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Synthesis of New Fluorine Derivatives via Mannich Reaction

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□ ABSTRACT □

Three New compounds N,N(substituted) amino,N(3(2-fluorenyl))propanone-3.(I_a),(I_b),(I_c), have been prepared using Mannich reaction from 2- Acetyl fluorine with formaldehyde and secondary amine. For(diethanol amine, diethyl Amine, N- methyl. N-phenyl amine) in an acidic medium HCl which gave these compounds:

(N, N bis (2- hydroxy ethyl) amino, N (3 (2-fluorenyl)) propanone-3 (Ia).

(N, N bis (ethyl) amino, N (3 (2- fluorenyl)) prpanone-3 (Ib).

N-methyl. N-phenyl amino, N (3 (2- fluorenyl)) propanone-3 (Ic).

The structure of these compounds have been checked by spectrum analysis: (IR, ^{1}H-NMR,^{13}c-NMR, LC-MS).

Key Words: Mannich reaction, Synthesis, Fluorine derivatives, 2- Acetyl Fluorine, Secondary Amine, Diethanol amine.

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اصطناع مشتقات جديدة للفلورين عبر تفاعل مانيش

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□ ملخّص □

تم تصنيع بعض المركبات الجديدةN,Nبيس (مستبدل) أمينو، N (3 (2 – فلورينيل)) بروبانون – 3 (Ic,Ib,Ia). عبر تفاعل مانيش بدءاً من 2– استيل فلورين مع الفورم ألدهيد وأمين ثانوي، مثال: (دي ايتانول أمين، دي ايتيل أمين، N– ميتيل.N– فينيل أمين)بوجود HCl. وهذه المركبات الجديدة هي:

Ia–N,Nبيس(2–هيدروكسي ايتيل) أمينوN(3(2– فلورينيل) بروبانون –3

Ib–N,Nبيس(ايتيل) أمينو، N (3(2– فلورينيل) بروبانون – 3

Ic–(N–ميتيل.N – فينيل) أمينو، N(3(2 – فلورينيل) بروبانون – 3

تم تحديد بنية المركبات والتعرف عليها باستخدام تحليل أطياف IR و^{1}H–NMR و^{13}C–NMRوLC–MS.

الكلمات المفتاحية: تفاعل مانيش، 2– استيل فلورين، اصطناع، مشتقات فلورين، أمين ثانوي، دي ايتانول أمين، دي ايتيل أمين، N– ميتيل.N– فينيل أمين.

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Introduction:

Mannich reaction is an important biosynthetic route in natural product synthesis,mainly alkaloids.Itis the condensation of a CH-activated (at alpha position) compound, usually a ketone or aldehyde,with a 1^0 or 2^0 amine (or ammonia) and a non-enolizable aldehyde or ketone to produce an amino-alkylated derivative AKA a Mannich Base [1].Reaction medium is usually a protic solvent:ethanol,methanol,water or acetic acid.In order to ensure a sufficiently high concentration of the electrophilic iminium ion [2].

Nowadays there is considerable interest in Chemical synthesis via Mannich reaction [3 -11]. In addition, there is great interest in rapid chemical synthesis under irradiation domestic microwave ovens[12], this method in synthesis is very good because the keeping in view the potential of microwave irradiation and biological importance of synthesis compounds[13].

Friedel-Crafts acylations are classic reactions in organic chemistry and are still of great importance in the synthesis of aromatic ketones. The reactions proceed generally with high selectivity and without rearrangements taking place although isomerizations have occasionally been observed. Fluorine-based aromatic ketones are of increasing interest as building blocks for the production of drugs and pharmaceuticals and as fine chemicals of industrial relevance. including applications in the production of thermosetting plastics and lubricating materials. In addition, fluorine-based polymers and copolymers are of interest owing to their unusual optical and electrical properties and are for that reason commonly used in organic light-emitting diodes, flat panel displays and in solar cells.In the nineteen thirties Dziewonski and Schnayder reported that the Friedel-Craftsacetylation of fluorine using acetylchloride (AcCl) and $AlCl_3$ in carbon disulfide gave 2- acetylfluorine[14].

In this paper, we have synthesized some new compounds from 2- acetyl fluorine with formaldehyde and diethanolamine,diethyl amine,N- methyl.N- phenyl amine, to give the compounds (Ia), (I_b), (Ic), respectively.

These compounds are:

- N, N bis(2- hydroxy ethyl) amino, N(3(2-fluorenyl))propanone-3. (Ia).
- N, N bis(ethyl) amino, N(3(2- fluorenyl))prpanone-3.(I_b).
- N-methyl. N-phenyl amino, N(3(2- fluorenyl))propanone-3.(Ic).

1- Importance and Aim of this work:

This work aims to synthesis new fluorine derivatives. May be, these Compounds have industrial applications and may be have biological activity also.

Experimentals Methods:

The used Instruments:

1- Infrared spectroscopy instruments(IR), Perkin-Emer FT-IR spectrum 200 spectrophotometer by using(KBr) Pills (Damascus University).

2- (Uv-Vis) spectrometer, T70 (Tishreen University).

3- Kofler hot – stage for melting point measurement(Tishreen University).

4- Nuclear Magnetic Resonance Bruker 400 MHZ, Avancespectrometer(^{1}H-NMR,^{13}C- NMR)(Syrian Atomic Energy Commission).

5- Euro Elemental Analyzer – Ajelent(Damascus University).

6- Rota Vapor type RERL(BÜCHI) (Tishreen University).

The used Materials:

1- 2- Acetyl Fluorine(sigma-Aldrich), 98%, M_{wt}= 208.26 g/mol, m.p =128-129 C°.

2- Formaldehyde, Diethanol amine, Diethyl amine, N- methyl, N- phenyl amine(Merck).

3- HCl, Absolute Ethanol, Methanol, Etherethyl(sigma- Aldrich).

General procedure for the preparation of Compounds (Ia),(Ib),(Ic) [12].

1-synthesis of N, N-bis (2- hydroxy ethyl) amino, N(3(2- fluorenyl)) propanone-3(Ia).

Amixture of 4.165g (0.02 mol), 2- acetyl fluorine, formaldehyde 1.6g (0.02 mol), diethanol amine 2.1g(0.02 mol), 200 ml absolute ethanol and a few drops of conc.HCl, was refluxed for 16 hr. the excess solvent was distilled under reduced pressure and a product separated as coloured oil (Green oil).

2- Synthesis of N, N- bis (Ethyl) amino, N (3(2- Fluorenyl)) Propanone-3 (Ib).

A mixture of 2-acetyl fluorine. 2.08 g (0.01 mol), formaldehyde 0.8g (0.01 mol). diethyl amine 0.73g (0.01 mol). absolute ethanol (200 ml) and a few drops of conc.HCl, was refluxed for 16 hr. the excess solvent was distilled under reduced pressure and a product separated as coloured oil (grey white oil).

3- Synthesis of N- Methyl.N-Phenyl amino, N (3 (2-Fluorenyl)) Propanone-3 (Ic).

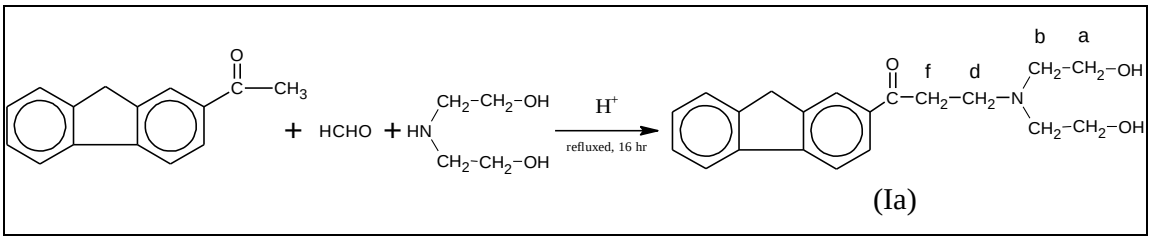
A mixture of 2.08 g (0.01 mol), 2-acetyl fluorine. formaldehyde 0.8g (0.01 mol). N-methyl, N-phenyl amine. 1.07 g (0.01 mol). absolute ethanol (200 ml) and a few drops of conc.HCl, was refluxed for 16 hr. the excess solvent was distilled under reduced pressure and a product separated as coloured oil (Brown oil).

Results and discussion:

Chemistry and characterization:

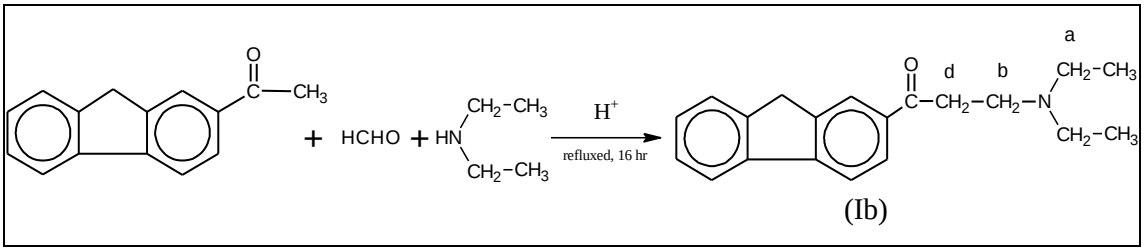
The present work involved three steps

First step: Include preparation of new compound (Ia) was prepared by reaction of secondaryamine (diethanol amine) with 2-acethyfluorine and formaldehyde. The synthesis of this compound was carried out lined in Scheme (1) and its physical propertiesas shown in table (1). Including melting point (oil) and % yield was (98) and this compound was identified by FT-IR Spectroscopy, LC-MS, ^{1}H-, ^{13}C-NMR. FT-IR spectrum of this compound showed characteristic absorption bands (1714.65)cm^{-1}, (2951,52)cm^{-1}, (1584.6)cm^{-1}, (3360.35)cm^{-1}, due to υ(C=O)str, υ(C-H)aliphatic, υ(C=C)aromatic, υ(OH), respectively. As shown in table (2). ^{1}H-NMR spectrum of compound (Ia) showed multiplet signals at (7.4 -8.16)ppm due to aromatic protons of fluorine and singlet signal at (2.35) ppm due to (OH) group proton and singlet signal at 3.76 ppm due to (CH_2) group protons of fluorine in addition to thriplet signals at (3.17)due to (CH_2)(a) group protons andthriplet signals at (2.48) due to (CH_2)(b) group protonsand thriplet signals at (2.57) due to (CH_2)(d) group protonsand thriplet signals at (2.48) due to (CH_2)(f) group protons. ^{13}C-NMR of compound (Ia) showedmultiplet signals at (127-142)ppm due to aromatic carbons of fluorine, signals at (41.85)ppm due to (CH_2) carbon of fluorine, signals at (200.9)ppm due to (C=O) carbon, signals at (62.06)ppm due to (CH_2)(a) carbon, signals at (59.65)ppm due to (CH_2)(b) carbon,signals at (47.46) ppm due to (CH_2)(d) carbonin addition tosignals at (43.05) ppm due to (CH_2)(f) carbon.



Scheme (1)

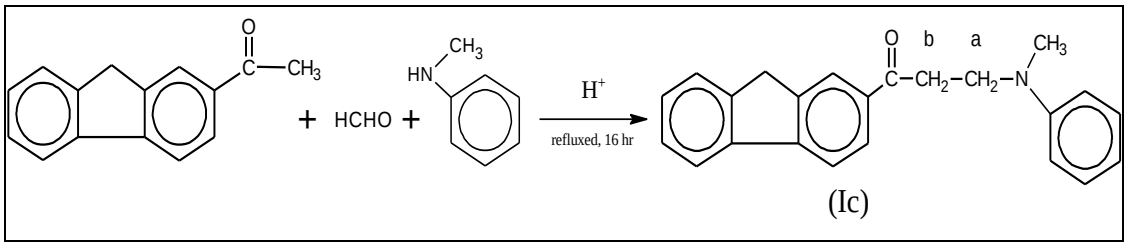
Secondstep: Second step includes preparation of new compound (Ib) was prepared by reaction of secondary amine (diethyl amine) with 2-acethy fluorineandformaldehyde. The synthesis of this compound was carried out lined in Scheme (2) and its physical propertiesas shown in table (1). including melting point (oil) and % yield was (93) and this compound was identified by FT-IR Spectroscopy, LC-MS, ^{1}H-, ^{13}C-NMR. FT-IR spectrum of this compound showed characteristic absorption bands (1675.34)cm^{-1}, (2992.98)cm^{-1}, (2854.13)cm^{-1}, (1557.78)cm^{-1}, due to υ(C=O)str, υ(CH_3), υ(CH_2), υ(C=C)aromatic, respectively. As shown in table (2). ^{1}H-NMR spectrum of compound (Ib) showed multiplet signals at (7.42 -8.16) ppm due to aromatic protons of fluorine anddisappearance of signals due to (OH) group proton and singlet signal at 3.76 ppm due to (CH_2) group protons of fluorine in addition to thriplet signals at (2.2) due to (CH_2)(a) group protons and thriplet signals at (2.57) due to (CH_2)(b) group protons and thriplet signals at (2.47) due to (CH_2)(d) group protonsand disappearance of signals due to (CH_2)(f) group protonswhich appeared for compound (Ia),in addition to thriplet signalsat 0.57 ppmdue to (CH_3) group protons. ^{13}C-NMR of compound (Ib) showed multiplet signals at (126 -142)ppm due to aromatic carbons of fluorine, signals at (41.80)ppm due to (CH_2) carbon of fluorine, signals at (200.9)ppm due to (C=O) carbon, signals at (49.08) ppm due to (CH_2)(a) carbon, signals at (46.8) ppm due to (CH_2)(b) carbon, signals at (42.9) ppm due to (CH_2)(d) carbon in addition to signals at (13.65) ppm due to (CH_3) carbon.



Scheme (2) .

Third step: this step includes preparation of new compound (Ic) was prepared by reaction of secondary amine (N-methyl, N-Phenyl amine.) with 2-acethy fluorineand formaldehyde. The synthesis of this compound was carried out lined in Scheme (3) and its physical properties as shown in table (1). including melting point (oil) and % yield was (83) and this compound was identified by FT-IR Spectroscopy, LC-MS, ^{1}H-, ^{13}C-NMR. FT-IR spectrum of this compound showed characteristic absorption bands (1746)cm^{-1}, (2828)cm^{-1}, (1456.13)cm^{-1}, (1558.14)cm^{-1}, due to υ(C=O)str, υ(CH_3), υ(CH_2fluorine ring), υ(C=C)aromatic, respectively. As shown in table (2). ^{1}H-NMR spectrum of compound (Ic) showed multiplet signals at (6.87-8.23) ppm due to aromatic protons of fluorine and disappearance of signals due to (OH) group proton and singlet signal at 3.5 ppm due to (CH_2) group protons of fluorine, in addition to thriplet signals at (2.7) due to (CH_2)(a)

group protons and thriplet signals at (2.3) due to (CH_2)(b) group protons and thriplet signals at (1.98) due to (CH_3) group protons and disappearance of signals due to (CH_2)(d) group protons which appeared for compound (Ib). ^{13}C-NMR of compound (Ic) showed multiplet signals at (112 -142) ppm due to aromatic carbons of fluorine ring and benzene ring, signals at (51.77)ppm due to (CH_2) carbon of fluorine, signals at (200.89) ppm due to (C=O) carbon, signals at (49.08) ppm due to (CH_2)(a) carbon, signals at (42.37) ppm due to (CH_2)(b) carbon, in addition to signals at (34.85) ppm due to (CH_3) carbon.



Scheme (3 .

Table(1):Melting points, yield, molecular formula (M.F.), molecular weight (M.Wt.), color and R_f

Comp.	M.Wt.	M.F.	Yield(%)	M.P. (^{0}C)	Color	R_f (eter:hexan) (1:3)
Ia	325	$C_{20}NO_3H_{23}$	98	oil	green	0.54
Ib	293	$C_{20}NOH_{13}$	93	oil	Grey white	0.6
Ic	327	$C_{23}NOH_{13}$	83	oil	brown	0.61

Table 2: Depacited elemental analysis (C.H.N)

Comp.	Found			Calculated		
	C%	H%	N%	C%	H%	N%
Ia	74.02	7.13	4.43	73.85	7.08	4.31
Ib	82	4.39	4.91	81.9	4.44	4.78
Ic	84.37	6.36	4.39	84.40	6.42	4.40

Table 3: Spectroscopial data

Comp. NO	Spectroscopy data
Ia	IR(KBr, cm^{-1}): 3360,35 [υ(OH)], 2951.52 [υ(C-H)Alipha],1714.65 [(C=O)], 1584.6 [υ(C=C)Ar],1103.08 [υ(C-N)],1067.41 [υ(C-O)],1455.21[υ(CH_2)] fluorine ring LC-MS: m/z =325.17 ^{1}H-NMR (400 MHz, $CDCl_3$, ppm)δH:2.35 (S, 1H, OH), 3.76 (S, 2H, CH_2fluorine ring), 3.17 (t, 2H, CH_2(a)),2.48 (t, 2H, CH_2(b)),2.57 (t, 2H, CH_2(d)),2.52 (t, 2H, CH_2(f)), 7.4-8.16 (m, 7H, aromatic ring ^{13}C-NMR(400MHz,$CDCl_3$,ppm)δC:200.9(C=O), 41,85(CH_2fluorene ring), 62.06(CH_2(a)), 59.65(CH_2(b)),47.46(CH_2(d)),43.05(CH_2(f)),127 -142(aromatic ring).
Ib	IR(KBr, cm^{-1}): 2992.98 [υ(CH_3)], 2854.13 [υ(CH_2)],1456.81[υ(CH_2)]fluorine ring],1675.34 [(C=O)], 1557.78 [υ(C=C)Ar], 1161.52 [υ(C-N)]. LC-MS: m/z =293.18 ^{1}H-NMR (400 MHz, $CDCl_3$, ppm)δH: 3.76 (S, 2H, CH_2 fluorine ring),0.57 (S,3H, CH_3),2.2 (t, 2H, CH_2(a)), 2.57 (t, 2H, CH_2(b)), 2.47 (t, 2H, CH_2(d)), 7.42 -8.16 (m,

	7H, aromatic ring) ^{13}C-NMR(400MHz,$CDCl_3$,ppm)δC:200.9(C=O), 41,80(CH_2fluorene ring), 49.08(CH_2(a)), 46.8(CH_2(b)), 42.9(CH_2(d)), 13.65(CH_3),126 -142(aromatic ring).
Ic	IR(KBr, cm^{-1}): 3046.68 [υ(CH)Ar],2828 [υ(CH_3)], 1456.13[υ(CH_2)] fluorine ring],1746 [(C=O)], 1558.14 [υ(C=C)Ar], 1131.65 [υ(C-N)] LC-MS: m/z =327.16 ^{1}H-NMR (400 MHz, $CDCl_3$, ppm)δH: 3.5 (S, 2H, CH_2 fluorine ring), 2.7 (t,2H, CH_2(a)), 2.3 (t, 2H, CH_2(b)), 1.98 (S, 3H,(CH_3)), 6.87 -8.23(m, 7H, aromatic ring) ^{13}C-NMR(400MHz,$CDCl_3$,ppm)δC:200.89(C=O), 41,97(CH_2fluorine ring), 51.77(CH_2(a)), 42.37(CH_2(b)), 34.85(CH_3),150.9(C-N),112 -142(aromatic ring).

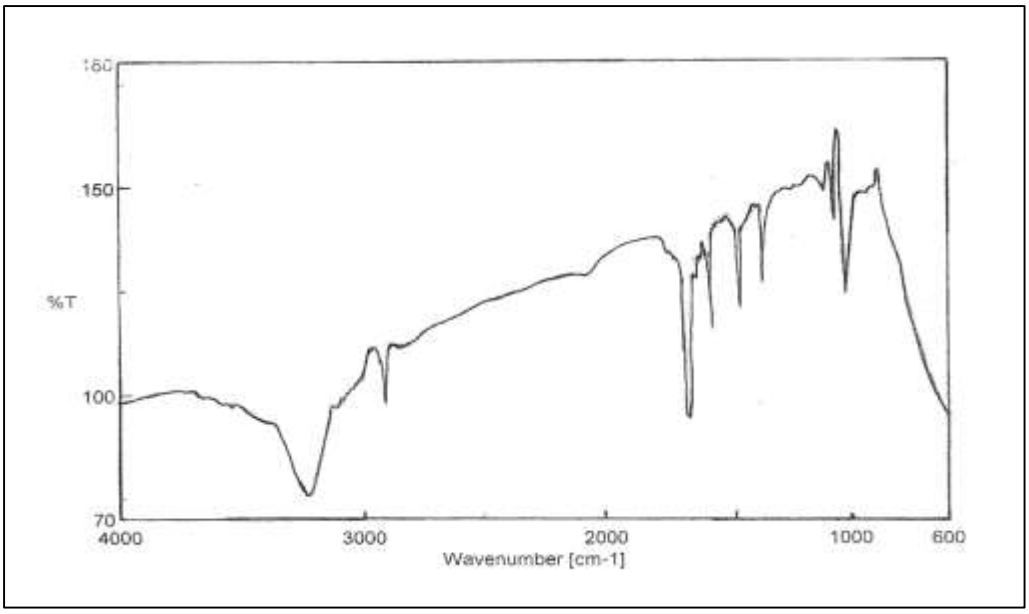


Figure (1). IR Spectra of (Ia)

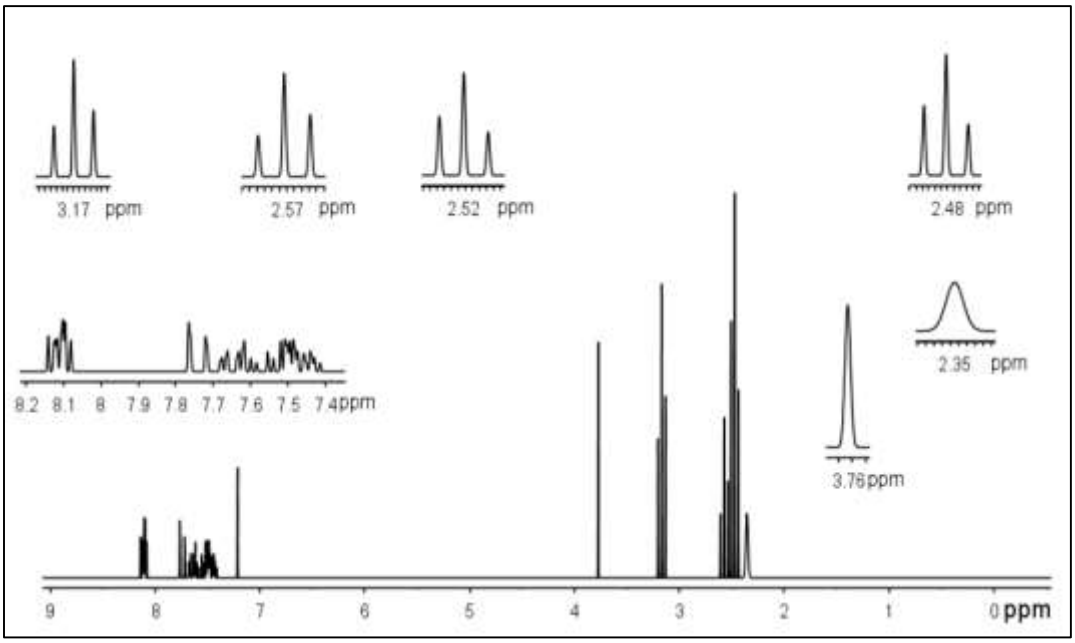


Figure (2). ^{1}H- NMRSpectra of (Ia)

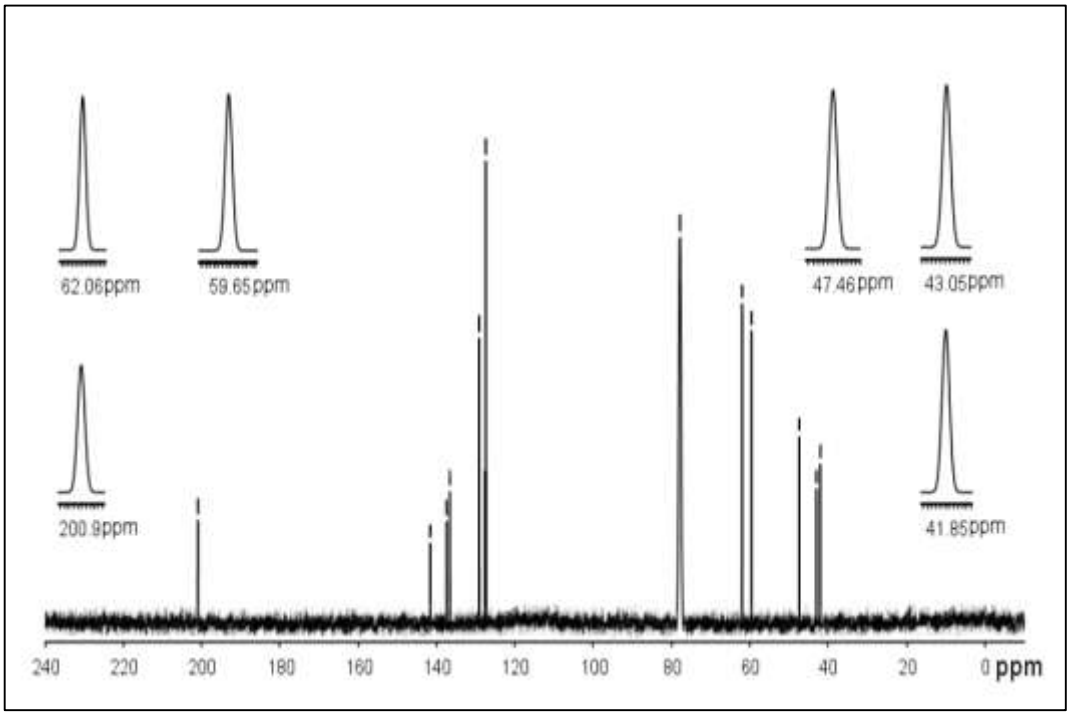


Figure (3). ^{13}C- NMR Spectra of (Ia)

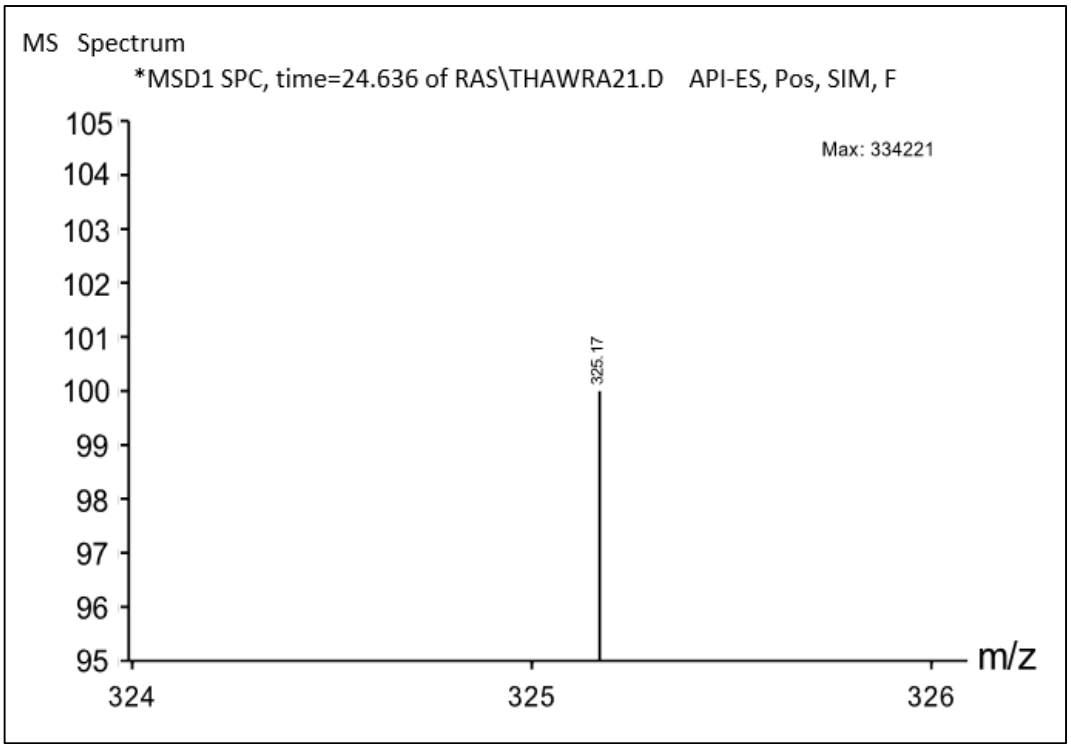


Figure (4). LC-MS Spectra of (Ia)

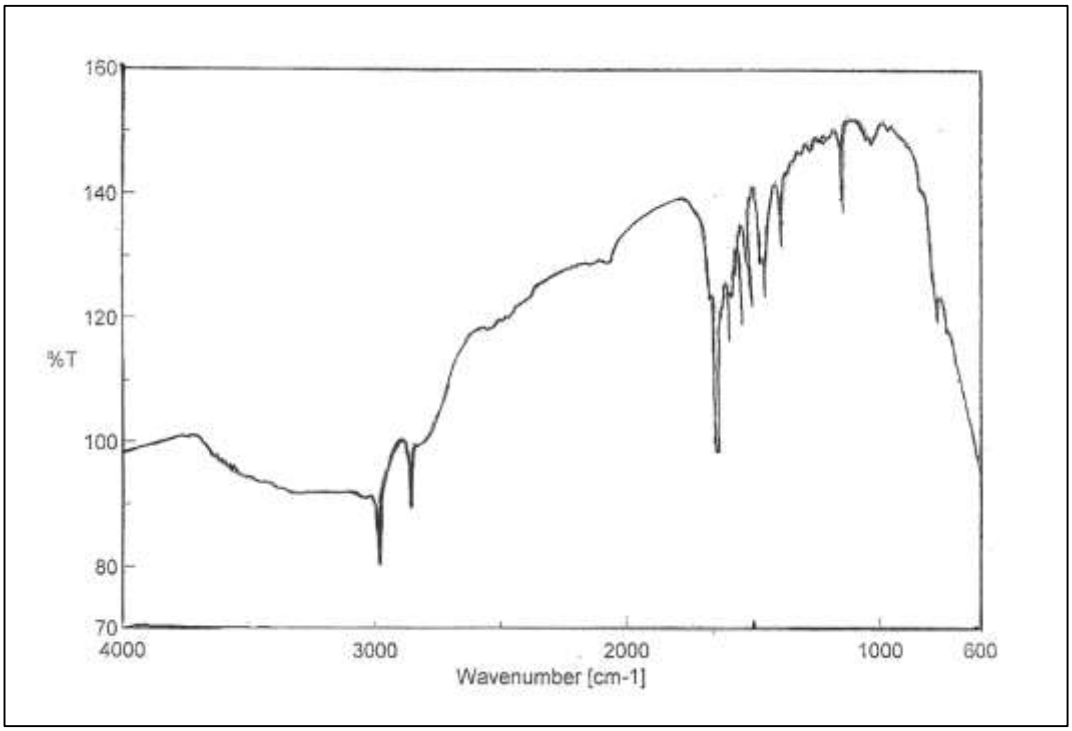


Figure (5). IR Spectra of (Ib)

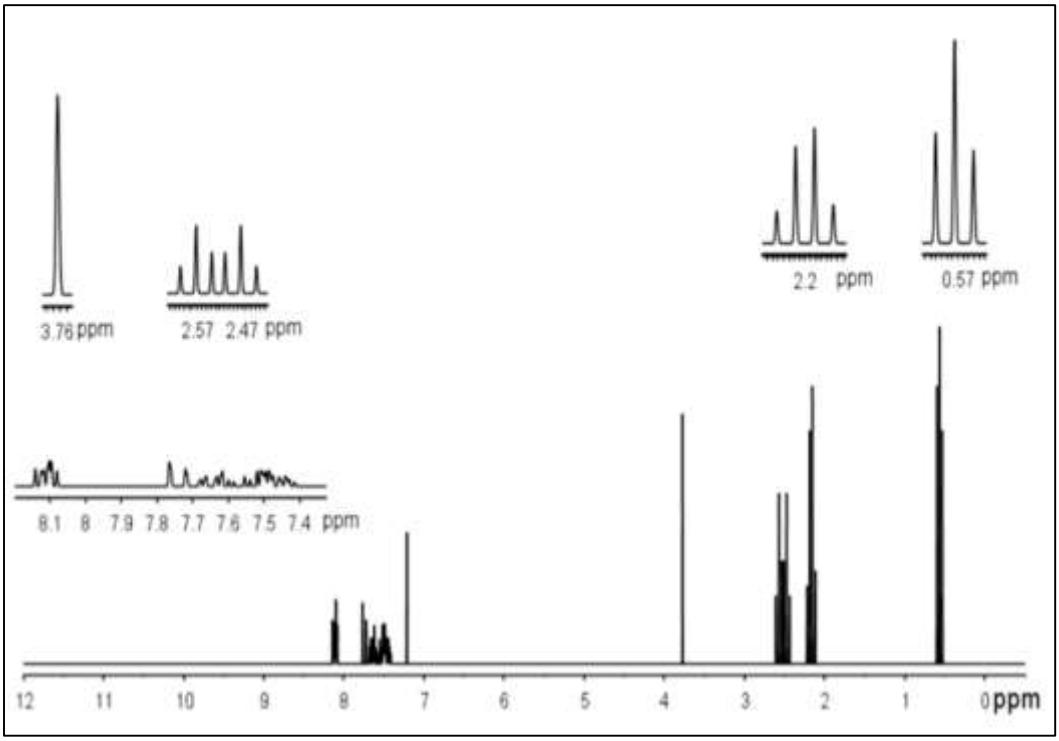


Figure (6). ^{1}H- NMR Spectra of (Ib)

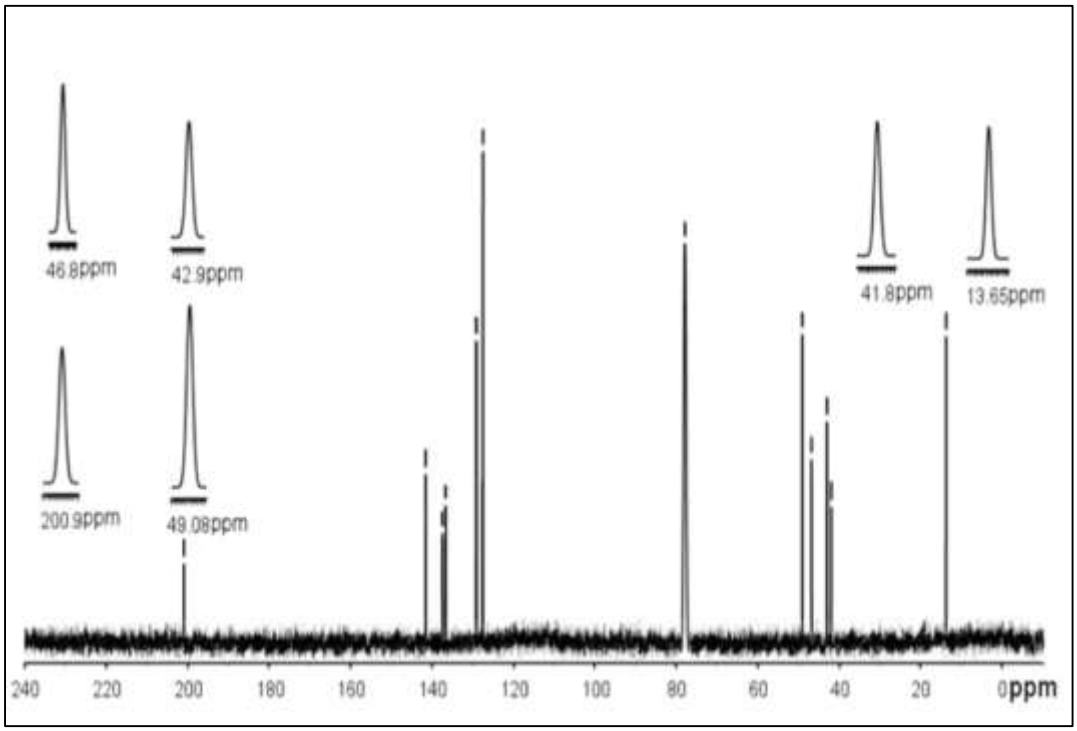


Figure (7). ^{13}C- NMR Spectra of (Ib)

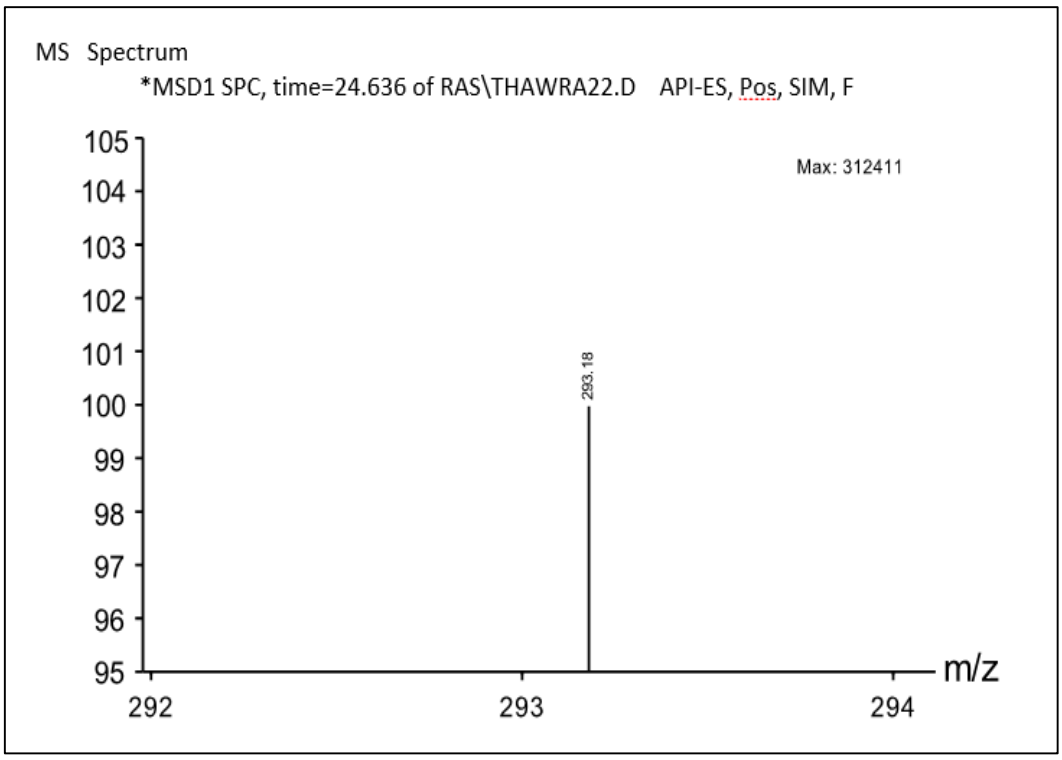


Figure (8). LC-MS Spectra of (Ib)

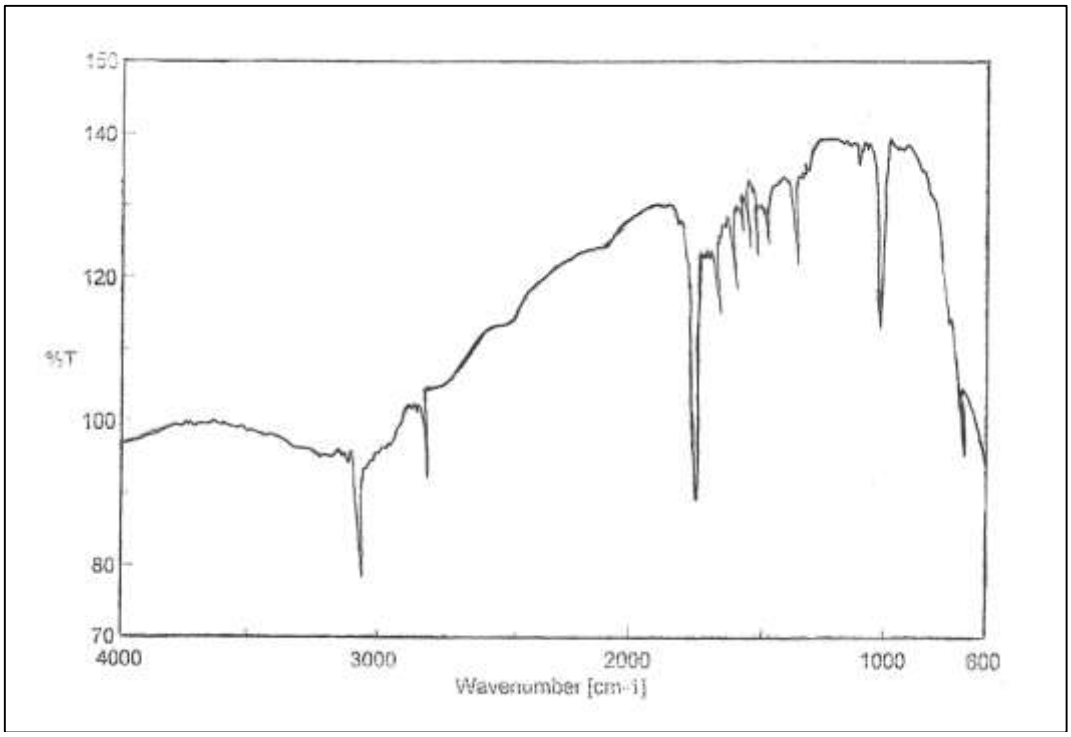


Figure (9). IRSpectra of (Ic)

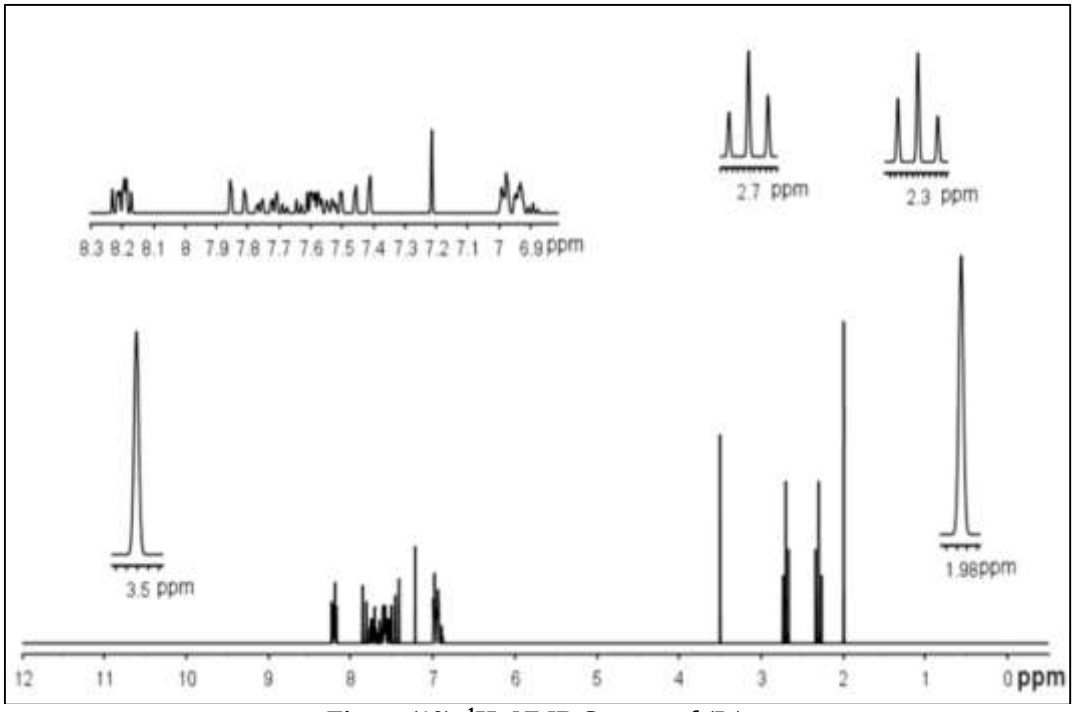


Figure (10). ^{1}H- NMR Spectra of (Ic)

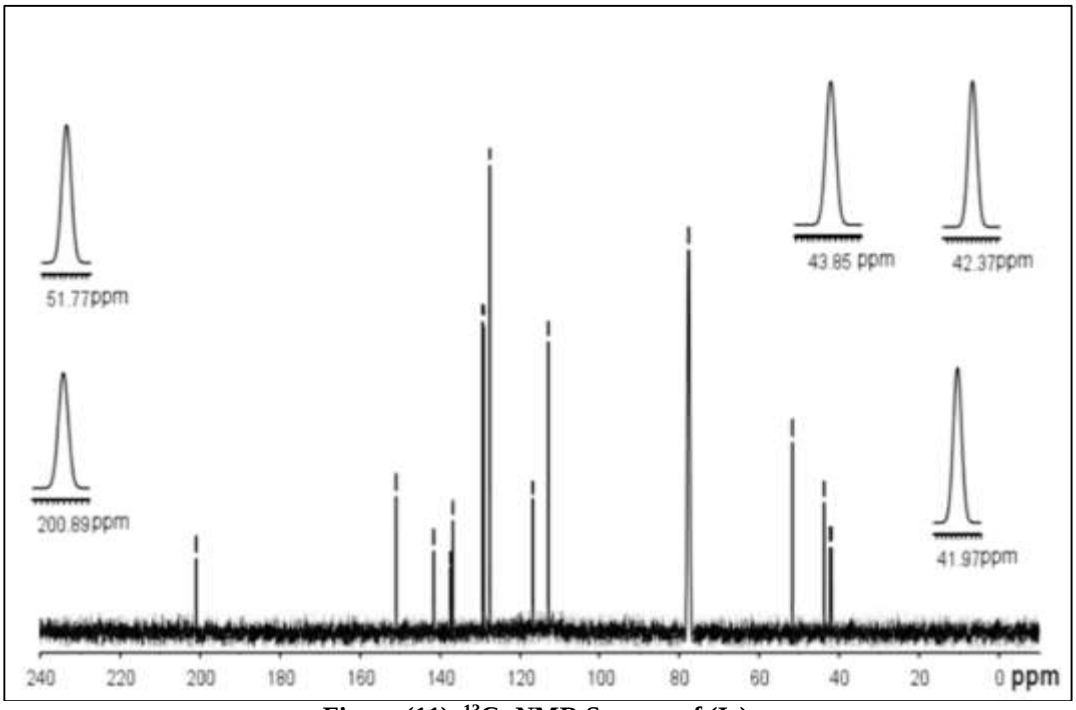


Figure (11). ^{13}C- NMR Spectra of (Ic)

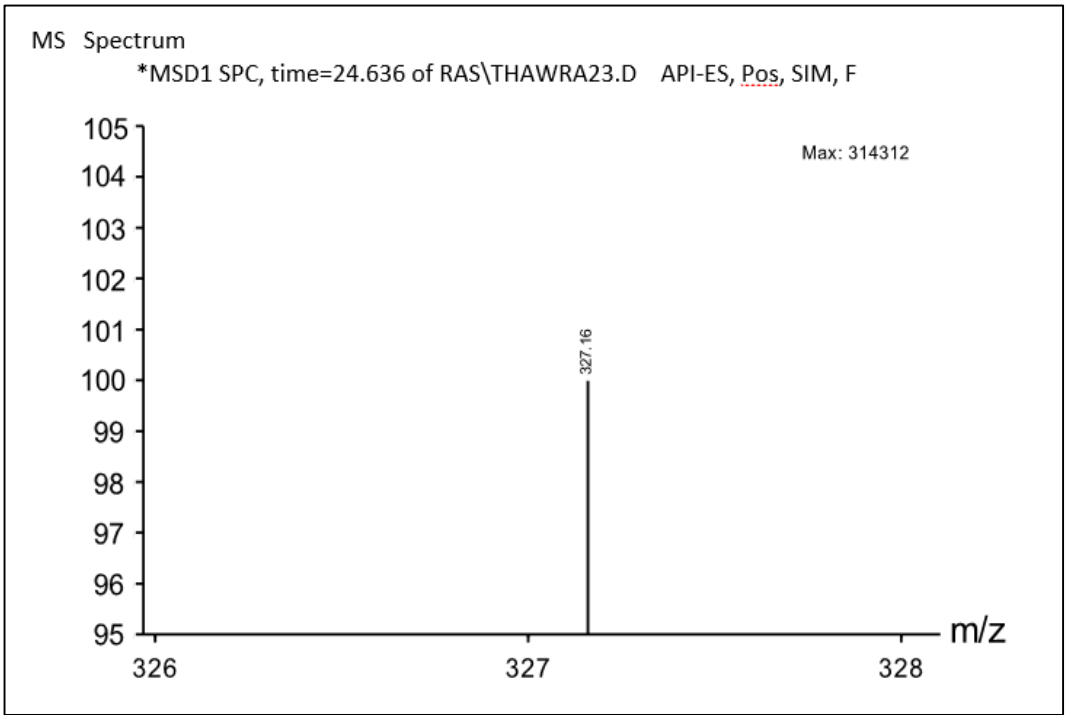


Figure (12).LC- MS Spectra of (Ic)

Conclusion:

The main aim of this study was to synthesize of new fluorine derivatives viaMannichreaction,these compounds were:

(N, N bis (2- hydroxy ethyl) amino, N (3 (2-fluorenyl)) propanone-3. (Ia)

(N, N bis (ethyl) amino, N (3 (2- fluorenyl)) prpanone-3. (Ib)

N-methyl. N-phenyl amino, N (3 (2- fluorenyl)) propanone-3. (Ic).

these compounds were identified by FT-IR Spectroscopy, LC-MS, ^{1}H-, ^{13}C-NMR.

these compounds have long been known for their diverse biological properties, mainly as antiviral, antibacterial, antifungal and anti-inflammatory agents,finallythey have biological activity [14]

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