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Synthesis, Identification and Anticancer Studying of Heterocyclic- Mefenamic Drug Via Thiosemicarbazide

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ABSTRACT

This study involvedsynthesisof (thiadiazole,triazole, thiadiazine, andheterocyclic-azo) andbio-studying of compounds that containing effective groups linked with mefenamicacid drug via cyclizationreaction ofthiosemicarbazide with mefenamicdrug toyieldnew drug- derivatives.All reactions are followedby (TLC) chromatographicand all the synthesized compounds have been identifiedbyusingvariouschemical techniques, like (^{1}H.NMR-spectra,^{13}C.NMR-spectra, FT.IR-spectra), melting points,physical propertiesand studying ofits effectonbreast cancer cells.

KEYWORDS

Mefenamic Acid Drug,Heterocyclic, Anticancer Studying,Breast Cancer, Thiadiazole, Triazole, Thiosemicarbazide, Thiadiazine, Azo.

Introduction

Mefenamicdrugis a derivative of anthranilic acid [1, 2],and is a non-steroidal anti-inflammatory (NSAIDs) that inhibits the action oftwo different types of ring oxidative enzymes (COX-2), (COX-1), and thus inhibits the production of prostaglandins (PGs) as the main cause of inflammation, pain and swelling [3-10].Heterocyclic compounds are one of the most important and largest types of organic compounds [11-16], covering about 65% of published research on organic chemistry[17-22], and methods of preparation for this type of compound have evolved using catalysts [23-30]. It has been reported that 1,2,4-triazole compounds and their derivatives possess a wide range[31-38] of bio activities being antimicrobial[39-41], anti-inflammatory, anti-inflammatory, antiviral, antifungal, analgesic, antihypertensive, tumor, anti-HIV andantioxidant [24-26].

ExperimentalandApparatuses

All chemicals used (purity 99.99 %), FT.IR-spectra: were recorded on Shimadzu 8300, KBr-disc, ^{1}HNMR-spectrawererecordedonvarian300MHZ spectrometerusingTMSas an internal standard, ^{13}C.NMR–spectra weremadein Kashan University, The Melting points were determined onGallenkamp M.F.B 600-010f melting point apparatus.

Synthesis ofMefenamicDrug Derivatives [1-3]

Treatment of mefenamic acid(0.01 mol) and thiosemicarbazide (0.01 mol) in the presence of ethanol absolute with (2 ml)sulfuric acid and then refluxing the mixture for (25 h) at (78ºC), the precipitate was filtered and dried with recrystallized presence of absolute ethanol to yield in the 78% of compound **[1]**, which (0.01 mol) of compound**[1]** coupling reaction (azotation step) with (0.01 mol) ofbenzene-1,4-diamine (p-phenylene diamine) the precipitate was filtered and dried with recrystallized to yield 80% of compound**[2]**, A mixture(0.01 mol) of compound **[2]** with (0.01mol) of copper acetatein the presence ofabsolute ethanol andrefluxed (3 hrs), the precipitate was filtered and dried with recrystallized to yield 74% of compound **[3]**accordingto studies (9-14).

Synthesis ofMefenamicDrug Derivatives[4-8]

Treatment of mefenamic acid (0.01 mol) and thiosemicarbazide (0.01 mol) in the presence of ethanol absolute with (8ml) sodium hydroxide and then refluxing the mixture for (25h) at (78ºC), the precipitate was filtered and dried with recrystallized presence of absolute ethanol to yield in the 70% of compound **[4]**, which (0.01 mol) of compound**[4]** react with (15ml) of bromo acetyl bromide in the presence ofpotassium carbonate with constant stirringfor (6h), the precipitate was filtered and dried with recrystallized to yield 78% of compound **[5]**, which (0.01 mol) of compound **[5]** coupling reaction (azotation step) with (0.01 mol) of4-aminoantipyrine the precipitate was filtered and dried with recrystallized to yield 80% of compound **[6]**, also taken (0.01 mol) of compound **[5]** coupling reaction (azotation

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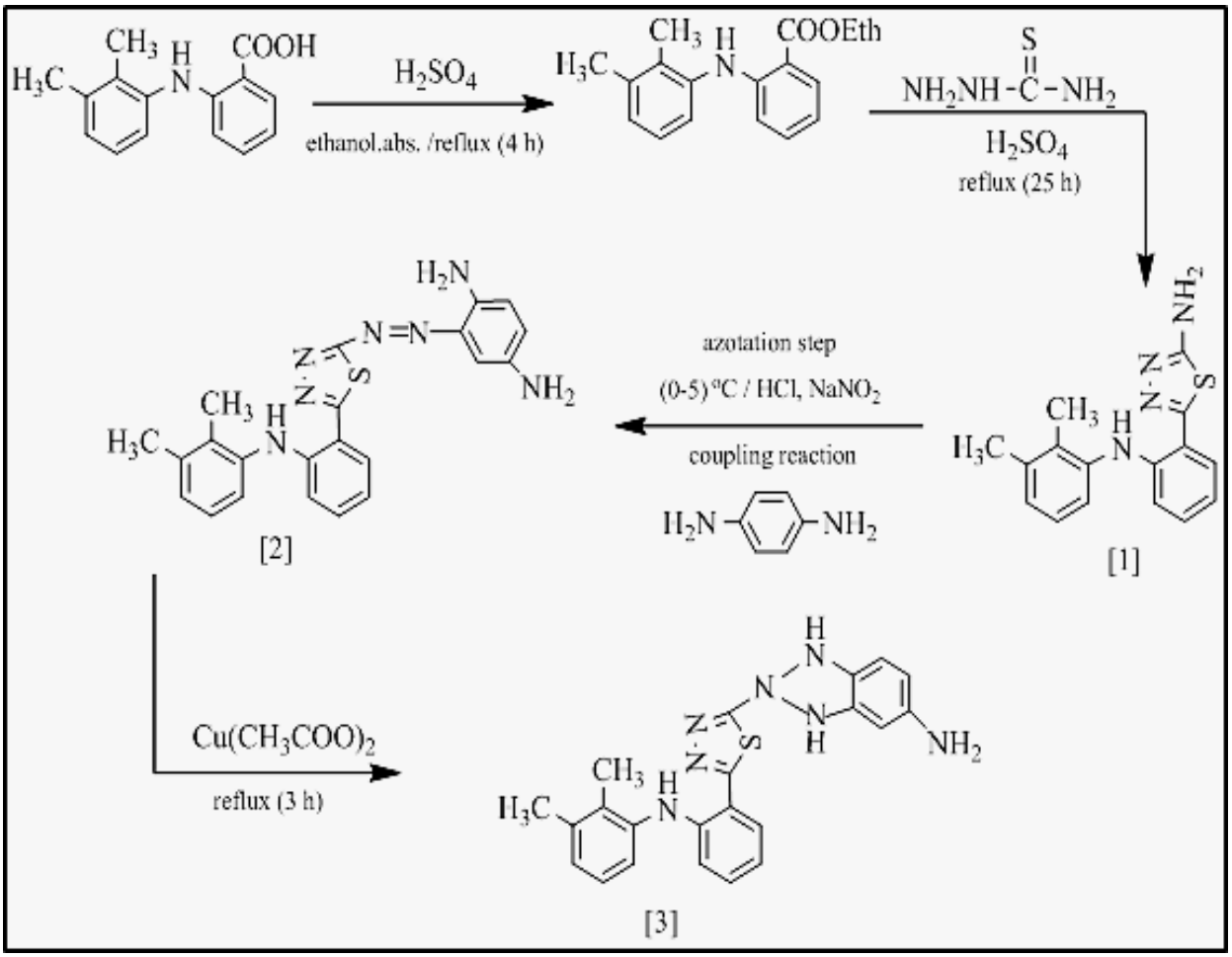
step) with (0.01 mol) of2-aminopyridine the precipitate was filtered and dried with recrystallized to yield 82% of compound **[7]**, also mixture (0.01 mol) of compound **[5]** coupling reaction (azotation step) with(0.01 mol) of2-aminophenol the precipitate was filtered and dried with recrystallized to yield 78% of compound **[8]**accordingto studies [(9-14)].

Synthesis ofMefenamicDrug Derivatives[9-11]

Treatment ofbenzil (0.01 mol) and thiosemicarbazide (0.01 mol) in the presence of ethanol absolute with (2ml)sulfuric acid and then refluxing the mixture for (10 h) at (78ºC), the precipitate was filtered and dried with recrystallized presence of absolute ethanol to yield in the 78% of compound **[9]**, which (0.01 mol) of compound **[9]** coupling reaction (azotation step) with (0.01 mol) ofbenzene-1,4-diamine (p-phenylene diamine) the precipitate was filtered and dried with recrystallized to yield 80% of compound [10], A mixture(0.01 mol) of compound **[10]** with (0.01mol) of copper acetate in the presence of absolute ethanol and refluxed (3h), the precipitate was filtered and dried with recrystallized to yield 82% of compound **[11]**accordingto studies [(9-14)].

Synthesis ofMefenamicDrug Derivative[12]

Treatment (0.01 mol) ofmefenamic acid and (0.01 mol) of compound **[9]**in the presence of ethanol absolute and then refluxing the mixture for (5 h) at (78ºC), the precipitate was filtered and dried with recrystallized presence of absolute ethanol to yield in the 78% of compound **[12],**accordingto studies [(9-14)].



Scheme 1. Preparation of Mefenamic Drug -Derivatives[1-3]

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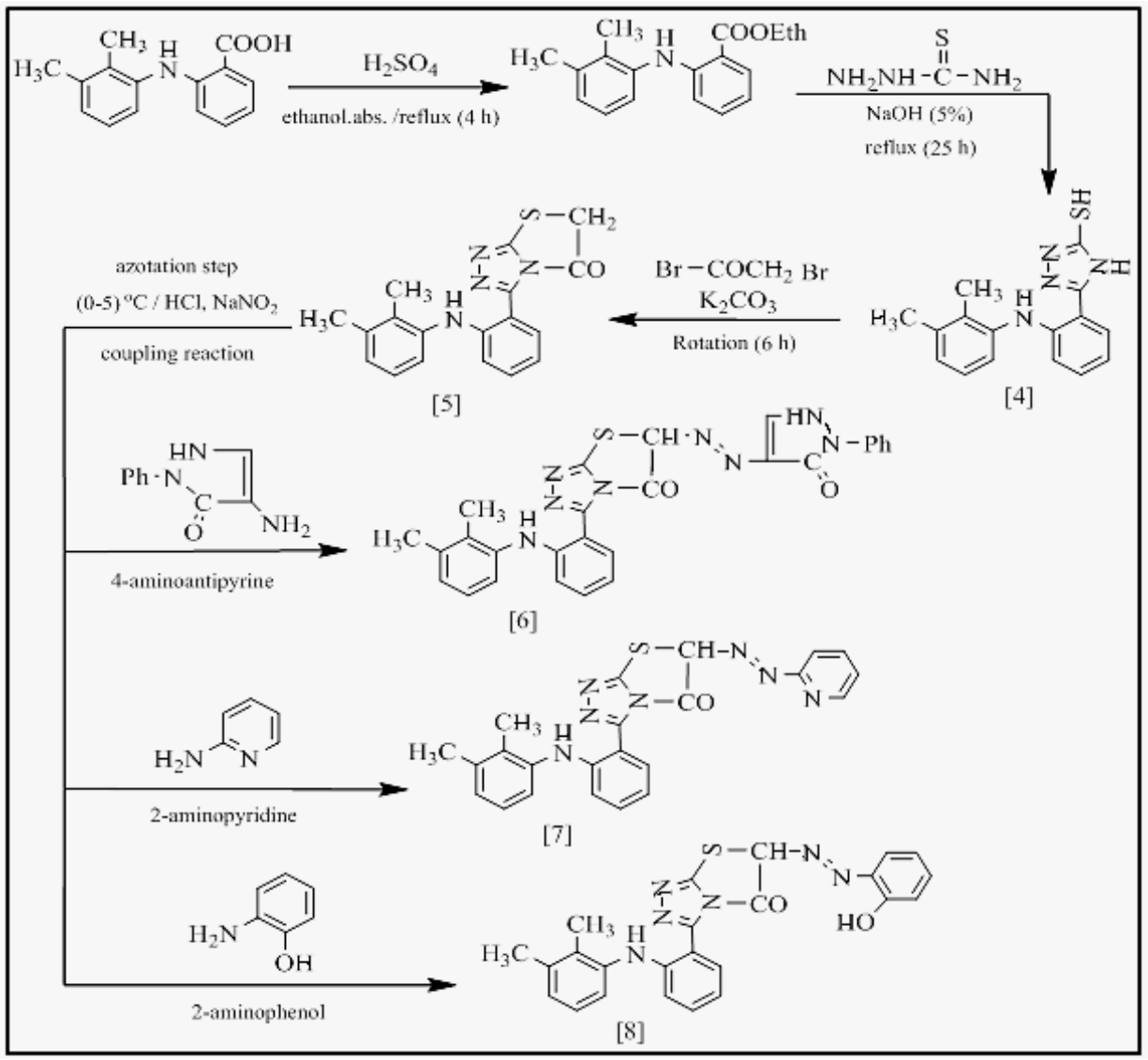
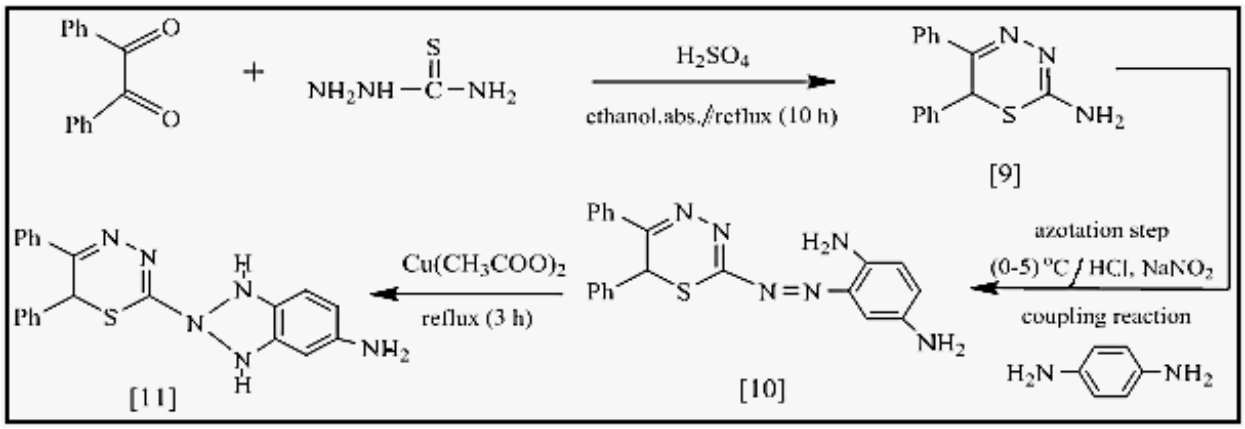


Scheme 2. Preparation of Mefenamic Drug -Derivatives [4-8]



Scheme 3. Preparation of Derivatives [9-11]

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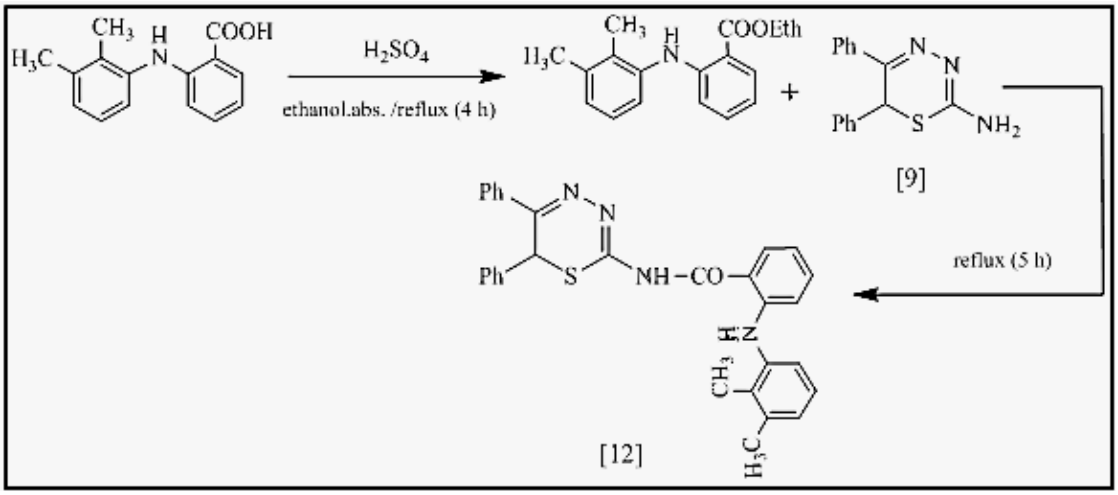

Scheme 4. Preparation of Mefenamic Drug -Derivative[12]

ResultsandDiscussion

FT.IR-spectra

The spectra showed absorption bands at (3444,3350) cm^{-1} due to (NH_2), absorption band at (3205) cm^{-1} due to (NH), absorption band at (1651) cm^{-1} due to (C=N) endo cycle of thiadiazole, absorption band at (750) cm^{-1} due to (C-S), absorption band at (2983) cm^{-1} due to (C-H) aliphatic, absorption band at (3000) cm^{-1} due to (C-H) aromatic in compound **[1]**, absorption band at (3387,3354) cm^{-1} due to (NH_2), absorption band at (3261) cm^{-1} due to (NH), absorption band at (1622) cm^{-1} due to (C=N) endocycle ofthiadiazole, absorption band at (746) cm^{-1} due to (C-S), absorption band at (2999) cm^{-1} due to (C-H) aliphatic, absorption band at (3088) cm^{-1} due to (C-H) aromatic, absorption band at (1467,1502) cm^{-1} due to (-N=N-) azo in compound **[2]**,absorption band at (3442,3372) cm^{-1} due to (NH_2), absorption band at (3288) cm^{-1} due to (NH), absorption band at (1676) cm^{-1} due to (C=N) endocycle ofthiadiazole, absorption band at (750) cm^{-1} due to (C-S), absorption band at (2990) cm^{-1} due to (C-H) aliphatic, absorption band at (3080) cm^{-1} due to (C-H) aromatic in compound **[3]**.Showed appearance absorption bends at (3409) cm^{-1} due to (NH), absorption band at (2264) cm^{-1} due to (SH) thiol, absorption band at (1658) cm^{-1}due to (C=N) endocycle of triazole, absorption band at (2978) cm^{-1} due to (C-H) aliphatic, absorption band at (3080) cm^{-1} due to (C-H) aromatic in compound **[4]**, absorption band at (3421) cm^{-1} due to (NH), absorption band at (1653) cm^{-1} due to (CO-N) carbonyl of amide, absorption band at (1222) cm^{-1} due to (CH_2-S), absorption band at (1614) cm^{-1} due to (C=N) endocycle of triazole, absorption, absorption band at (2993) cm^{-1} due to (C-H) aliphatic, absorption band at (3050) cm^{-1} due to (C-H) aromaticin compound **[5]**, absorption bends at (3444) cm^{-1} due to (NH), absorption band at (1662) cm^{-1} due to (CO-N) carbonyl of amide, absorption band at (1222) cm^{-1} due to (CH-S), absorption band at (1384,1463)cm^{-1} due to (-N=N-) azo, absorption band at (1643) cm^{-1} due to (C=N) endocycle of triazole, absorption, absorption band at (2999) cm^{-1} due to (C-H) aliphatic, absorption band at (3000) cm^{-1} due to (C-H) aromatic in compound **[6]**, absorption band at (3238) cm^{-1} due to (NH), absorption band at (1660) cm^{-1} due to (CO-N) carbonyl of amide, absorption band at (1246) cm^{-1} due to (CH-S), absorption band at (1442,1475)cm^{-1} due to (-N=N-) azo, absorption band at (1643) cm^{-1} due to (C=N) endocycle of triazole, absorption, absorption band at (2920) cm^{-1} due to (C-H) aliphatic, absorption band at (3059) cm^{-1} due to (C-H) aromatic in compound**[7]**,absorption bend at (3410) cm^{-1} due to (OH) hydroxyl of phenol, absorption band at (3172) cm^{-1} due to (NH), absorption band at (1662) cm^{-1} due to (CO-N) carbonyl of amide, absorption band at (1280) cm^{-1} due to (CH-S) sulfide, absorption band at (1460,1475) cm^{-1} due to (-N=N-) azo, absorption band at (1618) cm^{-1} due to (C=N) endocycle of triazole, absorption, absorption band at (2991) cm^{-1} due to(C-H) aliphatic, absorption band at (3088) cm^{-1} due to (C-H) aromatic in compound**[8]**. Showed appearance absorption bend at (3442,3381) cm^{-1} due to (NH_2),absorption band at (1692) cm^{-1} due to (C=N) endocycle of thiadiazine, absorption band at (1267) cm^{-1} due to (CH-S) sulfide, absorption band at (3000) cm^{-1} due to (C-H) aromatic in compound**[9]**,absorption bend at (3344,3311) cm^{-1} due to (NH_2), absorption band at (1443,1444) cm^{-1} due to (-N=N-) azo,absorption band at (1653) cm^{-1} due to (C=N) endocycle of thiadiazine, absorption band at (1255) cm^{-1} due to (CH-S) sulfide, absorption band at (3088) cm^{-1} due to (C-H) aromatic in compound **[10]**, absorption bend at (3365,3286) cm^{-1} due to (NH_2), absorption band at (3174) cm^{-1} due to (NH),absorption band at (1618) cm^{-1} due to (C=N) endocycle of thiadiazine, absorption band at (1205) cm^{-1} due to (CH-S) sulfide, absorption

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band at (2999.6) cm^{-1} due to (C-H) aromaticin compound **[11]**. Showed appearance absorption band at (3412) cm^{-1} due to (NH), absorption band at (3155) cm^{-1} due to (NH) amine of amide, absorption band at (1662) cm^{-1} due to (CO-N) carbonyl of amide, absorption band at (1618) cm^{-1} due to (C=N) endocycle of thiadiazine, absorption band at (1238) cm^{-1} due to (CH-S) sulfide, absorption band at (2991) cm^{-1} due to (C-H) aliphatic, absorption band at (3068) cm^{-1} due to (C-H) aromatic in compound **[12]**.

Table 1.FT.IR-data (cm^{-1}) of compounds [1-12]

Comp.	(C=N) endocycle	(NH)	(CO-N)	Other groups
1	1651	3205	------	(NH_2): 3444,3350., (C-S) endocycle:750., (CH) aliph:2983. (CH)arom:3000
2	1622	3261	------	(NH_2): 3387,3354., (C-S) endocycle:746.,(-N=N-) azo:1467,1502. (CH) aliph:2999. (CH)arom:3088
3	1676	3288	------	(NH_2): 3442,3372. (C-S) endocycle:750., (CH) aliph:2990. (CH)arom:3080
4	1637	3409	------	(SH) thiol:2264.,(CH) aliph:2978., (CH)arom:3080
5	1614	3412	1653	(CH_2-S):1222., (CH) aliph:2993., (CH) arom:3050
6	1643	3444	1662	(CH-S):1222.,(-N=N-) azo:1384,1463.,(CH) aliph:2993.,(CH) arom:3050
7	1612	3238	1660	(CH-S):1246.(-N=N-) azo:1442,1475.,(CH) aliph:2920. (CH) arom:3059
8	1618	3172	1662	(OH) phenol:3414.(CH-S):1280., (-N=N-) azo:1460,1475.(CH) aliph:2991. (CH) arom:3088
9	1629	------	------	(NH_2):3442,3381.(CH-S) sulfide:1267.,(CH) arom:3000
10	1653	------	------	(NH_2):3344,3311.(-N=N-) azo:1443,1444.,(CH-S) sulfide:1255. (CH) arom:3097
11	1618	3174	------	(NH_2):3465,3286. (CH-S) sulfide:1205., (CH) arom:2999.6
12	1618	3412	1662	(NH) amide:3155.(CH-S) sulfide:1238., (CH) aliph:2991. (CH) arom:3068

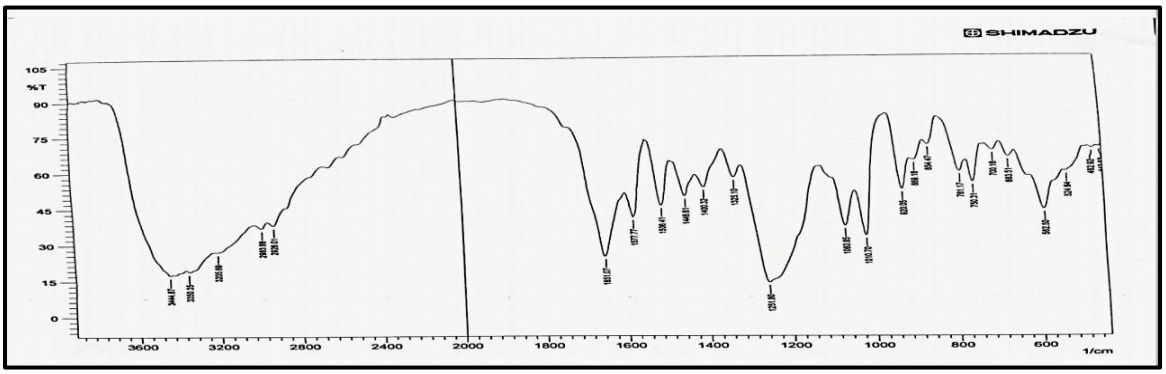

Fig. 1.FT.IR of Compound [1]

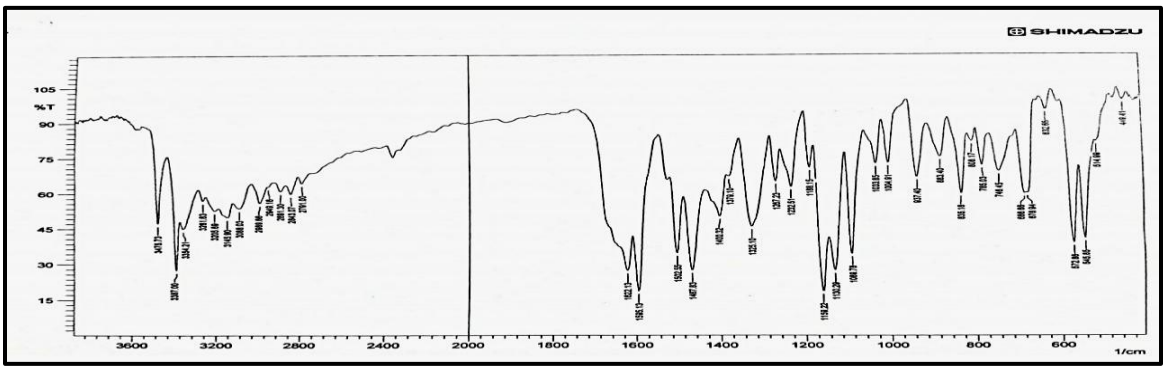

Fig. 2. FT.IR of Compound [2]

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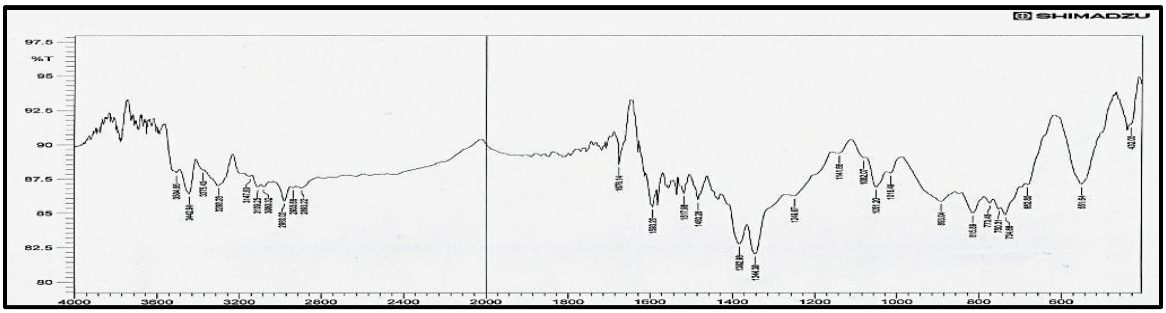

Fig. 3. FT.IR of Compound [3]

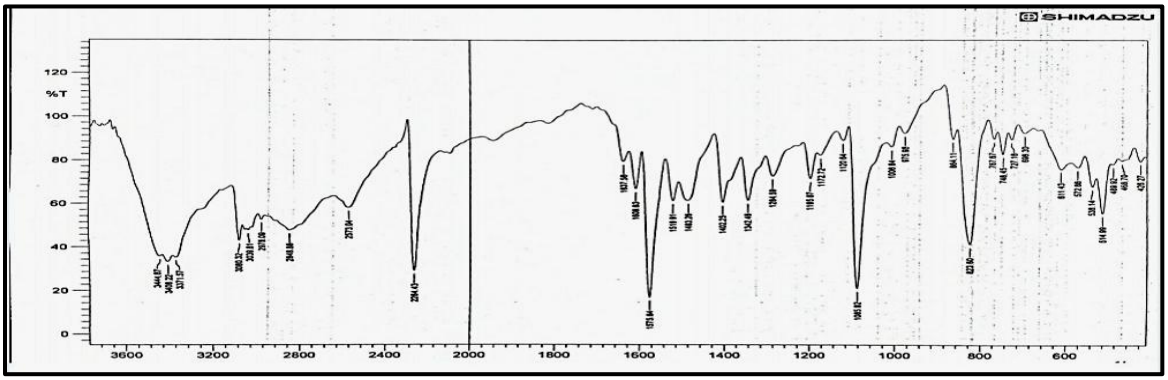

Fig. 4. FT.IR of Compound [4]

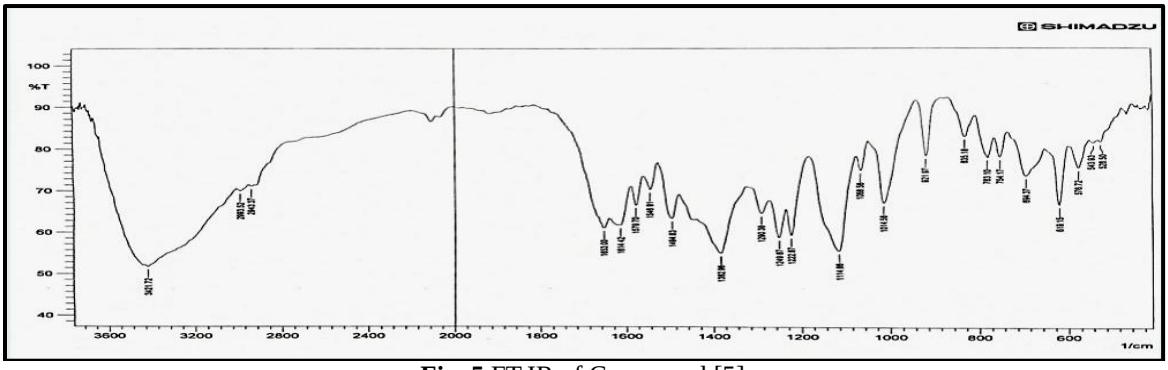

Fig. 5.FT.IR of Compound [5]

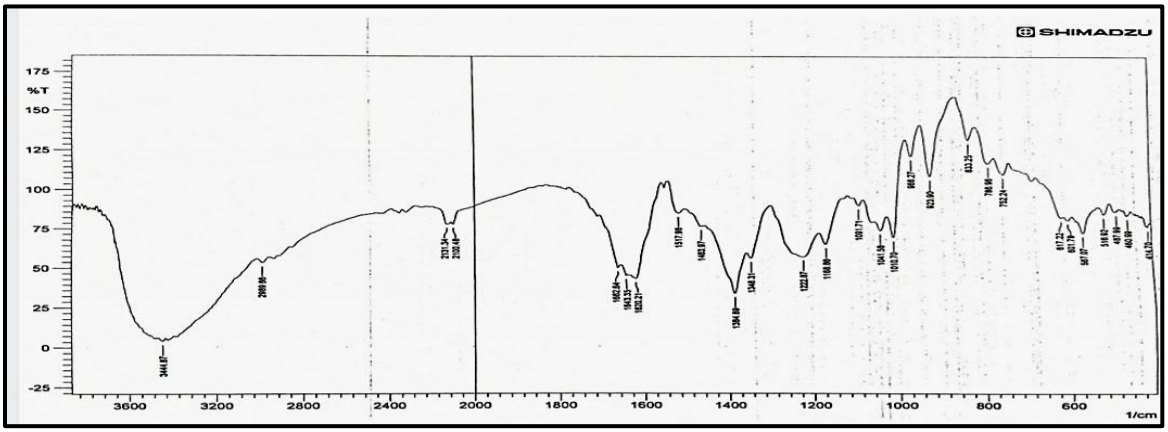

Fig. 6. FT.IR of Compound [6]

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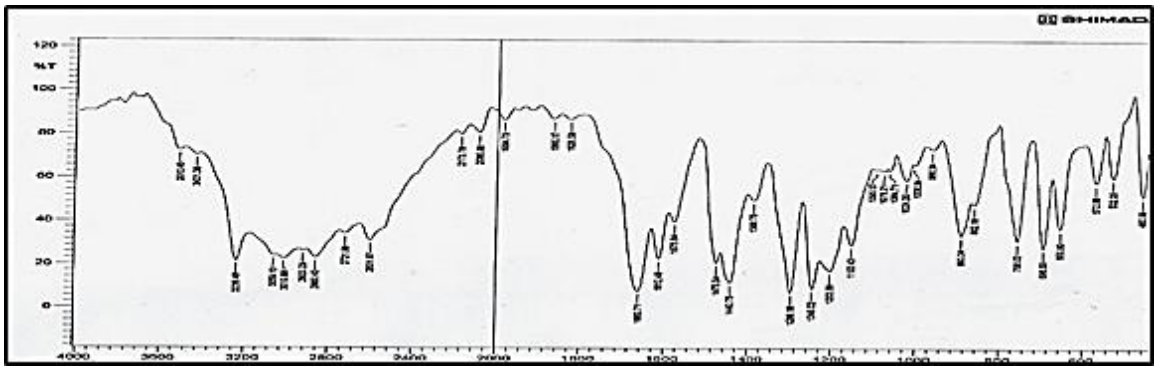

Fig. 7. FT.IR of Compound [7]

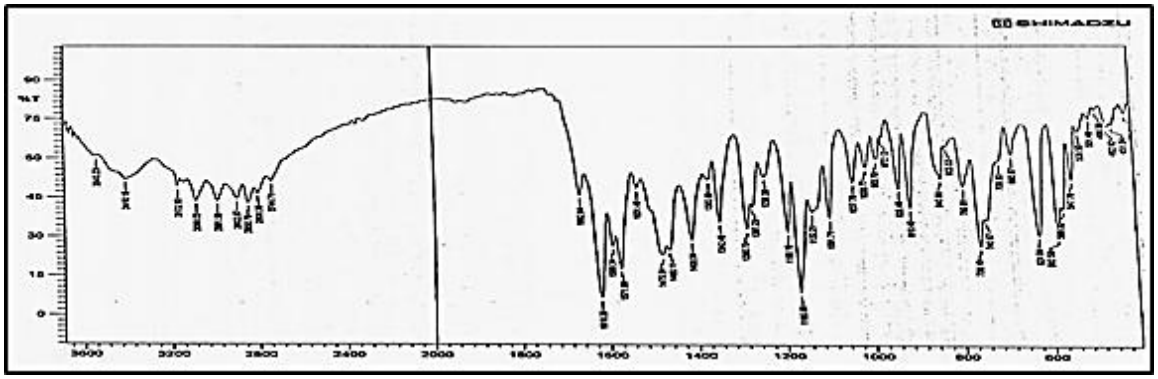

Fig. 8. FT.IR of Compound [8]

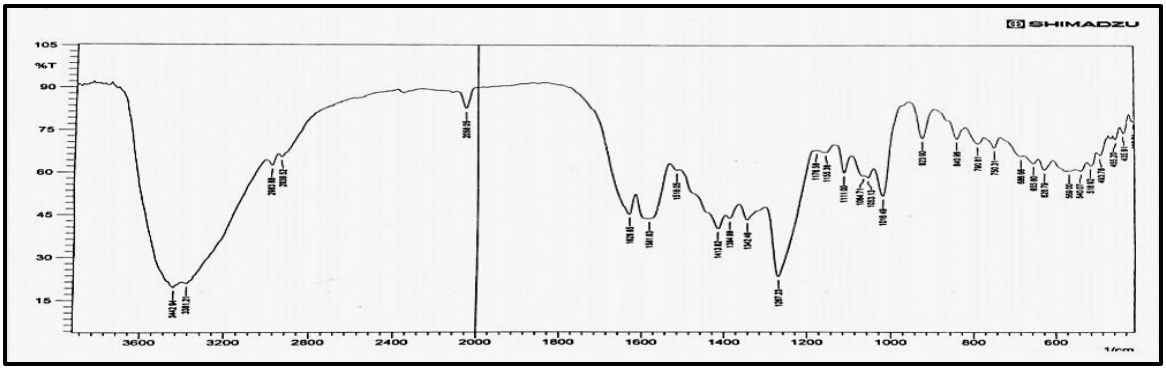

Fig. 9. FT.IR of Compound [9]

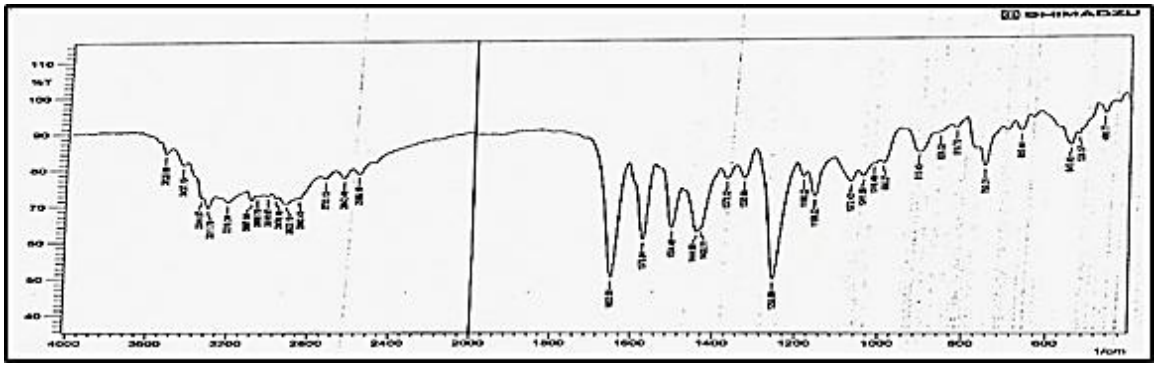

Fig. 10.FT.IR of Compound [10]

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 8521 - 8537
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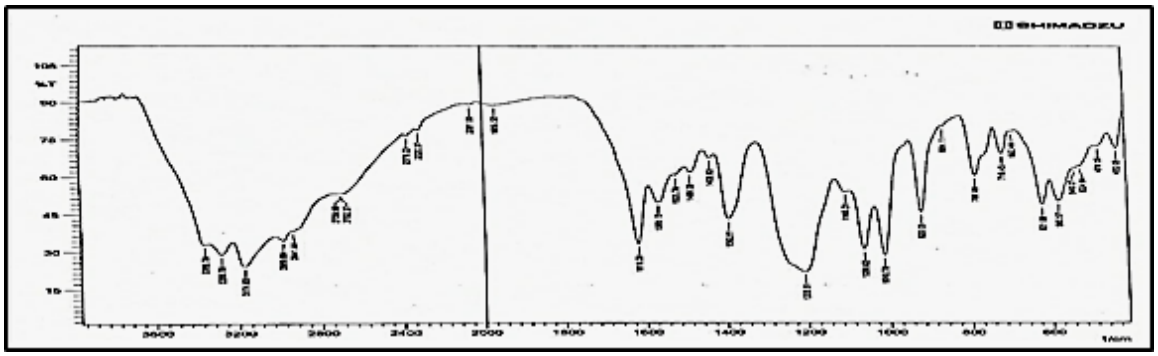

Fig. 11. FT.IR of Compound [11]

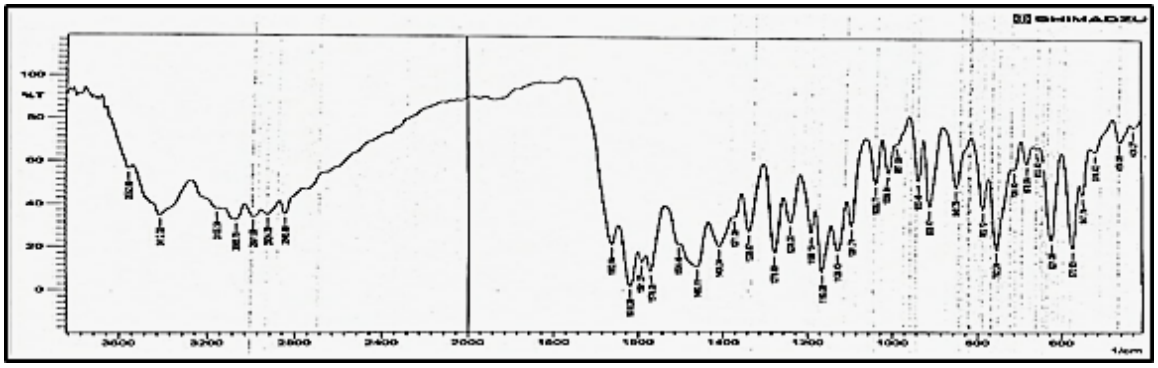

Fig. 12.FT.IR of Compound [12]

The ^{1}H.NMR Spectra

The spectra appeared signals at { δ(1.23,1.12) for protons of methyl groups (CH_3) and δ(5.10) for proton ofamine group (NH) and δ(5.32) for protons ofamine group (NH_2) andδ(7.15,6.82) for protons of aromatic rings }in compound **[1]**., which converted to signals at {δ(1.20,0.90) for protons of methyl groups (CH_3) and δ(4.48) for proton ofamine group (NH) and δ(5.50) and other (5.20) for protons ofamine group (NH_2) in (ortho, para) site andδ(7.50,6.76) for protons of aromatic rings } in compound **[2]**., which converted to signals at {δ(1.21,0.90) for protons of methyl groups (CH_3) and δ(4.50) for proton ofamine group (NH) and δ(4.21) for proton ofamine group (NH) endocycle of triazole and δ(5.12) for protons ofamine group (NH_2) andδ(7.89,6.67) for protons of aromatic rings } in compound **[3]**., which converted to signals at { δ(5.11) for proton ofthiol group (SH) and δ(5.49) for proton ofamine group (NH) endocycle of triazole and δ(4.57) for proton of amine group (NH) and δ(1.35,1.23) for protons of methyl groups (CH_3) and δ(7.50,7.13) for protons of aromatic ring } in compound **[4]**,which converted to signals at { δ(3.77) for protons ofmethylene group (CO-CH_2-S) and δ(4.72) for proton of amine group (NH) and δ(1.10,1.0) for protons of methyl groups (CH_3) and δ(8.0,7.16) for protons of aromatic ring } in compound **[5]**.,which converted to signals at { δ(3.10) for proton ofmethylene group (CO-CH-N=N) and δ(3.77) for proton of amine group (NH) and δ(1.29,1.0,0.95) for protons of methyl groups (CH_3) and δ(7.55,6.62) for protons of aromatic ring } in compound **[6]**, which converted to signals at { δ(3.72) for proton ofmethylene group (CO-CH-N=N) and δ(3.55) for proton of amine group (NH) and δ(1.09,1.03) for protons of methyl groups (CH_3) and δ(7.97,6.99) for protons of aromatic ring } in compound **[7]**., which converted to signals at{δ(11.75) for proton ofhydroxyl group (OH) of phenol and δ(3.75) for proton ofmethylene group (CO-CH-N=N) and δ(4.30) for proton of amine group (NH) and δ(2.04,1.09) for protons of methyl groups (CH_3) and δ(7.88,6.75) for protons of aromatic rings } in compound **[8]**.,which converted to signals at { δ(5.42) for protons ofamine group (NH_2) and δ(3.71) for proton ofmethylene group (-S-CH-C=N-) endocycle of thiadiazine andδ(7.70,7.40) for protons of aromatic rings } incompound **[9].**, which converted to signals at { δ(5.11) and other (5.32) for protons ofamine group (NH_2) in (ortho, para) siteand δ(3.67) for proton ofmethylene group (-S-CH-C=N-) endocycle of thiadiazine andδ(7.80,7.12) for protons of aromatic rings } in compound **[10]**.,which converted to signals at { δ(4.56) for proton ofamine group (NH) endocycle of triazole and δ(5.21) for protons ofamine group (NH_2) andδ(3.75) for proton ofmethylene group (-S-CH-C=N-) endocycle of thiadiazine and δ(7.40,6.80) for protons of aromatic rings } in compound **[11]**., which converted to signals at {δ(1.19,1.04) for protons of methyl groups (CH_3) and δ(4.96) for proton ofamine group (NH) and δ(9.10) for protonofamide group(-

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CO-NH) and δ(3.33) for proton ofmethylene group (-S-CH-C=N-) endocycle of thiadiazine and δ(7.51,6.68) for protons of aromatic rings } in compound **[12]**.

Table 2.[1]H.NMR- data (δ or ppm) of Compounds

Comp.	[1]H.NMR ((Important Peaks))
1	(1.23,1.12) for protons (CH_3).,(5.10) for proton (NH).,(5.32) for protons (NH_2)., (7.15,6.82) for protons of aromatic rings.
2	(1.20,0.90) for protons (CH_3).,(4.48) for proton (NH).,(5.50,5.20) for protons (NH_2).,(7.50,6.76) for protons of aromatic rings.
3	(1.21,0.90) for protons (CH_3).,(4.50) for proton (NH).,(4.21) for proton (NH) endocycle of triazole.,(5.12) for protons (NH_2).,(7.89,6.67) for protons of aromatic rings.
4	(5.11) for proton (SH).,(5.49) for proton (NH) endocycle of triazole.,(4.57) for proton(NH).,(1.35,1.23) for protons (CH_3).,(7.50,7.13) for protons of aromatic ring.
5	(3.77) for protons ($CO-CH_2-S$).,(4.72) for proton (NH).,(1.10,1.0) for protons (CH_3)., (8.0,7.16) for protons of aromatic ring.
6	(3.10) for proton (CO-CH-N=N).,(3.77) for proton (NH).,(1.29,1.0,0.95) for protons(CH_3).,(7.55,6.62) for protons of aromatic ring.
7	(3.72) for proton (CO-CH-N=N).,(3.55) for proton (NH).,(1.09,1.03) for protons (CH_3)., (7.97,6.99) for protons of aromatic ring.
8	(11.75) for proton (OH) of phenol.,(3.75) for proton (CO-CH-N=N).,(4.30) for proton (NH).,(2.04,1.09) for protons (CH_3).,(7.88,6.75) for protons of aromatic rings.
9	(5.42) for protons (NH_2).,(3.71) for proton (-S-CH-C=N-) endocycle of thiadiazine., (7.70,7.40) for protons of aromatic rings.
10	(5.11) and other (5.32) for protons (NH_2) in (ortho, para) site.,(3.67) for proton(-S-CH-C=N-) endocycle of thiadiazine.,(7.80,7.12) for protons of aromatic rings.
11	(4.56) for proton (NH) endocycle of triazole.,(5.21) for protons (NH_2).,(3.75) for proton (-S-CH-C=N-) endocycle of thiadiazine.,(7.40,6.80) for protons of aromatic rings.
12	(1.19,1.04) for protons (CH_3).,(4.96) for proton (NH).,(9.10) for proton (-CO-NH)., (3.33) for proton (-S-CH-C=N-) endocycle of thiadiazine.,(7.51,6.68) for protons of aromatic rings.

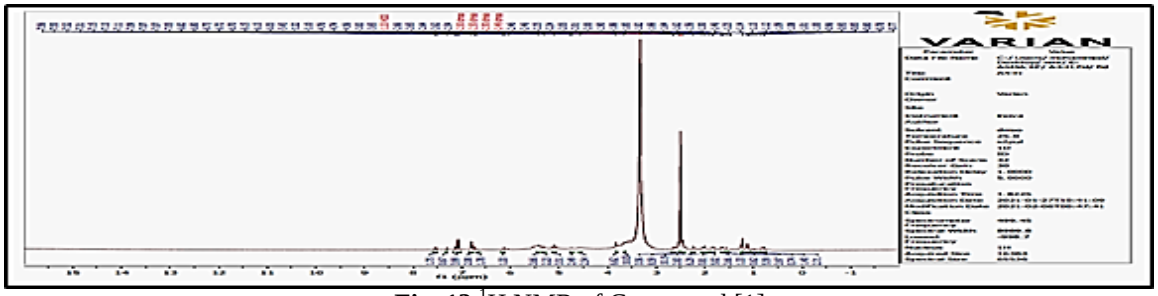

Fig. 13.[1]H.NMR of Compound [1]

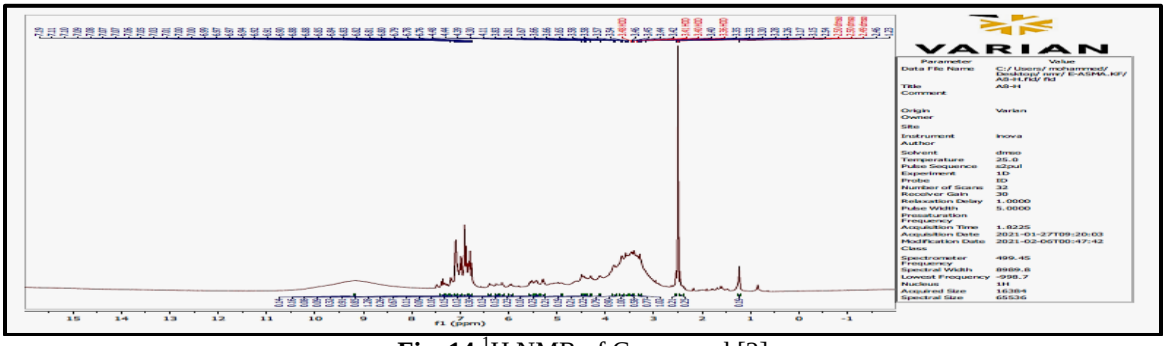

Fig. 14.[1]H.NMR of Compound [2]

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 8521 - 8537
Received 16 February 2021; Accepted 08 March 2021.

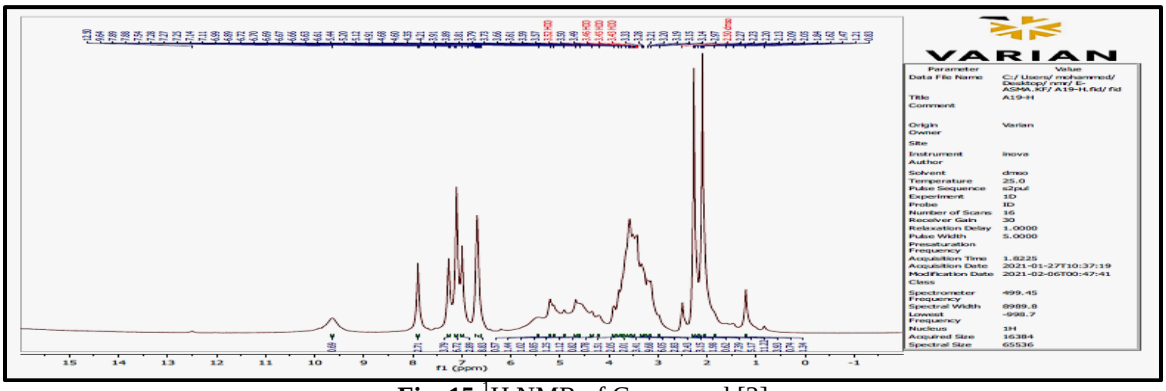

Fig. 15.[1]H.NMR of Compound [3]

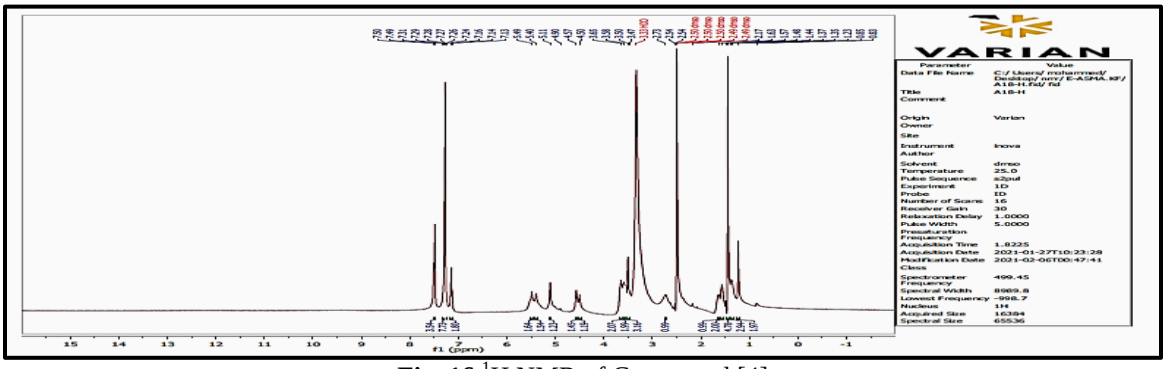

Fig. 16.[1]H.NMR of Compound [4]

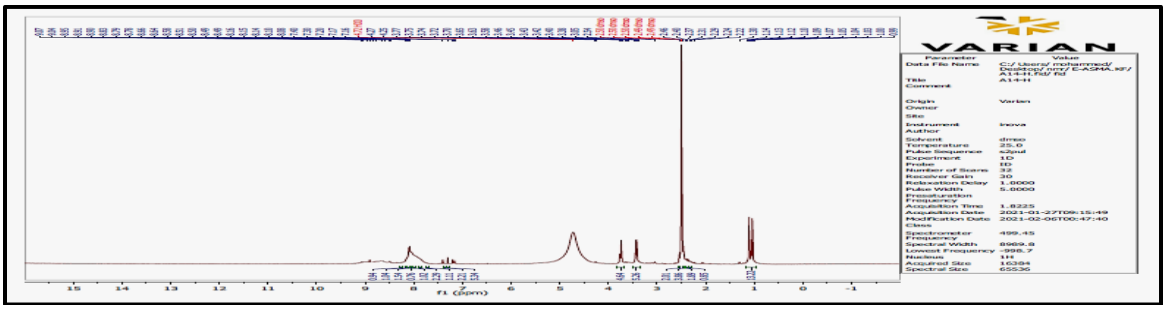

Fig. 17.[1]H.NMR of Compound [5]

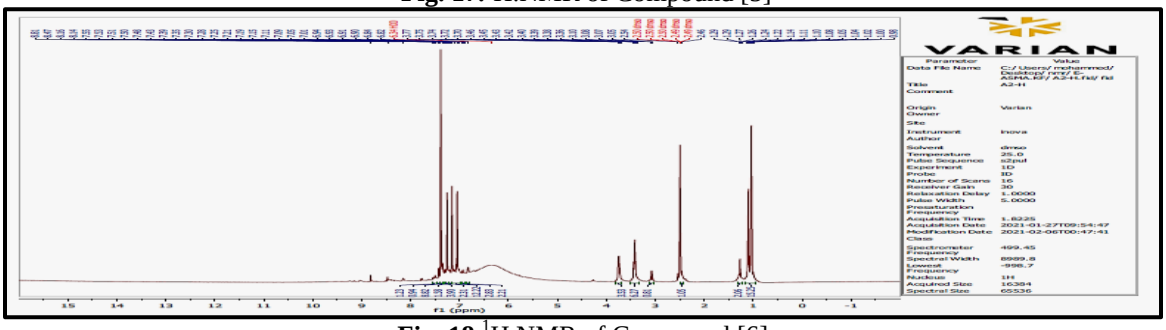

Fig. 18.[1]H.NMR of Compound [6]

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 8521 - 8537
Received 16 February 2021; Accepted 08 March 2021.

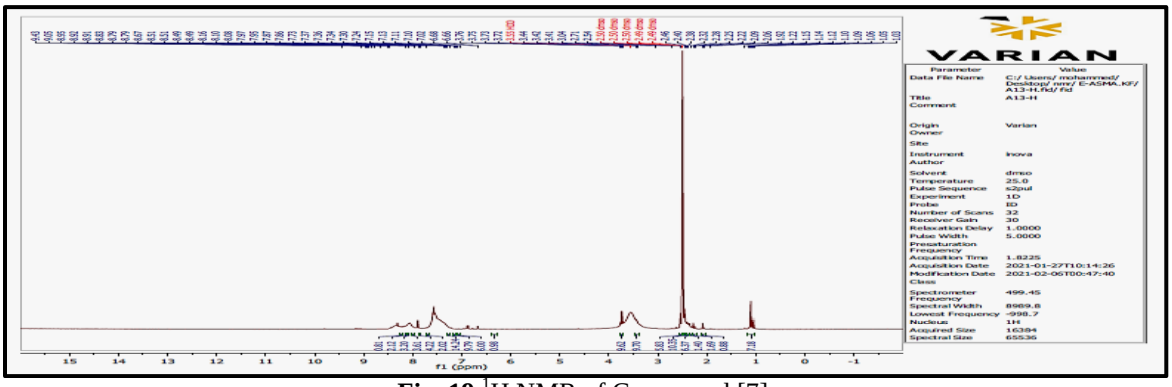

Fig. 19. ^{1}H.NMR of Compound [7]

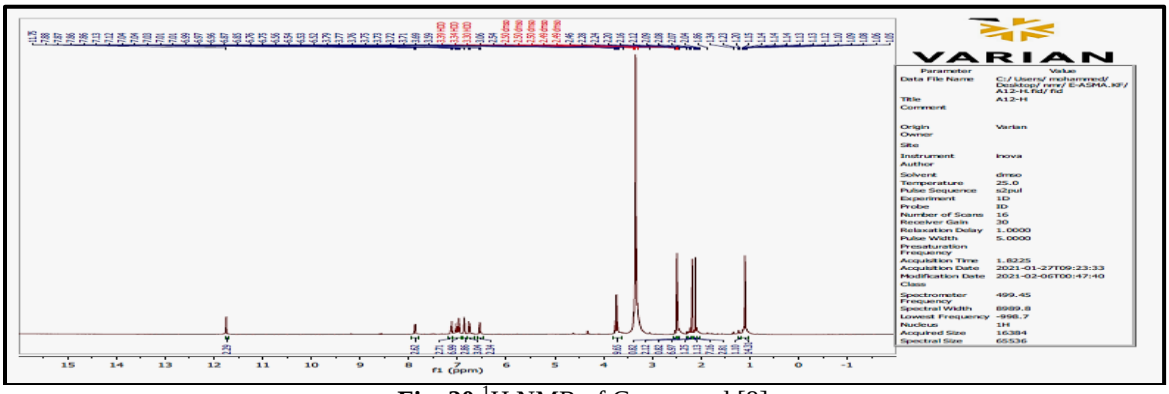

Fig. 20. ^{1}H.NMR of Compound [8]

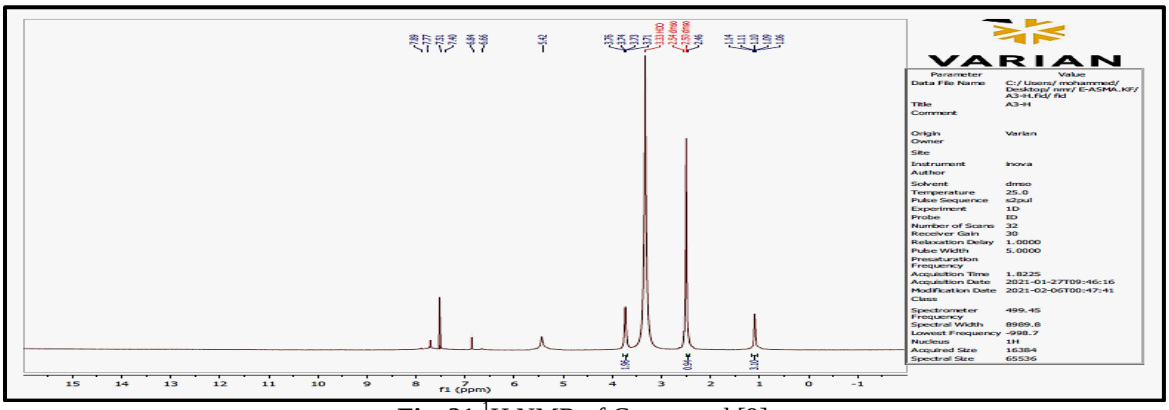

Fig. 21. ^{1}H.NMR of Compound [9]

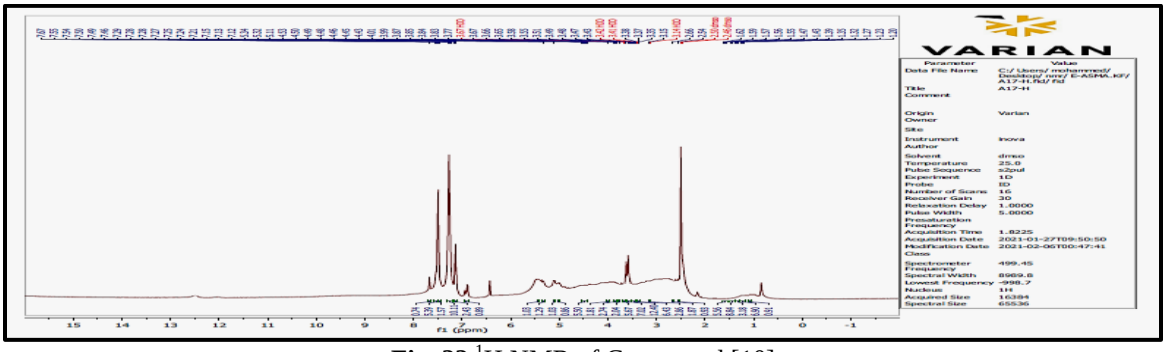

Fig. 22. ^{1}H.NMR of Compound [10]

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 8521 - 8537
Received 16 February 2021; Accepted 08 March 2021.

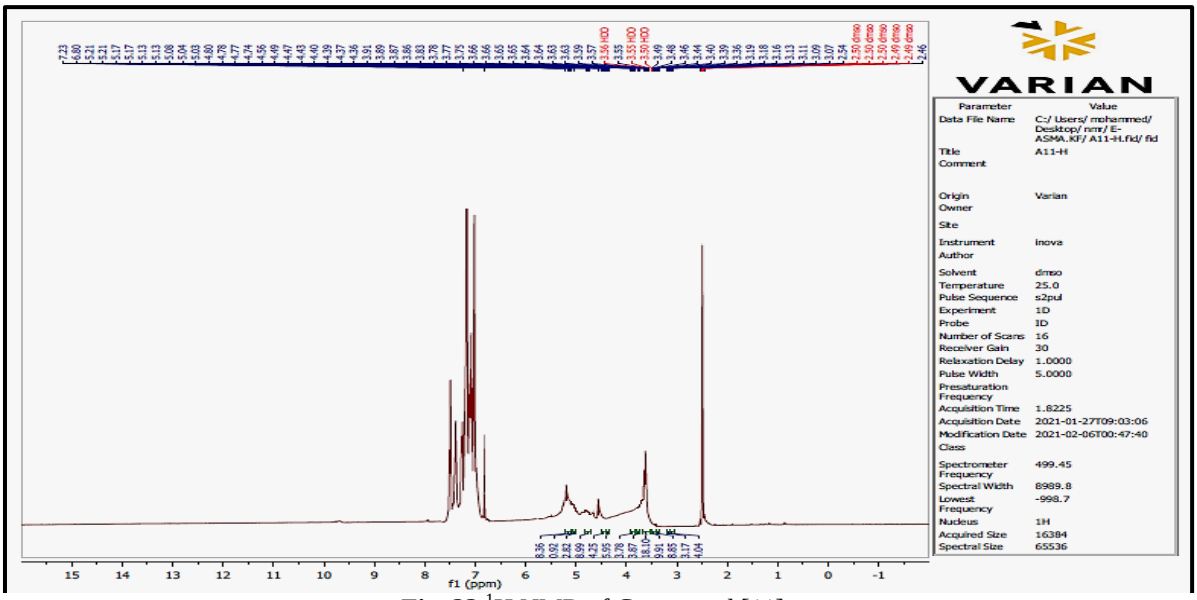

Fig. 23.[1]H.NMR of Compound [11]

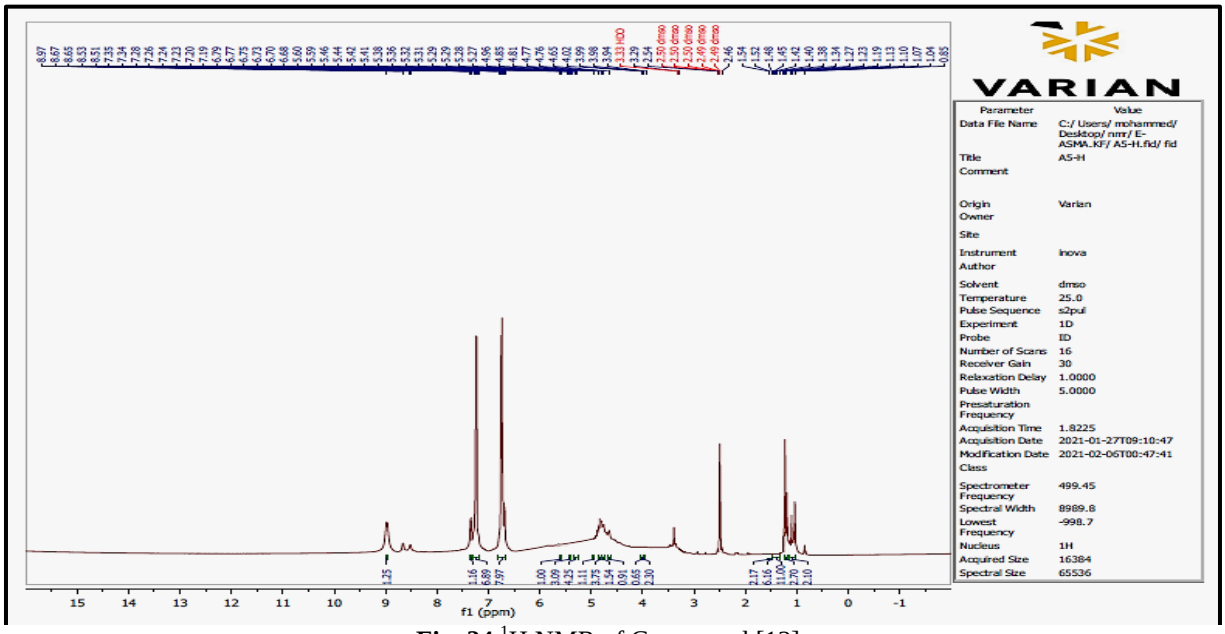

Fig. 24.[1]H.NMR of Compound [12]

The ^{13}C.NMR spectraldata ofsome compounds showed signals indicated to functional groups in these compounds, table (3).

Table 3.^{13}C.NMR- data (δ or ppm) of Compounds

Comp.	**^{13}C.NMR-data ((only Important Peaks))**
2	(162.2) (C, CO-N) carbonyl group in amide., (58.0) (C, CO-CH_2-S) in methylene.,(24.0,26.0) (C, methyl groups)., (110.0-130.0) (C, aromatic ring).
7	(60.0) (C, S-CH-C=N) in methylene., (82.0) (C,N=C-N=N-) near from azo., (105.0-138.0) (C, aromatic ring).
8	(61.95) (C, S-CH-C=N) in methylene., (65.5) (C,-N=C-N-NH-) near from amine group., (115.0-142.0) (C, aromatic ring).

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 8521 - 8537
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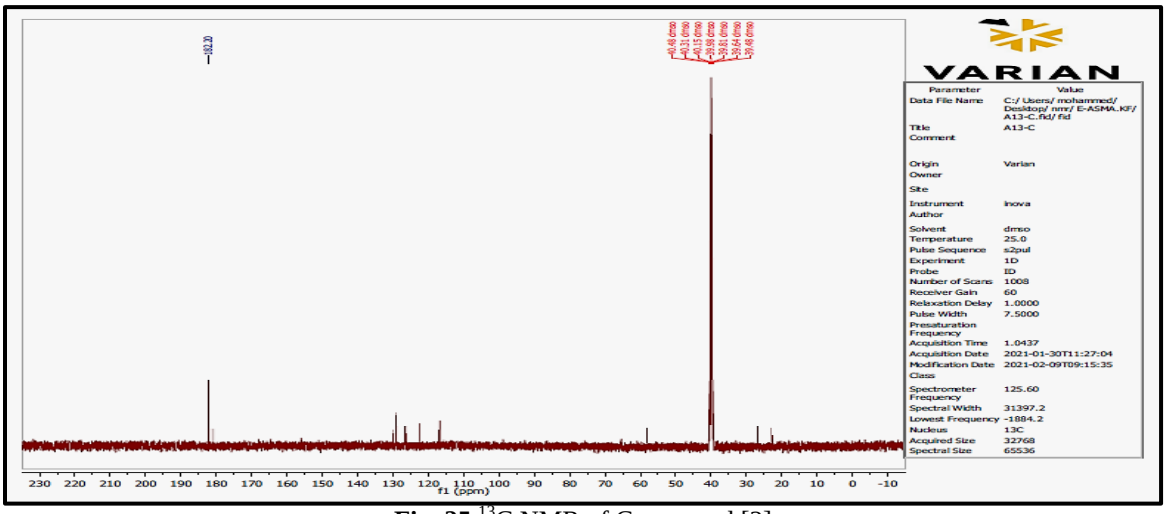

Fig. 25. ^{13}C.NMR of Compound [2]

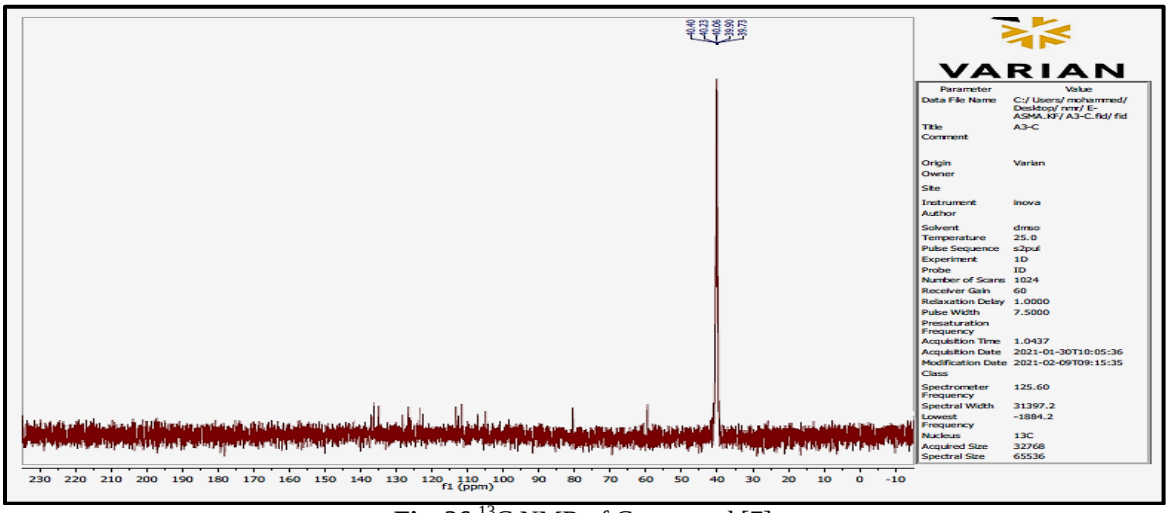

Fig. 26. ^{13}C.NMR of Compound [7]

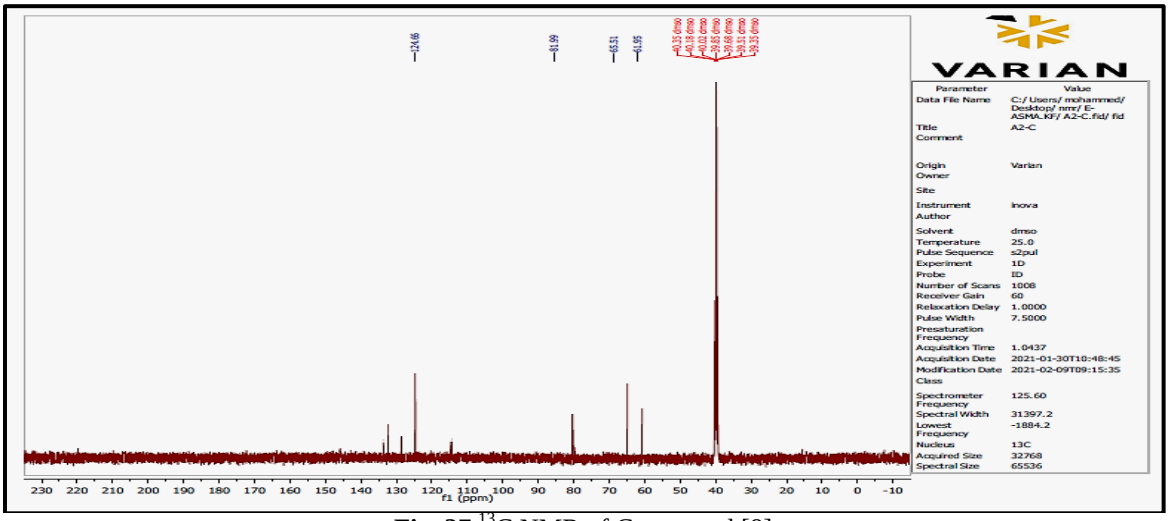

Fig. 27. ^{13}C.NMR of Compound [8]

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 8521 - 8537
Received 16 February 2021; Accepted 08 March 2021.

Initialization of Cancer Cell Line withMefinamic –Derivative (3)

Line processing and implantation ofbreast cancer cells and live cell line were carriedout at Biotechnology Center – the Nahrain (MCF-7 cell line) and (WRL cell line grew in 95% of RPMI–1640) supplemented with (10% FBS), cell suspension and incubation(13, 53) at (37 °C) in incubator {(CO2) % 5}accordingto studies [24-26]. The suspended cells were centrifuged at (250 g) for (10 minutes) and the supernatant was removed, the cells were re-suspended in a freezing medium, then placed at (-70 °C) in beaker for (1-3) days, the beaker wastransferred from the standard freezer boxes to the liquid (N_2) container., the results in table (4) andfigure (28):

ProcessingMethod[24-26]

MTT was used to determine cell viability by chromatic examination(64-70) of two (MCF-7 and WRL cell lines) accordingto studies [24-26]:

- Cell suspension (100 µL) was added to the wells of a small flat plate bottom.
- The solution was prepared by dissolving the crystals of 5 mg MTT in 1 ml of PBS solution (phosphate buffer solution).
- The concentrations of each innovative derivative of the prepared derivatives were used in this research (400, 200, 100, 50, 25, 12.5, 6.15)µg/ml of methanol, which were added to each well (three replicates per concentration).
- A 10 ml MTT solution was added to each well of a plate containing 96 wells and then incubated for 4 hours with a test sample at 37 °C (the solution became yellow).
- DMSO was added (200 µL (to each hole and stirred for 5 minutes (to become a purple DMSO solution).
- After the complete dissolution of the dye, the absorption of the colored solution from the living cells was read at (575 nm) using the ELISA reader.7- The mean absorption was calculated for each group of iterations and the validity ratio of the cells exposed to different treatments was obtained as follows:

Cell Vitality% = [(Absorption from the treated sample /Absorption from the untreated sample) X 100

Table 4. Showing the effect of different concentrations on the cancer cell line (MCF-7) and its toxic effect on the live cell line (WRL) ofMefinamic-Derivative (3)

Concentration ofCompound (μ g/Ml^{-1}) Heterocyclicderivative ofMefinamic acid (3)	**MCF-7**		**WRL**	
	Mean	**SD**	**Mean**	**SD**
400	38.93	4.30	81.17	3.41
200	51.85	3.61	89.12	1.51
100	66.05	2.70	93.13	0.64
50	75.54	5.21	95.83	0.31
25	90.70	4.80	95.37	0.90
12.5	94.56	1.33	94.71	1.27
6.25	94.95	0.48	95.68	0.41

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 3, 2021, Pages. 8521 - 8537
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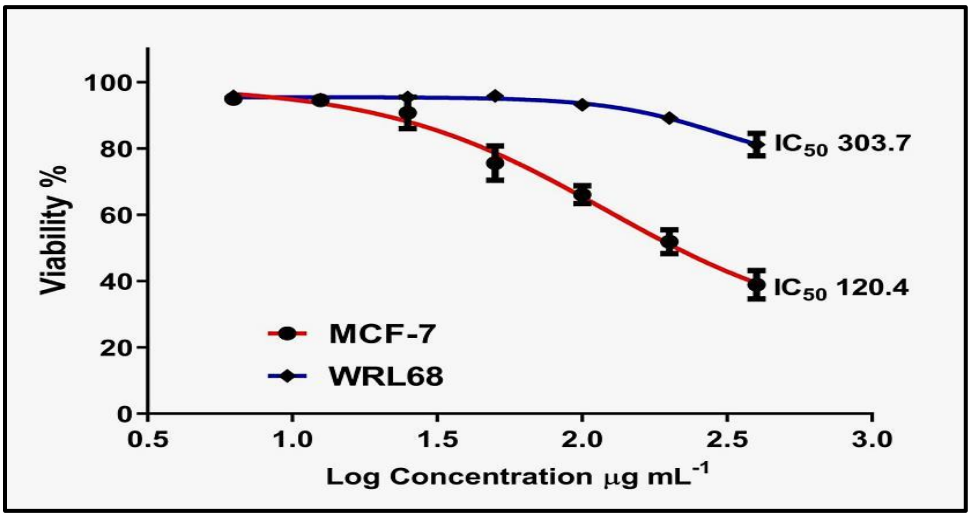

Fig.28. Percentage of remaining cells versus concentration of compound (3)

Conclusions

The results indicated to formation of these drug derivatives by appearance of new bands and disappearance of bands in starting compounds., besides to conclusions from our paper that gave good data for inhibition efficiency for these drug derivatives against cancer cells. Ourresults appeared good inhibition for carcinoma cells line forMefinamic derivative[3], and gave high response for derivative [3](it was = 73 % response percentage of derivative [3] for inhibition and killing of cancer cells due to heterocycleswhich linked withdrug liketriazoleand thiadiazole (heterocycles - Drug) that linked with drug which gave it more response against cancer cells also due to thiadiazole core in this derivative [3].

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