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Suzuki Miyaura Cross – Coupling Reactions of 4-Chloro Quinoline Derivatives and Studying of Biological Activity for some of Them

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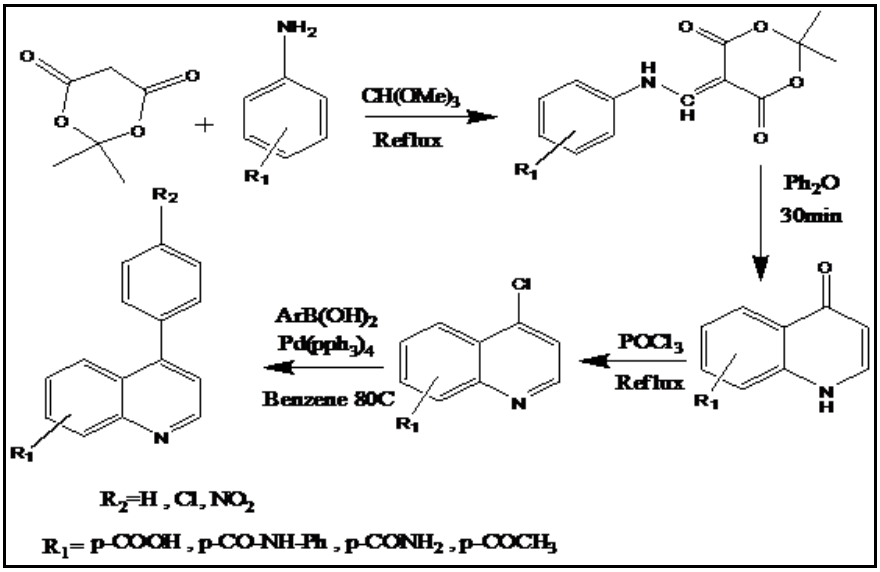
Abstract : The present work deals with the synthesis of arylated quinolines . The reaction of substituted aniline with meldrum acid in presence of tri methyl orthformate gives aniline-bis(methylene Meldrum's acid)derivatives , which was converted to substitute quinolone .The quinolone reaction with($POCl_3$) gives substituted 4-chloro quinoline. For that reaction of 4-chloro quinoline with different boronic acids in the presence of Tetrakis (triphenylphosphine) palladium (0) gives the arylatedquinolines.
Keywords :- Meldrum's acid, Quinolines, Suzuki coupling reactions.



1.Introduction

The Suzuki – Miyaura reaction (SMR) including the coupling of Organo- boron reagent and an Organic halide or Pseudo-halide and used palladium or nickel as catalyst and a base[1-4] . It's discovered in 1979 by Akira Suzuki and co-workers[5] . Suzuki-Miyaura cross-coupling reaction is a highly versatile methodology for generation of carbon carbon bonds[6]. Carbon-carbon bond formation reactions are important processes in chemistry, because they provide key steps in building complex, bio-active molecules developed as medicines

and agrochemicals. They are also vital in developing the new generation of ingeniously designed organic materials with novel electronic, optical or mechanical properties, likely to play a significant role in the burgeoning area of nanotechnology. It has now confirmed that all kinds of carbon–boron bonds including (sp3)C–B, (sp2)C–B, and (sp)C–B bonds are employed as cross-coupling partners in the coupling reactions[7]. This is a reaction of an aryl- or vinyl-boronic acid with an aryl-, vinyl- or an alkyl-halide catalyzed by palladium. It is vastly used to synthesize poly olefins, styrenes and substituted biphenyls[8]. The reactivities of aryl halides and aryl trifaltes are indicated as follows ;Ar-I > Ar-Br > Ar-OTf >> Ar-Cl. [9]

A general catalytic cycle for the Suzuki cross-coupling reaction is depicted[10] in Figure 1.2 .

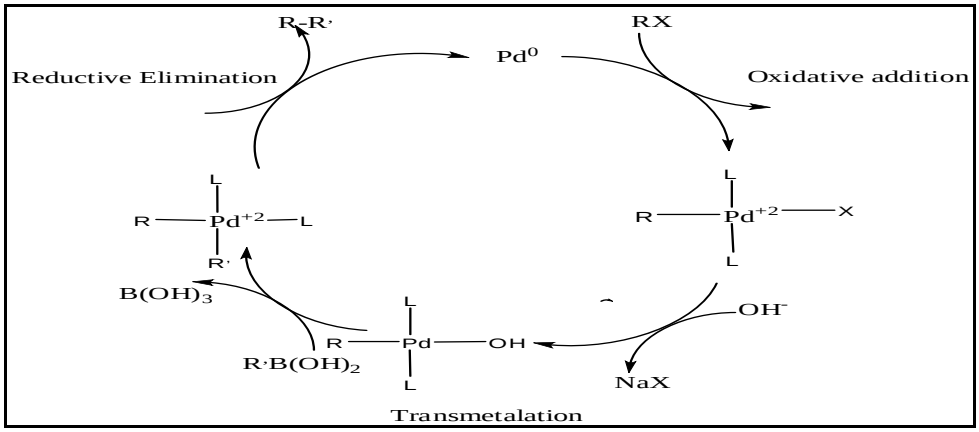


Figure 1.1. A general catalytic cycle for the Suzuki cross-coupling reaction

Oxidative addition:-

In an oxidative addition step an electrophilic compound X-Y adds to a metal complex. In this step, the XY bond is broken and two bonds are formed; M-X and M-Y, and mean while, oxidation state of the metal is raised by two. The coordination number of the metal also increases by two[11] .

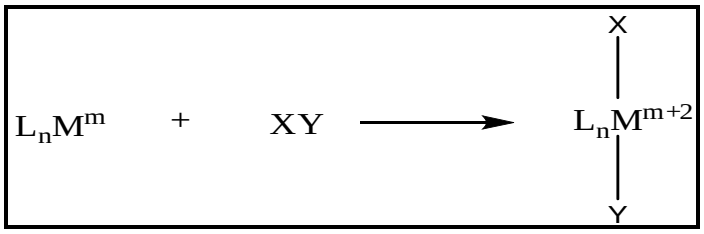


Figure 1.2. Oxidative Addition

Trans metallation Processes:-

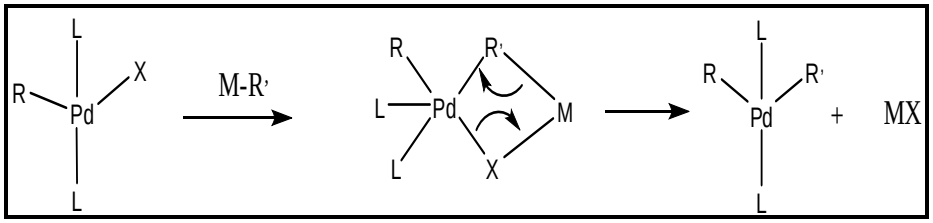


Figure 1.3. Transmetallation

In Suzuki reactions, trans metallation between organo palladium (II) halides and organ oboron compounds does not occur readily due to the low nucleophilicity of organic group on boron atom . However, the nucleophilicity of organic group on boron atom can be enhanced with base giving the corresponding “ate” complexes[12]

Reductive Elimination

Reductive elimination is simply the reverse reaction of oxidative addition. In this step, two carbon metal bonds are broken . The catalytic cycle is completed by reduction of the Pd(II) species into a Pd^0 species and finally coupling products[10] from Figure 1.4.

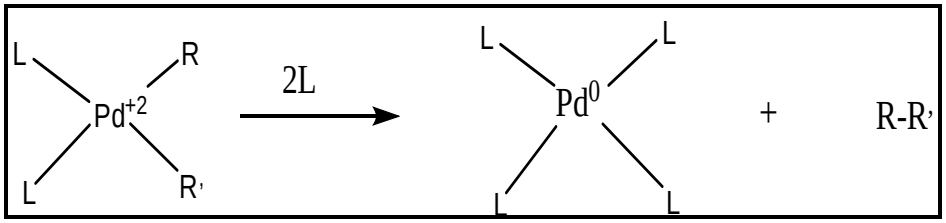


Figure 1.4. Reductive Elimination

2. Experimental

All chemicals were of highest purity and used as supplied by Fluka and Sigma-company . Measurements melting points, electro thermal 9300 , melting point engineering LTD , U.K of the synthesized compounds were determined in open capillary tube , All measurements were carried out by: FT-IR spectra ,Fourier transform infrared shimadzu (8400),H^1-NMR&C^{13}-NMR-spectra in (ppm) –unit were obtained in DMSO solution using (Bruker, Ultra Shield 300 MHz Switzerland), (Iran). Thin layer chromatography (T.L.C)was performed on silica gel for (T.L.C) and spots were visualized by Iodine vapors.

2.1.Preparation of compound (H)

2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid)[13]

Malonic acid (26g , 0.5 mol) , acetone (20 mL , 0.55 mol) and sulfuric acid (0.75 mL , 0.03 mol) were placed in a reactor at 0 ^oC with stirring under nitrogen purge . Within one half hour , addition of acetic anhydride (30mL , 0.6 mol) was begun dropwise at a rate of approximately 2mL/min . The mixture began as a white slurry and gradually turned pale yellow by the end of the addition of acetic anhydride ; the mixture was left out for 18 hrs at 0°C ; after which the mixture becomes a yellow slurry .Filtered the crystals of Meldrum's acid by suction, and washed three times with enough ice water to covered the cake. The air-dried product is afterwards purified by re crystallization. (7) Re crystallization of Meldrum's acid from acetone gave a colorless crystal with a M.P. of 95-97 °C. for a total of 18g (69.22 %yield) of Meldrum's acid .IR(KBr)cm^{-1}; 1791,1753(C=O) ketone, 3007(C-H) .H^1-NMR δ 1.72 (s,6H); δ 2.91(s,2H) .

2.2.Preparation of compound(2b,2c,2d,2f)[14]

A1 **:** 2 mixture of Meldrum's acid (0.85 g, 6 mmol)and $HC(OMe)_3$ (1.5 mL, 12.5 mmol) was heated under reflux for 4h, and the reaction mixture was then evaporated to dryness. The residue was dissolved in EtOH (10mL), aromatic amine (5 mmol) was added, and the reaction mixture was stirred at ambient temperature overnight. The resulting precipitate was filtered off, washed with EtOH, and re crystallized from EtOH.

2.2.1. (4-((2,2dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)methylamine)- benzoic acid (2b)

Orange powder ; (86%) ;mp(197-199)°C Rf: 0.55 IR(KBr)cm^{-1} ;1728(C=O), 1676,1629(C=O)ketone, 1600(C=C)alkenes, 3363(N-H), 3462(OH) ; H^1- NMR ($DMSO_{d6}$, MHz) δ 1.65 (s, 6H,CH_3), δ 6.5-7.8 (m, 4H), δ 11.2-11.3 (d, 1H,NH), δ 12.45(s,1H,COOH),δ7.94-7.96(s1H,CH=C=); C^{13}NMR($DMSO_{d6}$,MHz) 26.47,88.57,104.31,112.60,116.78,118.26,118.73,125.26,127.96,130.43,131.19,142.89,153.11,166.56,166.86,169.09 .

2.2.2. 4-((2,2dimethyl-1,3-dioxo-4,6-dioxan-5-ylidene)methylamino)-N-phenylbenzamide (2c)

White powder ; (85%) ;mp(258-259)°C Rf: 0.72 IR(KBr)cm^{-1} ; 1730,1685 (C=O)ketone, 1637(C=O) amide , 1602(C=C)alkenes, 3209,3338(N-H), ; H^1- NMR ($DMSO_{d6}$, MHz) δ 1.70 (s, 6H,CH_3), δ 6.5-7.8 (m, 8H), δ 11.35(s,1H,NH), δ 8.03(s1H,CH=C=), δ 10.27(s1H,NHamide);C^{13}NMR ($DMSO_{d6}$,MHz)26.99,88.08,

104.79,113.00,119.06,120,57,121.57,123.33,
124.17,128.91,129.81,132.53,139.53,140.26,141.59,152.60,153.53,164.31,164.90,165.75 .

2.2.3 4-((2,2dimethyl-1,3-dioxo-4,6-dioxan-5-ylidene)methylamino)- benzamide (2e)

Yellow powder (74%): mp(245-246)°C Rf: 0.7 IR(KBr)cm^{-1} ; 1728,1685(C=O)ketone, 1654(C=N), 1635(C=C)alkenes, 3317(N-H);3234-3404 (NH_2). H^1- NMR ($DMSO_{d6}$, MHz) δ 1.69 (s, 6H,CH_3), δ 7.55-7.95 (m, 4H), δ 11.28-11.33 (1H,NH) δ 8.01 (s1H,CH=C=), δ 8.64-8.66(2H,NH_2);C^{13}NMR($DMSO_{d6}$,MHz) 26.98,87.92,104.76,118.96,129.46,132.08,141.29,153.56,163.13,164.32,164.37 .

2.2.4 5-((4-acetyphenyl amino)methylene)-2,2-dioxane-4,6-dione (2l)

Orange powder (75 %): mp(208-210)°C Rf: 0.73 IR(KBr)cm^{-1} ; 1722,1668,1631(C=O)ketone, 1597(C=C)alkenes, 3157(N-H); H^1- NMR ($DMSO_{d6}$, MHz) δ 1.61 (s, 6H,CH_3), δ 1.62 (s, 3H,CH_3) δ 7.02-7.9 (m, 3H), δ 11.2 (s1H,NH), δ 8.5(s1H,CH=C=), C^{13}NMR ($DMSO_{d6}$,MHz)26.45,87.06,104.14, 119.94, 123.60,126.80,129.86,132.08,139.12, 153.68,162.81,163.62,166.59

2.3.Preparation of compound(3b,3c,3e,3l)[15]

(1 mmol) of (2b,2c,2e,2l) was added to Ph_2O (15ml) .The reaction mixture was heated at 260 ◦C for 30 min, and then quickly cooled to room temperature, and the precipitate was filtered off and washed with n-hexane .and add to phosphoryl chloride (4 ml) . the resulting mixture was reflux for (2 h) poured onto ice and water (40 ml) , neutralized with 10% NaOH extracted with CH_2Cl_2 (3× 20 mL) and the combined organic layers dried ($MgSO_4$) .

2.3.1 4-oxo-1,4-dihydroquinoline-6-carboxylic acid (3b)

Yellow powder ; (75.5%) ;mp(268-269)°C IR(KBr)cm^{-1} ;1700(C=O), 1681(C=O)ketone, 1631(C=C)alkenes, 3311(N-H), 3423(OH) ; H^1-NMR ($DMSO_{d6}$,MHz) δ 7.23-8.00(m, 3H), δ 10.75-10.79 (d, 1H,NH), δ 12.69 (s,1H,COOH) 6.9-7.1 (d 2H,CH=CH) .

2.3.2 4-oxo-N-phenyl-1,4dihydroquinoline-6-carboxamide (3c)

Green powder ; (70%) ;mp(206-208)°C IR(KBr)cm^{-1} ; 1680(C=O)ketone,1645(C=O)amide, 1600(C=C) alkenes, 3240,3300 (N-H), ; H^1- NMR ($DMSO_{d6}$, MHz) δ 7.07-7.12(d,2H,CH=CH) , δ 7.32-7.98(m,8H), δ10.03-10.07(d,1H,NH), δ10.10(s,NHCO);C^{13}NMR ($DMSO_{d6}$,MHz)110.96,115.11,120.68, 120.78,123.90, 128.49,129.02,129.89,139.79,143.69,143.89,165.14,169.43 .

2.3.3 4-oxo-1,4dihydroquinoline-6-carboxamide (3e)

Yellow powder (68.5 %): mp(218-220)°C,IR(KBr)cm^{-1} ; 1674(C=O)ketone,1653(C=O)amide ,1606(C=C) alkenes, 3192(N-H); H^1 NMR ($DMSO_{d6}$,MHz) δ 7.56-8.02 (m, 3H), δ 11.32 (s 1H,NH), δ 7.36-7.43(d, 2H,CH=CH),δ8.66-8.67(d,2H,NH_2) ;C^{13}NMR($DMSO_{d6}$,MHz)106.77,118.24, 123.91,128.80,128.88, 129.46, 129.57,129.64,129.82,130.52,132.07,141.30,164.32,167.83 .

2.3.4 6-acetylquinolin-4(1H)-one (3l)

Yellow powder (60 %): mp(156-158)°C IR(KBr)cm^{-1} ; 1692,1672(C=O)ketone, 1629(C=C)alkenes,3178(N-H); H^1 NMR ($DMSO_{d6}$,MHz) δ 8.04-8.74 (m, 3H), δ 11.31-11.36 (d 1H,NH), δ 7.29-7.36(d, 2H,CH=CH) , δ 2.63(s,3H,CH_3) ;C^{13}NMR($DMSO_{d6}$,MHz) 26.55,105.52, 117.51,130.59,135.06,141.40,147.17, 151.92,165.39, 196.25

2.4.1 4- chloroquinoline-6-carboxylic acid (4b)

Yellow powder ; (70 %) ;mp(232-234)°C IR(KBr)cm^{-1}; 1695(C=O), 1633(C=N)endocyclic, 1598(C=C) aromatic, 3200(OH) ; H^1-NMR ($DMSO_{d6}$, MHz) δ 7.09-7.91(m,4H), δ 11.65(s,1H,COOH) ,C^{13}-NMR ($DMSO_{d6}$,MHz)120.50,123.90,125.23,127.76,129.17,130.01,130.52,130.66,130.84,131.33,131.46,131.57,157.10,167.67.

2.4.2 4-chloro-N-phenylquinoline-6-carboxamide (4c)

Nutty powder ; (65 %) ;mp(171-173)°C IR(KBr)cm^{-1} ; 1658(C=O)amide 1647(C=N)endocyclic , 1585(C=C) aromatic, 3064 (C-H) aromatic,3410(N-H);H^1-NMR($DMSO_{d6}$,MHz) δ 6.97-8.14(m,8H), δ 10.20(s,1H,NHCO); C^{13}NMR($DMSO_{d6}$,MHz)119.08,120.60,120.89,123.92,129.04,129.83,130.53,140.30,145.52,153.57,157.10,158. 44,167.39 .

2.4.3 4-chloro-quinolin-6-carboxamide (4e)

Brown powder (69%): mp(185-187)°C IR(KBr)cm^{-1} ;1658(C=O)amide, 1629(C=N)endocyclic, 1585(C=C)aromatic, ; H^1-NMR ($DMSO_{d6}$,MHz) δ 7.42-8.83(m, 4H), δ 8.80-8.99 (d,2H,NH_2) .

2.4.4 1-(4-chloroquinolin-6-yl)ethanone (4l)

Black powder (50%): mp(193-194)°C IR(KBr)cm^{-1} ;1662(C=O)ketone,1637(C=N)endocyclic,1585(C=C) aromatic,; H^1 NMR ($DMSO_{d6}$,MHz) δ6.99-7.42(m,5H), δ 2.10 (s,3H,CH_3) ;C^{13}NMR ($DMSO_{d6}$,MHz)119.06, 123.90, 130.51,133.89,139.50,144.85,148.15,151.89,157.10,173.52

2.5 Suzuki – Miyaura cross- coupling

General procedure[14]. To a solution of the (4b, 4c, 4e, 4l) compounds (0.5 mmol) , boronic acid (0.5 mmol) in benzene (10 ml) and 1M Na_2CO_3 solution (1.2 ml) were introduced . The mixture was heated to 55°C , after which $Pd(pph_3)_4$ (0.02 mmol) was add. After stirring at 55°C for 18h – 20h , the mixture was allowed to cool to RT , and was then poured into water (6 ml), and extracted with CH_2Cl_2 (3×3 mL) . The combined organic layers were dried over Na_2SO_4 and evaporated to dryness .

2.5.1 4-(4-nitrophenyl)quinolin-6-carboxylic acid (5b)

Yellow powder ; (61 %) ;mp(>250)°C IR(KBr)cm^{-1} ;1672(C=O), 1635(C=N)endocyclic, 1598(C=C) aromatic, 1338-1508 (NO_2) 3504(OH) ; H^1- NMR ($DMSO_{d6}$, MHz) δ 7.37-8.20 (m, 9H), δ 11.39(s, 1H,COOH) carboxylic acid ,C^{13}- NMR ($DMSO_{d6}$,MHz) 113.91,122.50,129.16,129.32,131.89, 132.02,132.42 ,132.53,133.56,135.75,149.18,153.07,158.11,169.39 .

2.5.2 N,4-diphenyl-quinolin-6-carboxamide (5c)

Black powder ; (55%) ;mp(220-222)°C IR(KBr)cm^{-1} ; 1664(C=O)amide 1630(C=N)endocyclic , 1598(C=C)aromatic, 3057 (C-H) aromatic,3292(N-H) ; H^1- NMR ($DMSO_{d6}$, MHz) δ 7.37-8.40(m, 11H),δ9.75(s,1H,CONH); C^{13}NMR($DMSO_{d6}$,MHz)117.91,124.73,129.16,129.20,129.32,131.90, 132.02, 133.87, 140.13,142.63,151.29,153.49,156.11,168.04 .

2.5.3 4- phenyl-quinolin-6-carboxamide (5e)

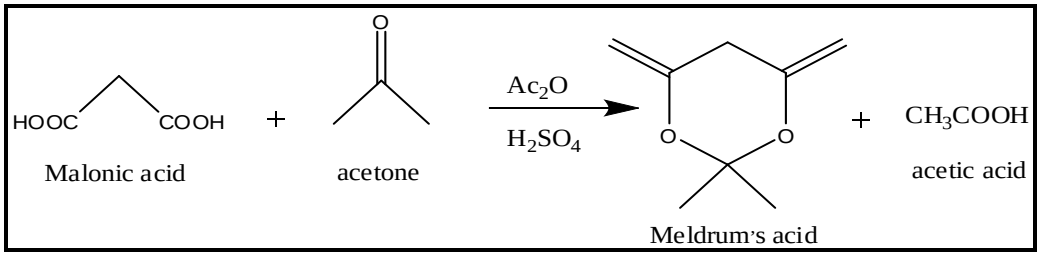
Green powder (50%); mp(181-183)°C IR(KBr)cm^{-1};1662(C=O)amide 1637(C=N)end cyclic, 1587(C=C) aromatic,3200-2385(NH_2) ; H^1 NMR ($DMSO_{d6}$,MHz)δ5.98-8.09(m,8H), δ8.35-8.38(d,2H,NH_2) ;C^{13}NMR ($DMSO_{d6}$,MHz)119.64,124.70,127.87,129.16,129.31,131.89,132.02,132.44,132.52,133.79,144.59, 148.07,167.37 .

2.5.4 1-(4-(4-chlorophenyl) quinolin-6-yl)ethanone (5l)

Nutty powder (47%): mp(>280)°C IR(KBr)cm^{-1} ;1681(C=O)ketone,1637(C=N)endcyclic, 1593(C=C) aromatic ; H^1 NMR ($DMSO_{d6}$,MHz) δ 2.52(s,1H,CH_3), δ 6.69-8.38 (m,8H) ;C^{13}NMR ($DMSO_{d6}$,MHz)26.85, 117.14, 19.07,124.70,126.95,129.16,129.31,130.52,131.89,132.02,132.51,132.55,133.81,144.59,148.08,191,13 .

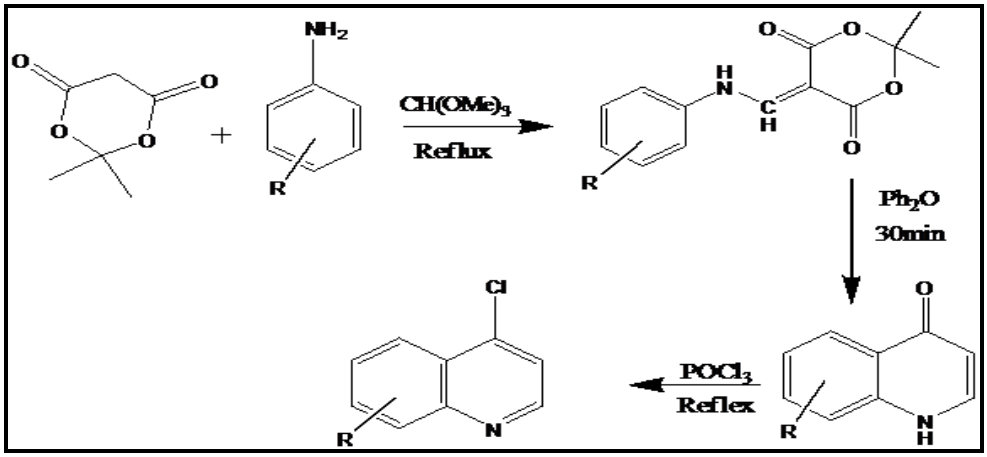
Results and Discussion

In our work for cyclization of phenyl amine derivatives -bis(methylene Meldrum's acid) to quinolone derivatives and preparation of 4-chloro quinoline derivatives involves the following steps: the first step involves the preparation of Meldrum's acid



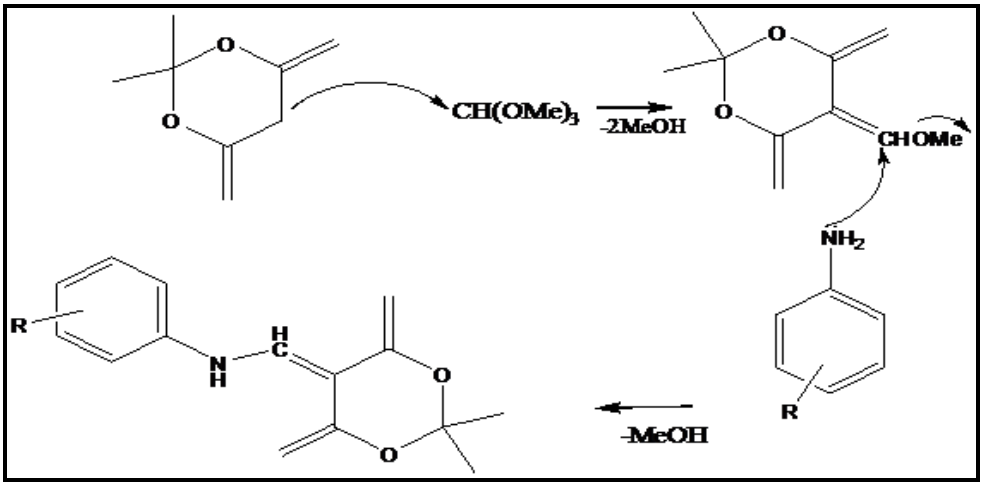
Scheme(1) :The prepared Meldrum's acid(H)

The prepared Meldrum's acid(H) was reacted with a number of aromatic amines which gave the Meldrum's acid derivatives in Scheme (2)

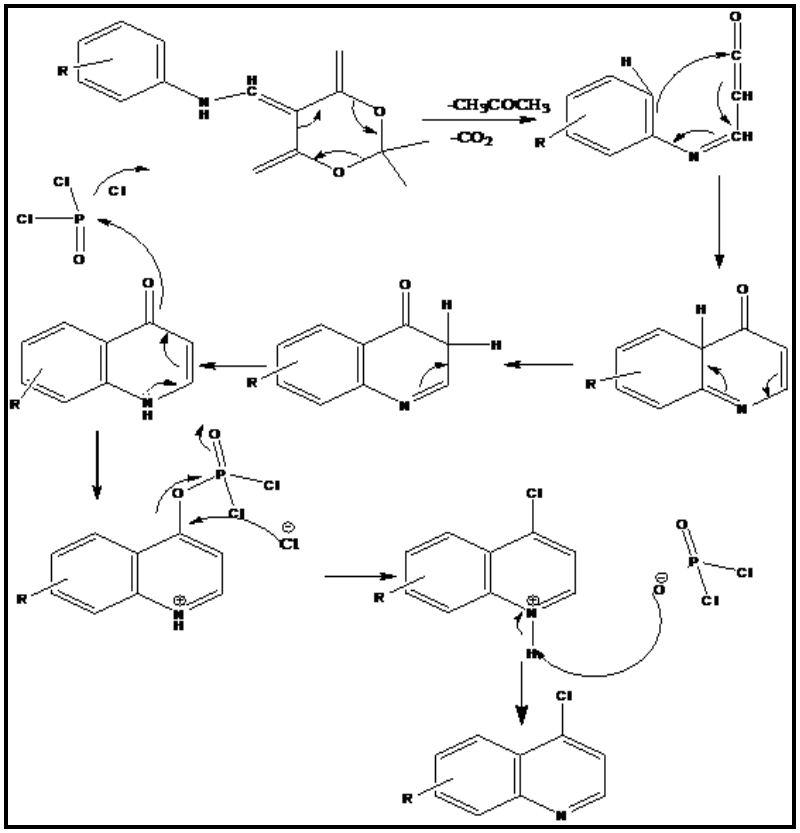


Scheme (2) Preparation of Compounds

The mechanism of this step is as followed:



The mechanism of cyclization step was suggested to be as follows :



Biological Activity

The biological activity[16,17] of the effect of some prepared compounds in this research on growth of three type of bacteria gram negative Escherichia coli **,** and Staphylococcus aureus . Streptococcus pneumonia as gram positive . was studied and the results were shown on table(III).

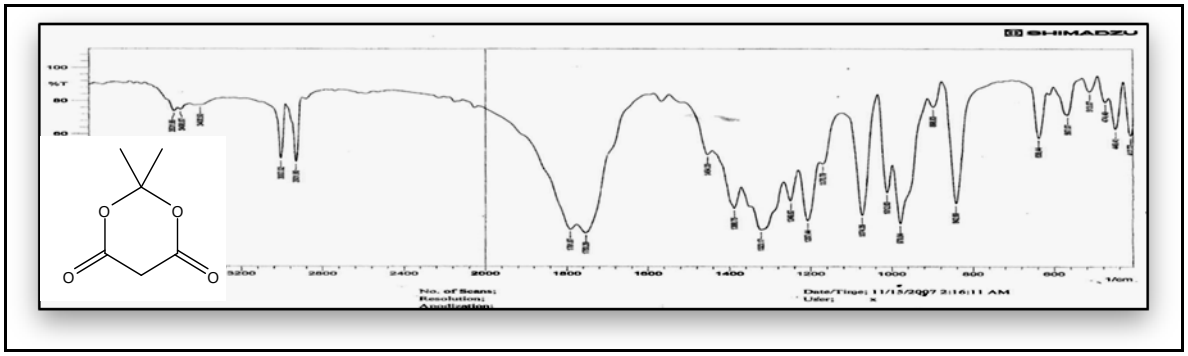
Meantime, the observable inhibition zone was determined during prepare concentration by dilution with DMSO (5, 10, 15) mg/ml[16,17] .

Table (I): Inhibition zone of some compounds

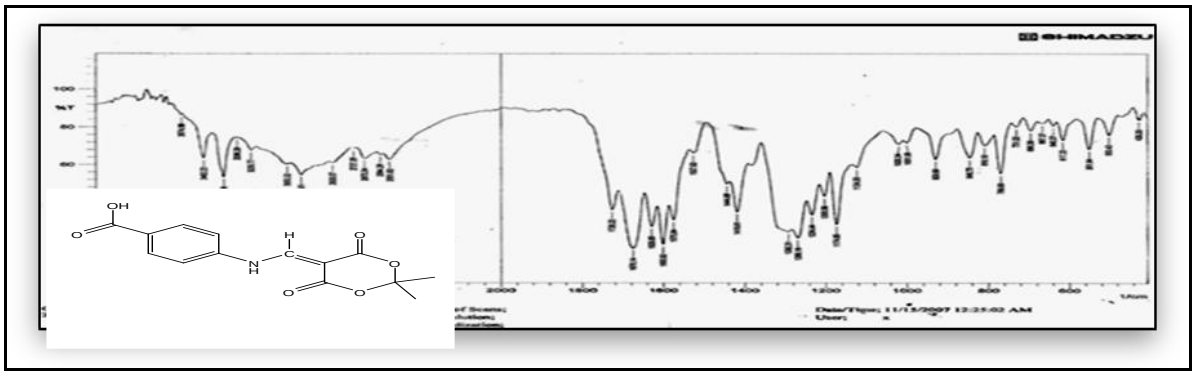
Conc. / Comp. No.	*Staphylococcus aureus*			*Streptococcus pneumonia*			*Escherichia coli*		
	5mg/ ml	**10mg/ ml**	**15mg/ ml**	**5mg/ ml**	**10mg/ ml**	**15mg/ ml**	**5mg/ Ml**	**10mg/ ml**	**15mg/ ml**
2b	+	+	++	_	_	_	_	_	_
2c	_	_	_	_	_	_	+	++	+++
2e	+	+	+++	_	_	+++	++	+++	+++
2l	++	+++	+++	++	++	+++	+	++	++
3b	+	++	++	_	_	_	++	++	+++
3c	++	++	++	_	_	_	+++	++	++
3e	+	+	+	_	_	+	_	_	_
4b	_	_	_	_	_	_	_	_	+++
4c	+	++	++	+	++	+++	+	++	+++
5b	_	_	_	_	_	+++	_	_	_
5c	+++	+++	+++	_	_	+	+++	+++	+++

Inhibition values = 0.1 – 0.5 cm beyond control = + (less active)

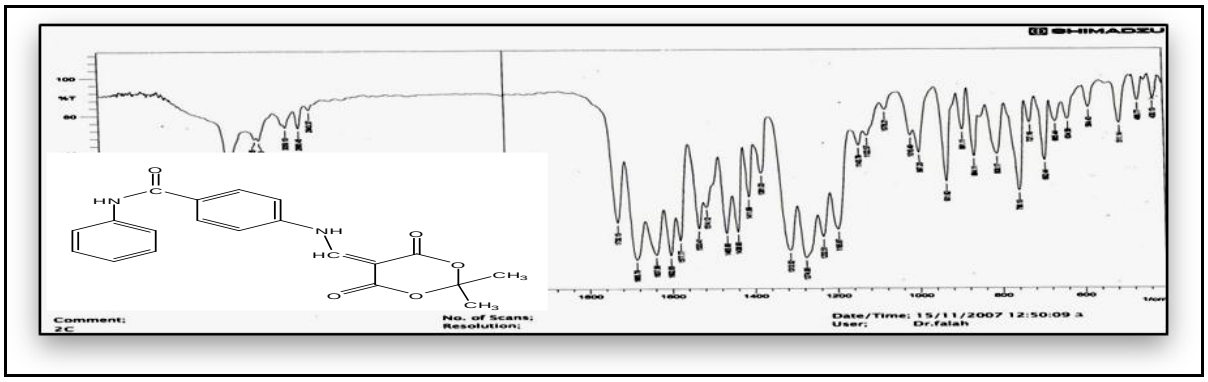
Inhibition values = 0.6 – 1.0cm beyond control = ++ (moderate active)
Inhibition values = 1.1 – 2.0 cm beyond control = +++ (highly active)



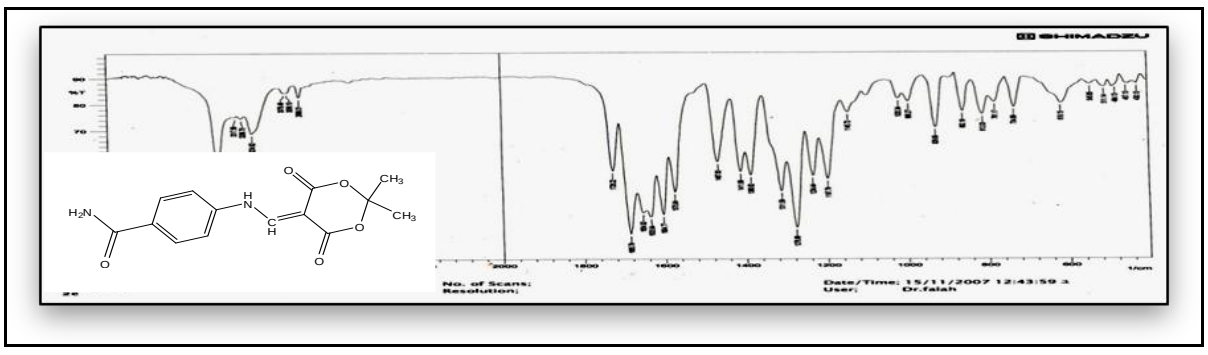
FT-IR Spectrum of Meldrum acid



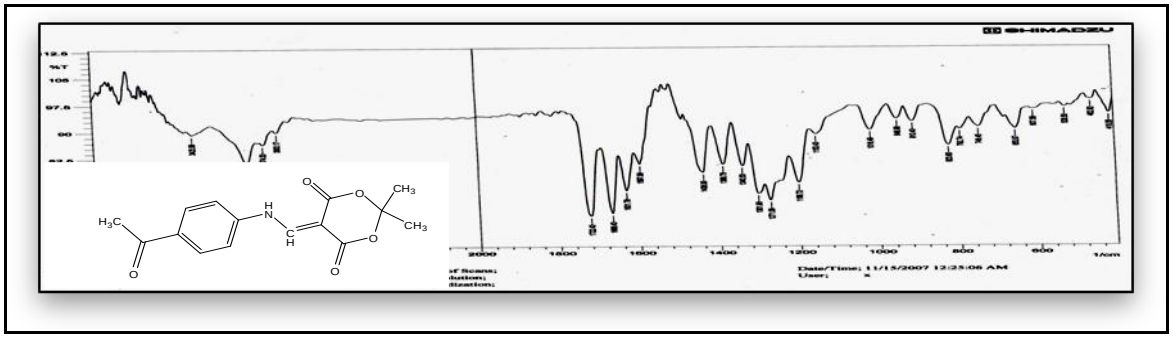
FT-IR Spectrum of Comp.(2b)



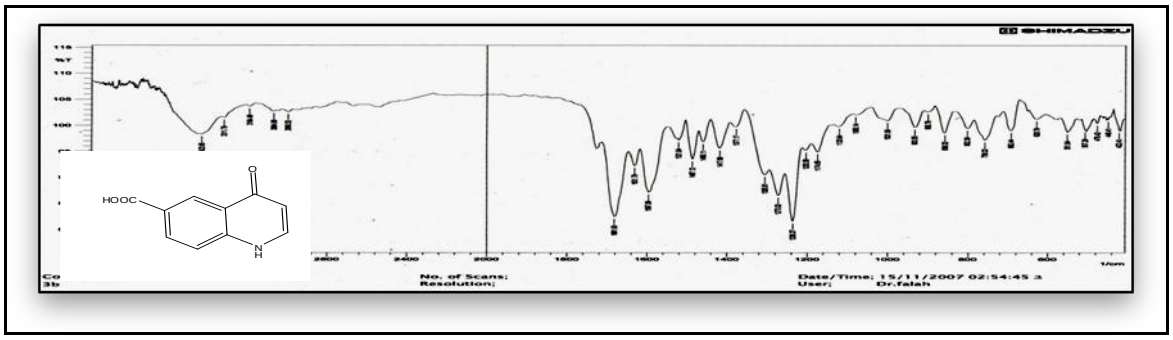
FT-IR Spectrum of Comp.(2C)



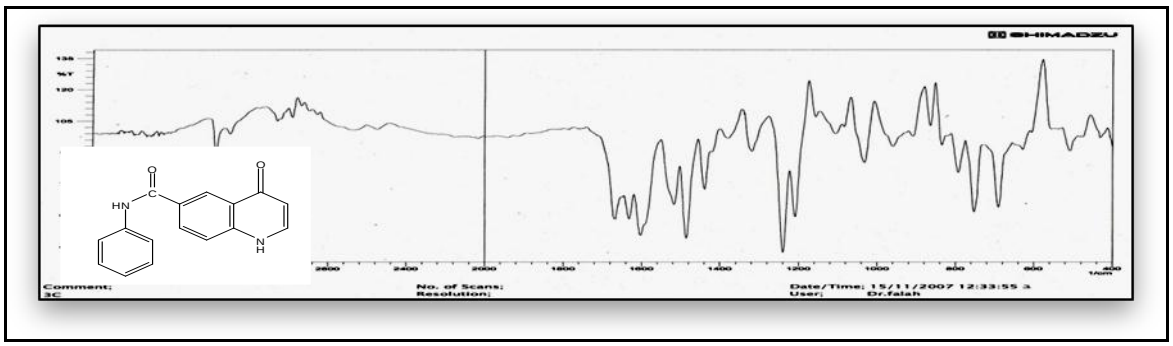
FT-IR Spectrum of Comp.(2E)



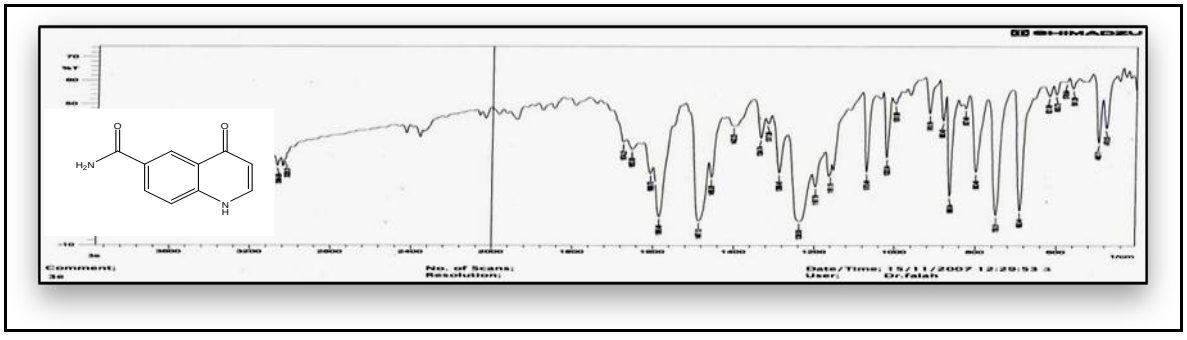
FT-IR Spectrum of Comp.(2L)



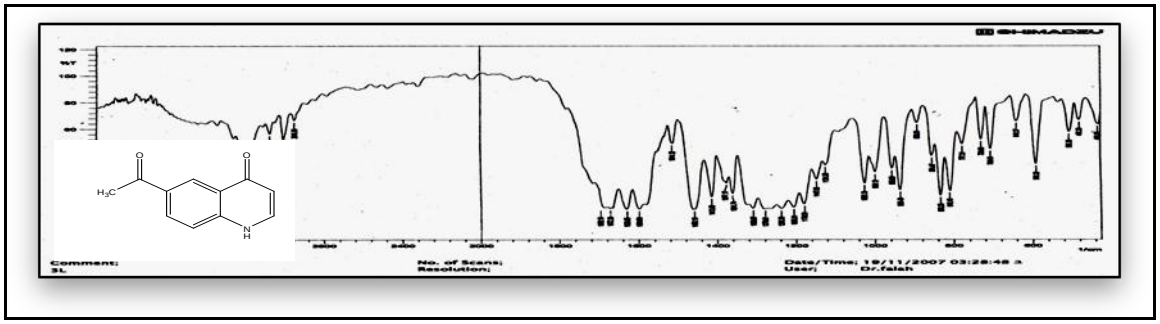
FT-IR Spectrum of Comp.(3b)



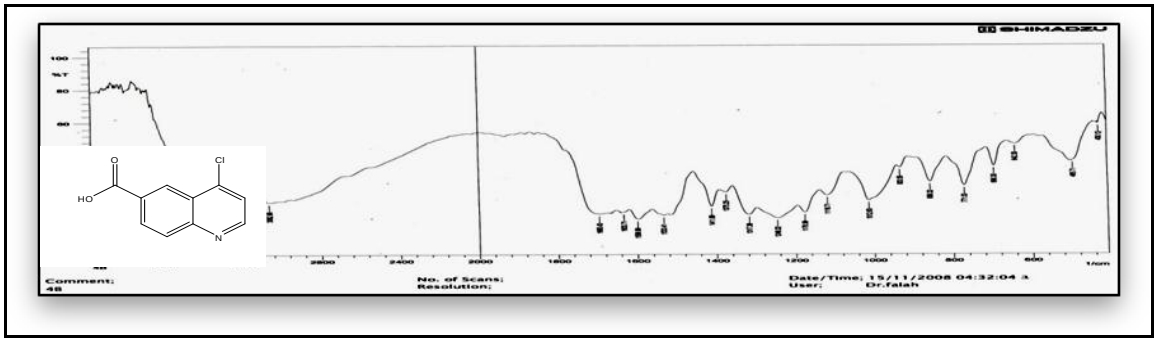
FT-IR Spectrum of Comp.(3C)



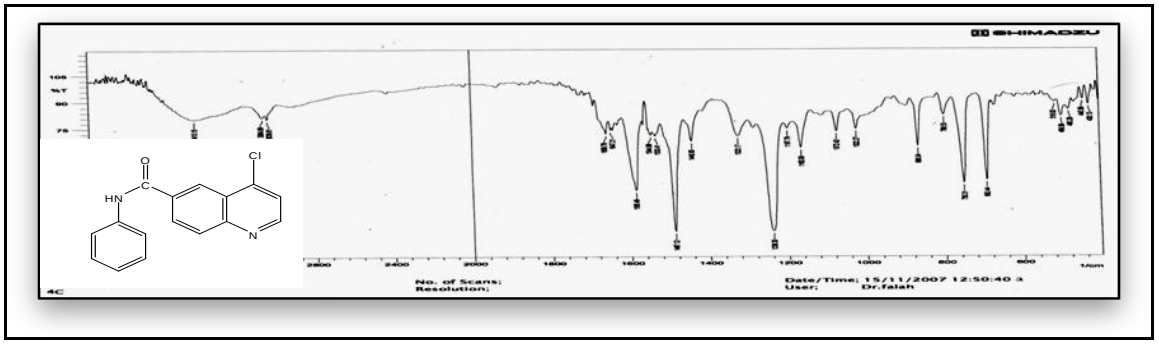
FT-IR Spectrum of Comp.(3E)



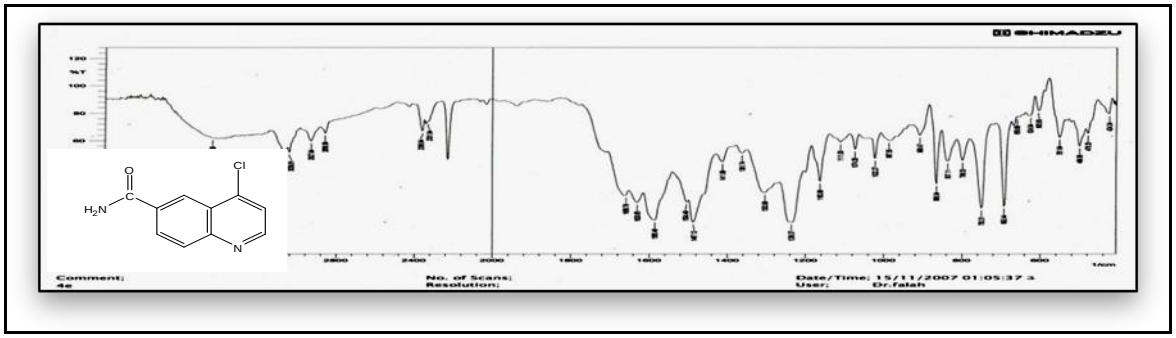
FT-IR Spectrum of Comp.(3L)



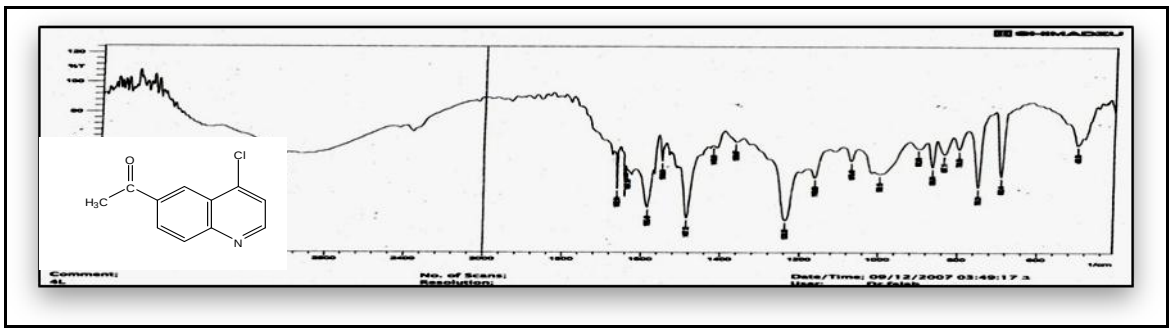
FT-IR Spectrum of Comp.(4B)



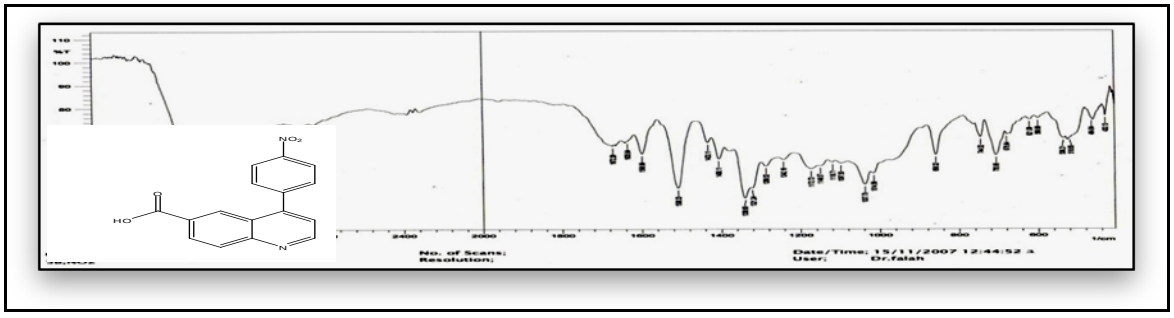
FT-IR Spectrum of Comp.(4C)



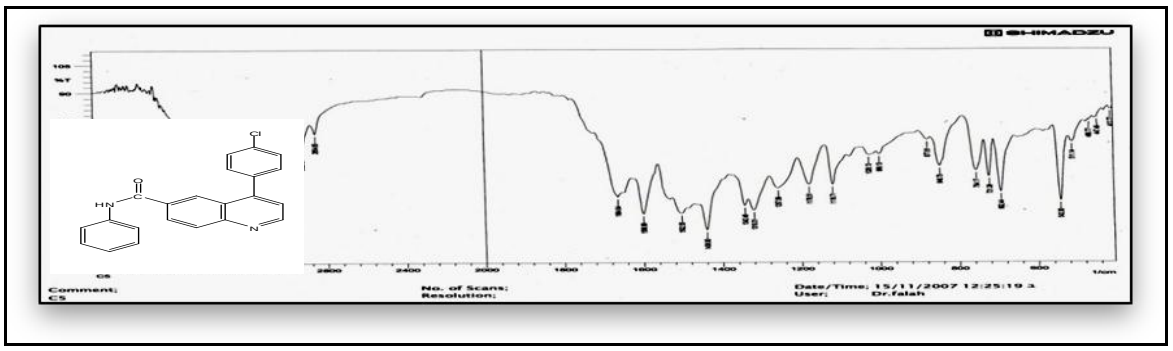
FT-IR Spectrum of Comp.(4E)



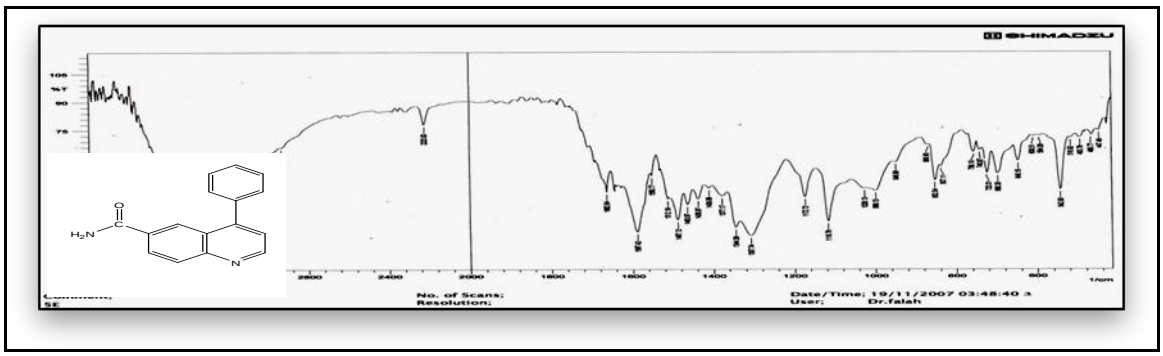
FT-IR Spectrum of Comp.(4L)



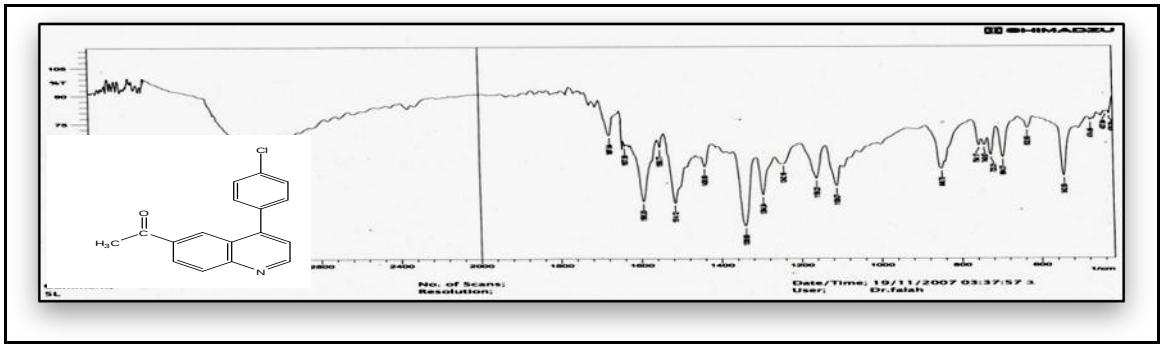
FT-IR Spectrum of Comp.(5B)



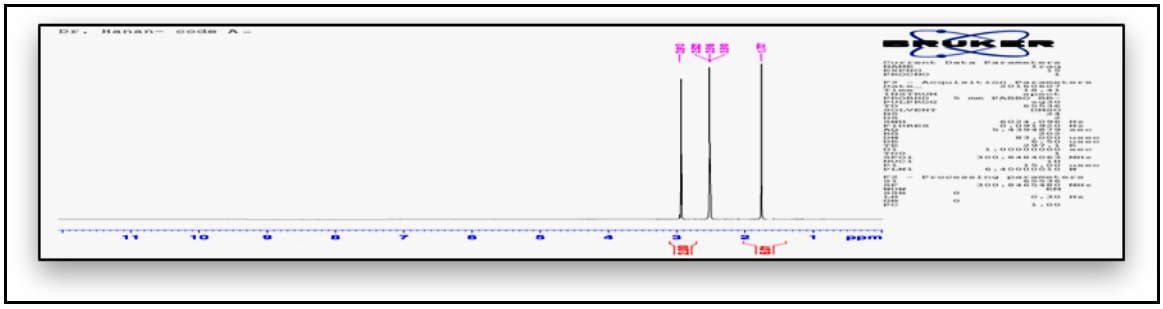
FT-IR Spectrum of Comp.(5C)



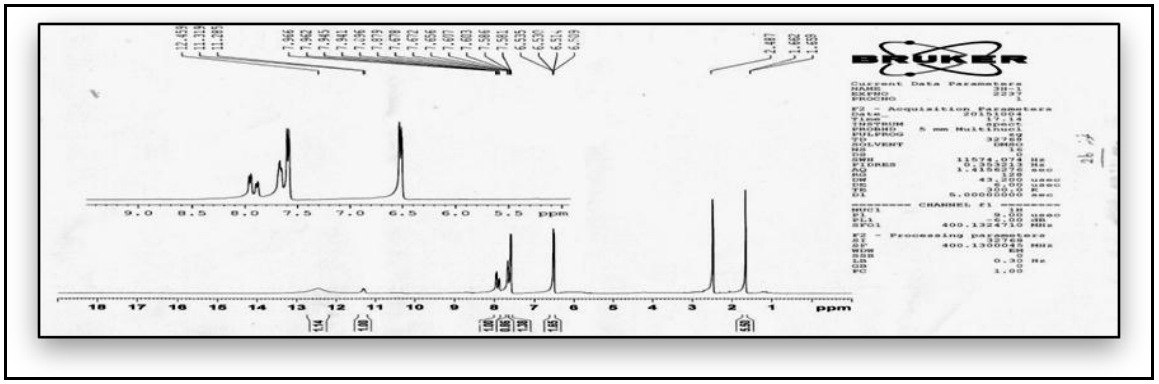
FT-IR Spectrum of Comp.(5E)



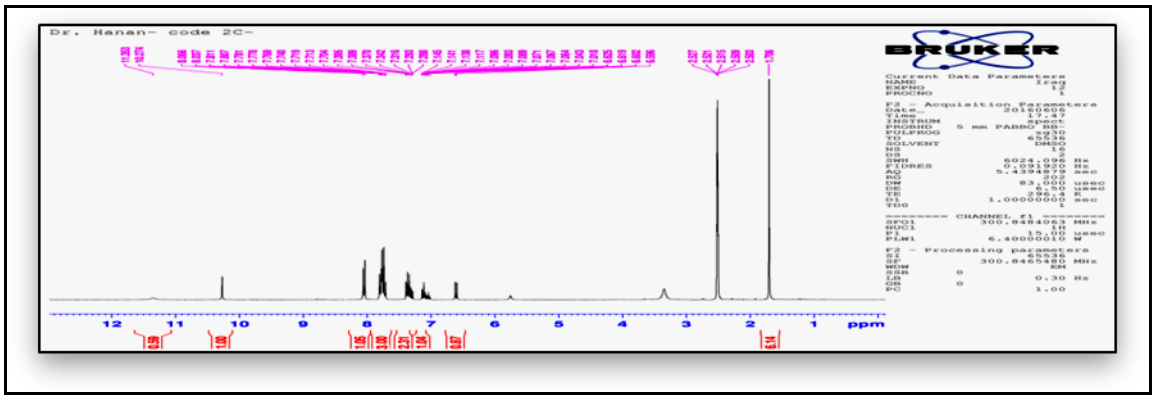
FT-IR Spectrum of Comp.(5L)



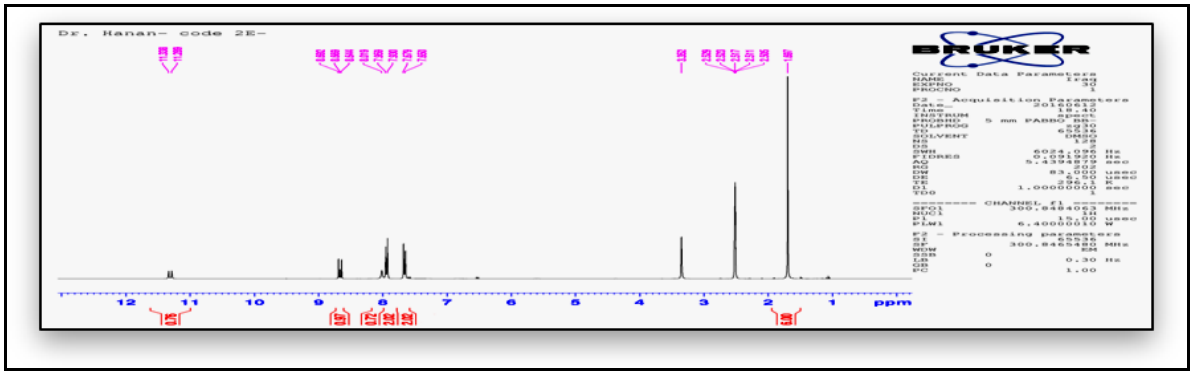
H[1]-NMR Spectra. Of Comp. (A) Meldrum's acid



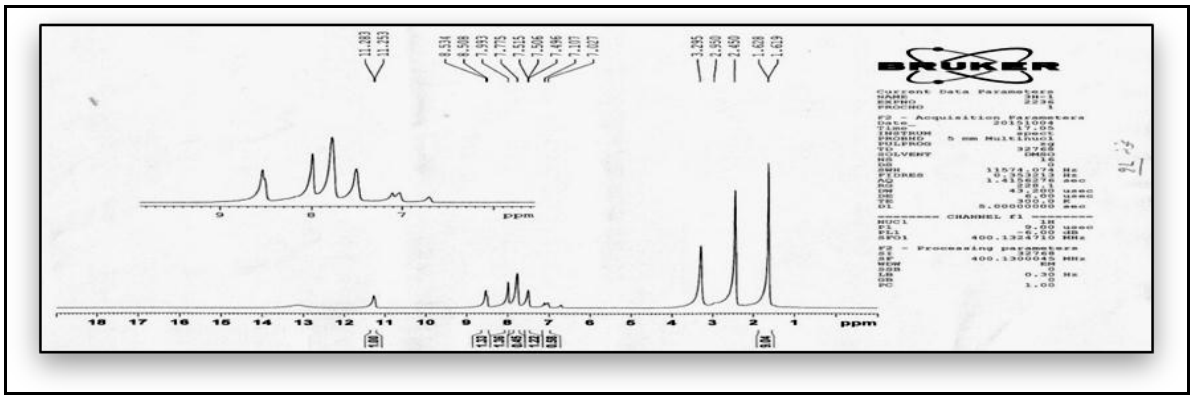
H[1]-NMR Spectra. Of Comp. (2B)



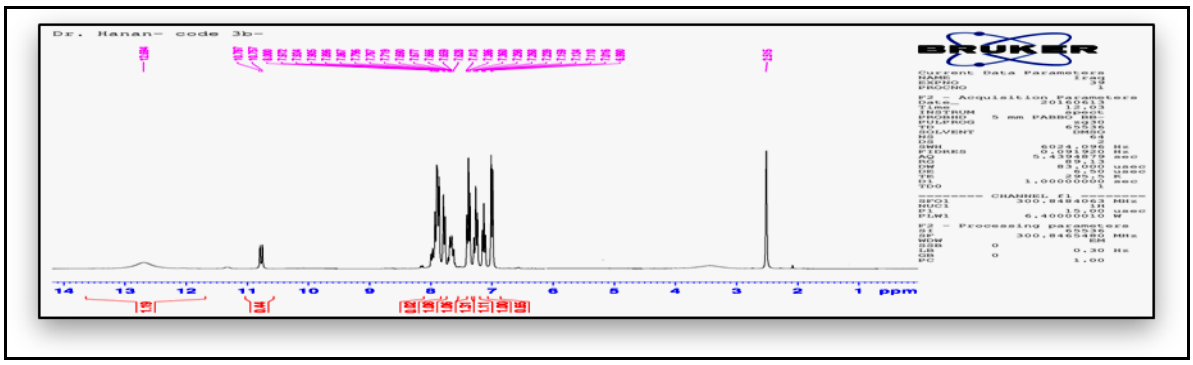
H[1]-NMR Spectra. Of Comp. (2C)



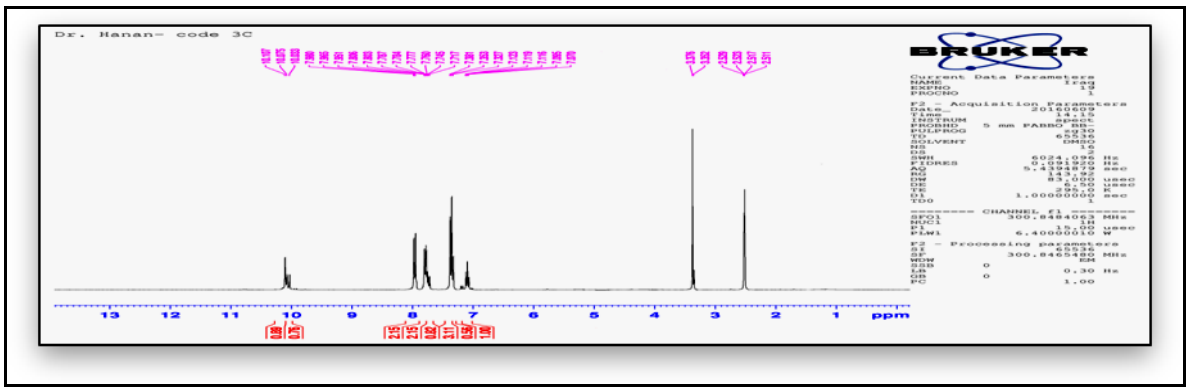
H^1-NMR Spectra. Of Comp. (2E)



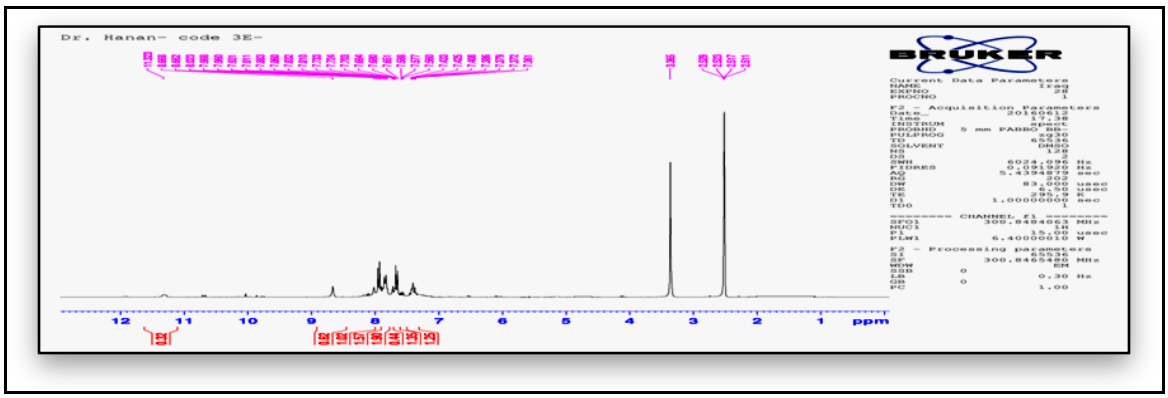
H^1-NMR Spectra. Of Comp. (2L)



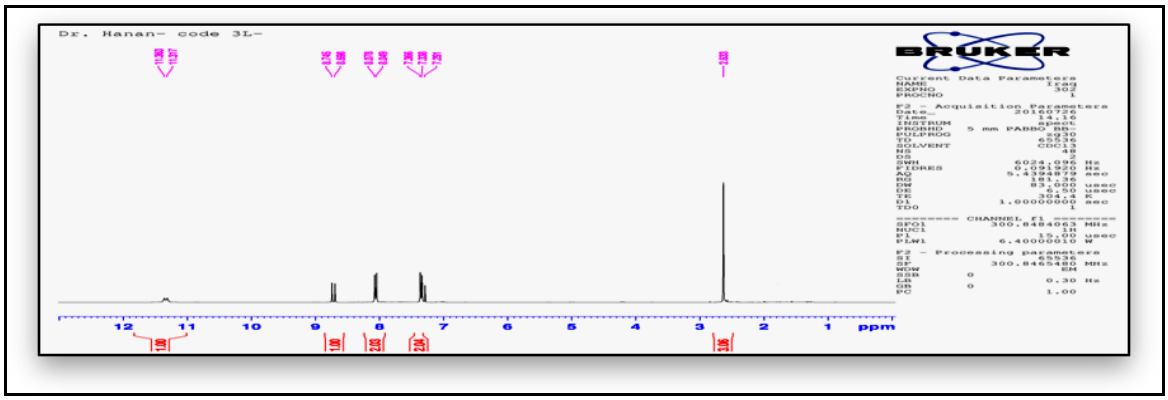
H^1-NMR Spectra. Of Comp. (3B)



H^1-NMR Spectra. Of Comp. (3C)



H[1]-NMR Spectra. Of Comp. (3E)



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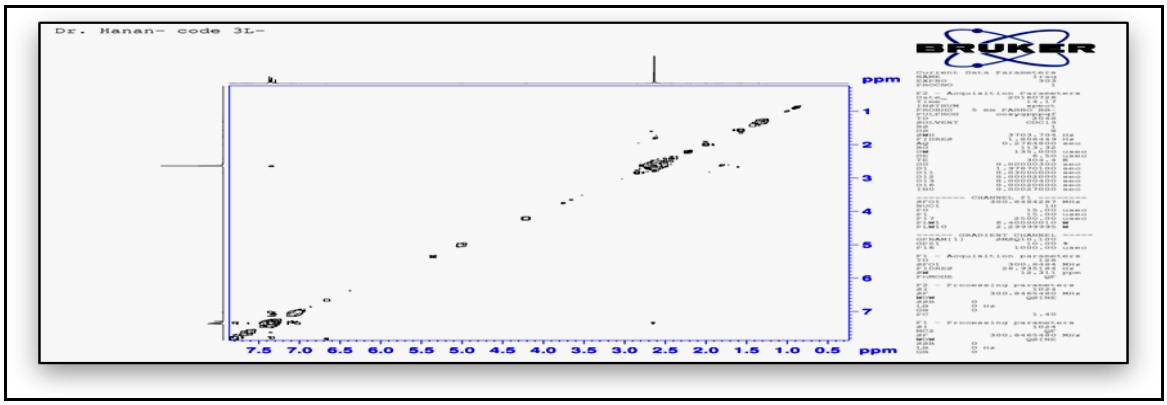
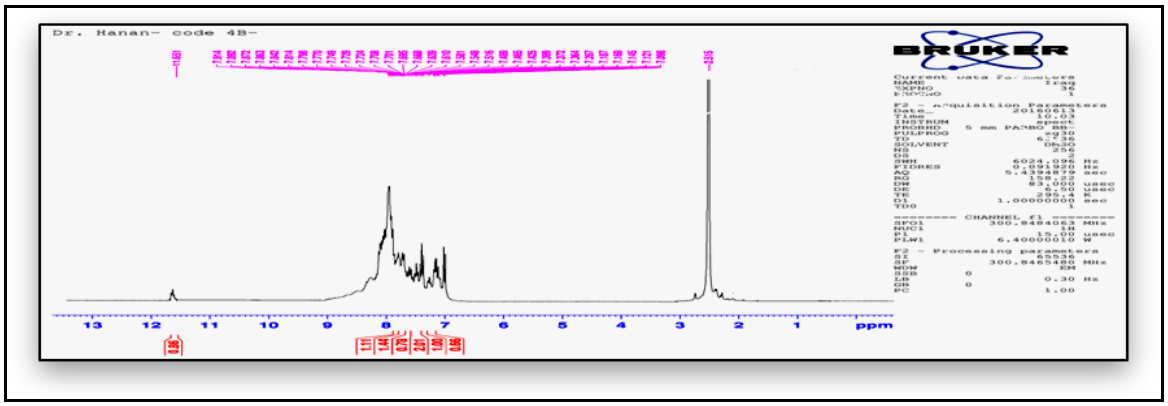
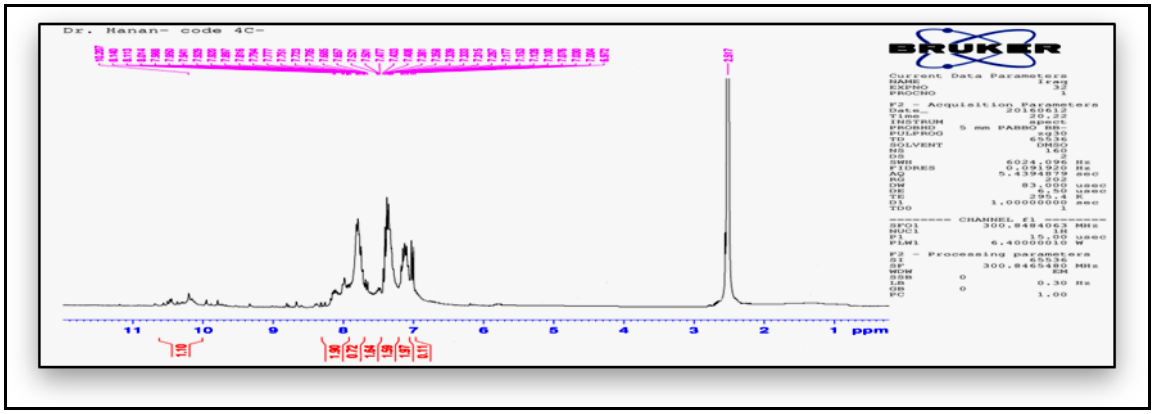


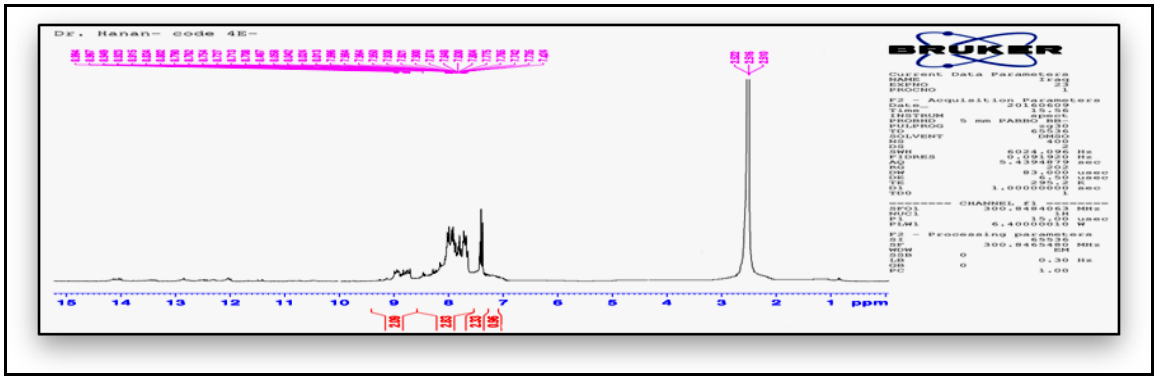
COSY 2D H[1]-NMR Spectra. Of Comp. (3L)



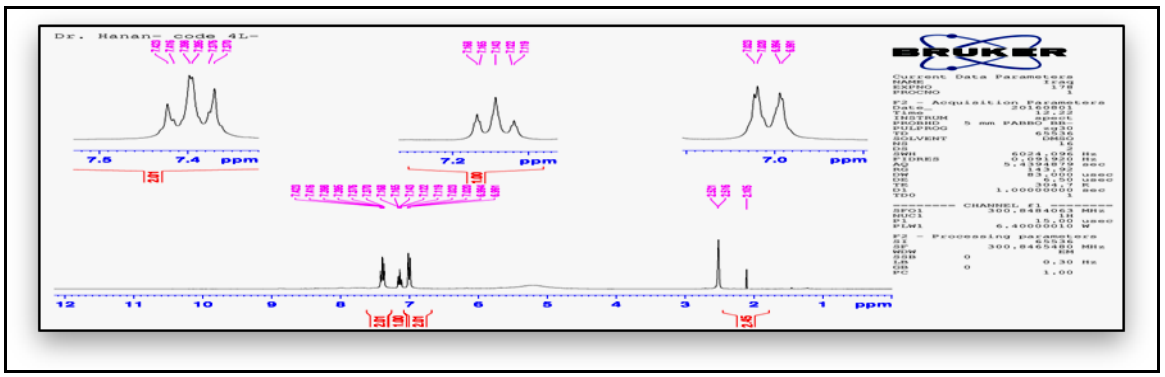
H[1]-NMR Spectra. Of Comp. (4B)



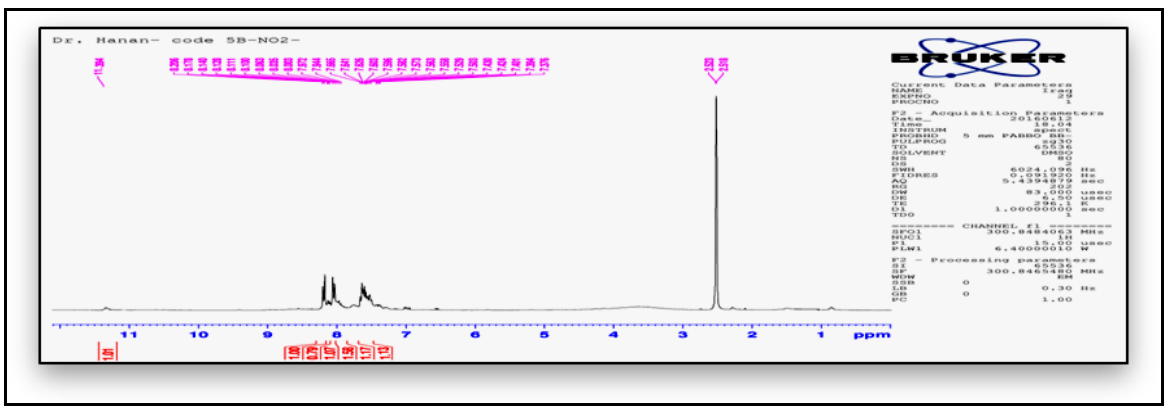
H^1-NMR Spectra. Of Comp. (4C)



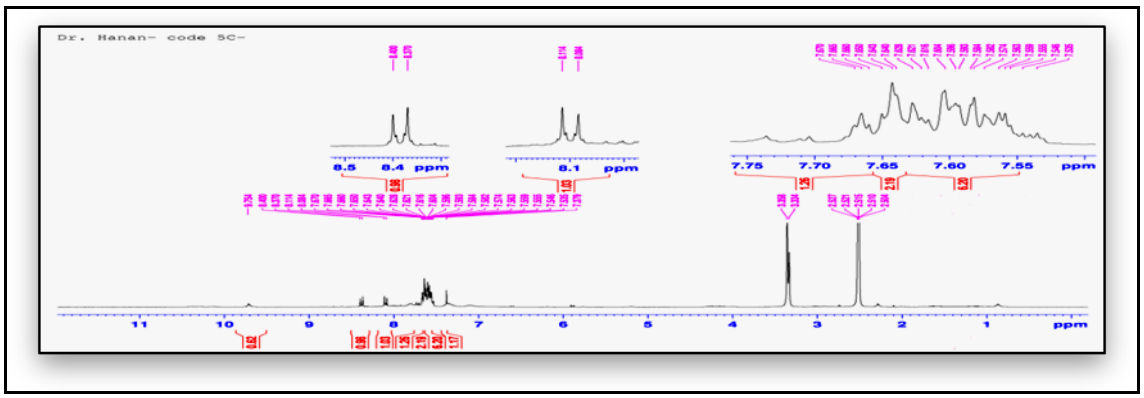
H^1-NMR Spectra. Of Comp. (4E)



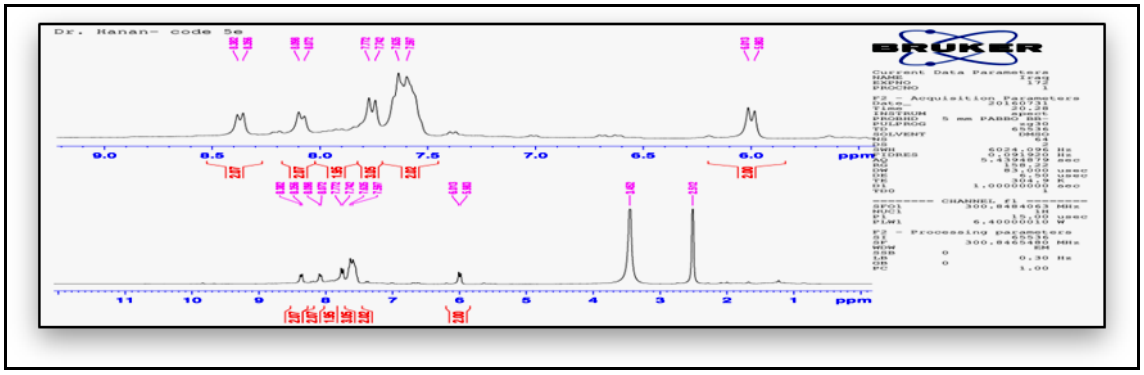
H^1-NMR Spectra. Of Comp. (4L)



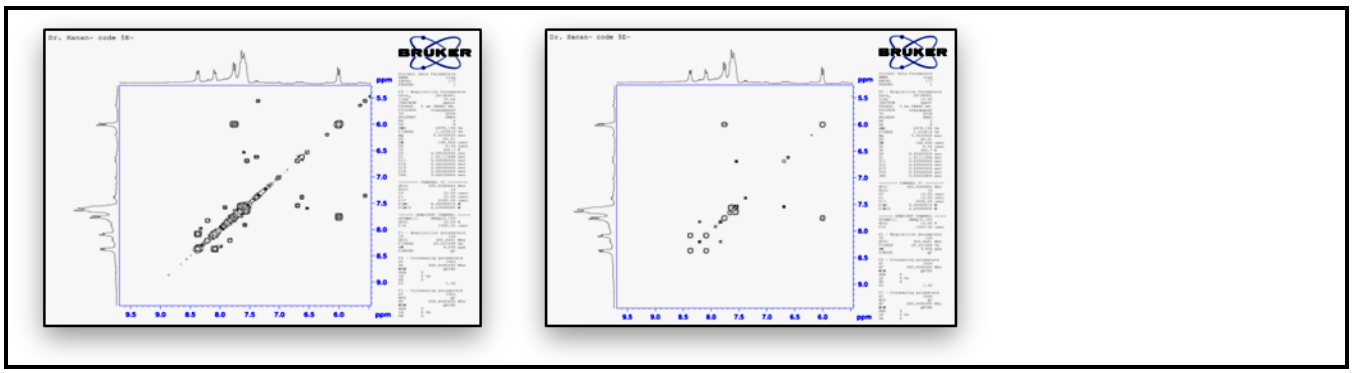
H^1-NMR Spectra. Of Comp. ($5BNO_2$)



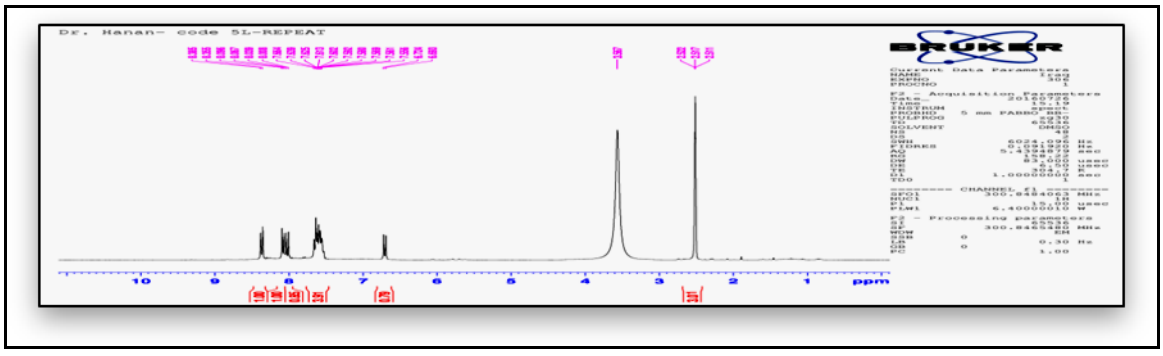
H^1-NMR Spectra. Of Comp. (5C)



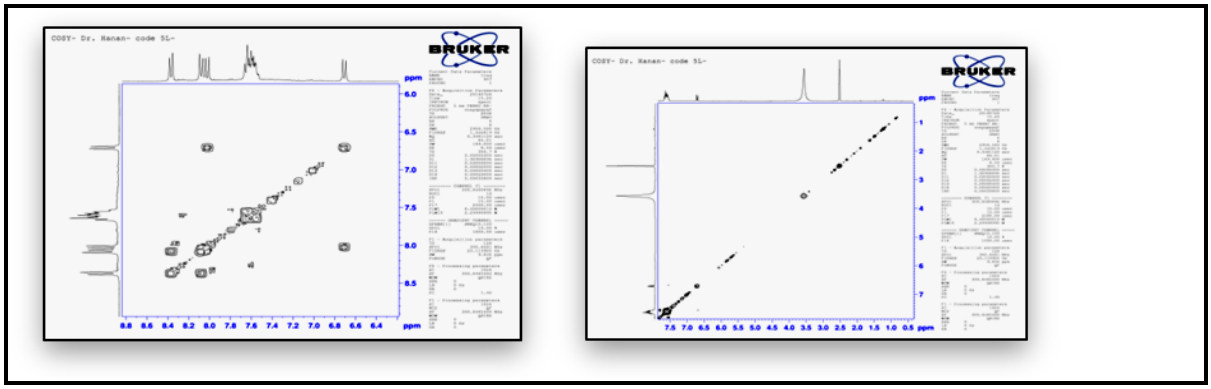
H^1-NMR Spectra. Of Comp. (5E)



COSY 2D H^1-NMR Spectra. Of Comp. (5E)



H^1-NMR Spectra. Of Comp. (5L)



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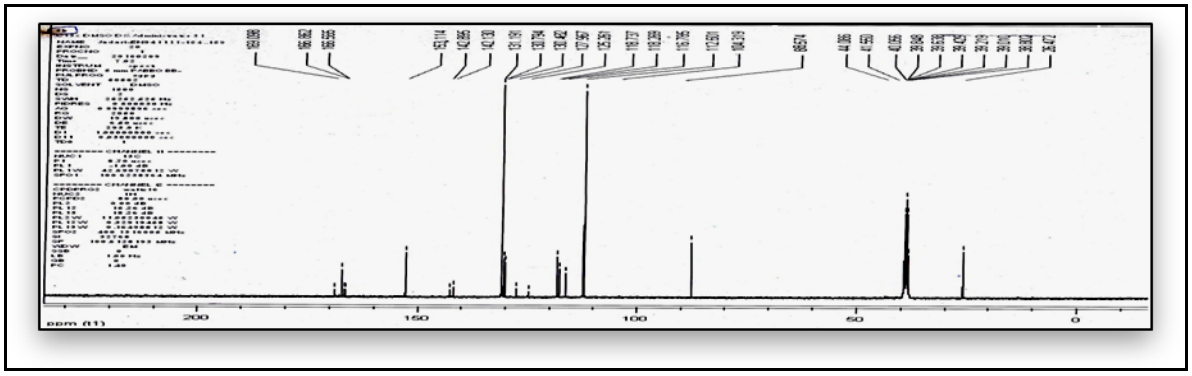
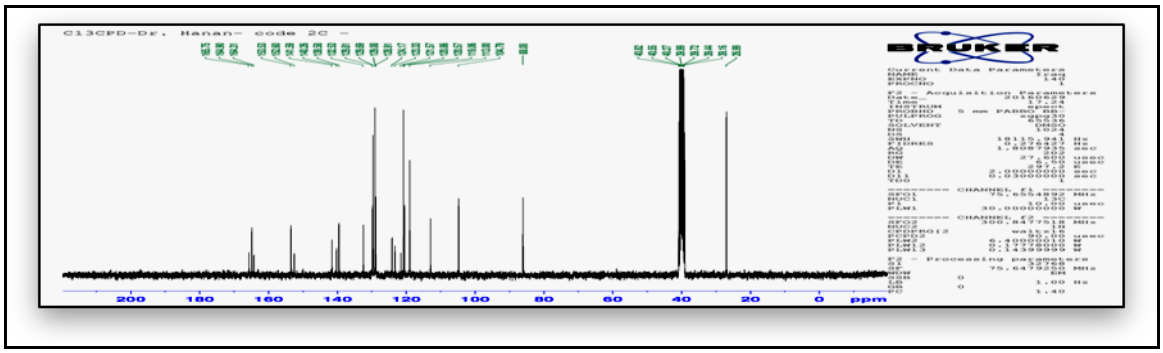
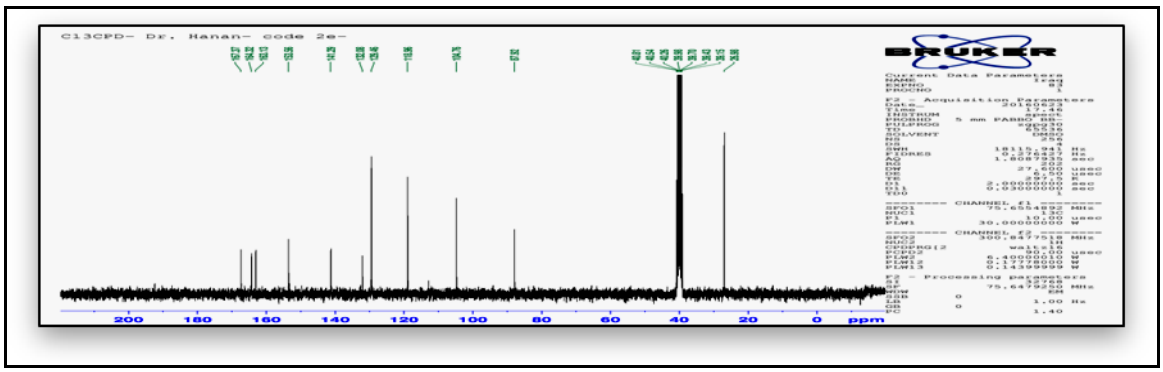


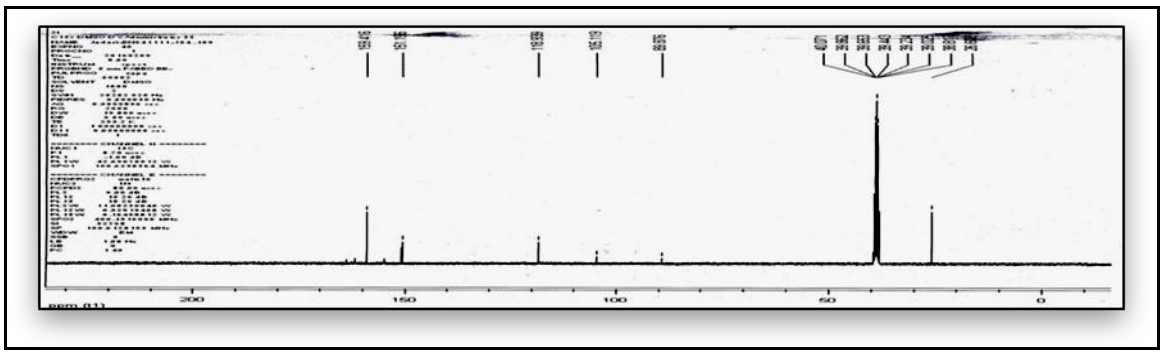
C^{13}-NMR Spectra. Of Comp. (2B)



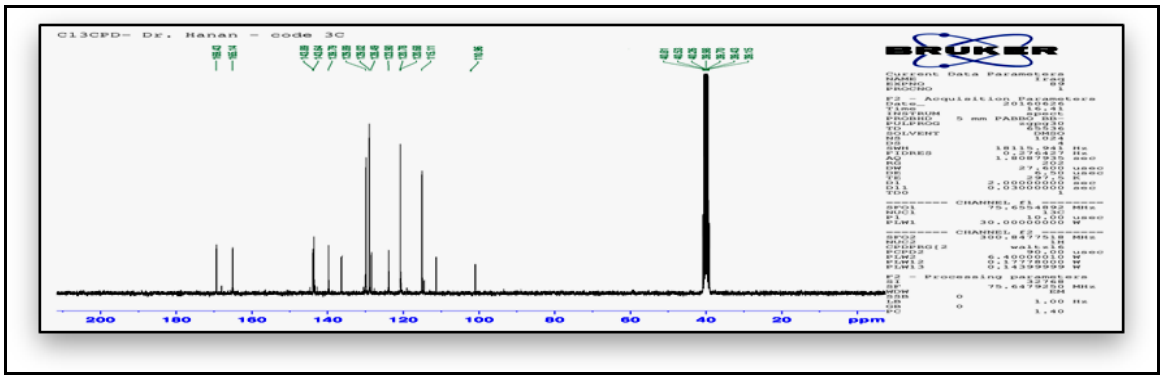
C^{13}-NMR Spectra. Of Comp. (2C)



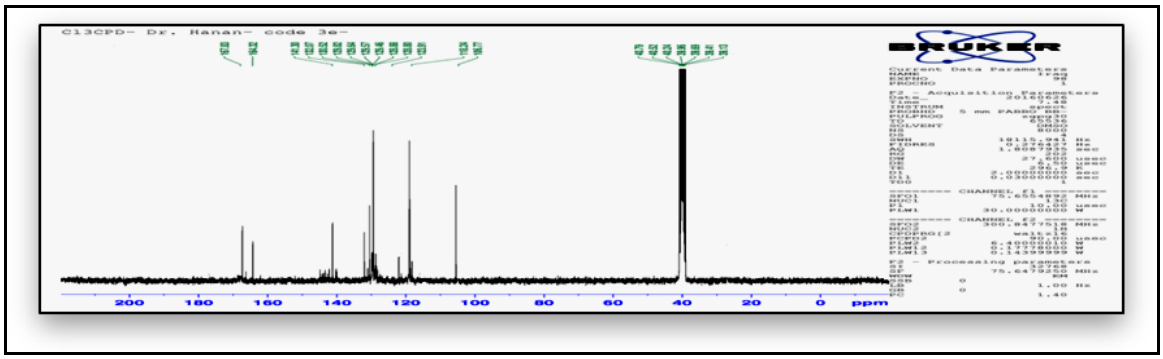
C^{13}-NMR Spectra. Of Comp. (2E)



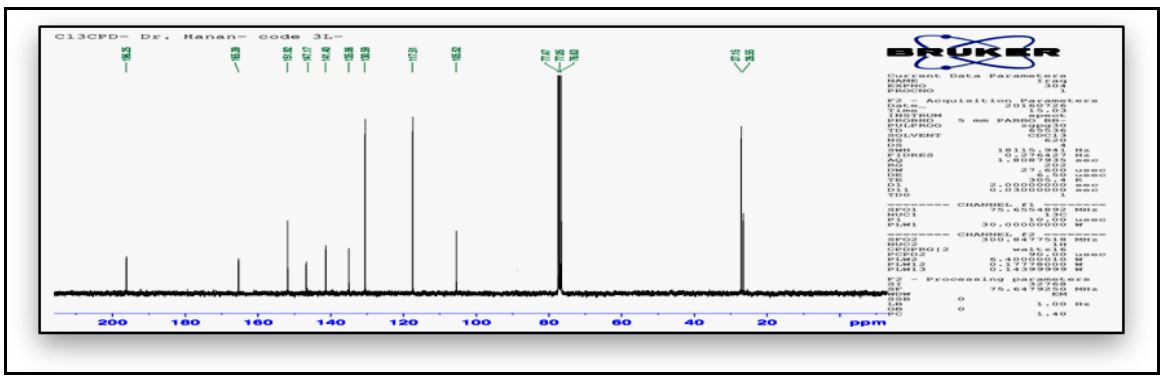
C^{13}-NMR Spectra. Of Comp. (2L)



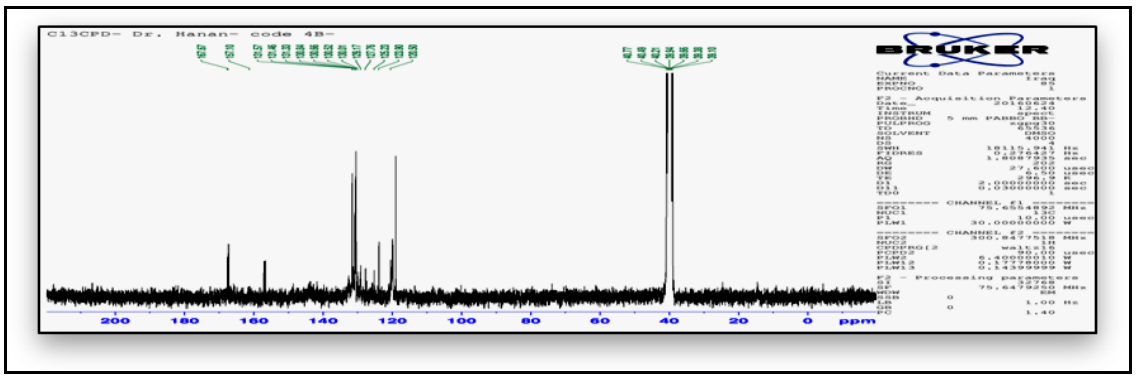
C^{13}-NMR Spectra. Of Comp. (3C)



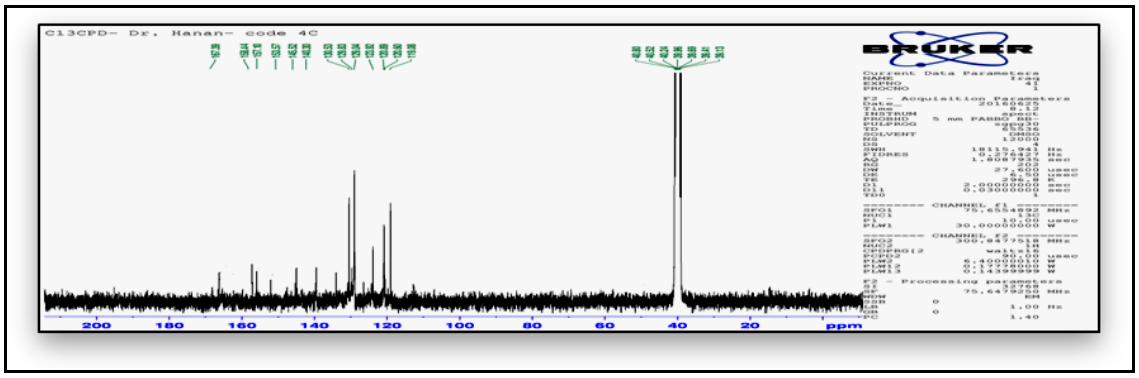
C^{13}-NMR Spectra. Of Comp. (3E)



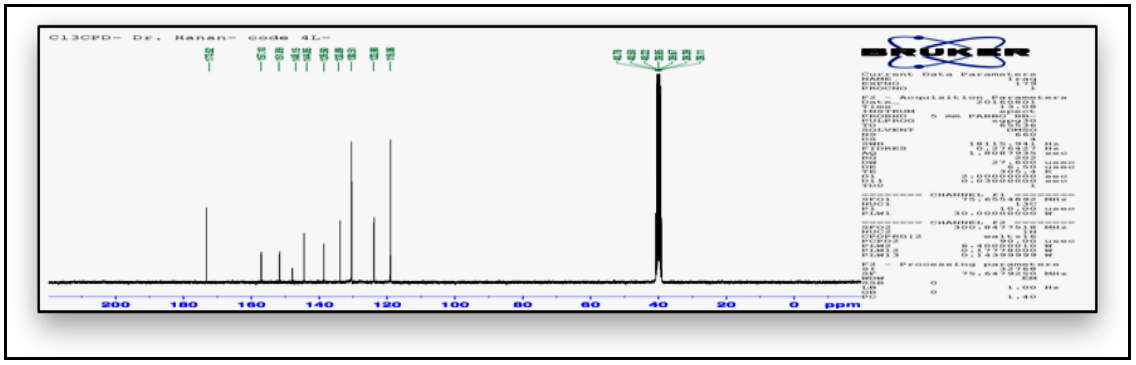
C^{13}-NMR Spectra. Of Comp. (3L)



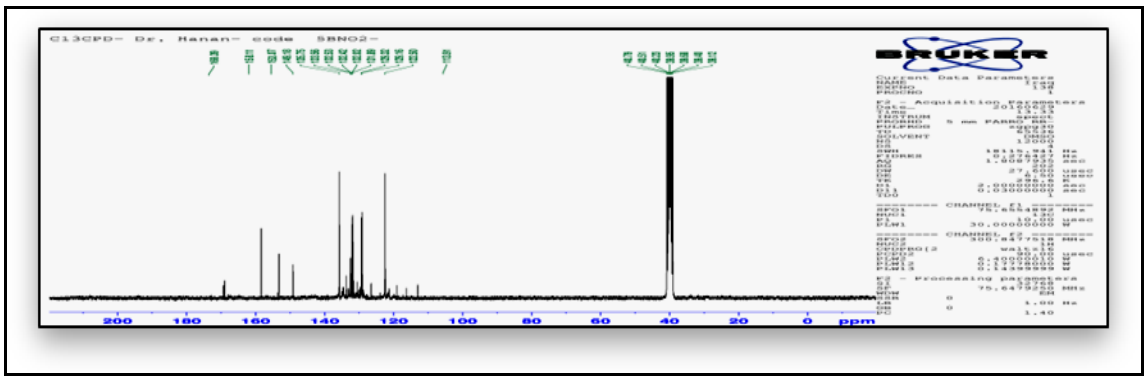
C^{13}-NMR Spectra. Of Comp. (4B)



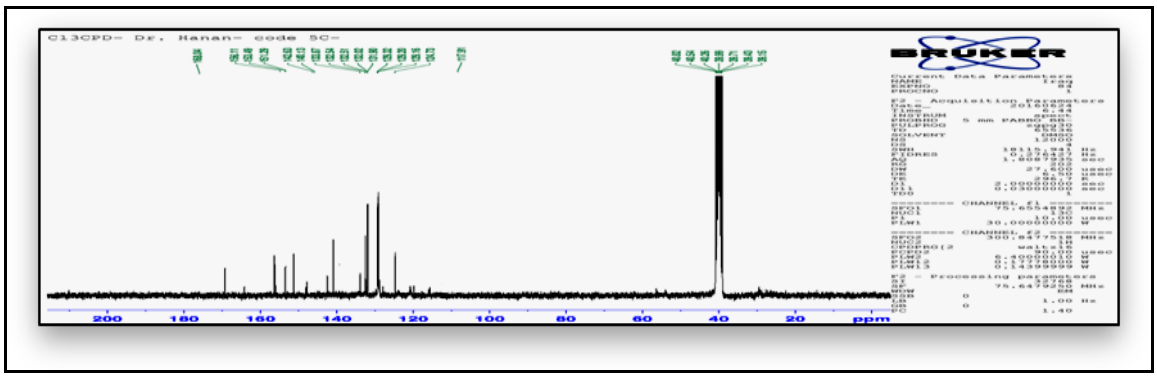
C^{13}-NMR Spectra. Of Comp. (4C)



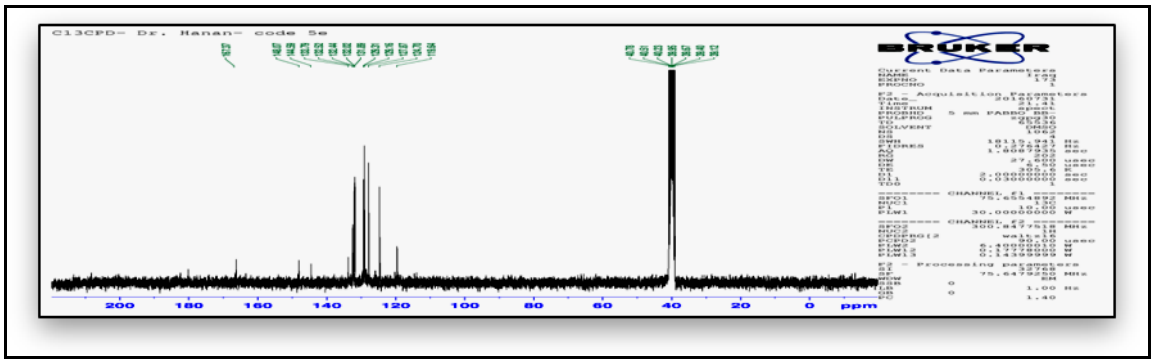
C^{13}-NMR Spectra. Of Comp. (4L)



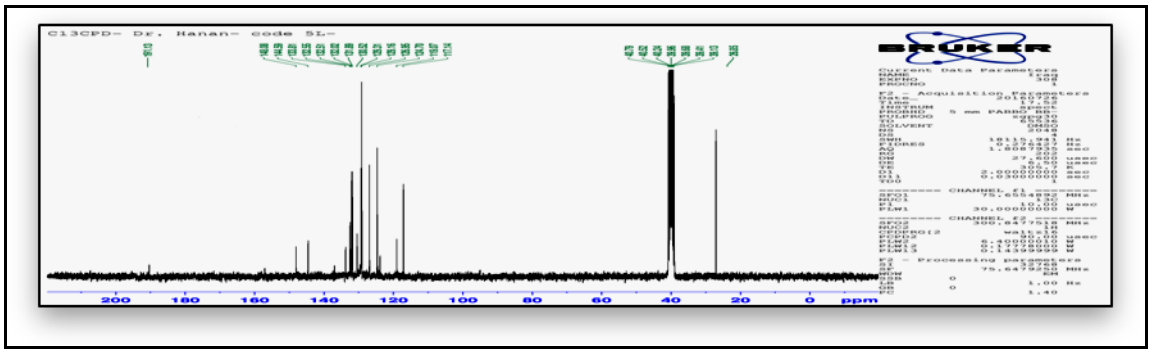
C^{13}-NMR Spectra. Of Comp. ($5BNO_2$)



C^{13}-NMR Spectra. Of Comp. (5C)



C^{13}-NMR Spectra. Of Comp. (5E)



C^{13}-NMR Spectra. Of Comp. (5L)

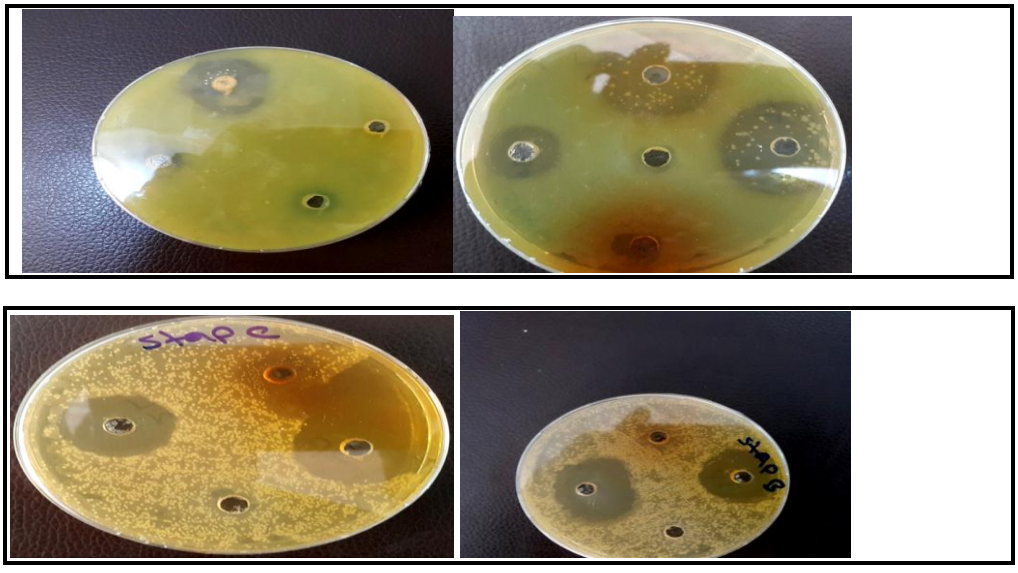


Fig (1-5) The biological activity of Preparing compounds

References

1. Miyaura, N. Cross-coupling reactions: A practical guide. Top. Curr. Chem. 2002 , 219, 11–59.
2. Jaheer M , Ranjith Reddy P , Shravan Kumar G , Divya Jyothi P, Mahmood S, Quinazolinone Derivatives as Growth Hormone Secretagogue Receptor Inhibitors: 3D-QSAR study , International Journal of ChemTech Research, 2016,9(5),896-903.
3. Geethalaksmi V, Theivarasu C , Synthesis and Characterization of Samarium (III) and Gadolinium (III) Complexes Containing2-Methoxy-6- ((2-(Piperazin-1yl) Ethylimino)Methyl) Phenol as Ligand , International Journal of ChemTech Research, 2016,9(5), 941-949.
4. Jaheer M , Ranjith Reddy P , Raghav Rao G , Divya Jyothi P , Shravan Kumar G , Three dimensional QSAR analysis of Quinazolinone derivatives as EGFR Inhibitors , International Journal of ChemTech Research, 2016,9(5), 887-895.
5. Bhave Ashish A , Chandrachood Pranav S , Deshpande Nirmala R , Kashalkar Rajashree V, Efficient route to synthesize Triazoles using copper on carbon catalyst via click chemistry ,International Journal of ChemTech Research, 2016,9(5),392-394.
6. Miyaura, N, Yamada, K, Suzuki, A , A new stereo specific cross-coupling by the palladium-catalyzed reaction of 1-alkenylboranes with 1-alkenyl or 1-alkynyl halides, Tetrahedron Lett. 1979, 20, 3437-3440.
7. R. B. Bedford, C. S.J. Cazin, D. Holder, The development of palladium catalysts for C–C and C–heteroatom bond forming reactions of aryl chloride substrates, Coord. Chem. Rev, 2004, 248,2283–2321.
8. Kurti L., Czako, B. Strategic Applications of Named Reactions in Organic Synthesis: Elsevier Academic Press 2005.
9. Nitinkumar B, Yashpalsinh J, 2, 4-Dihydroxy-5-Bromo [2'Methyl] Propiophenone Thiosemicarbazone [DHBMPT] as an Analytical Reagent: Studies on Pd (II) Chelate, International Journal of ChemTech Research, 2016,9(5),321-326.
10. Gülay, D. M sc. Thesis, Short-Time Suzuki reactions of Aryl halides catalyzed by Palladium-Loaded NaYZeolite under aerobic conditions ; İzmir Univ , 2006.
11. Amita V , Pathak Pratee K , Anjali T, Parjanya K , Piperazine bridged 4-aminoquinoline 1,3,5- triazine derivatives: Design, Synthesis, characterization and antibacterial evaluation , International Journal of ChemTech Research, 2016,9(4), 261-269.
12. Miyaura, N.; Suzuk A , Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds , Chem. Rev. 1995, 95, 2457–2483.
13. Nagham M Aljamali, Synthesis and Biological Study of Hetero (Atoms and Cycles) Compounds , Der Pharma Chemica, 2016, 8(6):40-48.
14. Nagham M Aljamali ,Synthesis and Chemical Identification of Branched Heterocyclic Compounds , European Journal of Scientific Research ,2015,134,1, 5-17.
15. Graf GI, Hastreiter D, Silva LE , Rebelo RA, Montalban AG, McKillop A , The synthesis of aromatic diazatricycles from phenylenediamine-bis (methylene Meldrum's acid) derivatives , Tetrahedron, 2002, 58 (44), 9095-9100.
16. Nagham M Aljamali , Intisar O , Synthesis of Sulfur Heterocyclic Compounds and Study of Expected Biological Activity , 2015, Research J. Pharm. and Tech. 8(9) ,1225-1242 , DOI: 10.5958/0974-360X.2015.00224.3
17. Sangdee K , Pimta J , Seephonkai P , Sangdee A , Antibacterial activity, time-kill profile and morphological effects of Streptomyces sp. SRF1 extracts against the foodborne pathogen Bacillus cereus , International Journal of ChemTech Research, 2016,9(6), 709-717.

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