

Synthesis of Schiff Bases Derivatives from Benzene Diamine Containing Acridine Moiety

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ABSTRACT

One side of (o, m and p) benzene diamine reacted with aromatic aldehyde to give Schiff bases (Ia-d) or (IIa-d) and (IIIa-d) respectively. The second amine group of the synthesized Schiff bases (Ia-d or IIa-d and IIIa-d) was reacted with substituted-9-chloroacridine to give the final compounds namely N-(Substituted benzylidene)-N'-(Substituted acridine -9-yl) (1,2 or 1,3 and 1,4) benzene diamine (V,VI,VII).The reaction progress was followed by thin layer chromatography (TLC), and R_f values were recorded. I.R. Spectral data for all the synthesized derivatives were reported. The U.V-Vis., and the ^1H NMR(300and 400MHz) were recorded for some derivatives to support the structure of the synthesized compounds.

Keywords: Acridine, Benzenediamine, Schiff bases.

(p, m, o)

(IIIa-d)	(IIa-d)	(Ia-d)	(IIIa-d)	(IIa-d)	(Ia-d)
(- 9-)-)-)-)-9
R_f			.	(1,4	1,3
			-	1,2)	
			(300 or 400)		
			:		

INTRODUCTION

Benzenediamine isomers are low to high toxic (Chong *et al.*, 2016), allergy (Ed Rietchel *et al.*, 2001) and used in hair dye (Al-Suwaidi *et al.*, 2010).

Many chemist researcher groups focused their attention on the development of Schiff bases (Gupta *et al.*, 2003) (El Ajaily *et al.*, 2013) (Boghaei *et al.*, 2002) and their metal complex (Genjal *et al.*, 2004) (Gaballa *et al.*, 2007), that possess cytotoxic activity (Fasina *et al.*, 2014). Due to the former notes, these complexes used as microbial active compounds (Benguzzi, 2007), (Hamil *et al.*, 2009), (Fasina *et al.*, 2012).

Condensation of 1,2-diamine compounds with carboxylic acids, dimethyl oxalate affords benzimidazole (Al Aqeel, 2017) and quinoxaline derivatives (Shekouhy *et al.*, 2008) respectively, which are used as wide range pharmaceutical agents.

Acridine and acridine derivative are reviewed (Kowalewska *et al.*, 2017) and have been extensively explored as potential therapeutic agents for the treatment of a number of diseases, such as cancer (Pethy *et al.*, 2008), Alzheimer's (Rodrigue, 2006), and as antimicrobial (Panda and Nayak, 2009), and antimalarial agents (Tomar *et al.*, 2010). Their mode of action is mainly attributed to DNA interaction and the subsequent effects on the biological processes linked to DNA and its related enzymes (Lang *et al.*, 2013). The above shortcomings have motivated our search and also in continuation to our work (Al-Luhaibe, 2013). Attempts have made to widening the scope and hence to synthesize some new Schiff base derivates from three of Benzene-diamine (1,2 or 1,3 and 1,4) isomers containing acridine moiety. The synthesized derivatives are expected to be highly potential biologically active.

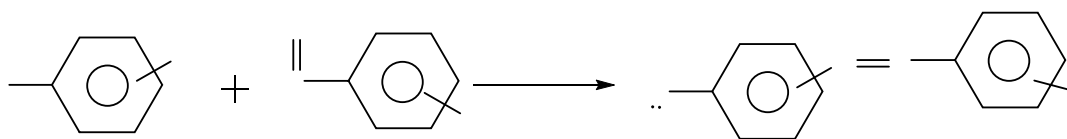
EXPERIMENTAL

All of the chemicals, solvent and reagents used of Purim grade (Note: simple or under vacuum distillation or recrystallization are some time carried out to purity chemicals). The purity of synthesized derivatives including intermediate was tested by thin layer chromatography (TLC) using silica gel (60-100 mesh), chromatography was eluted using a mixture of chloroform-methanol (9.5:0.5), or chloroform-ethyl acetate (5:5) and the spots were visualized by exposure to iodine vapour.

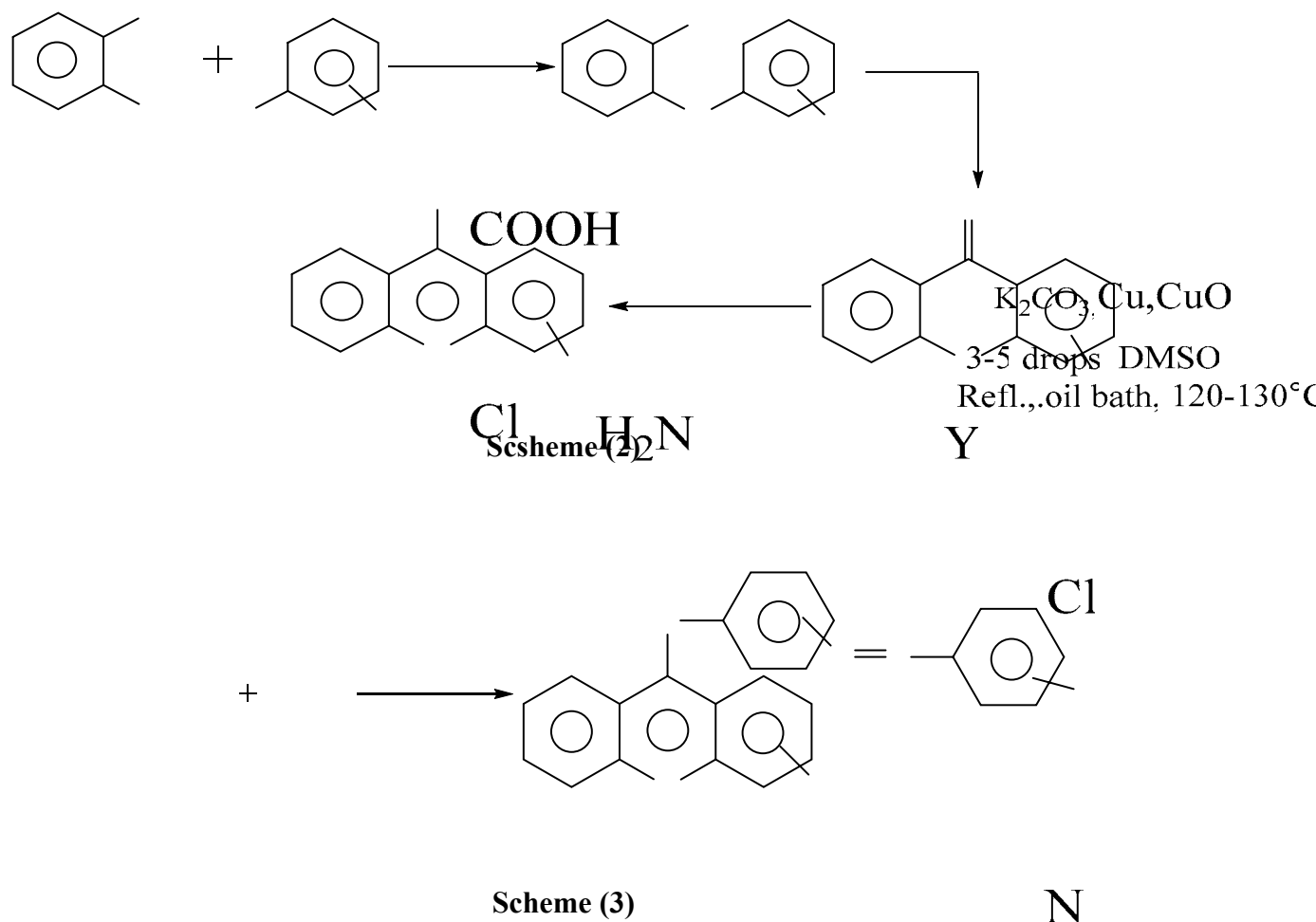
All melting points were uncorrected and determined by Electro thermal IA9000 Digital Melting apparatus. Complete spectra analysis was established to the synthesized derivatives. The U.V/Vis. absorbance recorded on A JASCOV - 630 UV / Vis spectrophotometer (Iraq, Mosul university, college of science). The I.R spectra were recorded on Alpha –Bruker ATR-FTIR (Iraq, Mosul, pharmacy college). ¹HNMR were recorded on Bruker Ultra shield 300 MHz, 400 MHz (Turkey, Gaze Entape Univ.) using DMSO-d₆, as solvent with TMS as internal standard.

General procedure for synthesis of N-(Sub. benzylidene) 1,2- benzene diamine(Ia-d) (Pati, S., 1970):

Equimolar of 1,2- benzene diamine (0.002mole) (0.216 g) and appropriate aromatic aldehyde (0.002 mole) dissolved and mixed in dry methanol (one drop of acetic acid was added if needed). The mixture was heated under reflux in a water bath for 3-5 hrs. and water was added to the crude product remained after solvent evaporation. The solid product was filtered off and washed several time.



Scheme (1)



times with child water-methanol mixture (Note : wash with petroleum ether 40-60, if required).

The above procedure was used to prepare N-(sub.benzylidene-1,3- benzene diamine(IIa-d) and N-(sub.benzylidene-1,4- benzene diamine(IIIa-d)). Tables (1, 2 and 3) show the physical and spectral data for the compounds (Ia-d; IIa-d; IIIa-d), respectively.

Table 1: The physical and spectral data for the Schiff bases are derived from 1,2- benzene diamine (Ia-d)

Compd. No.	R	yield %	color	m.p °C	R _f	IR (cm ⁻¹) NH ₂ , C=N, Others	¹ HNMR, δ ppm Ar, NH ₂ , N=CH, R,Y
Ia	4-OMe	96	Pale orange	74-76	0.50	3340, 1590, (OCH ₃)=1242,1164	-----
Ib	2-Cl	76	Brown	137-140	0.60	3528, 1624, (C-Cl)736	-----
Ic	= 4-N(Me) ₂	98	Brown	177-178	0.40	3063, 1594	Dry Methanol refl., 10 hrs
Id	4-Cl	66	Yellow	186-188	0.25	3441, 1624, (C-Cl)753	7.06, 6.85

(Ia-d, IIa-d, IIIa-d)

Table 2: The physical and spectral data for the Schiff bases are derived from 1,3- benzene diamine(IIa-d)

Compd. No.	R	yield %	color	m.p °C	R _f	IR(cm ⁻¹) NH ₂ ,C=N, Others	¹ HNMR, δ ppm Ar, NH ₂ , N=CH, R, Y
IIa	4-OMe	40	Dark red	78-80	0.60	3340, 1590, (OCH ₃)1242	7.02-9.85 (8H), 5.08, 6.89, 3.3 (OCH ₃).
IIb	2,3-di (OMe)	74	Brown	165-167	0.49	3340, 1616, (OCH ₃) 1263, 1227	-----
IIc	2-Cl	94	Dark Brown	170-172	0.31	3410, 1604, (C-Cl)730	-----
IIId	4-N(Me) ₂	88	Black	83-85	0.67	3188, 1581	6.35-9.65(8H), 3.25, 6.39, 2.85(2CH ₃), 2.90

Table 3: The physical and spectral data for the Schiff bases are derived from 1,4- benzene diamine(IIIa-d)

Compd. No.	R	yield %	color	m.p °C	R _f	IR(cm ⁻¹), NH ₂ , C=N, Others	¹ HNMR, δ ppm Ar.,NH ₂ ,N=CH,R,Y
IIIa	4-OMe	97	Yellow	139-141	0.89*	3040, 1592, (OCH ₃)1244	-----
IIIb	2,3-di (OMe)	96	Orange	127-128	0.40	3373, 1620, (OCH ₃)1267, 1217	7.54-8.91(7H), 3.85,7.39, 2.48,3.34(2OCH ₃)
IIIc	4-N(Me) ₂	88	Yellow	259-260	0.40	3438, 1586	-----
IIIId	2-NH ₂	90	black	97-99	0.80	3122, 1606, (NH ₂) 3235	5.95-7.60(8H), 5.01, 5.69, 5.43(NH ₂)

*Et Ac:CHCl₃(5:5)**General procedure for synthesis 9-chloro subs. acridine (IVa-f) (Acheson and Bottom, 1975), (Mahmood, 2013)**

To 50 ml of thionyl chloride (SOCl₂) (2-3 drop DMF) was added in round bottom flask, equipped by double surface condenser supported with CaCl₂ tube, 3g of subs. Acridone was added gradually with in (1-2 hrs) with continuous stirring. The stirring and reflux were continued in water bath (60-70°) for 3hrs. The reaction mixture finally converted to clear orange or sometimes dark brown. The excess of thionyl chloride was distilled off under vacuum. The crude product was added slowly to conc. Ammonia solution: ice mixture and digested for 1hr. The basic mixture was extracted 3 times with 25 ml of chloroform. The collected organic layer was dried with magnesium sulfate (for over night then), Filtered off and distilled under vacuum. The solid product is pure enough to continue the next step. (Note: ammonia: ethanol mixture was used as a solvent of crystallization if needed) (Mahmood 2013). The physical constants were listed in (Table 4).

Table 4: The physical constants of 9-chloro acridine

Compd. No.	R	Yield %	Color	m.p °C	R _f
IVa	2-Br	46	Orange	Oily	0.15
IVb	2-Me	76	Orange	92-94	0.32
IVc	4-Me	89	Orange	76-78	0.76
IVd	2-OMe	58	Dark orange	84-87	0.32
IVe	4-OMe	74	Orange	70-73	0.20
IVf	4-NO ₂	71	Dark orange	Oily	0.25

General procedure for synthesis of N-(subs. benzylidene)-N'-(subs.acridin-9-yl) 1,2- benzene diamine

Equimolar (0.001mole) of subs.-9-chloroacridine (IVa-f) was mixed with Schiff base (Ia-d or IIa-d and IIIa-d) in (30ml) of dry methanol. The reaction mixture was heated under reflux at least for 10 hrs. TLC monitor was at the end of the reaction. The solvent was removed by simple distillation, and crude product was washed with (10 ml) sodium bicarbonate (10%).The crude solid was washed with water then air dried .The product was washed several times with petroleum Ether (40-60) then dried under vacuum. This procedure was used to synthesize the 1,3 and 1,4 benzene diamine derivatives. Tables (5, 6 and 7) show the physical constants of these derivatives.

Table 5: The physical constants of N-(substituted benzylidene)-N -(substituted acridin-9-yl) 1,2 benzene diamine.

Compd. No.	Y	R	Yield %	Color	m.p °C	R _f
Va	2-Br	4-N(CH ₃) ₂	86	Reddish Orange	79-81	0.24
Vb	2-Br	2-Cl	83	Black Orange	80-82	0.53
Vc	4-CH ₃	4- Cl	83	Orange	62-64	0.73
Vd	4-CH ₃	4-N(CH ₃) ₂	89	Orange	149-151	0.59
Ve	2-CH ₃	4- OCH ₃	88	Red	57-58	0.44
Vf	2-CH ₃	4-N(CH ₃) ₂	86	Brown	103-105	0.37
Vg	2-OCH ₃	4- OCH ₃	89	Orange	54-57	0.68*
Vh	4-OCH ₃	4- OCH ₃	83	Black Orange	43-45	0.77
Vi	4-NO ₂	2-Cl	84	Black Orange	71-73	0.35
Vj	4-NO ₂	4-N(CH ₃) ₂	87	Orange	138-141	0.34

* EtOAc: CHCl₃ (50:50)

Table 6: The physical constants of N-(substituted benzylidene)-N -(substituted acridin-9-yl) 1,3 benzene diamine

Compd. No.	Y	R	Yield %	Color	m.p °C	R _f
Via	4-CH ₃	2,3-dimethoxy	69	Orange	142-145	0.77
VIb	4-CH ₃	2-Cl	63	Dark orange	85-87	0.66
VIc	2- CH ₃	2,3-dimethoxy	97	Pale brown	131-133	0.36*
VIId	2- CH ₃	2-Cl	98	Greenish black	209-212	0.34*
VIe	2-OCH ₃	4- OCH ₃	65	Black	132-134	0.40
VIIf	2-OCH ₃	2-Cl	98	Black	71-73	0.28
VIg	4-OCH ₃	2,3-dimethoxy	99	Reddish orange	201-203	0.72*
VIh	4-OCH ₃	2-Cl	97	Brown	208-210	0.51
VIIi	4-NO ₂	2,3-dimethoxy	37	Orange	Low temp.	0.42
VIJj	4-NO ₂	2-Cl	48	Brown	Low temp.	0.64

* EtOAc:CHCl₃ (5:5)

Table 7: The physical constants of N-(substituted benzylidene)-N-(substituted acridin-9-yl) 1,4 benzene diamine

Compd. No.	Y	R	Yield %	Color	m.p °C	R _f
VIIa	2-Br	4- OCH ₃	81	Brown	125-127	0.34
VIIb	2-Br	2,3-dimethoxy	83	Gray	117-119	0.30
VIIc	4-CH ₃	2,3-dimethoxy	95	Brown	153-155	0.89
VII d	2-CH ₃	4-N(CH ₃) ₂	96	Pale orange	138-141	0.58
VII e	2-CH ₃	4- OCH ₃	96	Brown	148d	0.34
VII f	2-OCH ₃	4- OCH ₃	93	Orange	97-100	0.94*
VII g	4-OCH ₃	4- OCH ₃	98	Orange	180-182	0.79*
VII h	4-OCH ₃	4-N(CH ₃) ₂	76	Black Orange	102-103	0.71
VII i	4-NO ₂	2,3-dimethoxy	71	Orange	Oily	0.32
VII j	4-NO ₂	2-Cl	86	Orange	84-87	0.30

* EtOAc:CHCl₃ (5:5)**Table 8: The IR and ¹HNMR of spectral data of some N-(substituted benzylidene)-N-(substituted acridin-9-yl)benzene diamine**

Compd. No.	IR(cm ⁻¹) NH,=CH, C=N, Other	¹ HNMR, δ ppm NH, Ar., N=CH,R,Y
Va	3225, 2921, 1596, 1511(aromatic),1367 (C-N), 1454(CH ₃)	12.18, 6.63-8.48(15H), 5.54,2.81-3.04(2CH ₃)
Vc	3047, 2920, 1581, 1517 (aromatic),736 (C-Cl)	10.66, 7.27-8.80(15H), 7.17, 2.61-2.69 (CH ₃)
Vj	3122, 2920, 1603, 1498 (aromatic)	11.49, 6.59-9.67(16H), 3.01(2CH ₃)
VI c	3321, 2918, 1626, 1580(aromatic), 1261(ROAr), 1369 (C-N)	11.76, 7.02-8.2 (14H), 6.81, 3.9 (m) (2CH ₃)
VI e	3340, 2918, 1670, 1590 (aromatic), 1242 (ROAr)	11.70, 7.0-9.87(15H), 6.68, 3.75-3.96(2OCH ₃)
VI g	3181, 2850, 1616,1571(aromatic), 1248(ROAr), 1466 (CH ₃), 1330 (C-N)	11.23, 7.08-8.31(14H), 6.88, 4.05,4.06,4.10(3OCH ₃)
VIIa	-----	9.87, 6.68-8.63 (15H), 6.59, 3.65 (OCH ₃)
VII d	-----	9.67, 6.70-8.50 (15H), 3.02, 2.33 (2CH ₃)
VII f	3367, 2920, 1587 (aromatic), 1242(ROAr), 1308 (C-N)	9.87, 6.77-8.65 (15H), 6.74, 3.85-3.87 (2CH ₃)

RESULT AND DISCUSSION

Electronic Spectra

U.V and Visible spectra of finally synthesized derivatives show maximum wave length bands (Log molar absorptivity) i.e. λ_{\max} (log ϵ). The 1,2-diamine derivatives (Va-j) show λ_{\max} of 330-340 nm, log ϵ of (4.204-3.69), while the 1,3-diamine derivatives (VIa-j) show more shift to higher wave length but with lower absorbance i.e. 375-400 nm (3.78-3.40), only the derivative (VIIa) shows good visible absorbance (430nm, log ϵ =3.95).The derivatives of 1,4 -diamine show two λ_{\max} of 450 nm and 475 nm with log ϵ of 3.87 and 3.30 respectively while only derivative (VII d) shows λ_{\max} 370, log ϵ of 4.38.

I.R spectra

All the synthesized compounds from (1,2-diamino) (Table 1) show that the range of ν NH, 3225-3065 cm⁻¹, ν =CH at 2918-2922 cm⁻¹, ν C=N at 1632-1584 cm⁻¹; these data are quite similar to that of I.R standard characteristic groups. For 1,3-diamine derivatives (Table 2) show ν NH at the range 3340-3045 cm⁻¹, ν =CH at range 2919-2848 cm⁻¹, also ν C=N at the range 1626-1616cm⁻¹, which are in very good manner of characteristic group of I.R. For 1,4-diamine derivatives.

(Table 3) shows ν NH at 3386-3199 cm^{-1} , ν =CH 2919-2830 cm^{-1} , also to ν N=C at 1632-1585 cm^{-1} . these data are good support to the foundation of characteristic groups (Parikh, V.M. 1974).

¹HNMR spectra

¹HNMR data excellently prove the synthesized compounds, (Table 8). shows the δ ppm of (NH), (H) aromatic, =CH, and other substituents CH₃,OCH₃, ...etc. these data were in agreement with literature and previous work (Sondhi *et al.*, 1997), (Sondhi *et al.*, 2004), (Mahmood, 2013), Fig (1-6).

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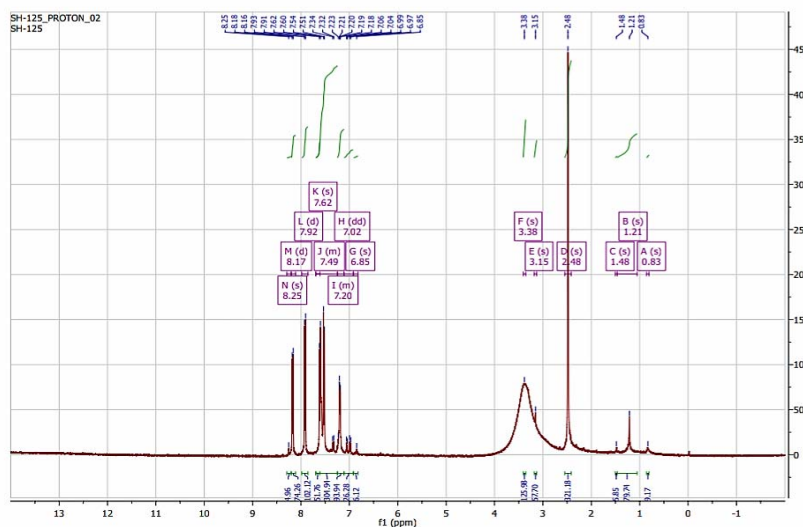


Fig. 1: ¹HNMR spectrum for compound (Id)

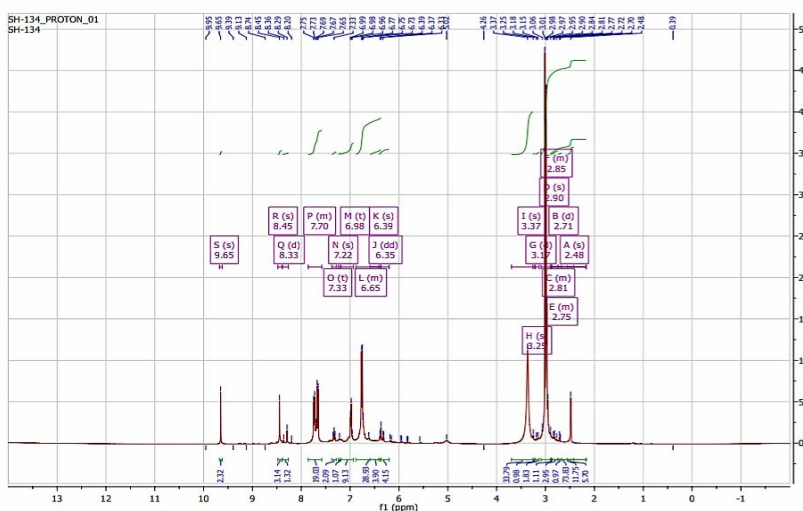


Fig. 2: ¹HNMR spectrum for compound (IId)

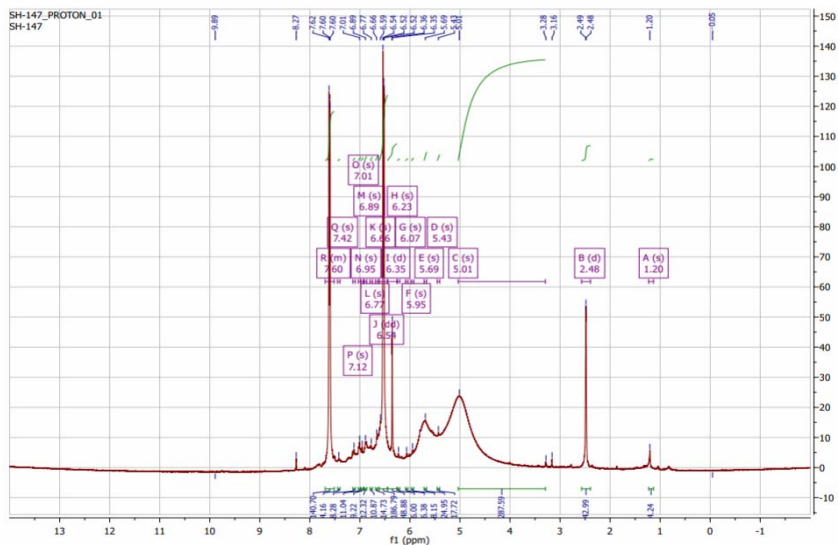


Fig. 3: ¹HNMR spectrum for compound (IIIId)

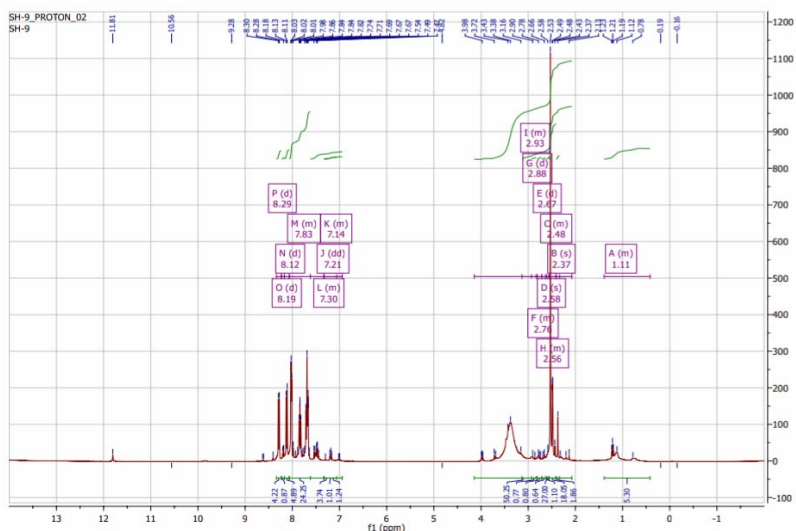
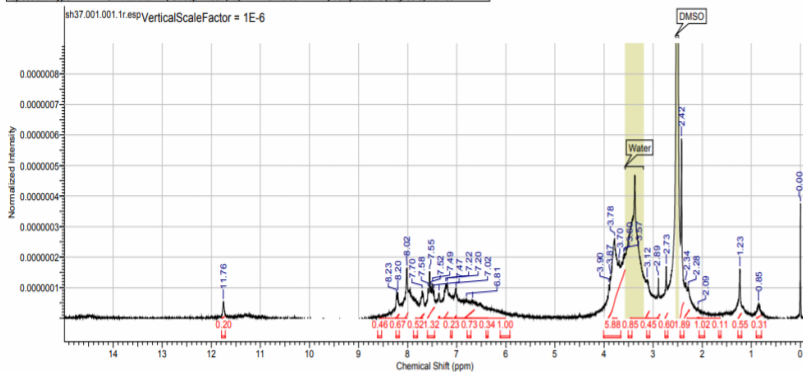


Fig. 4: ¹HNMR spectrum for compound (IVb)

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2	[3.20 - 3.57]	Water	1	mohand chem	13/03/2018 07:43:41		

Fig. 5: ¹HNMR spectrum for compound (VIc)

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