Preparation and Identification of some new isatin Schiff' s-mannich bases

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Abstract

Some isatin Schiff's bases (N_1– N_{12}) have been preparedby reaction with some aromatic amines then the resulting products were converted to the corresponding mannich bases (N_{13}-N_{23}) by reaction with some secondary amines and formaldehyde making use of active –NH group of isatin .All products have been identified by IR spectroscopy and for some by ^{1}H-NMR and^{13}C-NMR and C.H.N analyzer .

Keywords: Isatin , Isatinschiff's – mannich bases .

تحضير وتشخيص بعض قواعد شيف – مانخ للايساتين الجديدة

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الخلاصة

تم تحضير عدد من قواعد شيف للايساتين (N_{12}-N_1) بتفاعل الايساتين مع بعض الامينات الاروماتية وتم تحويل النواتج الى قواعد مانخ (N_{23}-N_{13}) بتفاعلها مع بعض الامينات الثانوية والفورملدهايد وبالاستفادة من مجموعة (-NH) الفعالة في

الايساتين. كل النواتج المحضرة تم تشخيصها باستخدام تقنية الاشعة تحت الحمراء (FT-IR) والبعض منها باستخدام تقنية الرنين النووري المغناطيسي (^{13}C-NMR-^{1}H-NMR) والتحليل الدقيق للعناصر (C.H.N).

كلمات مفتاحية: إيساتين ، قواعد شيف الايساتين ، قواعد مانخ

Introduction

Isatin (indoline -2,3-dione) is on of the indol derivatives of isatin which was prepared by oxidation of indigo[1] . Isatin Schiff's bases are known to posses biological activity such as antimicrobial and anticancer and analgesic[2-7].The other type of isatin derivatives and the isatinschiff's – mannich bases which combine both the azomethine and methylene amine linkage (CH_2-N) in one molecule and due to the intramolecular hydrogen bonding between the two groups and the probable biological activity it encouraged us to prepare these compounds .

Experimental Part

2.1 - Instruments and chemicals used :-

The uncorrected melting points were measured by electrothermal melting point apparatus (metler) and the infrared spectra were measured by infrared spectrophotometer (Perkin – Ulmer) . ^{1}H-NMR and ^{13}C-NMR spectra were measured in university of technology – Jordon using (Bruker Ultra shield 400MHz) instrument using DMSO-6d as a solvent and C.H.N analyzer of type (Evrovector EA 300A Italy) . All chemicals used were supplied from BHD , Flukacompanies .

2.2- Preparation of Schiff's bases (N_1-N_{12}).

Compound (N_1)in table (1) was chosen as typical example for the preparation :-

In around bottom flask fitted with condenser (1 gm , 0.007 mole) of isatin was dissolved in in (20 ml) of ethanol . A solution of (0.95 gm , 0.007 mole) in ethanol (15 ml) was treated with cat.ammount of glacial acetic acid (3-4 drops) ,and then the mixture was added to the above solution . The mixture was heated to reflux for 3 hrs and The precipitate appeared was filtered

and recrystallized from ethanol and after drying at room temperature ,M.P (281 – 283 ^{0}C) , %yield was 91% .

Table (1) physical properties of the prepared Schiff's bases($N_{12}N_{1}$-)

Comp.No	Chemical Formula	Colour	M.p^{0}C	% Yield	C.H.N	%C	%H	%N
N_1	$C_{14}H_{10}N_4O_2$	Pale orange	283 - 281	91	calculated found	63.02 63.15	3.60 3.79	21.03 21.14
N_2	$C_{14}H_9BrN_2O$	yellow	258 - 256	61				
N_3	$C_{14}H_9N_5O_5$	Pale brown	167 -165	68				
N_4	$C_{16}H_{11}N_3O$	yellow	227 - 225	87	calculated found	73.40 73.55	5.03 4.24	16.14 16.08
N_5	$C_{14}H_{10}N_2O$	yellow	220 - 218	72				
N_6	$C_{14}H_9ClN_2O$	Pale orange	257 - 255	80				
N_7	$C_{14}H_9ClN_2O$	yellow	225 - 222	60				
N_8	$C_{14}H_8Cl_2N_2O$	brown	174 - 172	69				
N_9	$C_{14}H_{10}N_2O_2$	Dark brown	320 - 318	60				
N_{10}	$C_{14}H_{10}N_2O_2$	Reddish-brown	229 - 227	76				
N_{11}	$C_{13}H_9N_3O$	Dark red	194 - 192	57				
N_{12}	$C_{13}H_9N_3O$	Dark brown	190 -188	48				

2.3 - Preparation of Schiff's - mannich bases (N_{13}-N_{23}).

Compound (N_{13}) in table (2) was chosen as typical example for the preparation :

(0.36 gm ,0.001 mole) of Schiff's bases containing isatin moiety was dissolved in methanol (25 ml) in a beaker (100 ml) then (0.015 mole) of formaldehyde (37%) (5 ml) was added to the mixture followed by (0.09gm,0.001 mole) of 2^0aminepiperidine when the mixture was cooled to 0 ^{0}C and left stirring for 3hrs then the reaction mixture was allowed to warm slowly at room temperature with stirring for 24hrs. Recrystallized from methanol to afford the tittle compound (N_{13}) as orange solid , m.p(204 – 206 ^{0}C) , %yield was 72% .

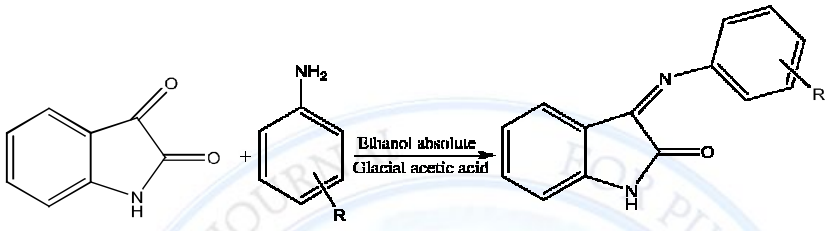
Table (2) physical properties of the prepared Schiff's –mannich bases ($N_{23}N_{13}$ -)

Com p.No	Chemical Formula	Colour	m.p^{0}C	% Yield	C.H.N	%C	%H	%N
N_{13}	$C_{20}H_{21}N_5O_2$	orange	206 - 204	72				
N_{14}	$C_{18}H_{18}N_4O_2$	Pale orange	168 - 166	79				
N_{15}	$C_{27}H_{20}BrN_3O$	Dark yellow	250 - 246	71				
N_{16}	$C_{19}H_{18}N_6O_6$	Dark yellow	175 -173	82				
N_{17}	$C_{22}H_{22}N_4O$	orange	164 -162	86				
N_{18}	$C_{19}H_{19}N_3O_2$	yellow	120 - 118	83				
N_{19}	$C_{19}H_{18}ClN_3O_2$	Pale yellow	134 - 132	76				
N_{20}	$C_{19}H_{21}N_5O_2$	Pale orange	166 - 164	72				
N_{21}	$C_{19}H_{18}ClN_3O_2$	Pale yellow	180 - 178	57				
N_{22}	$C_{20}H_{21}N_3O$	Pale yellow	152 - 150	57	calculated found	74.78 75.21	6.35 6.63	13.14 13.16
N_{23}	$C_{21}H_{20}N_4O_2$	yellow	168 -166	%80	calculated found	69.51 69.98	5.53 5.59	15.83 15.55

Results and Discussion

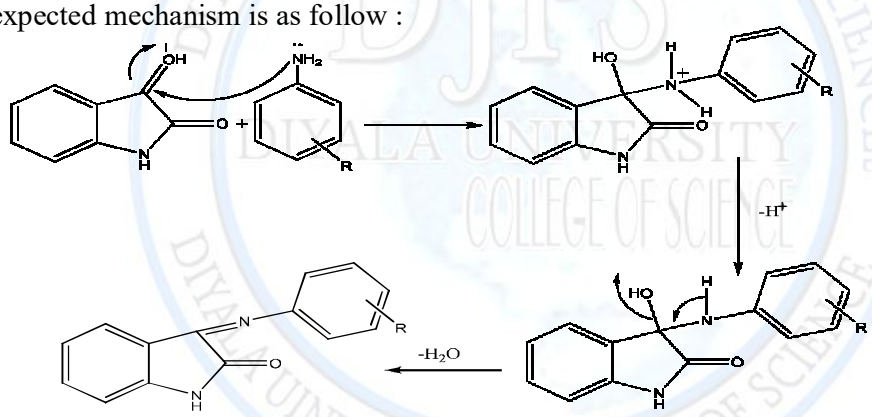
3.1 – preparation of isatin Schiff's bases ($N_1 – N_{12}$) :-

Isatin Schiff's bases have been prepared by condensing isatin with primary amines in the presence of glacial acetic acid as a catalyst and ethanol as a solvent :



R= - 4Br , 4-CH_2CN , 4-Cl , 3-Cl , 2,4-Di-Cl , 4-OH , 4-NH_2 , -2OH , 2-NH_2 , 4-F , 4 -COOH , 2-NO_2 , 4-$COCH_3$

The expected mechanism is as follow :

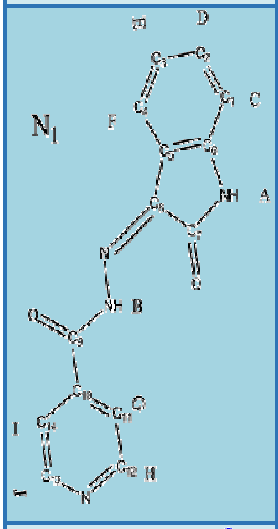
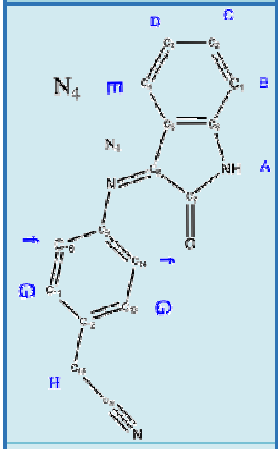
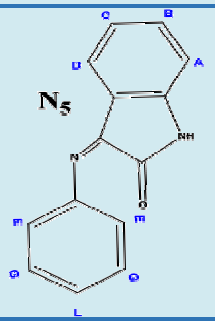


The productswas identified by its physical properties and IR – spectra using FT-IR instrument which showed the characteristic absorption band and also the C.H.N analysis which was shown in table (2),(3) .Also the ^{1}H-NMR and ^{13}C-NMR spectra for compounds N_1 ,N_4 , N_5 are shown in table (4) [8,9,10] .Atypical IR and NMR spectra for Comp.N1are shown in fig (1),(2),(3)

Table (3) FT-IR absorption frequencies of isatin Schiff's bases (N_1 - N_{12})

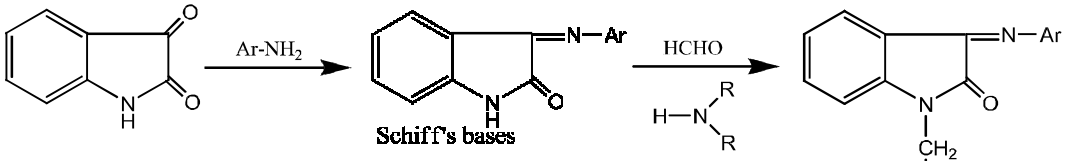
Comp.No	IR v cm^{-1} (KBr)		
	C=N (isomethine)	C=C Aromatic	Others
N_1	1620	1468-1545	(3234)N-H for isatin (3165) N-H for isonazide (3060)for C-H Ar (1721)C=O amide for isatin (1594) C=N for pyridine ring (660-877)for(HC=) Ar bending
N_2	1652	1463-1615	(3271)N-H for isatin (1743)C=O amide for isatin (583-833)for(HC=) Ar bending (749)for C-Br
N_3	1685	1458-1619	(3193)N-H for isatin (3037)for C-H Ar (1737)C=O amide for isatin (1336 sy-1458 asy)for NO_2 (630-846)for(HC=) Ar bending
N_4	1660	1463-1502	(3205)N-H for isatin (2724 sy-2881 asy)for CH_2 (2244) for CN nitrile (1746)C=O amide for isatin (663-837)for(HC=) Ar bending
N_5	1655	1459-1611	(3168)N-H for isatin (1741)C=O amide for isatin (690-992)for(HC=) Ar bending
N_6	1652	1463-1614	(3266)N-H for isatin (1742)C=O amide for isatin (748-945)for(HC=) Ar bending (1080) for C-Cl
N_7	1658	1462-1587	(3206)N-H for isatin (1747)C=O amide for isatin (651-799)for(HC=) Ar bending (1080) for C-Cl
N_8	1667	1413-1556	(3188)N-H for isatin (1717)C=O amide for isatin (1084)for(C-Cl)
N_9	1672	1452 -1507	(3148)N-H for isatin (3251) for OH phenol (1724)C=O amide for isatin (665-887)for(HC=) Ar bending
N_{10}	1617	1470	(3108)N-H for isatin (3368) for OH phenol (1688)C=O amide for isatin (749-837)for(HC=) Ar bending
N_{11}	1682	1402	(3194)N-H for isatin (3060)for C-H Ar (1618) C=N for pyridin (1740) C=O amide for isatin (736 -884) for(HC=) Ar bending
N_{12}	1681	1403-1490	(3194)N-H for isatin (3060)for C-H Ar (1490)for C=N pyridin (1740)C=O amide for isatin (736 -884)for(HC=) Ar bending

Table (4) Approximate values ^{1}H-NMR and ^{13}C-NMR spectra for compounds N_1 ,N_4 , N_5

sample	Chemical shifts ^{1}H-NMR (ppm)	No.of protons	Types of protons	Chemical shifts ^{13}C-NMR (ppm)
 N_1	6.97-7.11 7.42-7.62 7.79 8.87 11.44 14.00	2 2 2 2 1 1	Aromatic protons for six membered ring of isatin (E,D) Aromatic protons for six membered ring of isatin (C,F) Aromatic protons for six membered ring of isoniazid (G,I) Aromatic protons for six memberedring of isoniazid (J,H) Proton of (N-H) for isoniazid(B) Proton of (N-H) for isatin(A)	C1-C6= 119 – 143.3 C7= 168.5 C8=134.7 C9=163.4 C11=C14=121.6 C12=C13=151.3
 N_4	4.10 6.72-7.46 11.00	2 8 1	Protons of (CH_2-CN) group (H) Aromatic protons (B,C,D,E,F,G) Proton of (N-H) for isatin(A)	C1-C6= 118.4-150 .2 C7=C8= 155.9 C9-C14= 122.2-143 C15=22.4 C16=118
 N_5	6.73-7.60 11.00	9 1	Aromatic protons (A,B,C,D,E,G,L) Proton of (N-H) for isatin(H)	

3.1 – preparation of isatin Schiff's –mannichbases (N_{13} – N_{23}) :-

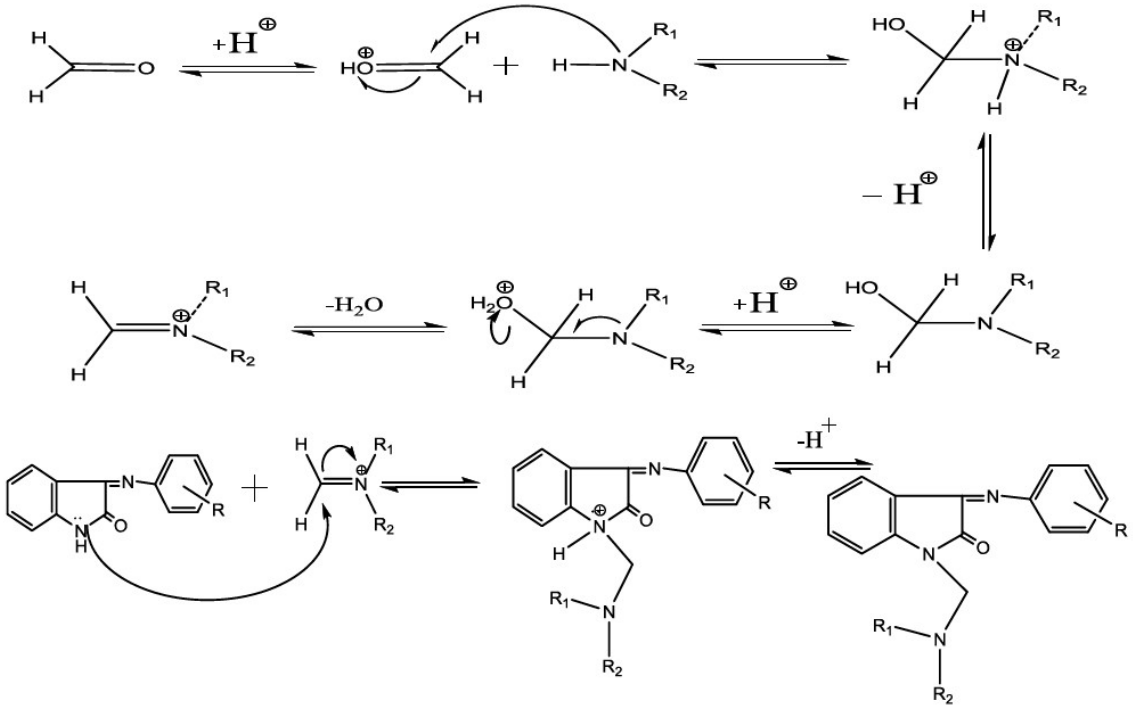
Schiff's – mannich bases (N_{13}-N_{23}) were prepared by reacting Schiff's bases of isatin with secondary amines and formaldehyde in absolute methanol or ethanol as shown in the equation



a. Ar = m-F-C_6H_4-
b. Ar = m-Cl-C_6H_4-
c. Ar = p-Cl-C_6H_4-
d. Ar = p-Br-C_6H_4-
e. Ar = p-I-C_6H_4-
f. Ar = p-$CH_3OC_6H_4$-
g. Ar = p-$H_2NO_2SC_6H_4NH$-

R = CH_3 , C_2H_5 ,  , C_4H_8O ----etc

And the expected mechanism is shown below :



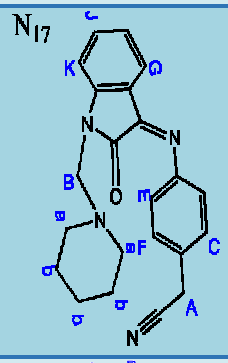
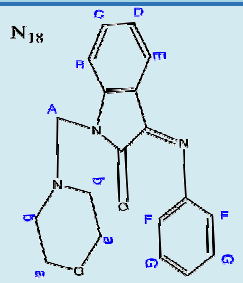
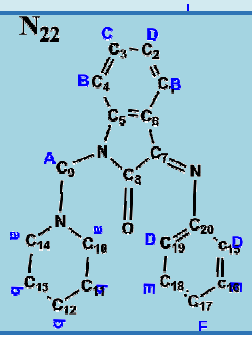
The products also were identified through the physical properties and IR-spectra using FT-IR instrument which showed the characteristic absorption bands and C.H.N analysis tables (2),(5).Also the identification included the ^{1}H-NMR and ^{13}C-NMR for compounds N_{17},N_{18},N_{22},N_{23} and the related data are shown in table (6)[8,9,10] .Atypical IR and NMR spectra for Comp.N_{22} are shown in fig (4),(5),(6) .

Table (5) FT-IR absorption frequencies of isatin Schiff's-mannich bases (N_{13}– N_{23}).

Comp .No		IR v cm^{-1} (KBr)			
	C-H aliphatic	C-N aliphatic	C=N isomethine	C=C Aromatic	Others
N_{13}	2863 3034	1346	1675	1409 1545	(3233)for N-H for isatin (3034)for C-H Ar (1721)C=O amide for isatin (1620)for C=N (715 -877)for(HC=) Ar bending
N_{14}	2856 2950	1335	1611	1348 1467	(3039)for C-H Ar, (1936)C=O amide for isatin (1151)for C-O morpholin (710 – 855)for(HC=) Ar bending
N_{15}	2877	1335	1652	1464 1614	(1741)C=O amide for isatin (748 -883)for(HC=) Ar bending (582) for C-Br
N_{16}	2855 2949	1336	1268	1428	(3109)for C-H Ar (1736)C=O amide for isatin (1460 asy)for NO_2 (1151) for C-O morpholin (710 -848)for(HC=) Ar bending
N_{17}	2804 2935	1344	1659	1465 1501	(2246)for CN nitrile (1731)C=O amide for isatin (696-847)for(HC=) Ar bending
N_{18}	2892 2959	1340	1660	1468	(3049)for C-H Ar (1727)C=O amide for isatin (1152) for C-O morpholin (750 -862)for(HC=) Ar bending
N_{19}	2827 2946	1360	1661	1427 1465	(3068)for C-H Ar (1731C=O amide for isatin (1151) for C-O morpholin (714 -829)for(HC=) Ar bending (1082) for C- Cl
N_{20}	3032	1347	1695	1408 1483	(3234)for N-H of isonazide (3058) for C-H Ar (1722)C=O amide for isatin (1593) C=N for pyridine ring (717 -841)for(HC=) Ar bending

N_{21}	2864 2889	1356	1659	1399 1469	(3067) for C-H Ar (1731)C=O amide for isatin (712 -837)for(HC=) Ar bending (1084)for(C-Cl)
N_{22}	2800 2850	1437	1664	1468	(3021) for C-H Ar (1726) C=O amide for isatin (753 -860) for(HC=) Ar bending
N_{23}	2854 2960	1336	1658	1428 1465	(2960) C-H aromatic (1729)C=O amide for isatin (1163)for C-O morpholin (756 -869)for(HC=) Ar bending

Table (6) Approximate values of ^{1}H-NMR and ^{13}C-NMR spectra for compounds N_{17} ,N_{18}, N_{22} ,N_{23}

Sample	Chemical shift ^{1}H-NMR (ppm)	No.of protons	Type of protons	Chemical shift ^{13}C-NMR (ppm)
N_{17} 	1.54 3.41 4.49 5.21 6.72- 7.75	6 4 2 2 8	Protons of sixmembered ring for piperidine (a) Protons of sixmembered ring for piperidine (b) Protons of (N-CH_2-N) for mannich bases (B) Protons of (CH_2-CN) (A) Aromatic protons (C,D,E,G,F,I,J,K)	
N_{18} 	2.49 3.36 4.47 6.36 – 7.64	4 4 2 9	Protons of six membered ring for morpholin (b) Protons of six membered ring for morpholin (a) Protons of (N-CH_2-N) for mannich bases (A) Aromatic protons(B,C,D,E,G,F,I)	
N_{22} 	1.54 3.21 4.45 6.72- 7.75	6 4 2 9	Protons of six membered ring for piperidine (b) Protons of six membered ring for piperidine (a) Protons of (N-CH_2-N) for mannich bases (A) Aromatic protons (B,C,D,E, F,)	C1-C6 = 128.5-115.9 C7=C8=163.4 C15-C20= 117.5-148.2 C9=62.3 C10=C14=51.3 C11-C13=26.1

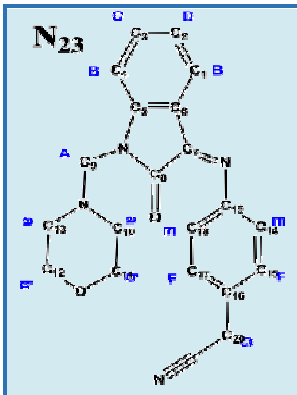
	3.63 4.02 4.52 5.27 7.05 – 7.88	4 4 2 2 8	Protons of sixmembered ring for morpholin (b) Protons of six membered ring for morpholin (a) Protons of (N-CH_2-N) for mannich bases (A) Protons of (CH_2-CN) (G) Aromatic protons(B,C,D,E, F)	C1-C6=125.3-116.9 C7=C8=164.8 C14-C19= 118.5-150.1 C9=69.6 C10=C13=51.6 C11-C12=66.6

Fig (1) : FT-IR spectrum for compound N_1

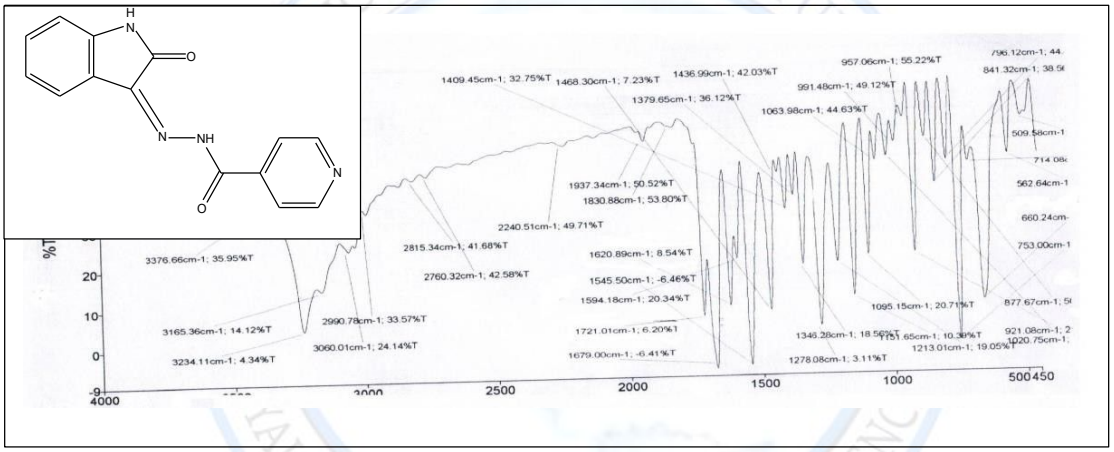


Fig (2) : ^{1}H-NMR spectrum for compound N_1

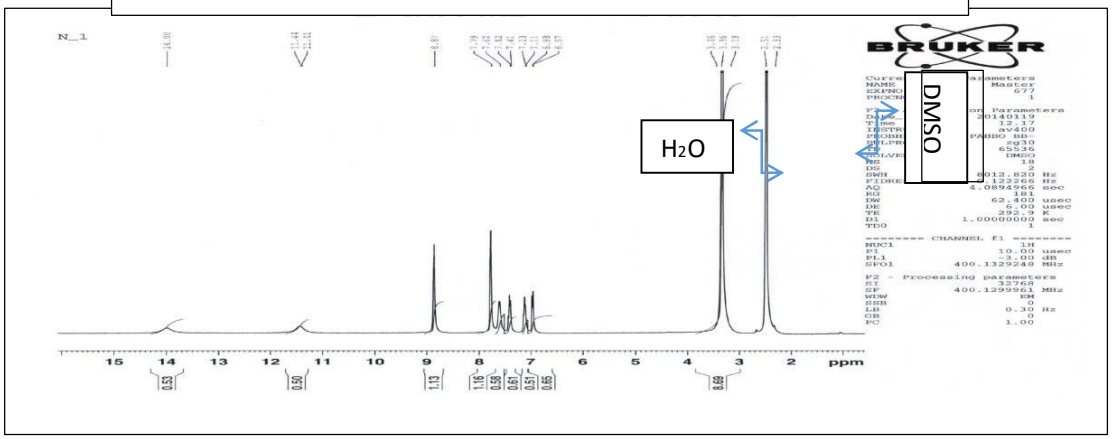


Fig (3) : ^{13}C-NMR spectrum for compound N_1

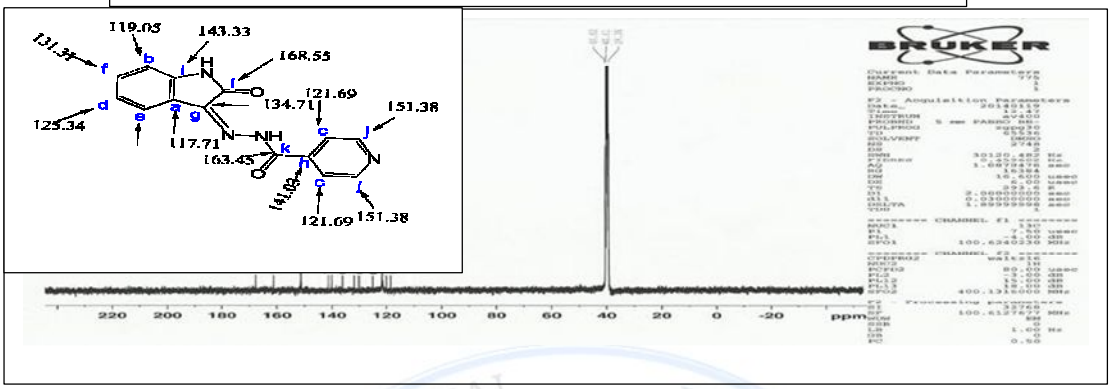


Fig (4) : FT-IR spectrum for compound N_{22}

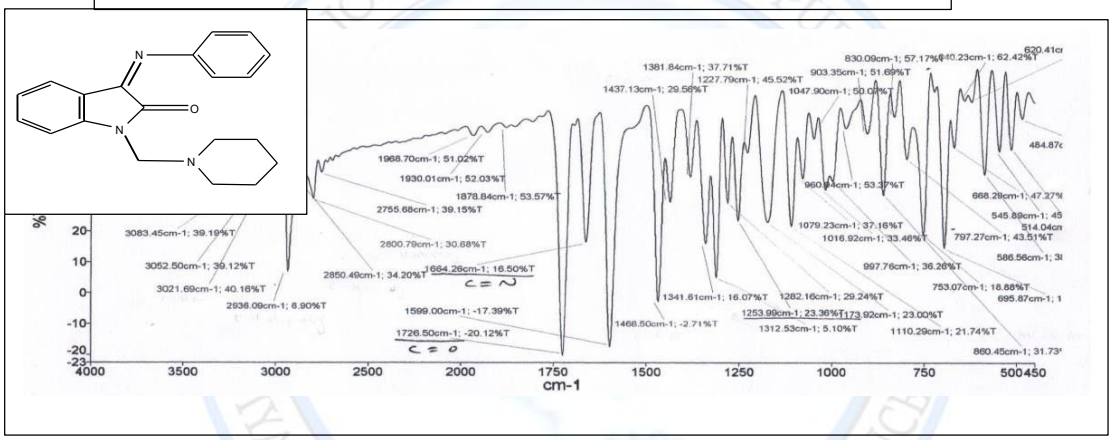


Fig (5) : ^{1}H-NMR spectrum for compound N_{22}

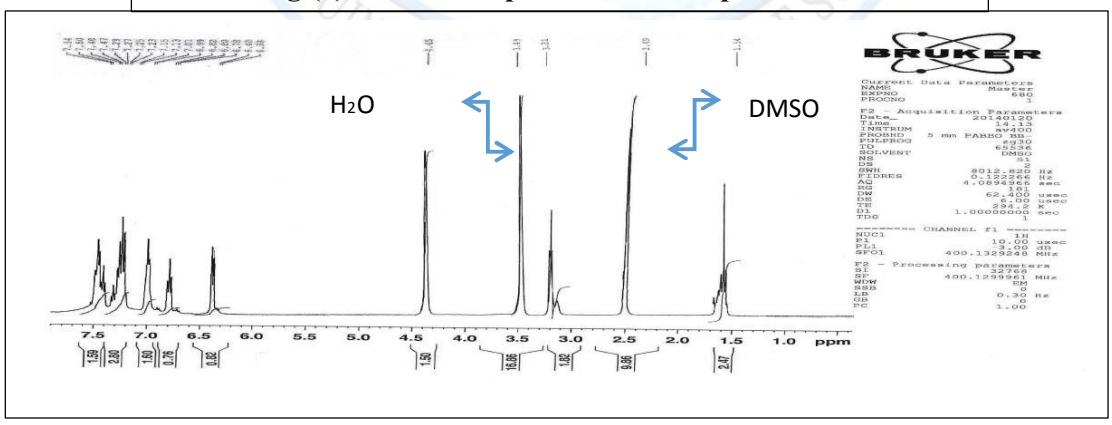
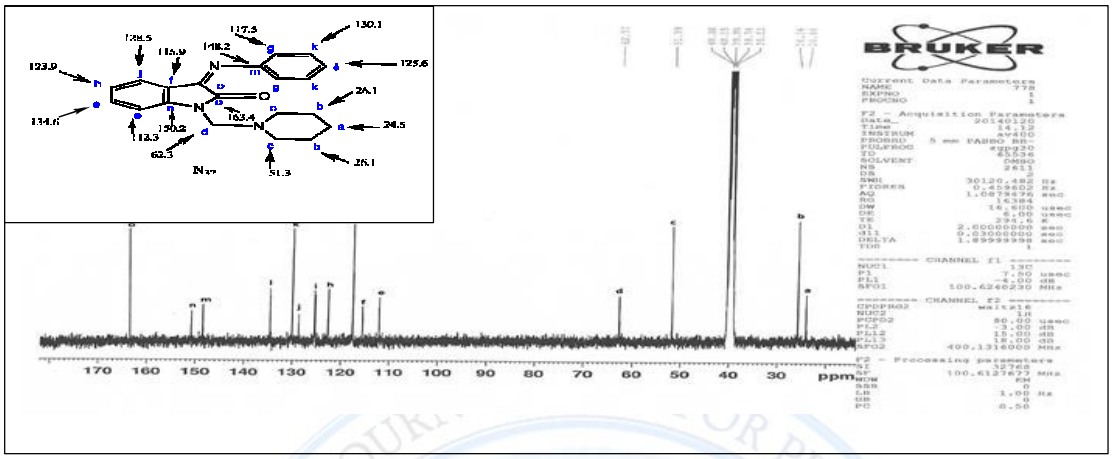


Fig (6) : ^{13}C-NMR spectrum for compound N_{22}



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