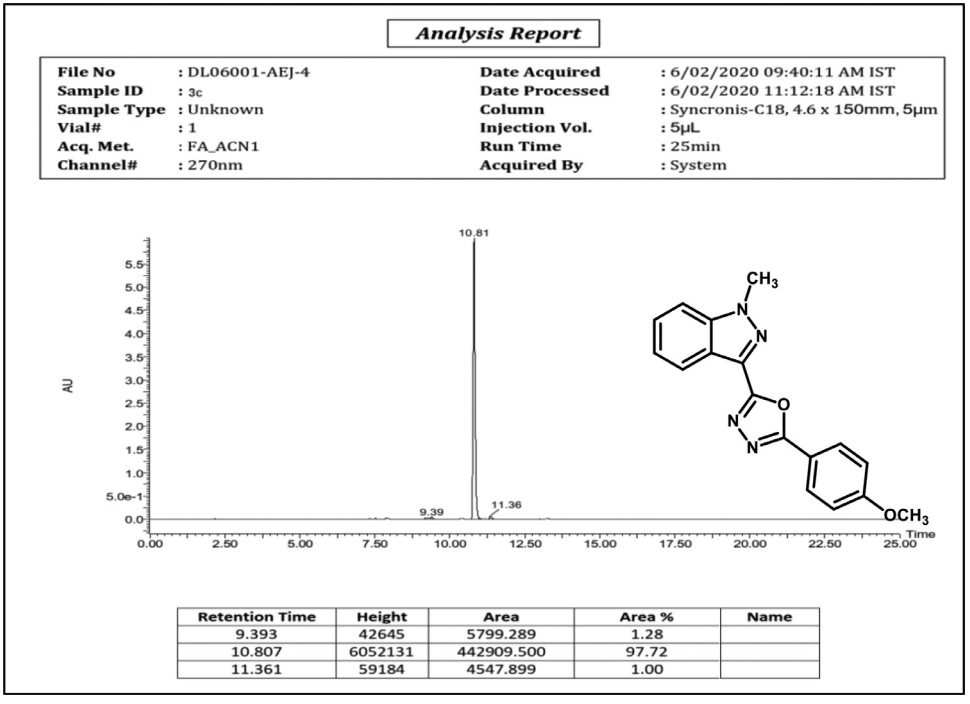


Fig. 10. Mass spectrum of **3c**.



Retention Time	Height	Area	Area %	Name
9.393	42645	5799.289	1.28	
10.807	6052131	442909.500	97.72	
11.361	59184	4547.899	1.00	

Fig. 11. HPLC spectrum of **3c**.

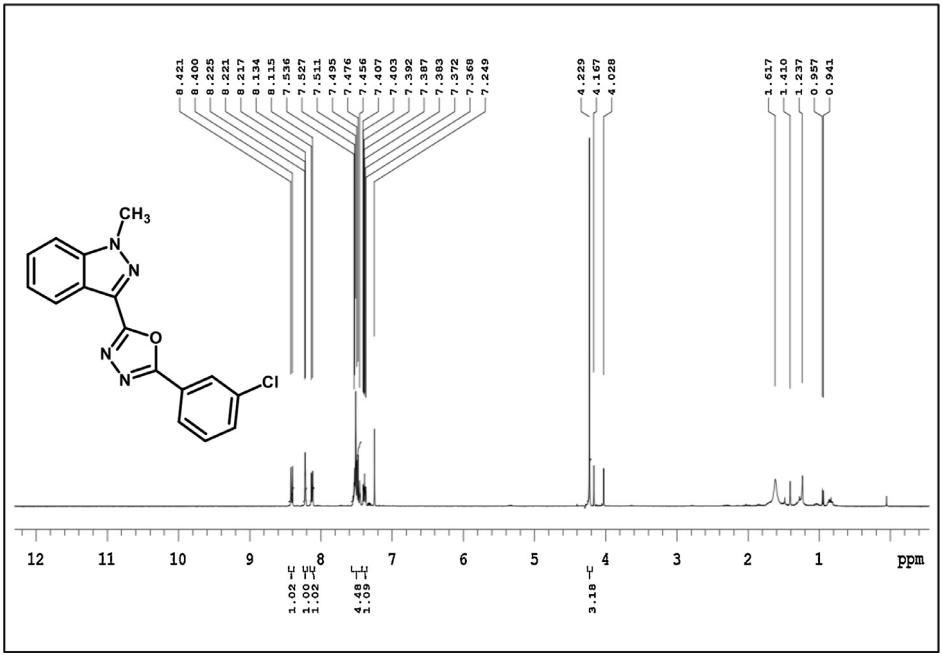


Fig. 12. ^{1}H NMR spectrum of **3d**.

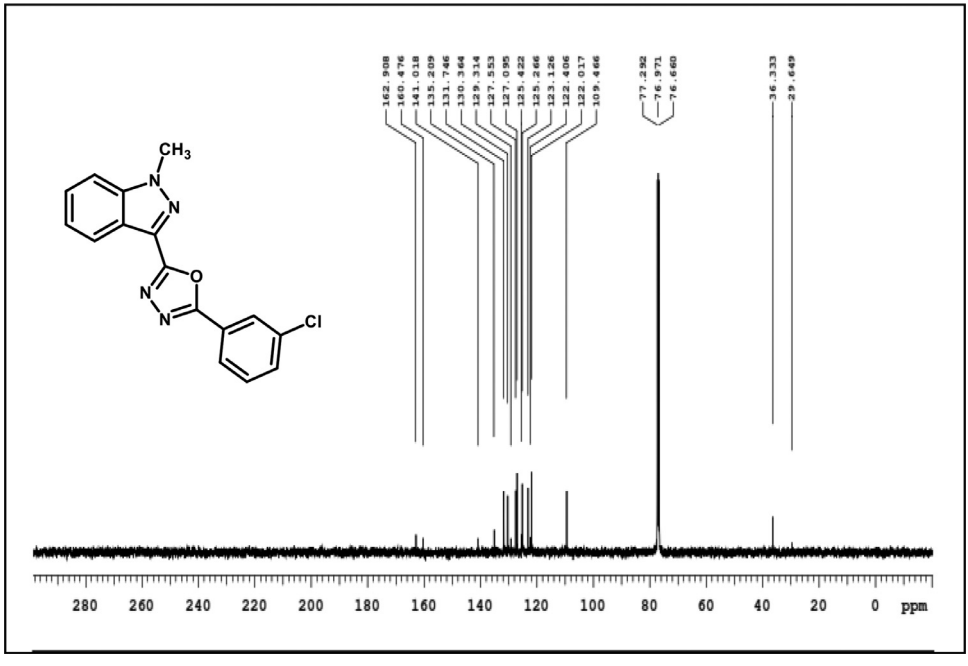


Fig. 13. ^{13}C NMR spectrum of **3d**

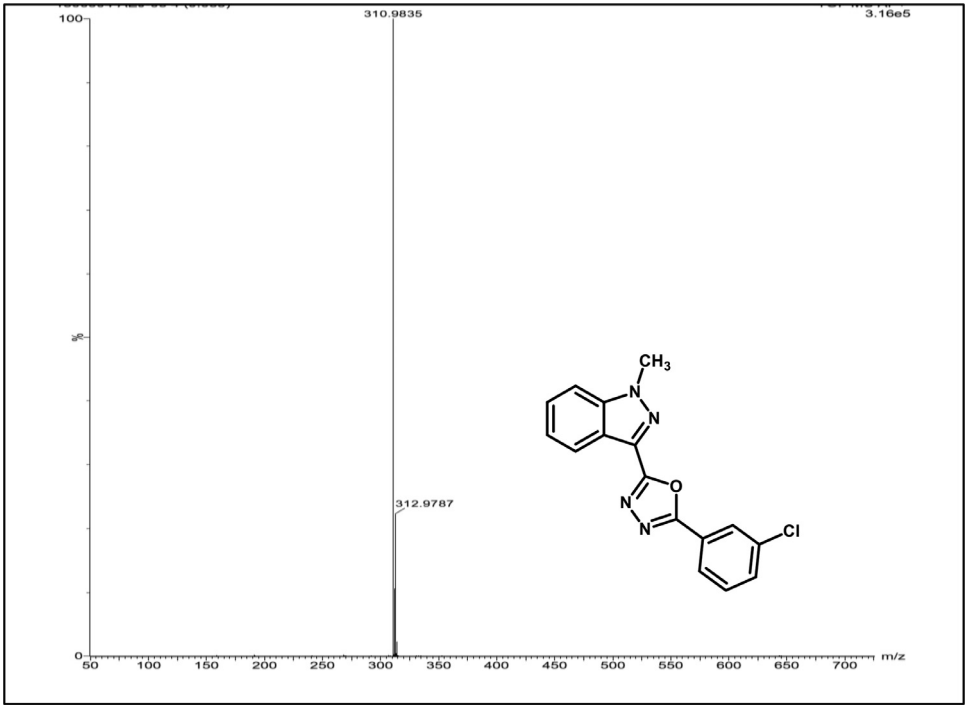
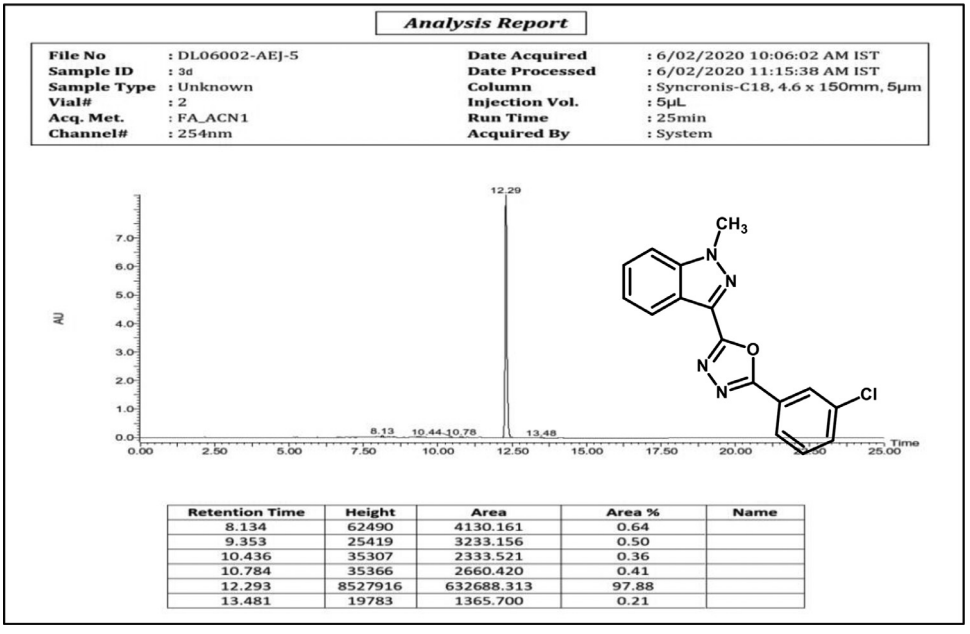


Fig. 14. Mass spectrum of **3d**



Retention Time	Height	Area	Area %	Name
8.134	62490	4130.161	0.64	
9.353	25419	3233.156	0.50	
10.436	35307	2333.521	0.36	
10.784	35366	2660.420	0.41	
12.293	8527916	632688.313	97.88	
13.481	19783	1365.700	0.21	

Fig. 15. HPLC spectrum of **3d**

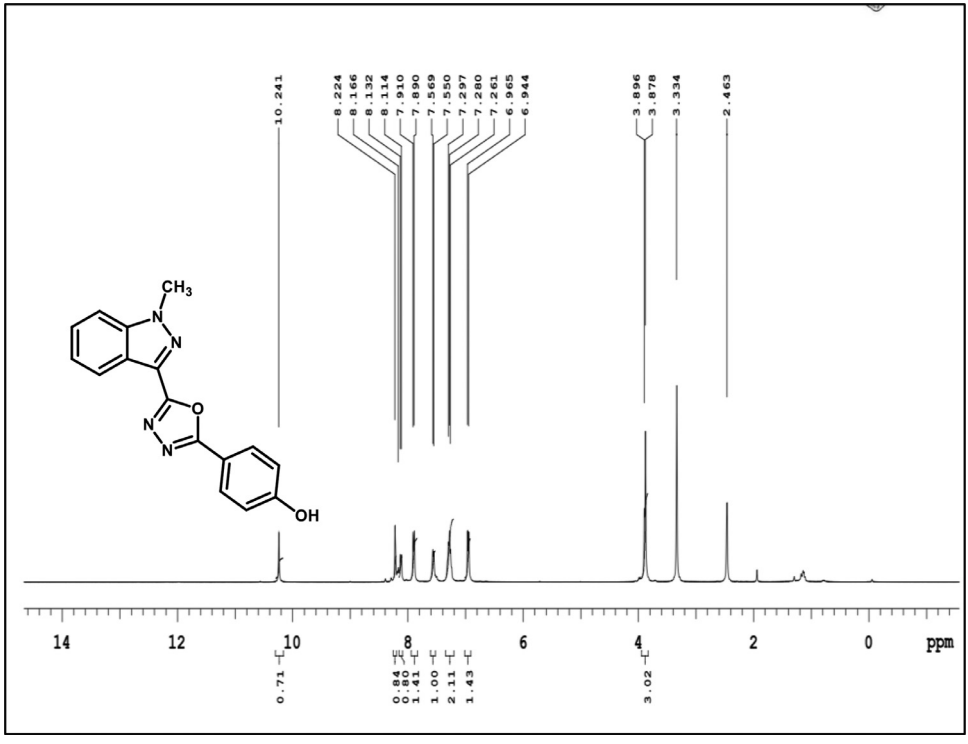


Fig. 16. [1]HNMR spectrum of **3e**.

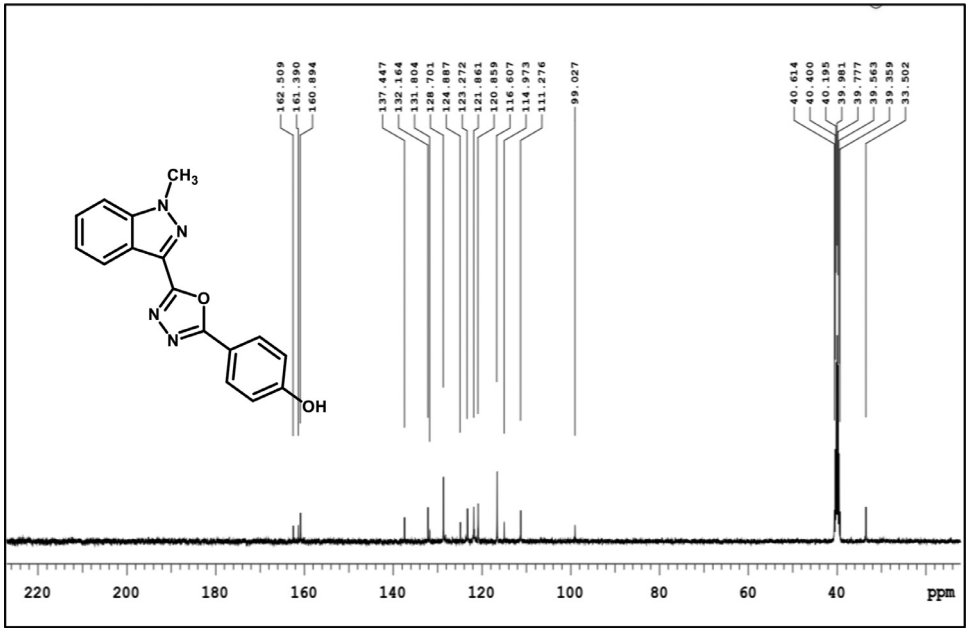


Fig. 17. [13]C NMR spectrum of **3e**.

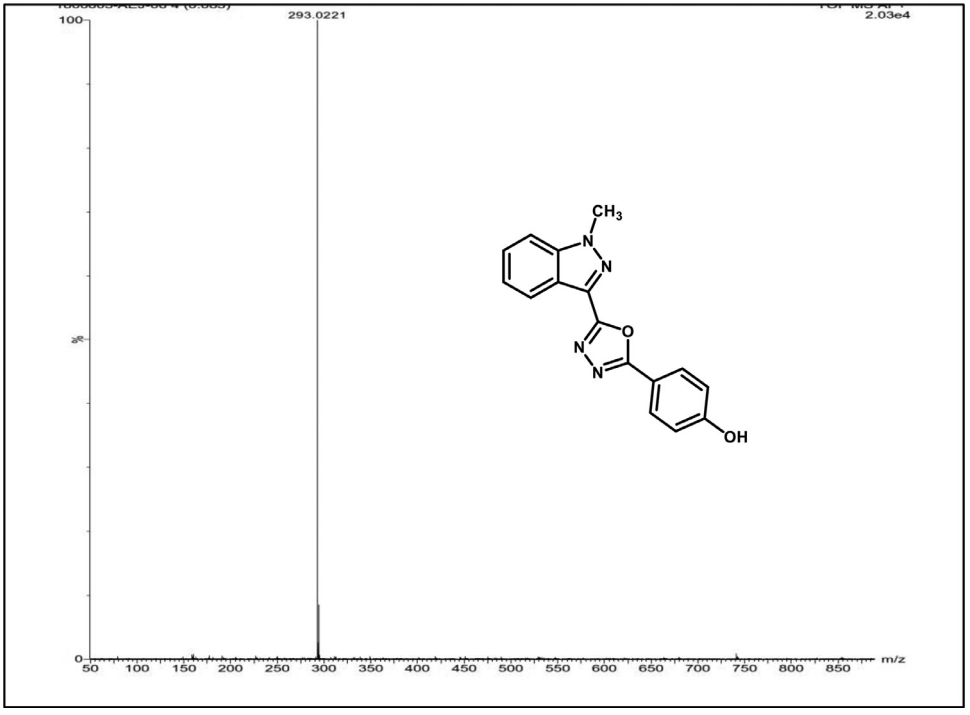


Fig. 18. Mass spectrum of **3e**.

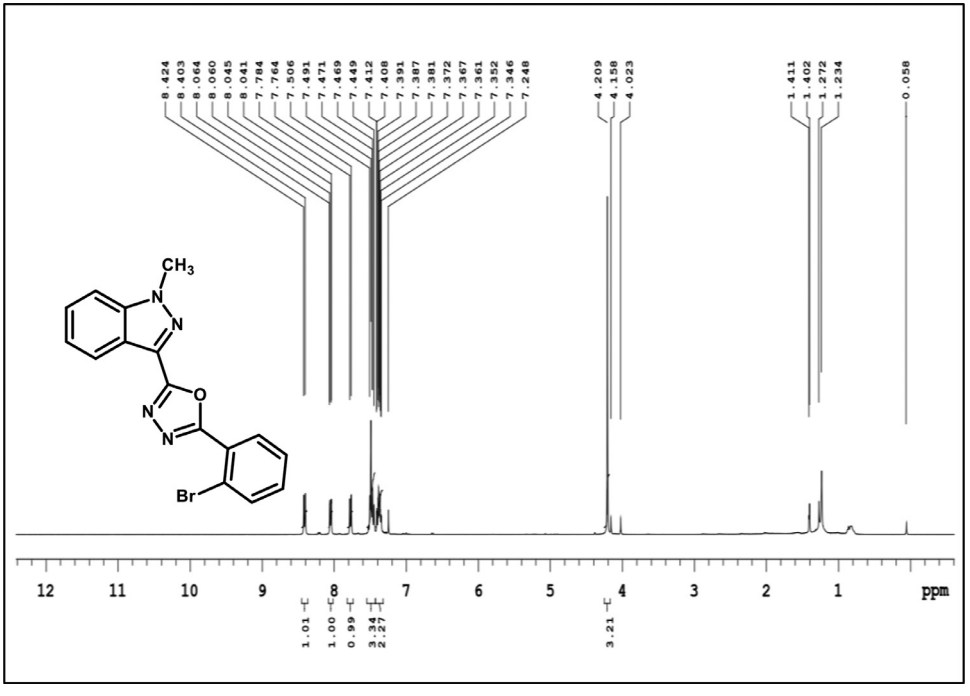


Fig. 19. ^{1}H NMR spectrum of **3f**.

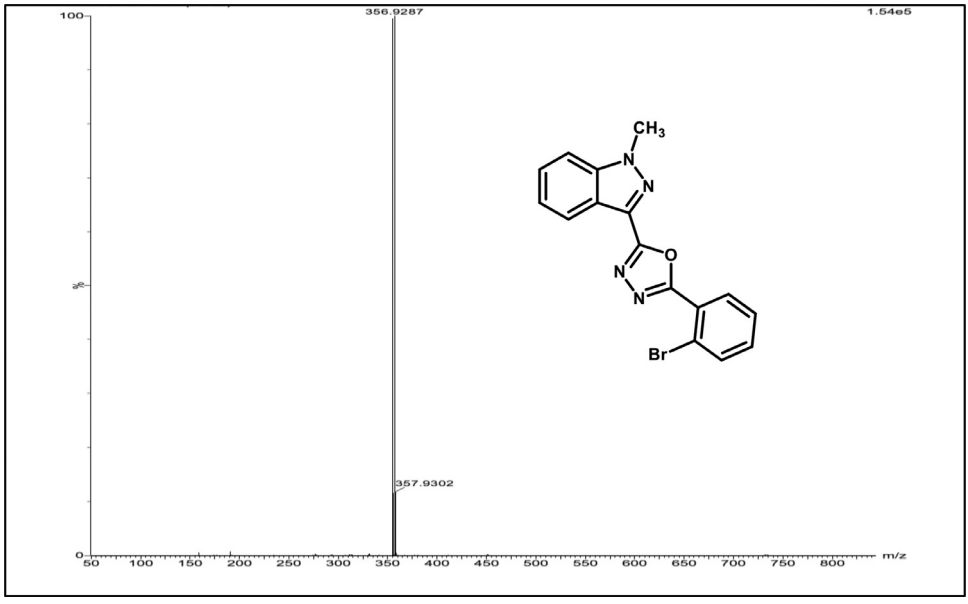


Fig. 20. ^{13}C NMR spectrum of **3f**.

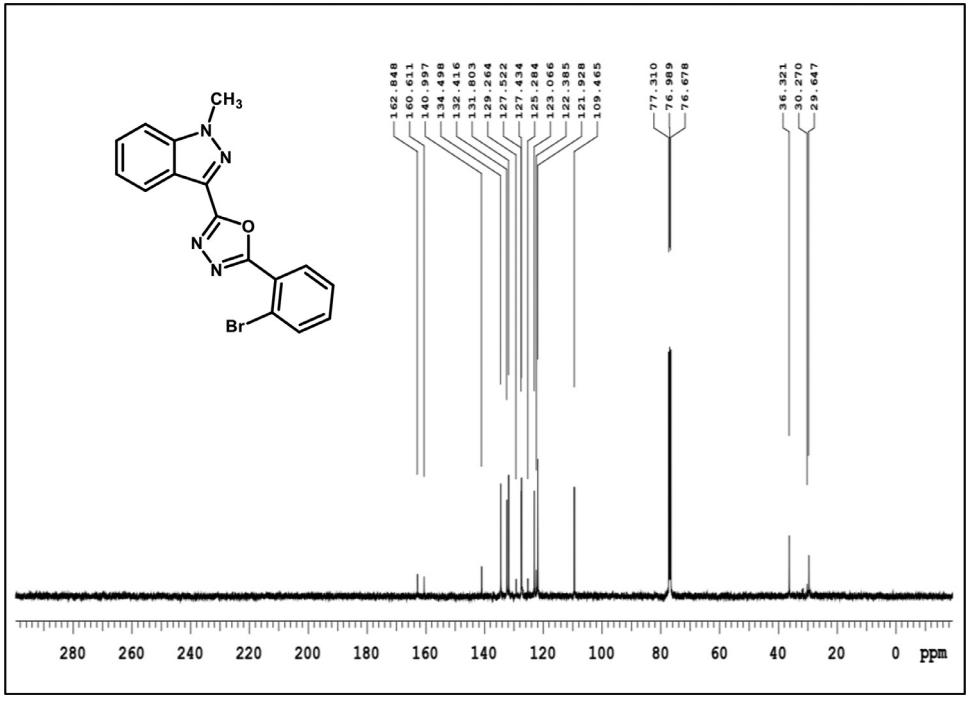
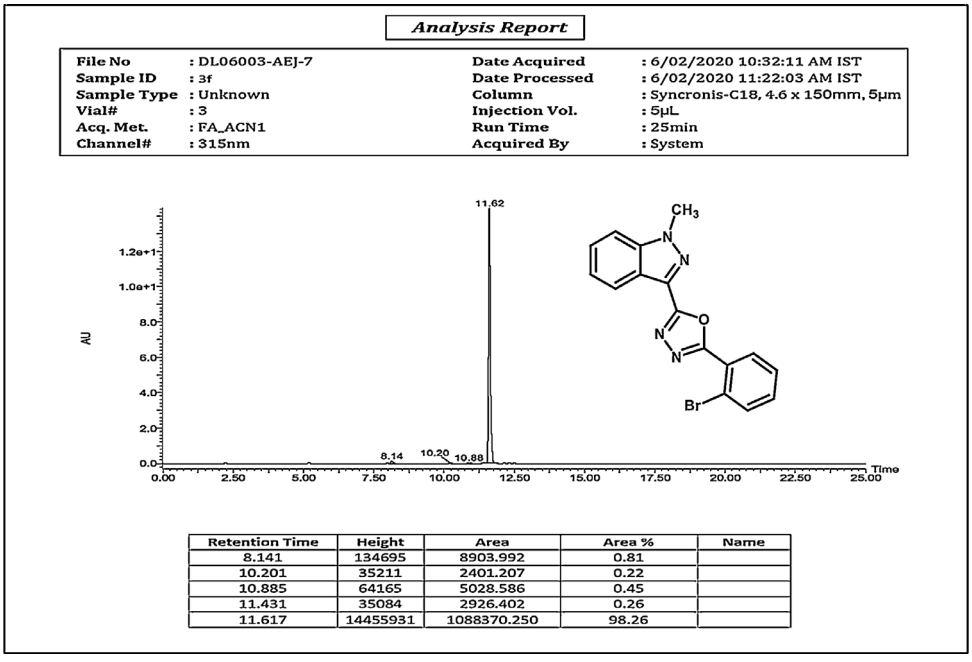


Fig. 21. Mass spectrum of **3f**.



Retention Time	Height	Area	Area %	Name
8.141	134695	8903.992	0.81	
10.201	35211	2401.207	0.22	
10.885	64165	5028.586	0.45	
11.431	35084	2926.402	0.26	
11.617	14455931	1088370.250	98.26	

Fig. 22. HPLC spectrum of **3f**.

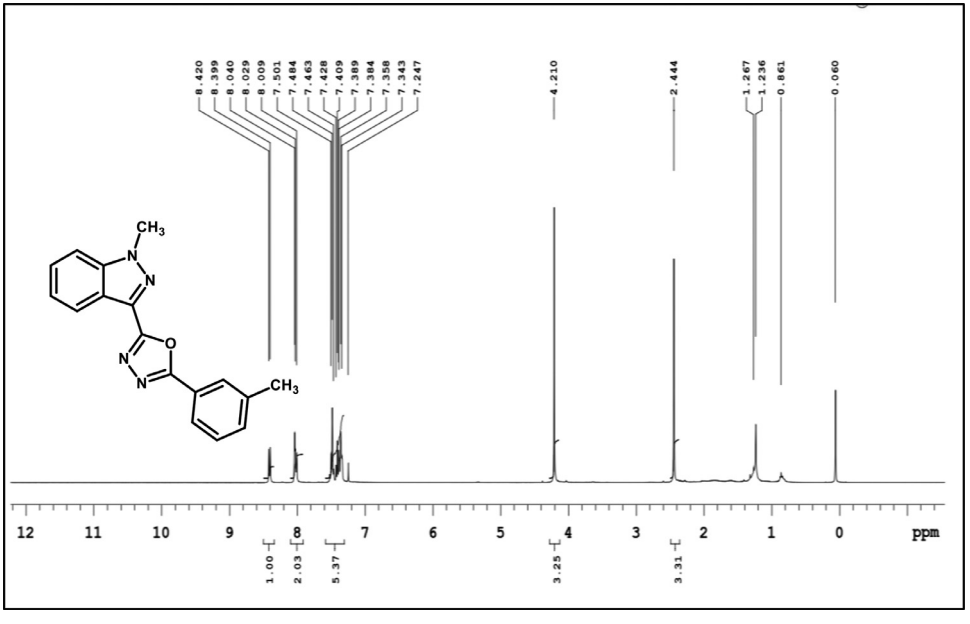


Fig. 23. [1]HNMR spectrum of **3g**.

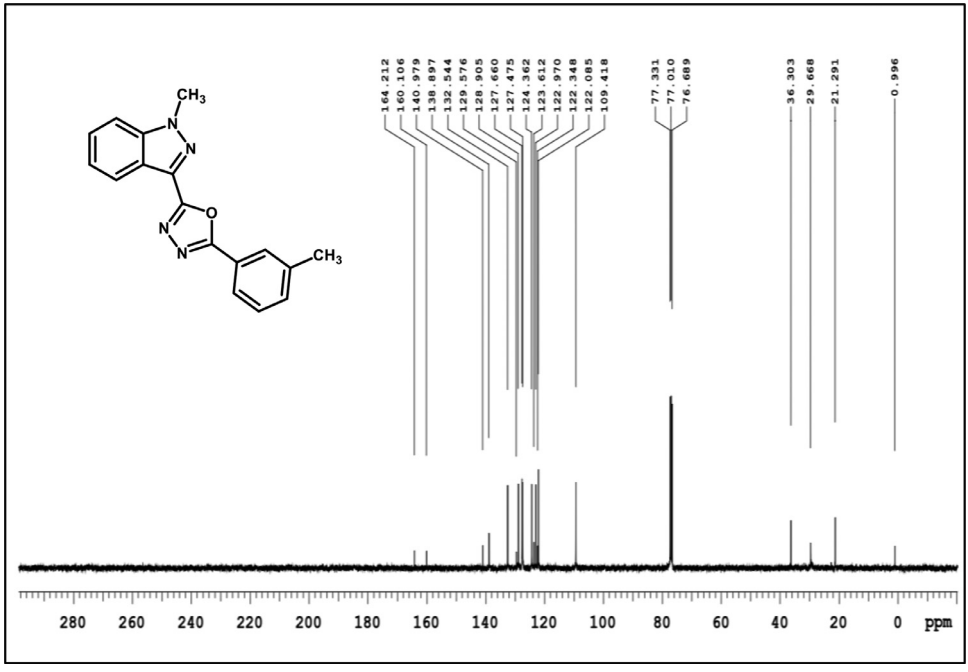


Fig. 24. ^{13}C NMR spectrum of **3g**.

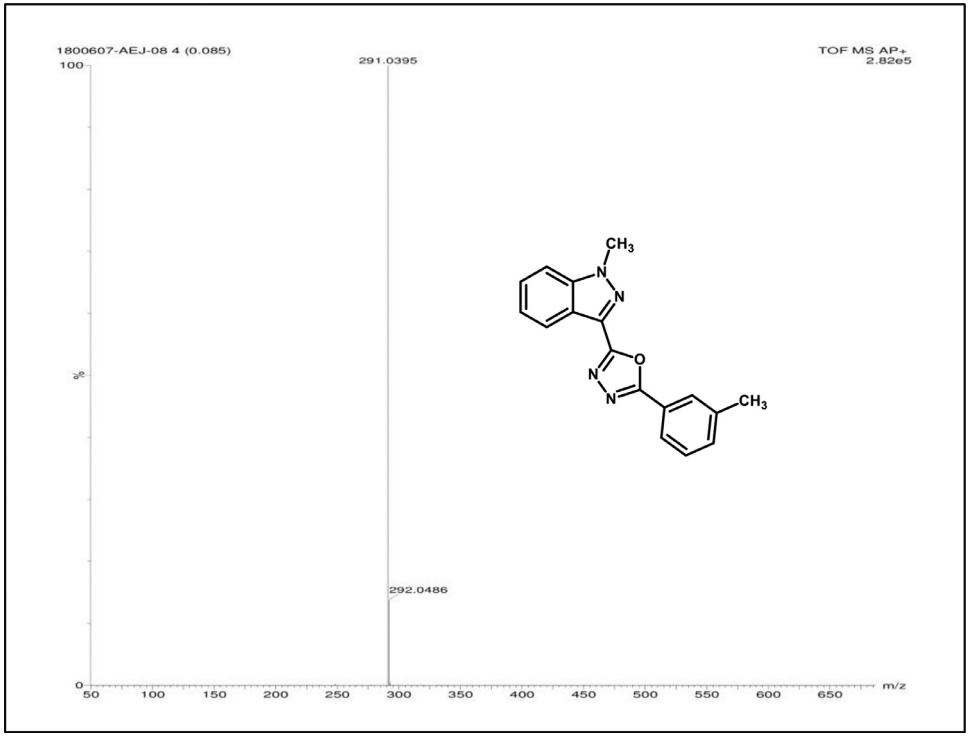


Fig. 25. Mass spectrum of **3g**.

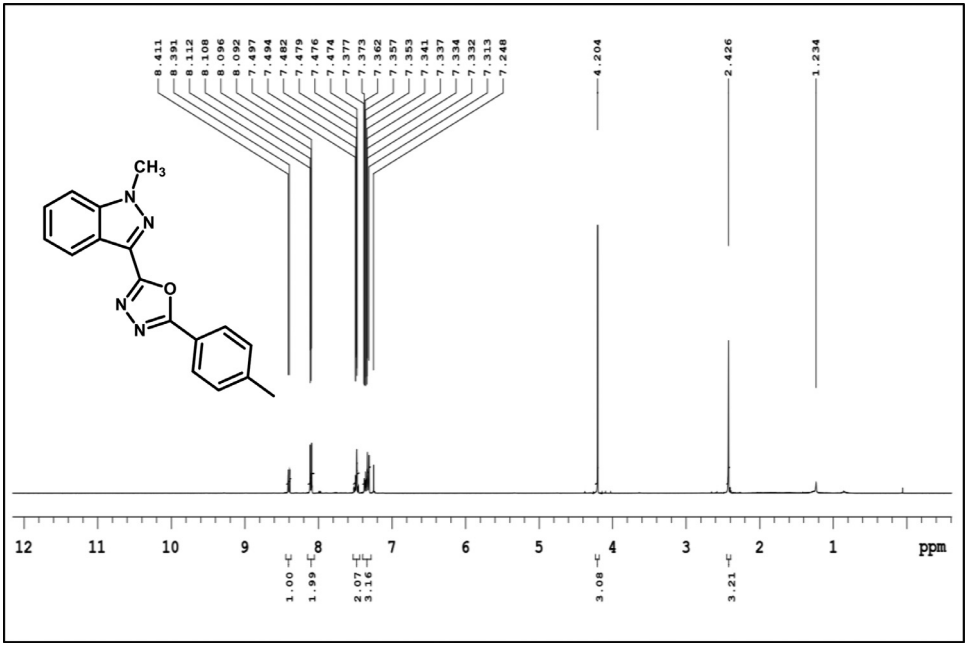


Fig. 26. [1]HNMR spectrum of **3h**.

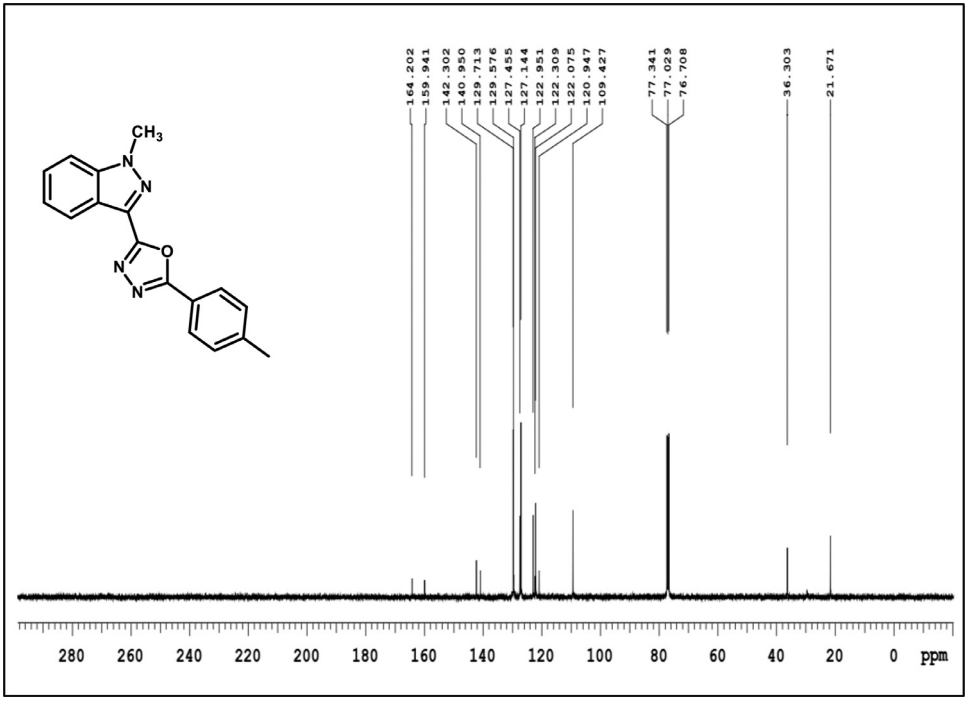


Fig. 27. [13]C NMR spectrum of **3h**.

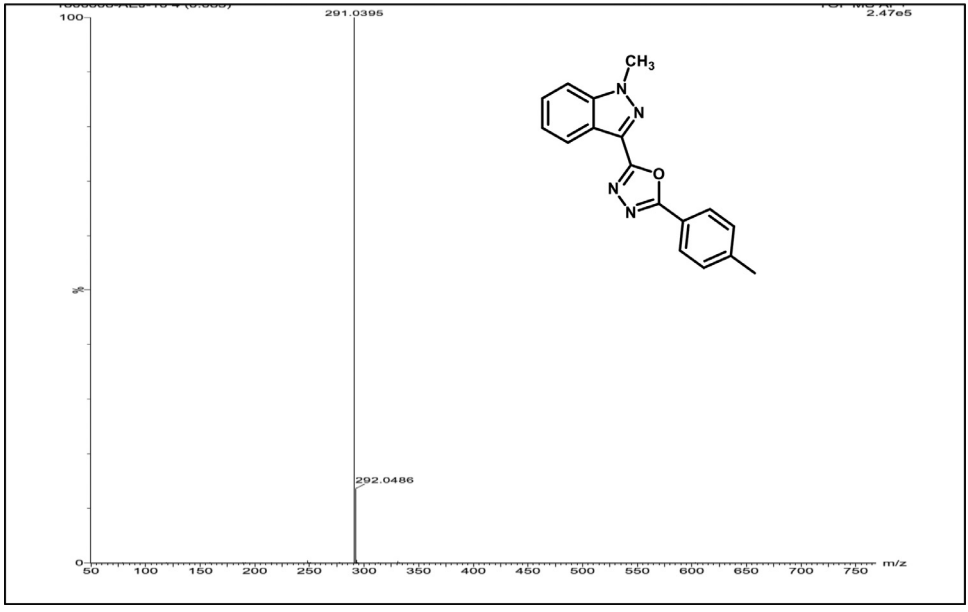


Fig. 28. Mass spectrum of **3h**.

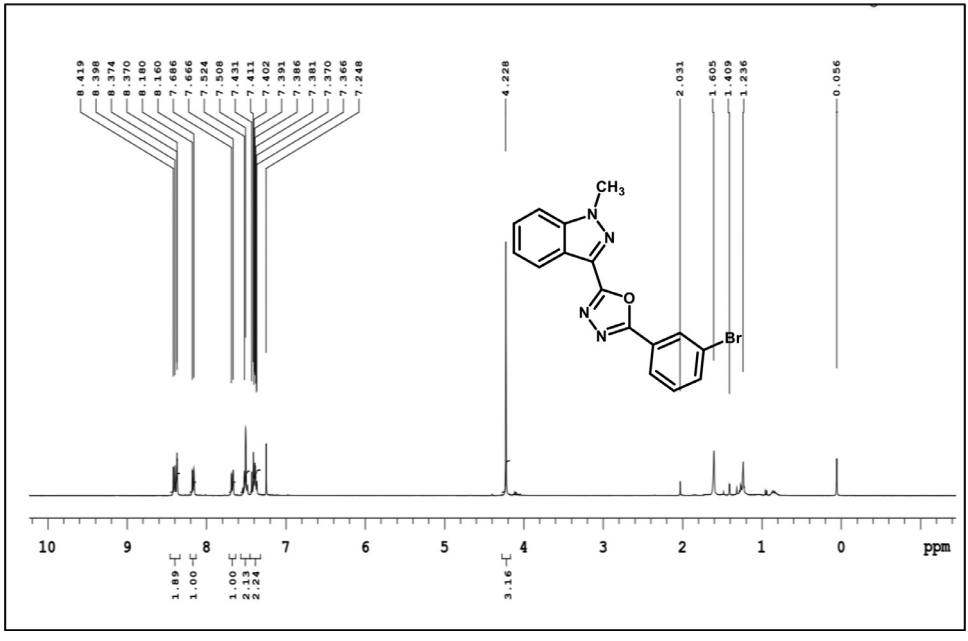


Fig. 29. [1]HNMR spectrum of **3i**.

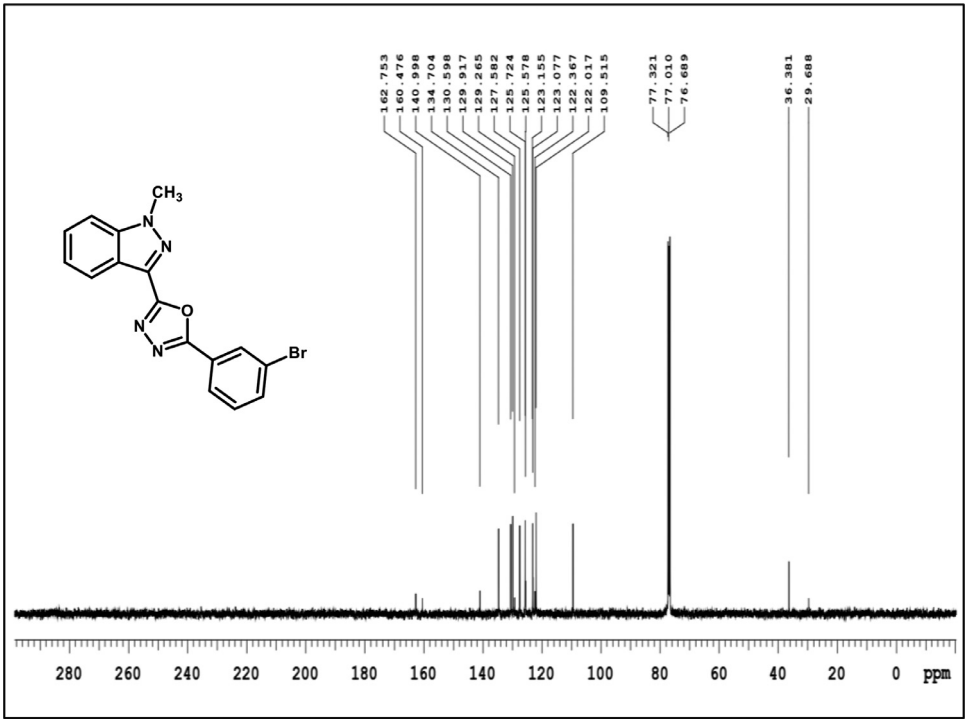


Fig. 30. ^{13}C NMR spectrum of **3i**.

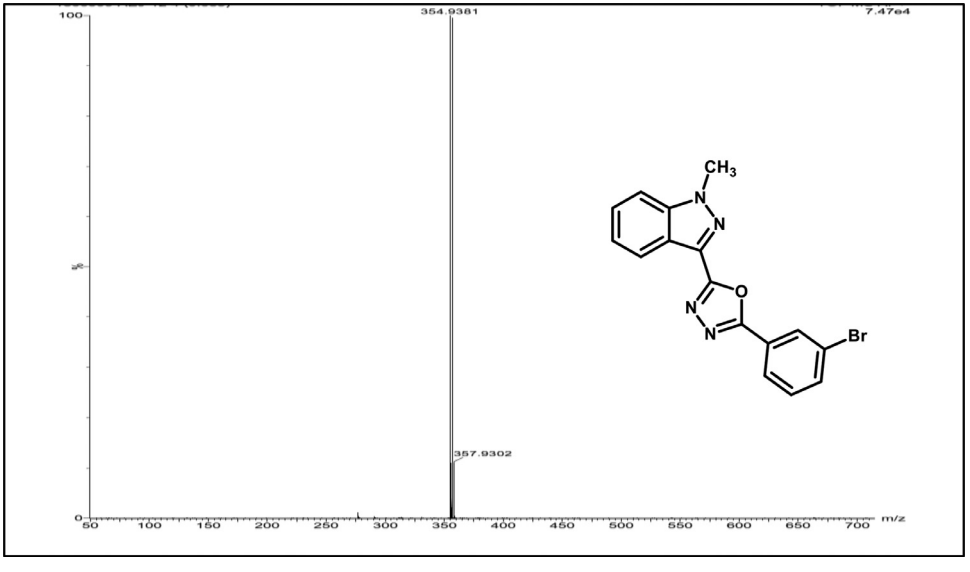
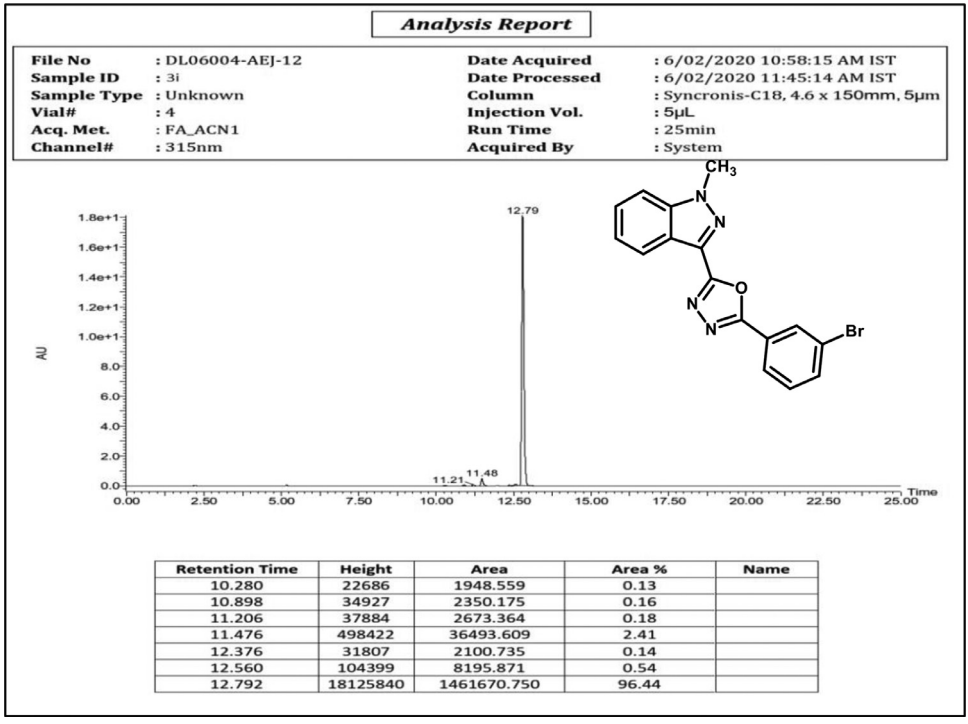


Fig. 31. Mass spectrum of **3i**.



Retention Time	Height	Area	Area %	Name
10.280	22686	1948.559	0.13	
10.898	34927	2350.175	0.16	
11.206	37884	2673.364	0.18	
11.476	498422	36493.609	2.41	
12.376	31807	2100.735	0.14	
12.560	104399	8195.871	0.54	
12.792	18125840	1461670.750	96.44	

Fig. 32. HPLC spectrum of **3i**.

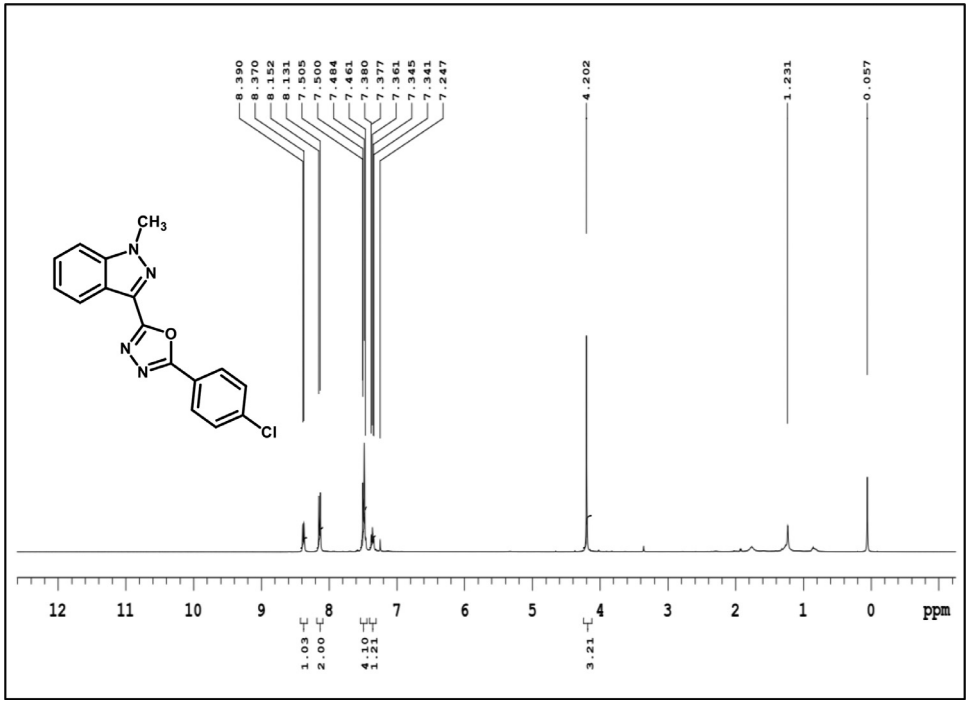


Fig. 33. ^{1}H NMR spectrum **3j**.

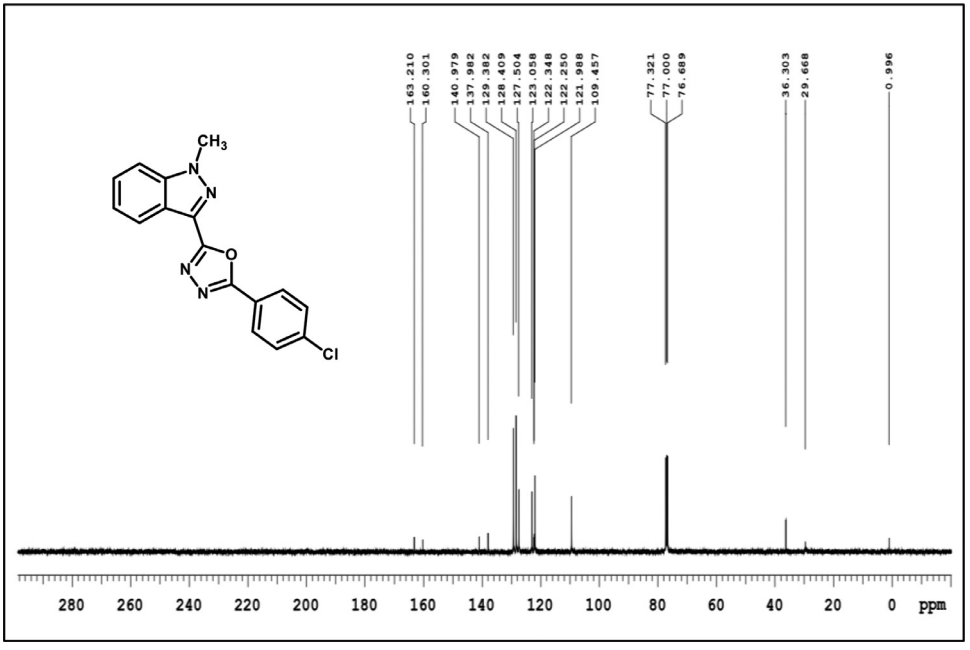


Fig. 34. ^{13}C NMR Spectrum of **3j**.

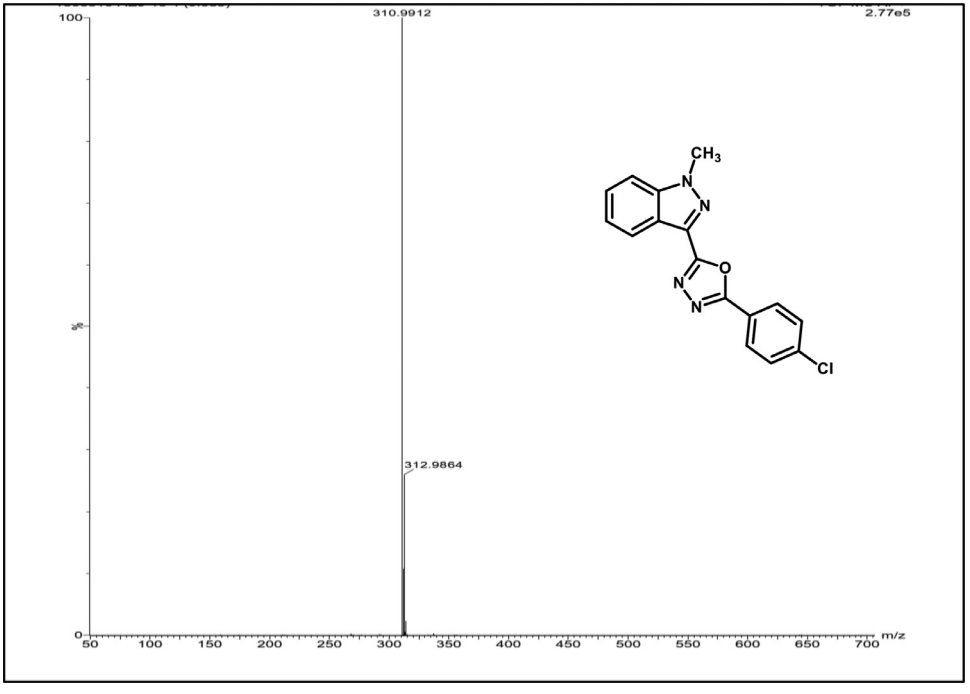


Fig. 35. Mass spectrum of **3j**.

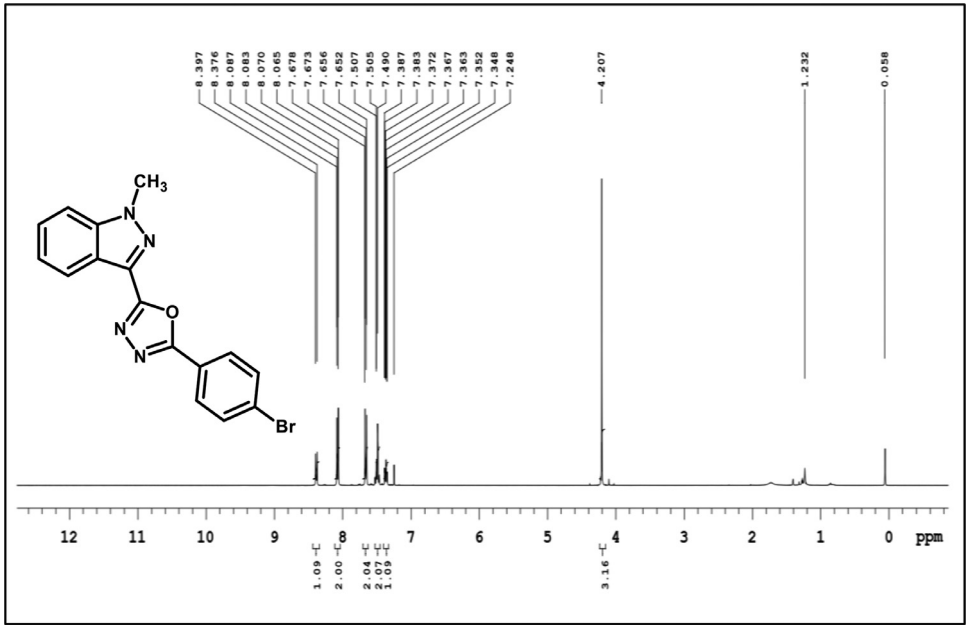


Fig. 36. ^{1}H NMR spectrum of **3k**.

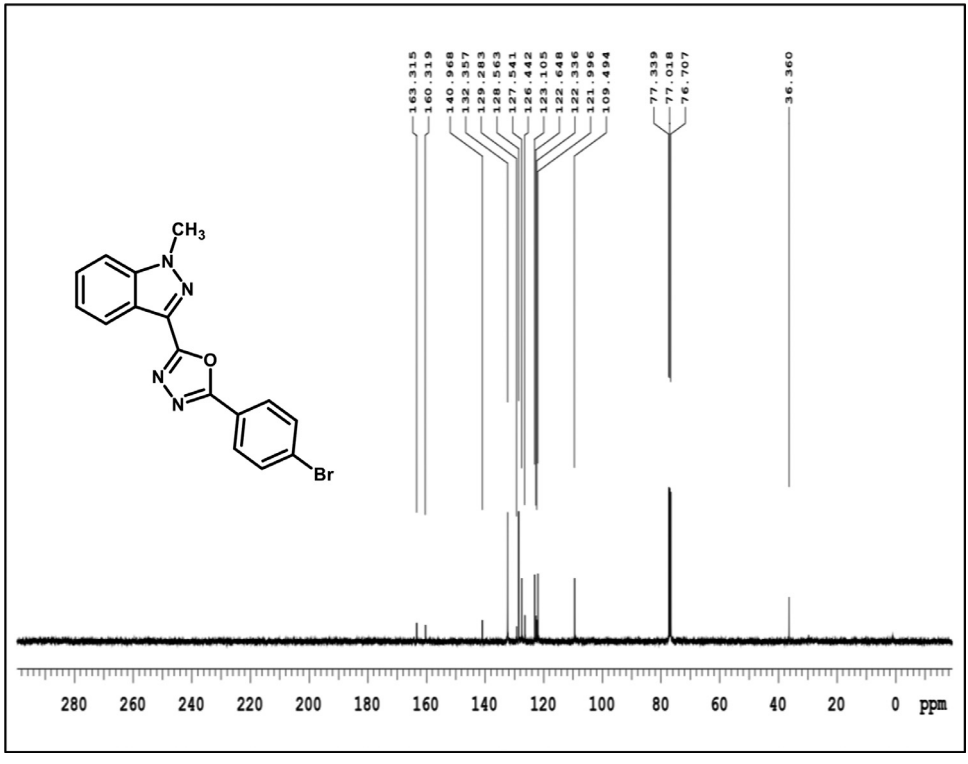


Fig. 37. ^{13}CNMR spectrum of **3k**.

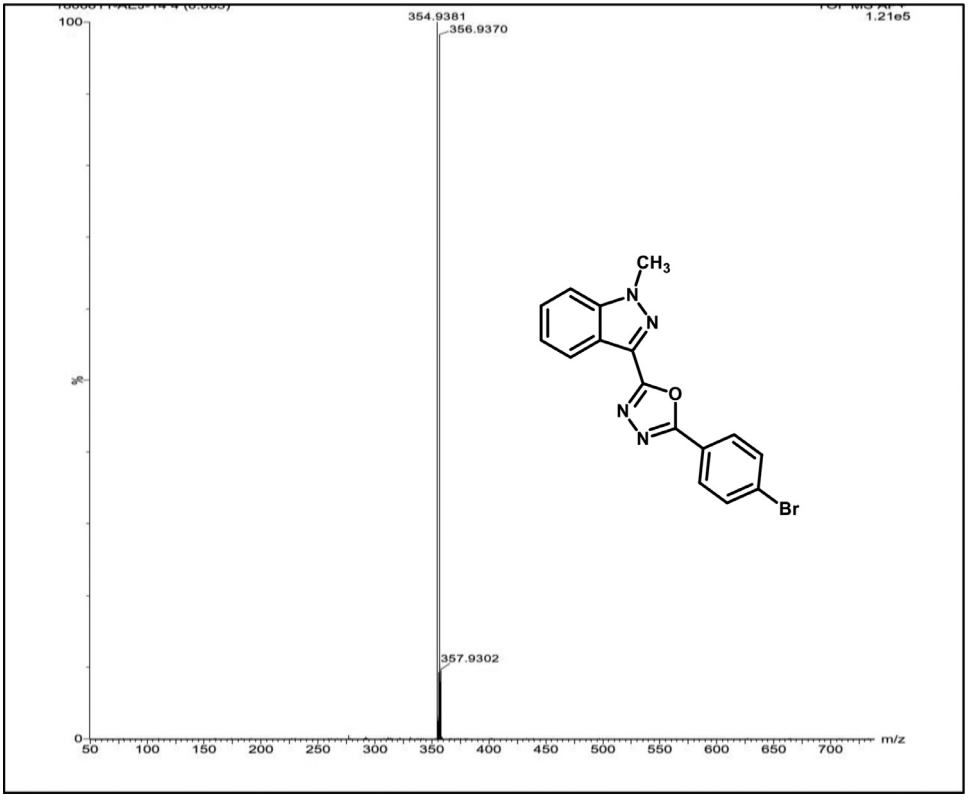


Fig. 38. Mass spectrum of **3k**.

using Waters (USA) connected to W2998 Photo-Diode Array Detector, Column: Syncronis-C18, 4.6 × 150 mm, 5 μm, Mobile Phase-A: 0.1% Formic acid in Water, Mobile Phase-B: Acetonitrile.

The OTDs were screened for their anti-proliferative potency against human hepatocellular carcinoma cell lines (HepG2, HCCLM3) and normal Liver human cell line (LO2) using MTT assay [2].

2.2. General procedure

To a stirred solution of 1-methyl-1H-indazole-3-carboxylic acid (1 gm, 0.0056 mol) in anhydrous ethanol (15 mL). The catalytic amount of conc. Sulfuric acid was added and refluxed for 6 h. The excess of ethanol was concentrated off on a rota-evaporator. The reaction mixture was cooled and the contents of the flask were transferred to a separating funnel containing about 250 mL of distilled water. The synthesized ester was extracted three times with 50 mL Ethyl acetate each. The organic layers were mixed and washed with brine and dried over Sodium sulfate. Ethyl acetate was then distilled off under reduced pressure to get the ester **1** in 89% yield.

To a stirred solution of ethyl 1-methyl-1H-indazole-3-carboxylate **1** (0.5 gm, 0.0024 mol) taken in a round bottom flask containing 250 mL of ethanol, 99% hydrazine hydrate (0.15 mL, 0.0029 mol) was added and refluxed for 6 h. The excess of ethanol and hydrazine hydrate were distilled off under reduced pressure. Ice-cold water was poured into the above reaction mixture and the precipitate so obtained was filtered off and recrystallized from a suitable solvent and the product N-methy indazole-acid hydrazide [3] was obtained in 92% yield.

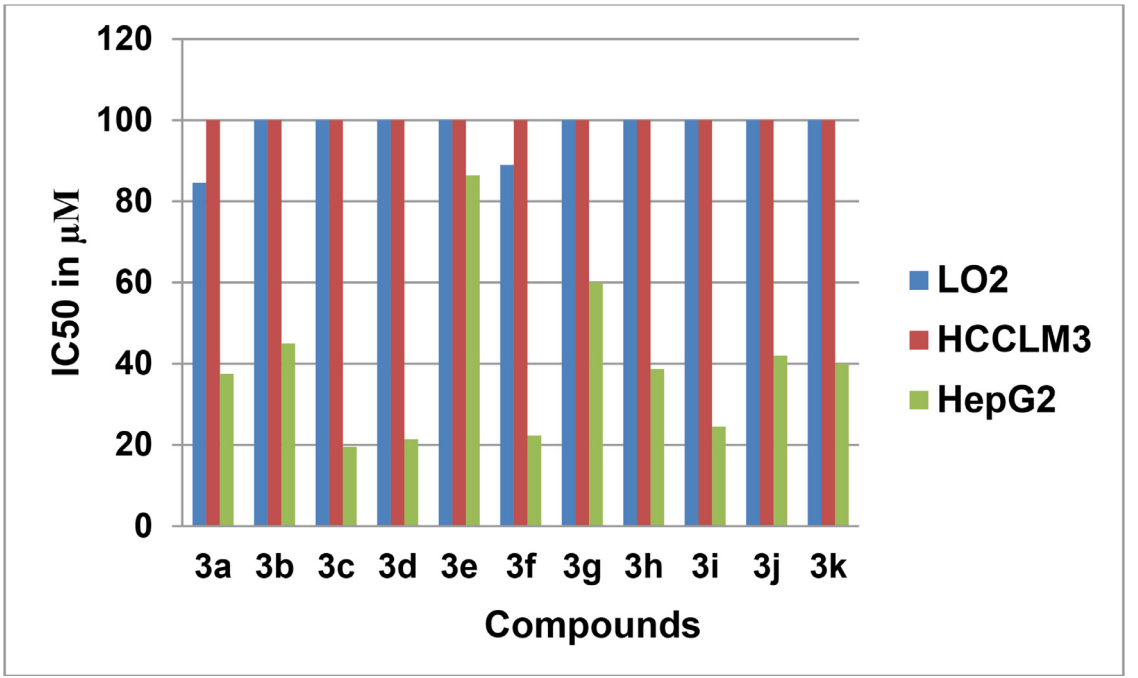


Fig. 39. Anti-proliferative activity of Oxadiazoles as determined by MTT Assay.

2.3. Procedure for the synthesis of 3a-k

A mixture of 1-methyl-1H-indazole-3-carbohydrazide (1eq), different aromatic acids (**2a-k)** (1eq) and phosphorus oxychloride ($POCl_3$) (2 mL) were taken in round bottom flask and refluxed for 8 h. The contents of the reaction mixture were cooled and poured onto the crushed ice. The solid obtained was filtered, treated with potassium carbonate, washed with water and purified by column chromatography using ethyl acetate and hexane as eluent to afford oxadiazoles.

2. 3 characterization data

2-(1-methyl-1H-indazol-3-yl)-5-phenyl-1,3,4-oxadiazole, 3a:
White Solid; mp178–182°C; 81% yield;^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.35(d, J=8.4 Hz, 1H), 8.18–8.16 (m, 2H), 7.44–7.49 (m,5 H), 7.31–7.33 (m, 1H), 4.16 (s, 3H); ^{13}C NMR: 163.05, 159.19, 139.97, 130.74, 128.49, 128.01, 126.49, 126.19, 122.74, 122.01, 121.35, 121.04, 108.45, 35.33; LCMS (ESI): *m/z* Calcd for $C_{16}H_{12}N_4O$ $[M+H]^+$: 277.1044; Found: 277.0432.

2-(2-chlorophenyl)-5-(1-methyl-1H-indazol-3-yl)-1,3,4-oxadiazole, 3b: White solid; mp 160–164°C; 78% yield;^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.08–8.6(m,1H),8.05–7.45 (m,1H), 7.45–7.43 (m,1H),7.42–7.37(m,3H), 7.36–7.31(m,2H) 4.15 (s,3H);^{13}CNMR:161.32,159.56, 139.97,132.34,131.36,130.38,130.21,128.22,126.45,126.03,122.08,122.37,120.90,108.49,35.36; LCMS (ESI): *m/z* Calcd for $C_{16}H_{11}ClN_4O$ $[M+H]^+$: 311.0654; Found:310.9835.

2-(4-methoxyphenyl)-5-(1-methyl-1H-indazol-3-yl)-1,3,4-oxadiazole,3c: Off white solid; mp 196–200°C; 83% yield;^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.39 (d, J=8 Hz,1H), 8.15 (d, J=8. 8 Hz,2H), 7.49–7.45(m,2H),7.37–7.34(m,1H),7.01(d, J=8.8 Hz, 2H),4.20(s,3H),3.87 (s, 3H); ^{13}CNMR:164.00,162.35,159.73,140.94, 128.97, 128.544, 127.44,122.91, 122.28,122.08, 116.24, 114.43,109.42,55.46,36.29;LCMS (ESI): *m/z* Calcd for $C_{17}H_{14}N_4O_2[M+H]^+$: 307.1150; Found:307.0354.

2-(3-chlorophenyl)-5-(1-methyl-1H-indazol-3-yl)-1,3,4-oxadiazole,3d: White solid; mp180–184°C; 86% yield;^{1}H NMR ($CDCl_3$,400 MHz)δ: 8.41(d, J=8.4 Hz,1H), 8.23–8.22(m,1H),8.12 (d J=8 Hz, 1H),7.54–7.46(m,4H), 7.417.37 (m,1H), 4.22(s,3H); ^{13}CNMR: 162.90, 160.47, 141.01, 135.21,131.75,130.36,129.31,127.55,127.09,125.42,125.26,123.13,122.40,122.02,109.47,36.33;LCMS (ESI): *m/z* Calcd for $C_{16}H_{11}ClN_4O[M+H]^+$: 311.0654; Found:310.9835.

4-(5-(1-methyl-1H-indazol-3-yl)-1,3,4-oxadiazol-2-yl)phenol,3e:off white solid; mp170–174°C; 88% yield;^{1}H NMR (DMSO-D6, 400 MHz) δ: 10.24 (s,1H),8.22 (s, 1H), 8.12(d, J=7.2 Hz,1H),7.9(d, J=8 Hz,1H),7.56 (d, J=7.6 Hz,1H),7.29–7.26 (m, 2H), 6.95(d, J=8.4 Hz,2H), 3.87 (s,3H);^{13}C NMR:162.51, 160.89, 137.45, 132.16, 128.70, 124.89, 123.27, 121.86, 120.86, 116.61,114.97, 111.27, 99.03, 33.50;LCMS (ESI): *m/z* Calcd for $C_{16}H_{12}N_4O_2[M+H]^+$: 293.0993; Found:293.0221.

2-(2-bromophenyl)-5-(1-methyl-1H-indazol-3-yl)-1,3,4-oxadiazole,3f:white solid; mp160–165°C; 88% yield;^{1}HNMR($CDCl_3$,400 MHz) δ:8.41(d, J=8.4 Hz,1H), 8.06–8.04(m,1H),7.68–64(m,1H),7.51–7.45(m,3H),7.41–7.35(m,2H),4.21(s,3H);^{13}C NMR:162.85,160.61,140.9, 134.49,132.41,131.80,129.26,127.52,127.43,125.28,123.07,122.38,121.93(2),109.47,36.32;LCMS (ESI): *m/z* Calcd for $C_{16}H_{11}BrN_4O[M+H]^+$: 356.0095; Found:356.9287.

2-(1-methyl-1H-indazol-3-yl)-5-(m-tolyl)-1,3,4-oxadiazole,3 g:off white solid; mp150–152°C; 85% yield;^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.41(d, J=8.4 Hz,1H), 8.04–8.01(m,2H), 7.50–7.34(m,5H), 4.21 (s,3H), 2.44 (s,3H); ^{13}C NMR: 164.21, 160.10, 140.98, 138.89, 132.89, 132.54, 129.57, 128.90, 127.66, 127.47, 124.36, 123.61, 122.61, 122.97, 122.35, 122.08, 109.42, 36.30,29.67;LCMS (ESI): *m/z* Calcd for $C_{17}H_{14}N_4O[M+H]^+$: 291.1201; Found: 291.0395.

2-(1-methyl-1H-indazol-3-yl)-5-(p-tolyl)-1,3,4-oxadiazole,3h:off white solid; mp182–186°C; 83% yield; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.4(d, J=8 Hz,1H), 8.11–8.09 (m,2H), 7.5–7.47(m,2H), 7.38–7.31(m,3H), 4.20(s,3H), 2.43(s,3H); ^{13}C NMR: 164.20, 159.94, 142.30, 140.95,129.71,129.58,127.45,127.14,122.95,122.31,122.07,120.95,109.43,36.30,21.67;LCMS (ESI): *m/z* Calcd for $C_{17}H_{14}N_4O[M+H]^+$: 291.120; Found: 291.0395.

2-(3-bromophenyl)-5-(1-methyl-1H-indazol-3-yl)-1,3,4-oxadiazole,3i: Pale yellow solid; mp172–176°C; 77% yield; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.42–8.37(m,2H),8.17 (d, J=8 Hz, 1H), 7.68 (d, J=8 Hz, 1H),7.52–7.50 (m,2H), 7.437.37 (m,2H), 4.23 (s,3H); ^{13}C NMR: 162.75,160.48,140.99,134.70,130.59,129.92,129.26,127.58,125.72,125.57,123.15,123.08,122.37,122.02, 109.51,36.38;LCMS (ESI): *m/z* Calcd for $C_{16}H_{11}BrN_4O[M+H]^+$: 355.0116; Found: 354.9381.

2-(4-chlorophenyl)-5-(1-methyl-1H-indazol-3-yl)-1,3,4-oxadiazole,3j:off white solid; mp180–186°C; 87% yield;^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.38 (d, J= 8 Hz,1 H), 8 . 1 4 (d, J=8.4 Hz, 2H), 7.50–7.46 (m.4H), 7.38–7.34 (m,1H), 4.02(s,3H); ^{13}C NMR: 163.21,160.30, 140.98, 137.98, 129.38, 128.41, 127.50, 123.06, 122.35, 122.25, 121.99,109.46,36.30;LCMS (ESI): *m/z* Calcd for $C_{16}H_{11}ClN_4O[M+H]^+$: 311.0621; Found: 310.9912.

2-(4-bromophenyl)-5-(1-methyl-1H-indazol-3-yl)-1,3,4-oxadiazole,3k:off white solid; mp184–190°C; 85% yield;^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.39(d, J=8.4 Hz, 1H), 8.09–8.06 (m,2H), 7.68–7.65 (m,2H), 7.501–7.49 (m,2H),7.39–7.35(m,1H),4.21(s,3H);^{13}C NMR:163.31, 160.32, 140.97, 132.36, 129.28, 128.56, 127.54, 126.44, 123.11, 122.65, 122.36, 121.99,109.49,36.36;LCMS (ESI): *m/z* Calcd for $C_{16}H_{11}BrN_4O[M+H]^+$: 356.0095; Found: 356.9370.

Declaration of Competing Interest

The authors declare that they are no known competing financial interests reported in this article.

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References

[1] Dukanya, M.K. Shanmugam, S. Rangappa, P.K. Metri, S. Mohan, Basappa, K.S. Rangappa, Exploring the newer oxadiazoles as real inhibitors of human SIRT2 in hepatocellular cancer cells, Bioorg. Med. Chem. Lett. 30 (2020) 127330, doi:10.1016/j.bmcl.2020.127330.

[2] P. F.McAuliffe, G.B.Mills F.Meric-Bernstam, A.M. Gonzalez-Angulo, Deciphering the role of PI3K/Akt/mTOR pathway in breast cancer biology and pathogenesis, Clin. Breast Cancer 10 (2010) S59–S65, doi:10.3816/CBC.2010.s.013.

[3] M.Patel S.Zakir, M. Farooqui, Synthesis of new α aminophosphonate system bearingIndazole moiety and their biological activity, Eur. J. Med. Chem. 50 (2012) 39–43, doi:10.1016/j.ejmech.2012.01.024.