CHAPTER-4

C_3 Symmetric Molecules with Asymmetric Recognising Centres

4. C_3 Symmetric Molecules with Asymmetric Recognising Centres

4.1 Introduction

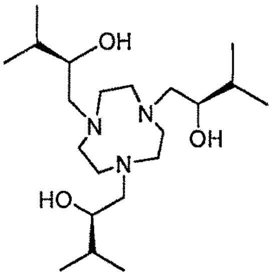
Chirality is the most important property of asymmetric molecules. The word chirality has been derived from the Greek word *kheir* meaning hand or handedness, as hands of an individual possess a similar relationship, which is present in two enantiomers of chiral compound, and it is readily understandable by using them as a model. The presence of chirality in a number of natural products and biomolecules reflects the highly ordered functioning of biological systems at the fundamental level. The building of biomolecules is not random or without a purpose. Only biologically active and useful enantiomers are produced by nature. Thus chirality and synthesis of chiral molecules is an intrinsic and important character of a biological process. Non-covalent interactions play an extremely important role for this phenomenon. On a supramolecular level, chirality is expressed in organization of molecules. A large number of natural products including some vitamins and biopolymers are chiral because of the dissymmetric influence exerted by enzymes and other biomolecules during the biochemical pathway. The secondary and tertiary structure of proteins, enzymes, membranes, cell or tissues all inherit this property.

In organic chemistry too, chirality and chiral synthesis have been the most important factors to be considered by practicing scientists. Therapeutic agents containing a chiral centre have only one of the enantiomers biologically active and therefore the objective of synthesis of the chiral drugs and separation of a racemic mixture have become parts of medicinal chemistry and new drug discovery.

In addition to the beauty present in C_3-symmetric compounds, they are found important in asymmetric synthesis and chiral recognition for which they need to be asymmetric or need to possess asymmetric centres in their structure. Chirality and symmetry appear to be paradoxical. Chiral active centers in the molecules having a rigid frame-work and an element of symmetry can be advantageous. Too many chiral centers of different types in a molecule result in no or decreased enantiomeric recognition due to decrease in structure complementarity.[1] A C_3- symmetric chiral ligand offers only one type of chiral site for substrate co-ordination because all the three sites are equivalent. The reduced number of competing asymmetric environment leads to high enantioselectivity in catalytic reactions involving metal centers bearing chiral tripodal C_3 symmetrical ligands. Chiral systems with C_3 –symmetry attain contribution in a variety of dendrimers[2], molecular receptors[3], ion channel mimics[4], chromatographic stationary phases[5] and organomettalic ligands. [3]

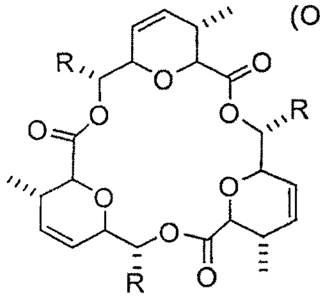
Chirality in C_3 symmetric systems may arise from chiral starting materials or reagents or from a twist in molecular structure or from an achiral centre generating during their synthesis. In the first case, the compounds may be synthesized directly in enantiomerically pure form, whereas resolution is necessary in the latter. Most of the homochiral C_3 symmetric chiral molecules so far reported consist of three chiral arms radiating from a central unit. Homochiral C_3 –symmetric molecules attain extra rigidity in which the three chiral arms radiate from a ring. Such systems constitute of three parts: a central ring, a donor group and a chiral unit. An excellent review on C_3 symmetry molecules in chiral applications has been presented by Moberg.[3]

The small triazacyclo compound have been N-substituted with a variety of pendant arms.[6] N-Substitution of the nonacyclic compound giving chiral arms e.g. N,N',N"-tris(2(R)-2-hydroxy-3-methylbutyl)-1,4,7- triazacyclononane **1** has been carried out.[7,8]



1

A C_3-symmetric macrocyclic host made up of hydropyrane rings and lactone linkages have been reported with substituted amino **2**, phosophono **3**, and furan **4** pendant groups as unnatural ionophores.[9]



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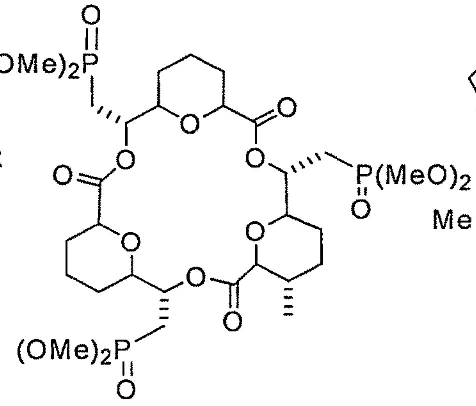

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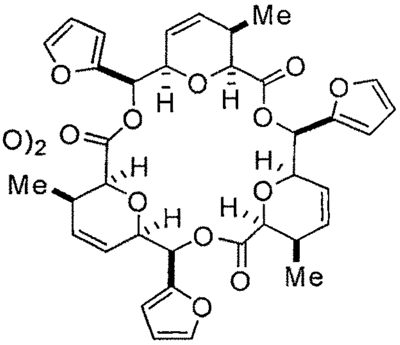

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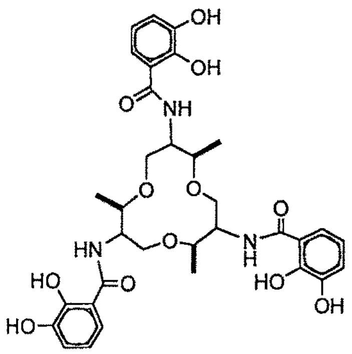
Enterobactin **5** is a naturally occuring C_3-symmetric cyclic tri-lactone having catechol as pendant groups forms complex with iron and regularise its transport through the cell membrane. Several chiral enterobactin analogs have been prepared based on tris-aminoethylamine and 1,3,5-tris(bromomethyl)mesitylene and their iron (III) binding properties examined.[10]



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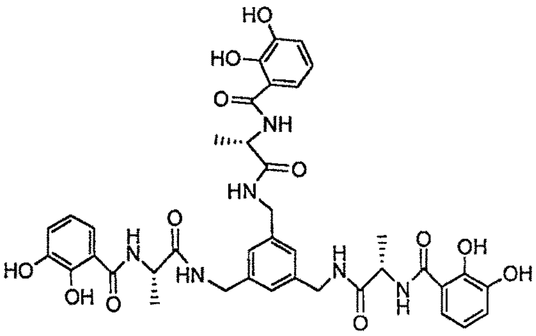

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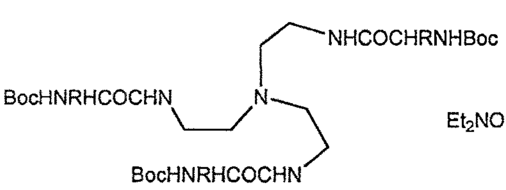
Several C_3- symmetric chiral compounds (e.g. **7-10**) have been prepared with carbon, nitrogen, silicon, and phosphorus at the centre having a variety of pendant groups including binaphthyl, pyridyl, oxazolyl, imidazolyl and aryl groups.[3]



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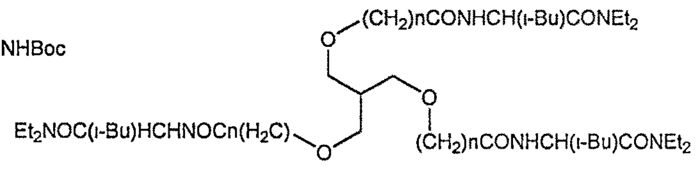

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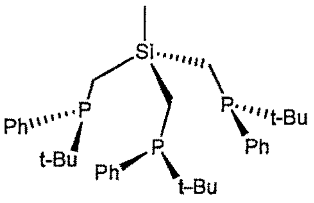

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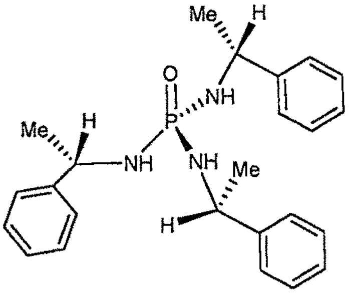

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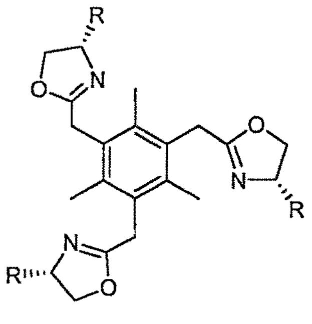
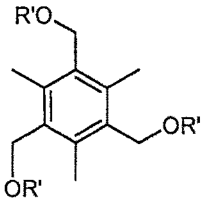
C_3- symmetric chiral oxazoline receptors **11** have been reported to exhibit chiral molecular recognition discriminating between (R)- and (S)-α-phenylethylamine.[11] Similar tripodal oxazoline receptors have been studied and observed to have selective recognition of NH_4^+ over K^+.[12] 1,3,5-Tris(bromomethyl)mesitylene has been employed in the synthesis of the oxazoline receptors **11**.



R= Ph, i-Pr, Bn

11

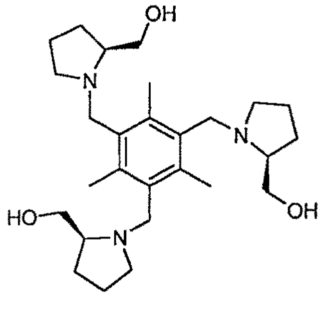
Armstrong *et al* have prepared C_3- symmetric homochiral molecules **12** by linking natural mono-terpene alcohols with 1,3,5-tris(bromomethyl)mesitylene as potential ligands.[13]



R' = (-)-menthol,(-)-isopinocampheol, (-)-borneol, (+)-terpinen-4-ol, (S)(+)-2-methyl-1-butenol

12

Homochiral C_3- symmetric triols **13** and triamines **14** have been prepared by the same group and their use as ligands explored briefly.[14,15]



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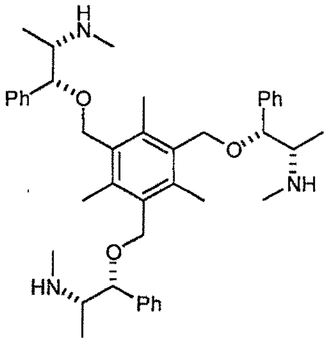
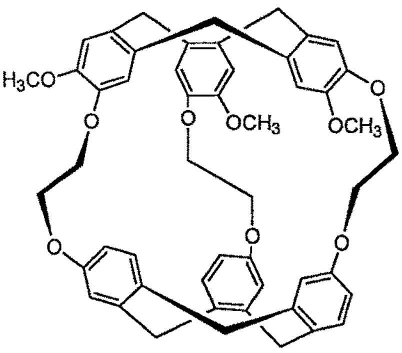


14

The C_3-symmetric closed structures (**15-18**) have been prepared using perhydrotriquinacene triaryl benzene, cyclotriveratrylenes, calixarenes, S- triazines, or porphorins.[3,16]



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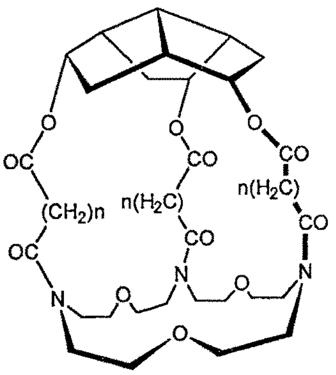

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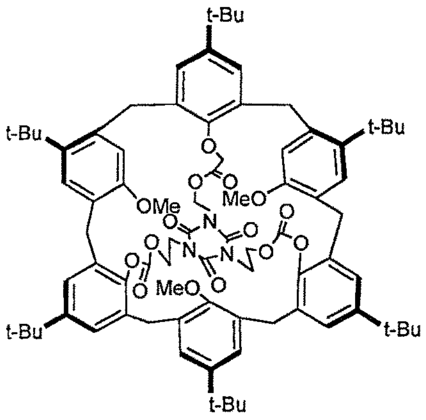
t-Bu
t-Bu
t-Bu
O
O
O
N
OMe
MeO
O
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N
N
O
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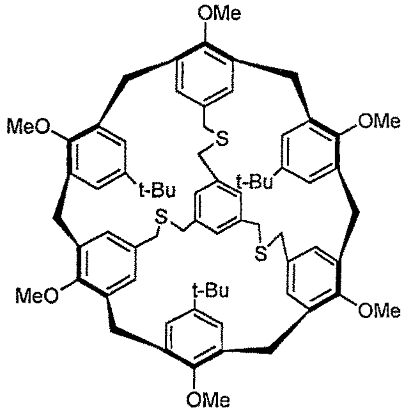
O
O
MeO
t-Bu
t-Bu
t-Bu

17


OMe
MeO
OMe
S
t-Bu
t-Bu
S
S
MeO
t-Bu
OMe
OMe

18

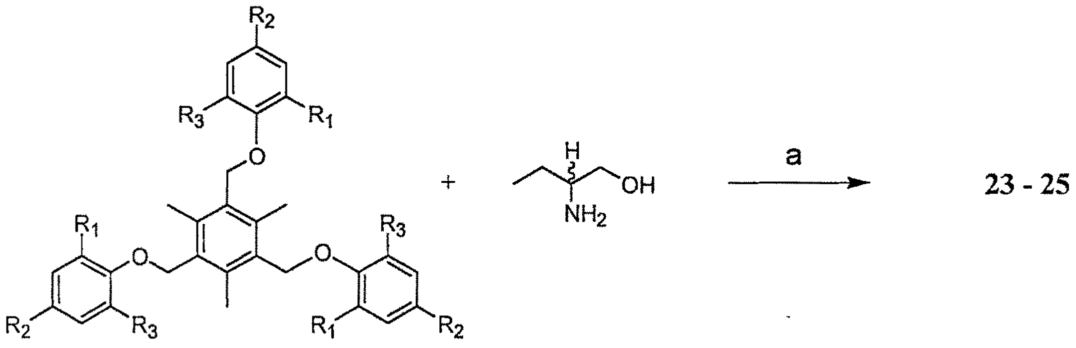
4.2 Aims and objectives

Coupling of tris(bromomethyl)mesitylene with a variety of phenolic aldehydes as reported in the previous chapter has yielded C_3-symmetric building blocks with different structural features which can be applied for the synthesis of compounds useful for important applications. Looking at the importance of C_3-symmetric chiral compounds in asymmetric synthesis and chiral recognition, described hitherto, the introduction of chiral sensors in the new molecules was an obvious goal for us. The presence of one or more donor sites is required for chiral recognition in the moiety to be introduced in C_3 -symmetric triformyl compounds (Chapter 3) with the central rigid aromatic palm connecting the aromatic podand groups useful for holding guest molecules or ions. Among the chiral molecules, which can react smoothly with the formyl groups located in the C_3 -symmetric compounds, chiral amino compounds are more attractive choice. The chiral amino compounds include amino aromatic compounds, amino alcohols and one of the most important biomolecules, amino acids. We decided to apply some of these in the synthesis of C_3-symmetric homochiral imino compounds.

4.3 Results and discussion

For introduction of chiral functionalities to the C_3-symmetric compounds prepared, we decided to employ readily available chiral amino alcohols at the first place. Optically pure L-2-aminobutanol **22** was made readily available by a Lupin Laboratories, Ankleshwar, which generates it in a large quantity. Its D-isomer was also obtained from other sources for our studies. The 2-aminobutanols were subjected to react with the three of the C_3-symmetric aldehydes using different reaction conditions. Different solvents were employed for the condensation in good yields to non-formation of the triply condensed product. Acetonitrile was found to be the solvent of choice and gave the C_3-symmetric products in all the cases. In ethanol, some of the tripodal substrates were insoluble. So all the reactions could not be studied using ethanol as a solvent. The 4-formylphenyl derivative was soluble but did not give the targeted product. The condensation reactions were also carried out using THF as a solvent but its lower polarity compared to acetonitrile might be the major reason for failure of the reaction to give the triple condensation for some of the combination of the substrates for which the reactions were carried out. Apart from the solvent, the suitable reaction condition was found to be refluxing a mixture of tris(formylaryl)ether with three equivalents of either D- or L-2-aminobutanol **22** in acetonitrile for about two hours with stirring. The C_3-symmetric aldehydes used for these reactions are 1,3,5-tris((4-formylphenoxy)methyl)-2,4,6-trimethylbenzene, 1,3,5-tris((2-formyl-6-methoxyphenyloxy)methyl)-2,4,6-trimethyl benzene and 1,3,5-tris((4-formyl-2-methoxyphenyloxy)methyl)-2,4,6-trimethylbenzene (**Scheme-1**). All the products were solid in nature and were crystallized using appropriate solvents.

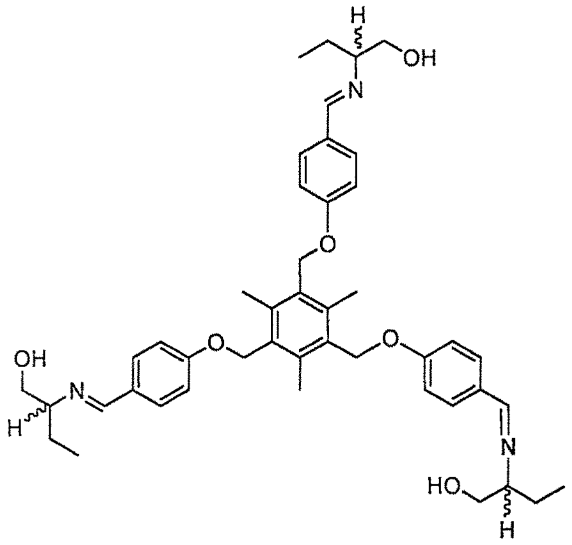
Scheme-1



R_1, R_2, R_3 = H/CHO/OCH_3 **R or S**

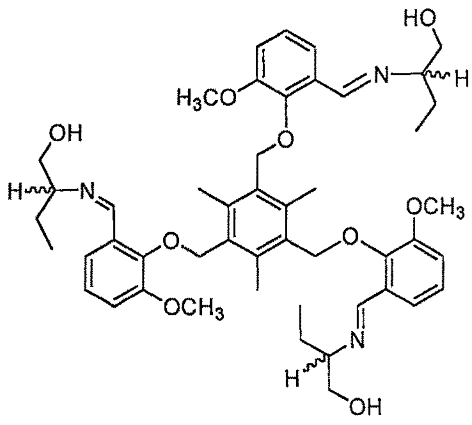
19-21 **22**

Reagents and Conditions: a) acetonitrile, Δ, 2h, 50-60%.



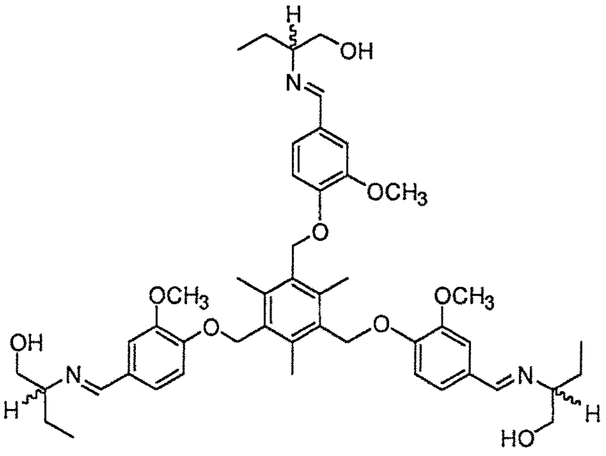
(R) or (S)

23



(R) or (S)

24



(R) or (S)

25

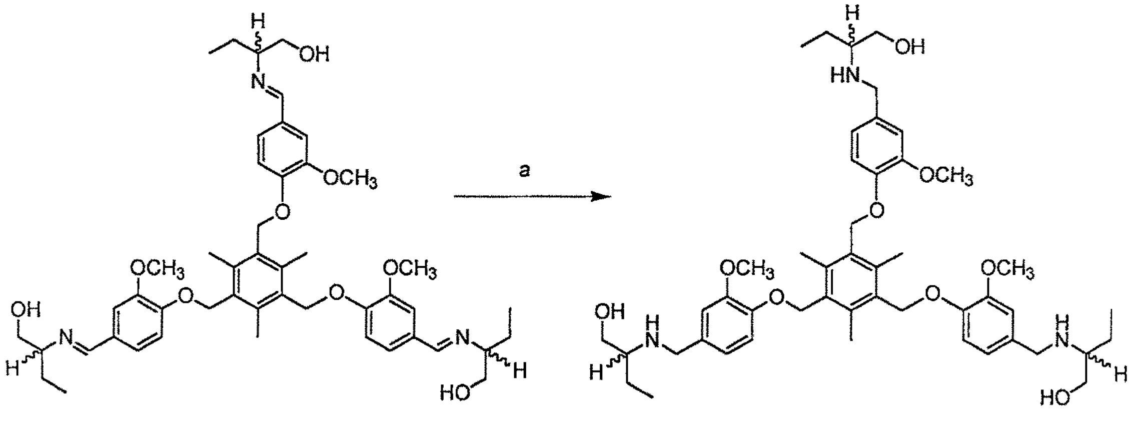
The C$_3$-symmetric chiral compounds obtained in crystalline form were fully characterized using IR, NMR, and elemental analysis. FAB-Mass were obtained for a couple of samples. All the products were optically active and the rotation was measured using a polarimeter. The physical data are well in agreement with the proposed structures.

The IR spectra clearly show that the products have no carbonyl group and the carbonyl group stretching frequencies seen in the IRs of the starting trialdehydes have disappeared and a broad band for the OH-stretching frequency around 3400 cm^{-1} is observed. A strong band for asymmetric C-O-C stretching was observed between 1214 to 1270 cm^{-1} (refer the spectral section).

Analysis of the PMR spectrum shows that the C_3 symmetric imino compound derived from (4-formylphenyloxy)methylmesitylene shows all the characteristic proton signals clearly. The diagnostic signals include methyl and methylene protons attached to the central ring, doublets of the p-substituted phenyl ring, and doublets of p-substituted phenyl ring. The methine proton on the carbon doubly bonded to N absorbs at 8.38 ppm. The proton on the asymmetric carbon atom at 3.48ppm, a doublet for $-CH_2$ protons attached to the –OH group and the protons for the ethyl group attached to the asymmetric carbon atom are also clearly observed in PMR. The 2-formyl 3-methoxy analog has an additional singlet at 3.95 ppm with different pattern for the aromatic protons. The 1,3,5-tris((4-formyl-2-methoxyphenyloxy)methyl)-2,4,6-trimethylbenzene derived imino compound is not completely soluble in $CDCl_3$. Its PMR spectrum in DMSO displayed the methoxy proton at 3.8 ppm while each proton on the methylene group attached to the –OH group seems to be separately appearing at 4.55 ppm and at 3.52 ppm.

The double bond of CH=N of the latter product was reduced to $-CH_2NH-$ (**Scheme-2**) after which the compound was soluble in $CDCl_3$ with disappearance of the methane proton and $-CH_2NH-$ protons appearing at 3.7ppm to 3.88ppm and –NH proton as a broad singlet at 1.9ppm. Two protons of $-CH_2OH$ are still observed separately at 3.4ppm and 3.7ppm

Scheme-2

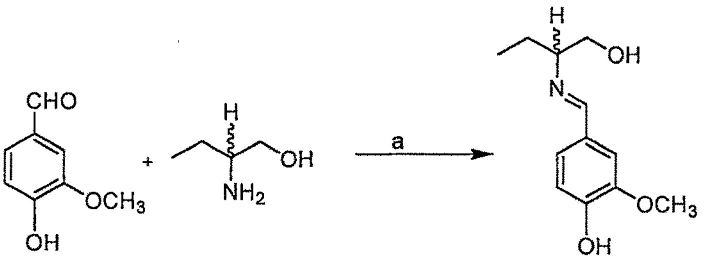


25 (R or S) **26 (R or S)**

Reagents and Conditions: a) EtOH, $NaBH_4$, Δ, 2h, 54.1%.

For comparison and confirmation of our C_3 symmetric compounds, the aminobutanols were reacted directly with one of the aromatic aldehydes, vanillin without the central connecting unit to give the corresponding imine **(Scheme-3)**.

Scheme-3



27 **22** **28**

Reagents and Conditions: a) THF, Δ, 1h, 76.2%.

Proton NMR spectrum of **28** when compared with that of the corresponding C_3-symmetric compounds has been found different according to the expectation. It was reported earlier that imine formation of 2-amino butanol with aromatic aldehydes results in cyclisation of the product to an oxazolidine ring[17] but in our study we have not observed formation or presence of oxazolidine ring and the presence of an imine group is clearly observed.

The ^{13}CNMR for the imino product obtained from 4-formylphenyloxymethyl compound which has a local symmetry also present. It shows the characteristics signals at 161.2 ppm for the methine carbon (CH=N) and at 74.5 ppm for the carbinol carbon, benzyl carbons forming the ether linkage are seen at 66.3 ppm and the asymmetric carbons are observed at 65.1 ppm in addition to the signals for other aromatic and aliphatic carbons.

For *o* and *p*-vanillins as the local symmetry is absent, more of aromatic signals are observed and a clear signal around 55 ppm is observed for the methoxy carbon. The imine derived from the 4-formyl-2-methoxy compound reduced to tris(secondary amine) does not have the signal for the imino carbon and shows the signal for the benzyl amine carbon at 50.7 ppm.

FAB-Mass spectrum for one of the tris(amino alcohol) products has been obtained showing M+2 peak at 827 (might be due to the abstractions of protons from the matrix used). The next lower prominent peak observed is due to the cleavage of one of the butanol side chains. The base peak derived is after cleavage of all the three imino groups. The LC-MS of the sample also shows the M+2 peak. The reduced product has also been subjected to FAB-mass, which shows M+2 product at 831 the base peak. The peak corresponding to the loss of butanol side-chain is also observed (see he spectral section).

In our study optically pure D- and L-2-aminobutanols have been employed for the preparation of the C_3 symmetric chiral molecules. The resulting condensation product must retain chirality because the reaction is not disturbing the chiral carbon. Totally three D- and L- pairs have been synthesised. One of these products has been reduced to give the tris-amino product as mentioned earlier and should also retain the optical activity. Specific rotation for all these compounds have been measured and the values are reported in **Table 1.**

Table 1 **Specific Rotations of Enantiomers of the Compounds 22 to 26.**

Compound	*L*	*D*
22	-0.17^0	$+0.11^0$
23	-29.40^0	$+28.00^0$
24	-23.68^0	$+22.60^0$
25	-30.22^0	$+28.60^0$
26	-37.52^0	

The specific rotation has been measured by taking 0.1% solution of the compound in chloroform on an auto-polarimeter.

As can be observed the D- and L- isomers show specific rotation of nearly same value in opposite directions. The rotation angle values for the L- products are about 1° more than the values observed for the D- isomers. This must be due to the difference in optical purity of the starting 2-aminobutanol. The results show that the chiral centre is not disturbed during the reaction carried out and therefore these C_3 symmetrical chiral products can be further employed for binding studies with chiral guest molecules.

The study of binding ability of the chiral host molecules requires a detailed NMR titration studies. Such NMR titrations have been planned using optically pure amino acids. As this study requires long hours on a NMR machine, it has not been materialised so far. The binding studies would lead to some interesting results and help in designing of suitable guest molecule and applicability of the designed host molecule.

4.4 Experimental

Reagents, Solvents and Instrumentation .

L-2-amino butanol was obtained from Lupin Laboratories and D-2-amino butanol obtained was of S.d.-fine Chemical co. All the solvents and other chemicals were obtained from Suvidhinath Chemicals. Solvents were purified by standard methods and reagents were used without purification.

Melting points have been recorded on a Gallenkamp 350 micro melting apparatus by open capillary method and are uncorrected. Optical rotations are measured on a Jasco-Dip 370 polarimeter at 25^0C in chloroform. Infrared spectra have been recorded using Perkin-Elmer 16PC as KBr discs between 4000-600 cm^{-1}. ^{1}H-NMR spectra are recoreded on Bruker-AVX instruments at 200 MHz and 400 MHz at **Sun Pharmaceutical and Research Centre** and ^{13}C-NMR spectra have been recorded on Jeol-300 machine at 75 MHz at **Kwangju Institute of Science and Technology, Korea.** ^{1}H- and ^{13}C-NMR spectra are recorded in $CDCl_3$, except in some cases where not soluble, DMSO-d_6 is used with TMS as the internal standard. Elemental analysis has been carried out using Perkin-Elmer 240 CHN analyser. FAB-Mass spectra are recorded on a JEOL SX 102/DA-6000 mass spectrophotometer data system using Argon/ Xenon (6kv, 10mA) as the FAB gas at accelerating voltage 10 kv at room temperature using m-nitrobenzyl alcohol as the matrix at **CDRI Lucknow**.

Synthesis of the Tri-imines (23-25)

General Procedure:

To a solution of tri-aldehyde (3 mmol) in 20 mL acetonitrle in 100mL two necked RB flask was added, a solution of (R) or (S) 2-amino-1-butanol (1.2 mmol) in 10 mL acetonitrile dropwise using a dropping funnel within 30min. while refluxing with stirring. The mixture was further refluxed for 2hrs after which half of the solvent was distilled off. The mixture was left overnight at room temperature to yield the corresponding product, which was recrystallised using appropriate solvent.

(R)-or (S)- 1,3,5-Tris((4-(1-hydroxybutyl-2-iminomethylidene)-phenyloxy)methyl)-2,4,6-trimethylbenzene (23)

1,3,5-Tris((4-formyl-phenyloxy)methyl)-2,4,6-trimethylbenzene (0.174 mg.,0.3 mol) and (R) or (S) 2-amino-1-butanol (0.106 gm., 0.113 mL, 1.2 mol) were reacted as described above. The white solid product was recrystallised from ethanol.

Yield	:	50.34% (0.370 gm)
M.P.	:	140^0 C
$[\alpha]_D^{25}$ (0.1% in $CHCl_3$)	:	$+28.00^0$ and -29.40^0
IR (KBr, cm^{-1})	:	3401,2961, 2927, 2872, 1459, 1239, 1642, 1604, 1510, 992.
^{1}H-NMR (δppm):	:	0.88 (9H, t, $-CH_2-CH_3$), 1.6 (6H, q, $-CH_2-CH_3$), 2.46(9H, s, Ar-CH_3), 3.19 (3H, s, $-CH-CH_2-OH$),

3.73 (6H,m, -CH_2-OH of hydroxy but-2-yl), 5.1 (6H, s, Ar-CH_2-O-Ar), 7.0 (d) & 7.6 (d), arom. protons), 8.2 (3H,s, -CH=N-).

^{13}C-NMR (δppm): 10.7 (-CH_2-CH_3), 25.0 (-$\underline{C}H_2$-CH_3), 66.2 (-CH-CH_2-OH), 74 (-CH_2-OH of hydroxy but-2-yl), 15.9 (Ar-CH_3), 77.0(Ar-CH_2-O-Ar), 115,129,130,132,132.5,139 (arom.carbons), 161.2 (-CH=N-).

Anal. Calcd. for $C_{45}H_{57}N_3O_6$: % **C** 72.8, **H** 7.6, **N** 6.4

Found: For **D** % **C** 73.9, **H** 7.7, **N** 5.5

For **L** % **C** 74.2, **H** 7.9, **N** 5.5

(R)or(S)1,3,5-Tris-((2-(1-hydroxybutyl-2-iminomethylidene)-6-methoxyphenyloxy) methyl)-2,4,6-trimethyl benzene(24)

1,3,5-Tris ((2-formyl-6-methoxyphenyloxy)methyl)-2,4,6-trimethylbenzene (0.204 gm., 0.3 mol) and (R) or (S) 2-amino-1-butanol (0.106 gm., 0.113 mL, 1.2 mol) were reacted as described and recrystallised from acetonitrile to white pellets.

Yield: 57.5% (0.475gm.).

M.P.: 160^0 C.

$[\alpha]_D^{25}$ (0.1% in $CHCl_3$): +22.60^0 -23.68^0

IR (KBr, cm^{-1}): 3413, 2962, 2927, 2872, 1636, 1581, 1475, 1271, 1203, 1072, 953.

^{1}H-NMR (δppm):	0.75 (9H, t, -CH$_2$-**CH$_3$**), 1.50 (6H, m, -**CH$_2$**-CH$_3$), 2.54 (9H, s, Ar-**CH$_3$**), 3.0 (3H, s, -**CH**-CH$_2$-OH), 3.55 (6H,m, -**CH$_2$**-OH of hydroxy but-2-yl), 4.0 (9H, s, Ar-O-**CH$_3$**), 5.2 (6H, s, Ar-**CH$_2$**-O-Ar), 7.0 (2H, m, aromatic), 7.5 (1H, m, aromatic), 8.5 (3H, s, -**CH**=N-).
^{13}C-NMR (δppm):	10.6 (-CH$_2$-**CH$_3$**), 25 (-**CH$_2$**-CH$_3$), 66 (-**CH**-CH$_2$-OH), 74 (-**CH$_2$**-OH of hydroxy but-2-yl), 16 (Ar-**CH$_3$**), 70.2 (Ar-**CH$_2$**-O-Ar), 55.9 (Ar-O-**CH$_3$**), 153, 148, 140, 132, 130, 124, 119, 114 (arom. carbons), 158.0 (-**CH**=N-).
FAB Mass:	827 (M+2).
Anal. Calcd. for $C_{48}H_{63}N_3O_9$:	% **C** 69.3, **H** 7.58, **N** 5.77
Found: For **D**	% **C** 69.45, **H** 7.89, **N** 4.81
For **L**	% **C** 68.8, **H** 8.3, **N** 4.6

(R)or(S)1,3,5-Tris-((4-(1-hydroxybutyl-2-iminomethylidene)-2-methoxyphenyloxy) methyl)-2,4,6-trimethylbenzene (25)

1,3,5-Tris-((4-formyl-2-methoxyphenyloxy)methyl)-2,4,6-trimethylbenzene (0.204gm., 0.3 mol) & (R) or (S) 2-amino-1-butanol (0.106 gm., 0.113 mL, 1.2 mol) were reacted as described in general procedure. The white solid product was recrystallised from methanol.

Yield: 54.4%(0.450gm)

M.P: 200^0 C

$[\alpha]_D^{25}$ (0.1% in $CHCl_3$): $+28.60^0$ and -30.22^0

IR (KBr cm^{-1}): 3412, 2962, 2929, 2873, 1639, 1597, 1510, 1266, 1138.

^{1}**H-NMR** (δ ppm): 0.80 (9H, t, $-CH_2-$**CH_3**), 1.44 & 1.62 (6H, **$-CH_2-$**CH_3), 2.4 (9H, s, Ar-**CH_3**), 3.2 (3H, s, -**CH**-CH_2-OH), 3.65 (6H,m, -**CH_2**-OH of hydroxy but-2-yl), , 3.8 (9H, s, Ar-O-**CH_3**), 5.1 (6H, s, Ar-**CH_2**-O-Ar), 7.3 & 7.4 (s, arom. protons), 8.2 (3H,s, -**CH**=N-).

^{13}**C-NMR** (δppm): 10.8 ($-CH_2-CH_3$), 15.9 (Ar-CH_3), 25 ($-CH_2-CH_3$), 66.23 ($-CH-CH_2-OH$), 74.30 ($-CH_2$-OH of hydroxy but-2-yl), 66.6 (Ar-CH_2-O-Ar), 55.9 (Ar-O-CH_3), 151, 150,140, 131, 130, 123, 113, 110 (arom. carbons), 161 (-CH=N).

Anal. Calcd. for $C_{48}H_{63}N_3O_9$: % **C** 69.3, **H** 7.58, **N** 5.77

Found: For **D** % **C** 70.45, **H** 7.8, **N** 4.4

For **L** % **C** 69.7, **H** 7.3, **N** 5.14

(R) or (S) 1,3,5-Tris-((4-(1-hydroxybut-2-yl aminomethyl)-2-methoxyphenyloxy) methyl)-2,4,6-trimethyl benzene(26)

(R)- or (S)-1,3,5-Tris-((4-(1-hydroxybutyl-2-iminomethylidene)-2-methoxyphenyloxy) methyl)-2,4,6-trimethyl benzene (0.826 gm. ,0.1 mmol) was dissolved in 20 mL methanol and $NaBH_4$ (0.378 gm., 10 mmol) was added in small portions at refluxing temperature. The completion of the reaction was monitored using TLC. After 2h the reaction was worked up by removal of solvent under reduced pressure. Water (15ml) was added to give a residue further extracted with DCM. The DCM extracts were dried over anhy. Na_2SO_4. The product obtained after removal of solvent was crystallized from acetonitrile.

Yield: 54.1 % (0.450gm)

M.P.: 140°C

$[\alpha]_D^{25}$ (0.1% in $CHCl_3$): -37.52°

IR (KBr, cm^{-1}): 3383, 2958, 2931, 2873, 1590, 1514 (s), 1464, 1261, 1227, 1137,1037, 989.

^{1}H-NMR (δ ppm): 0.9 (9H, t, -CH$_2$-$\mathbf{CH_3}$), 1.5 (6H, m, -$\mathbf{CH_2}$-CH$_3$), 1.9 (3H, Br.s, -**NH**), 2.45(9H, s, Ar-$\mathbf{CH_3}$), 2.6 (3H, m, -**CH**-CH$_2$-OH), 3.35 & 3.65(6H,m, -$\mathbf{CH_2}$-OH of hydroxy but-2-yl), 3.75 (d, -$\mathbf{CH_2}$ of benzylamine), 3.82 (9H, s, Ar-OCH$_3$),5.1 (6H, s, Ar-$\mathbf{CH_2}$-O-Ar), 7.0 (d) & 6.9 (m) (arom. protons).

^{13}C-NMR (δppm): 10.7 (-CH$_2$-$\mathbf{CH_3}$), 25.0 (-$\mathbf{CH_2}$-CH$_3$), 66.2 (-CH-CH$_2$-OH), 77.0 (-CH$_2$-O of hydroxy but-2-yl),

	15.9 (Ar-CH_3), 77.0 (Ar-CH_2-O-Ar), 114-139.4 (aromatic carbons).
FAB Mass:	833 (M+2).
Anal. Calcd. for $C_{48}H_{69}N_3O_9$:	**% C** 69.3, **H** 8.3, **N** 5.05
Found:	**% C** 68.82, **H** 8.37, **N** 4.62.

(R) or (S)- 4-(1-Hydroxybut-2-yl-iminomethylidene)-2-methoxyphenol(28)

4-Hydroxy-3-methoxybenzaldehyde (vanillin) (0.152g, 1mmol) was taken in 10 mL of THF. (R) or (S)-2-amino-1-butanol (O.O89gm., 0.094 mL, 1 mmol) was added to the solution of 4-hydroxy-3-methoxybenzaldehyde in 5 mL THF with stirring during 30 min under reflux temperature. Reaction was continued for 1h more and solvent was removed. The solid obtained was crystallized from toluene to get yellow crystals.

Yield:	76.2% (0.170gm)	
M.P.:	145^0C	
$[\alpha]_D^{25}$: (0.1% in $CHCl_3$):	$+17.98^0$	-16.60^0
IR (KBr, cm^{-1}):	3288, 2964, 2933, 2874, 1654, 1590, 1518, 1464, 1364, 1130, 1030, 825.	
^{1}**H-NMR** (δppm):	0.84 (3H, t, -CH_2-$\mathbf{CH_3}$), 1.59 (2H, q, -$\mathbf{CH_2}$-CH_3), 3.2 (1H, m, -**CH**-CH_2-OH), 3.75 (2H, m, -$\mathbf{CH_2}$-OH of hydroxy but-2-yl), 3.76 (3H, s, Ar-OCH_3),	

5.1 (br.s, Ar–**OH**), 6.8, 7.0 & 7.3 (m, arom. protons), 8.04(3H,s, -**CH**=N-).

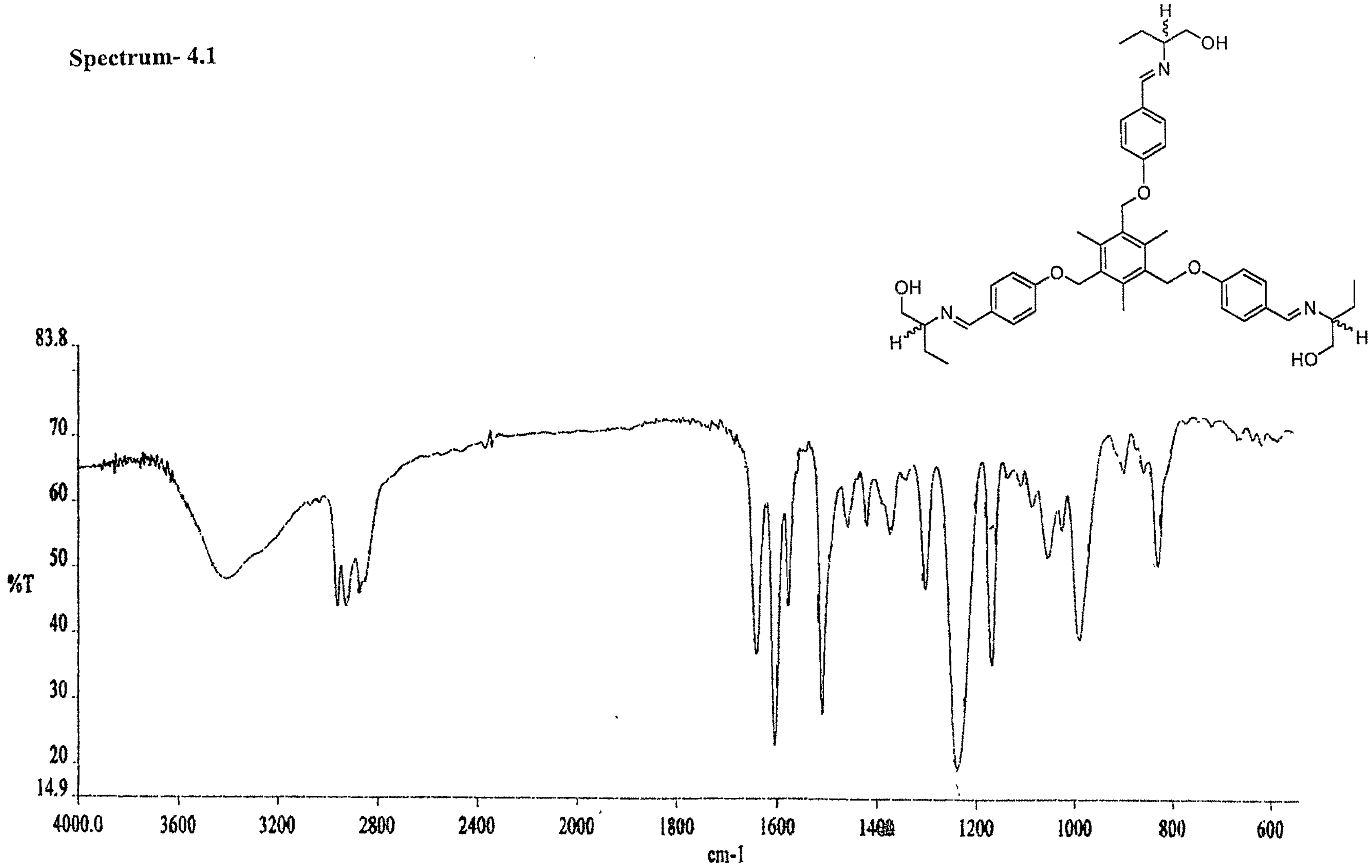
^{13}**C-NMR** (δppm): 10.7 (-CH_2-$\mathbf{CH_3}$), 25.0 (-$\mathbf{C}H_2$-CH_3), 66 (-**C**H-CH_2-OH), 74 (-**C**H_2-O-of hydroxy but-2-yl), 109, 114.3, 124.1, 128, 147.0, 149 (arom. carbons), 161.9 (-CH=N-), 58.8 (-OCH_3).

Anal. Calcd. for $C_{12}H_{17}NO_3$: % **C** 64.57, **H** 7.62, **N** 6.27

Found: For **(S)** % **C** 65.41, **H** 7.83, **N** 6.21

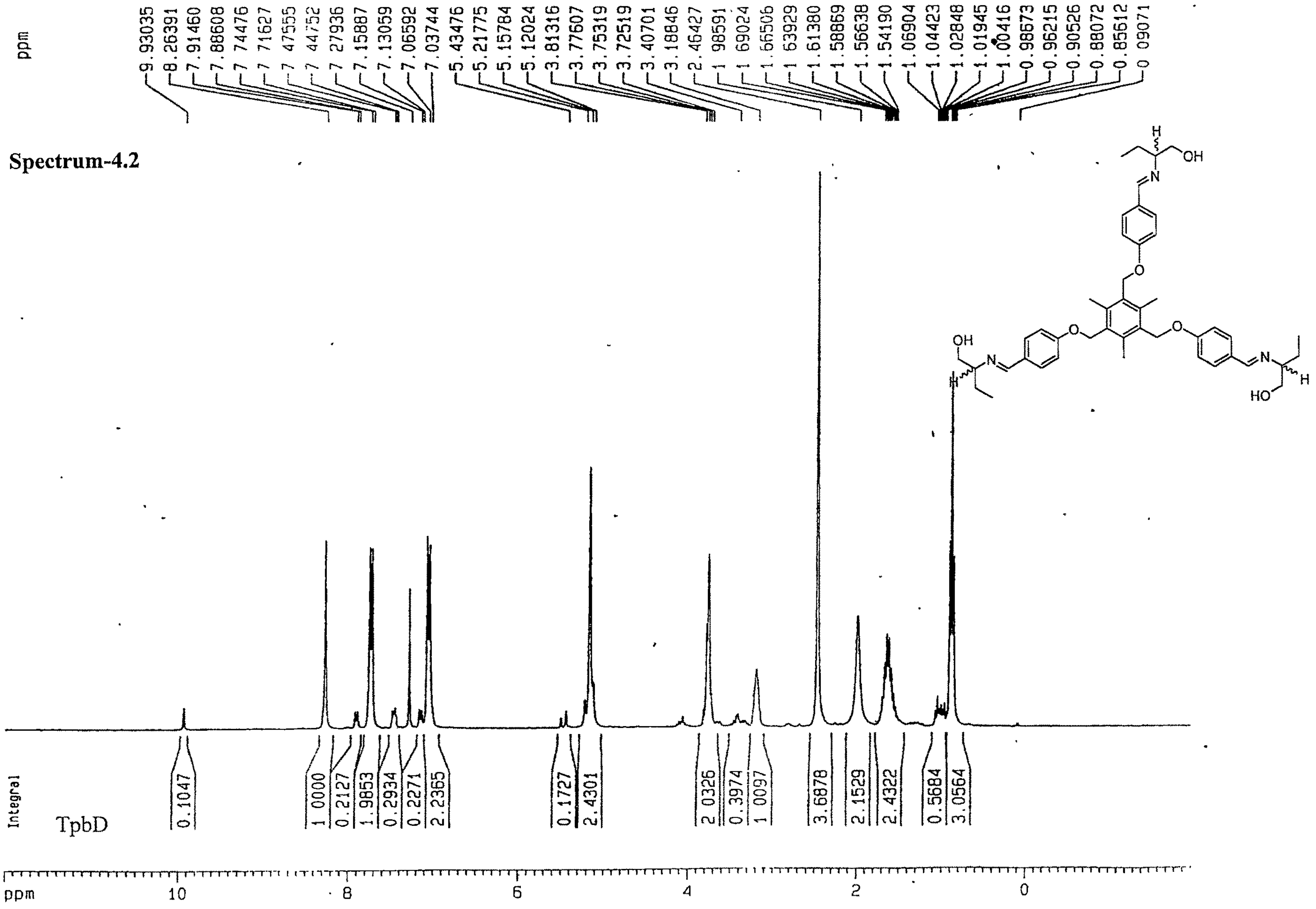
For **(R)** % **C** 65.3, **H** 7.4, **N** 6.14

Spectrum- 4.1



TpbD-IR

Spectrum-4.2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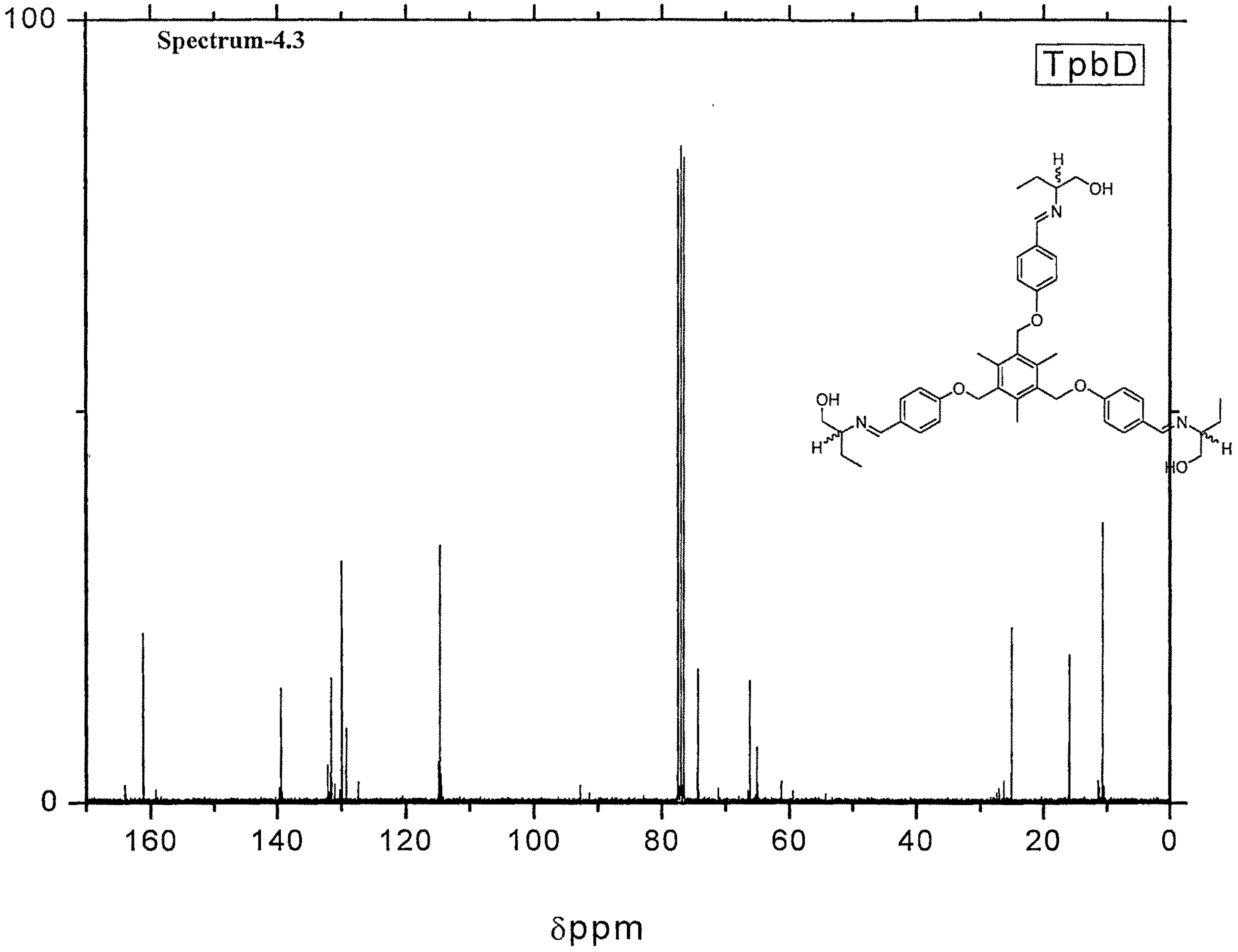
8
6
4
2
0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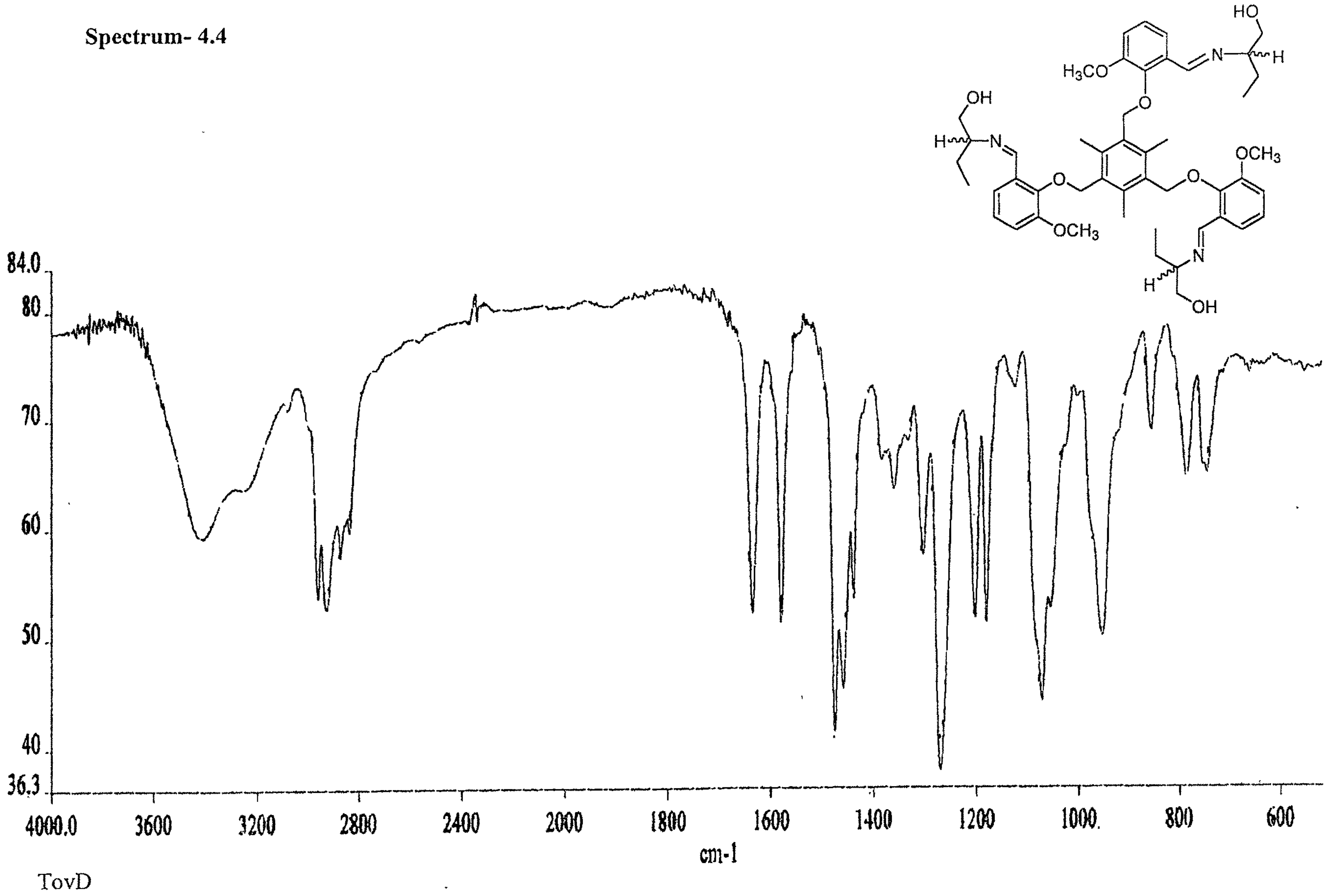
0
δppm

Spectrum- 4.4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H
OH
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N
O
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O
O
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N
H
OH
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80
70
60
50
40
36.3
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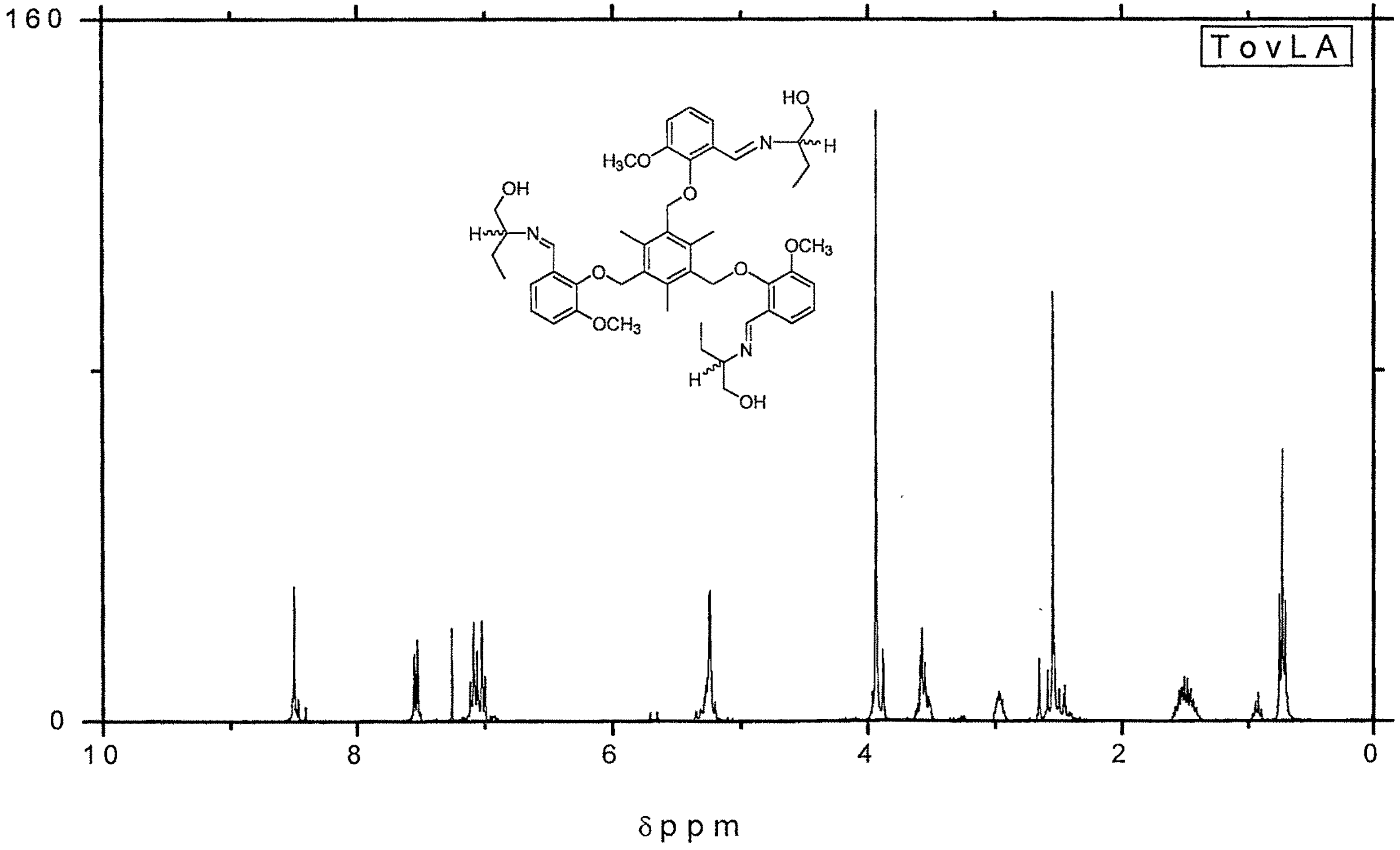
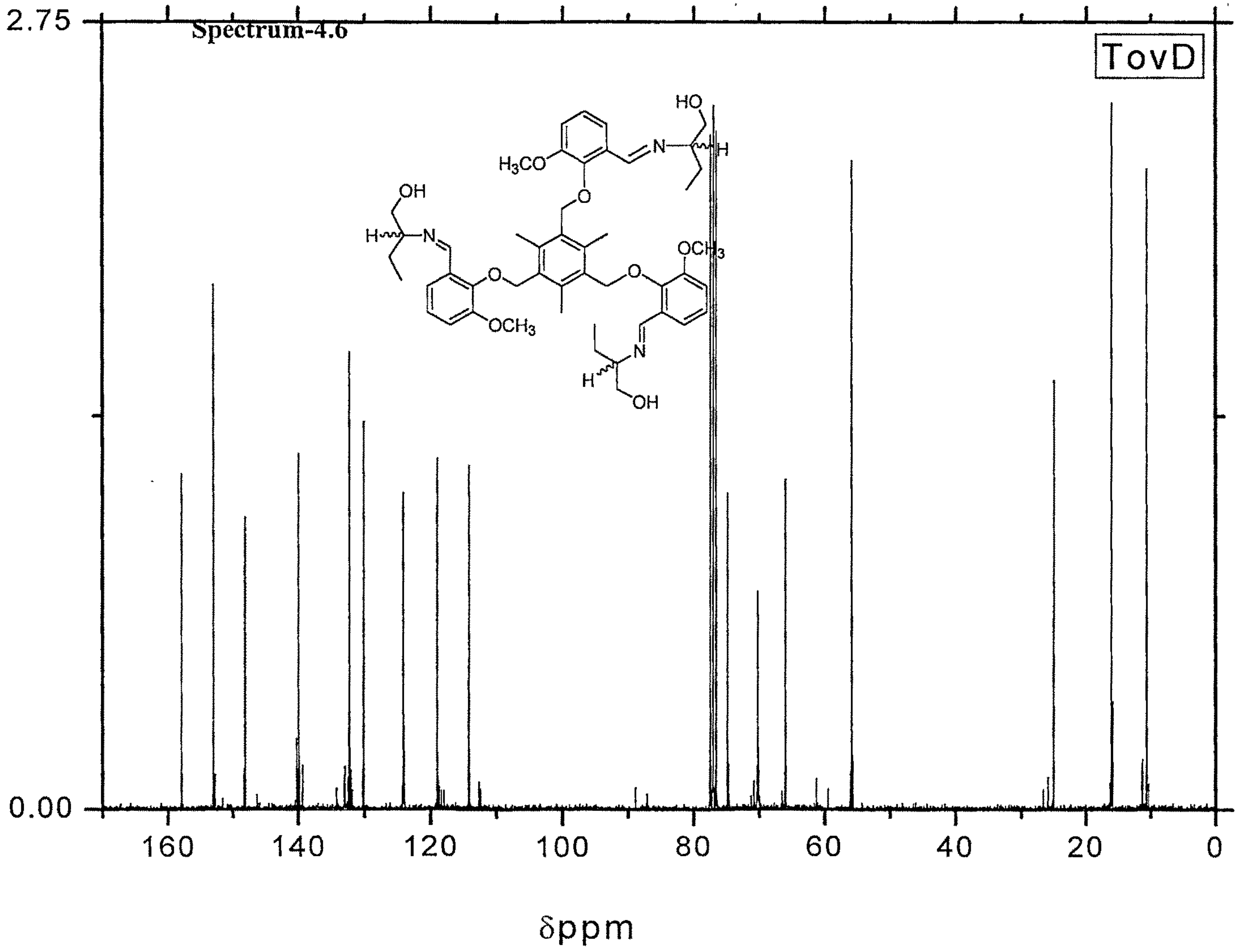
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
cm-1
TovD

Spectrum-4.5



Spectrum-4.6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OH
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N
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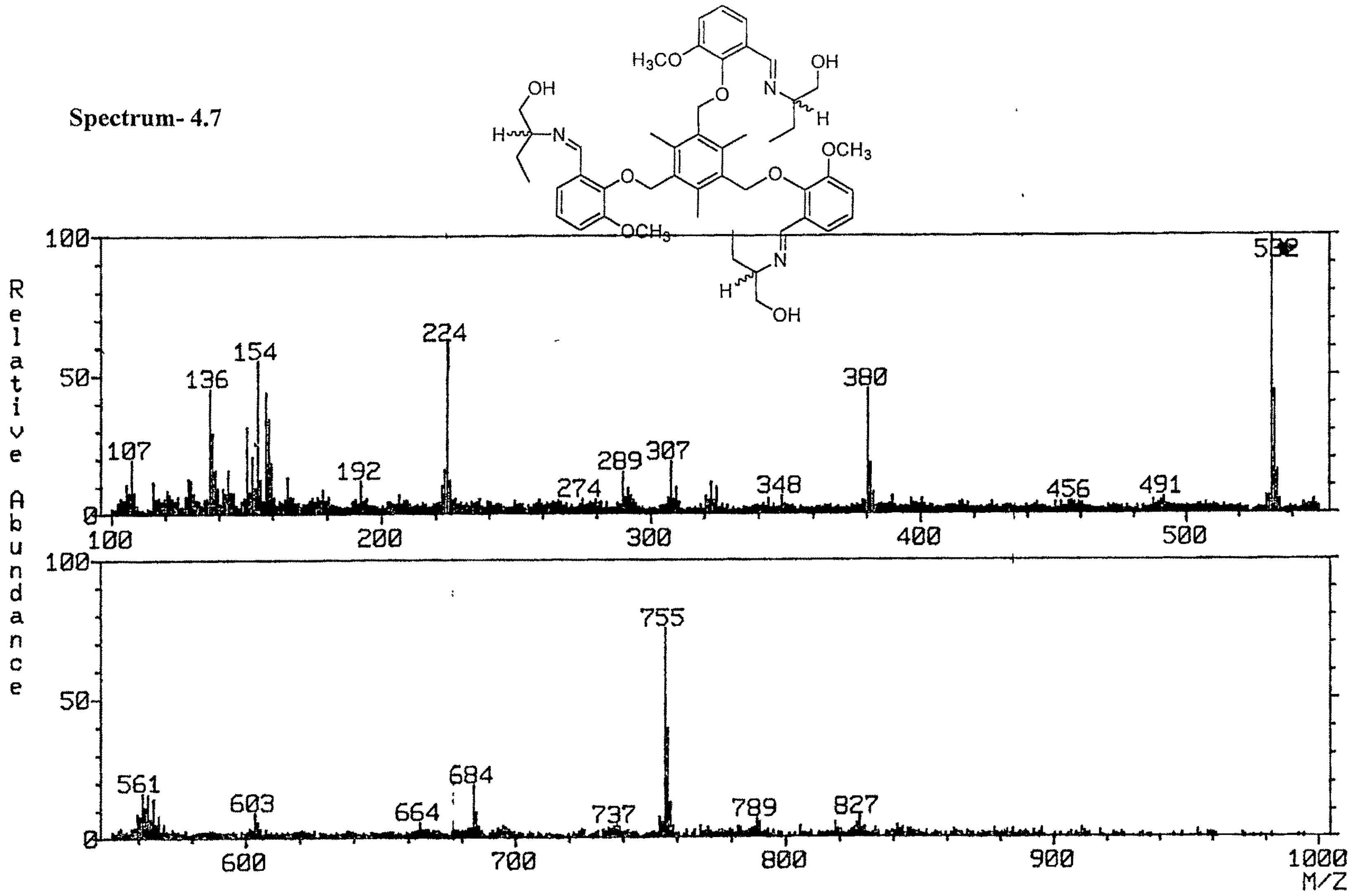
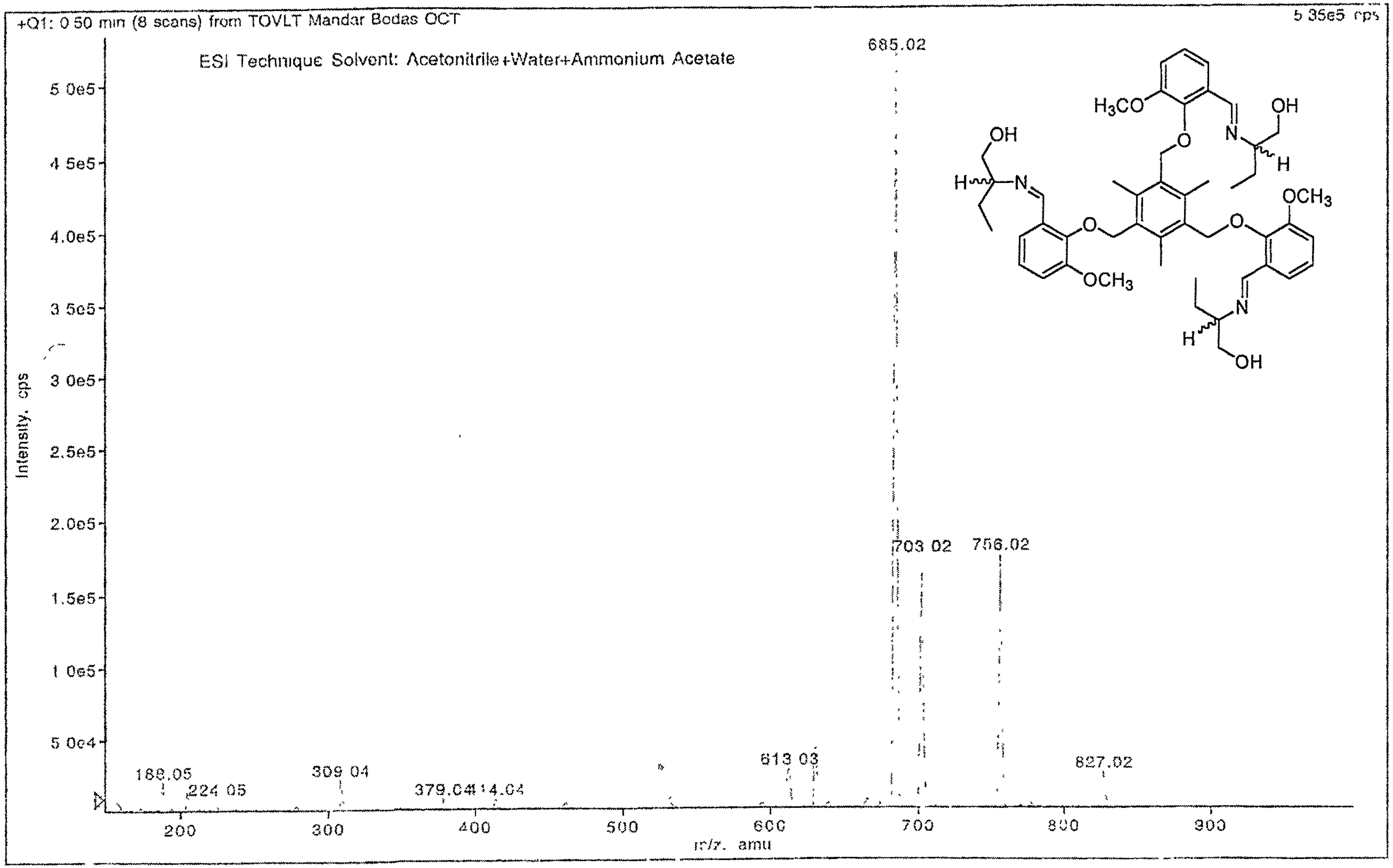
O
OCH3
O
N
H
OH

Spectrum- 4.7



Tovd

Spectrum- 4.8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5 35e5 cps
ESI Technique Solvent: Acetonitrile+Water+Ammonium Acetate
Intensity, cps
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4 5e5
4.0e5
3 5e5
3 0e5
2.5e5
2.0e5
1.5e5
1 0e5
5 0e4
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703 02
756.02
827.02
613 03
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414.04
309 04
224 05
188.05
200
300
400
500
600
700
800
900
m/z, amu
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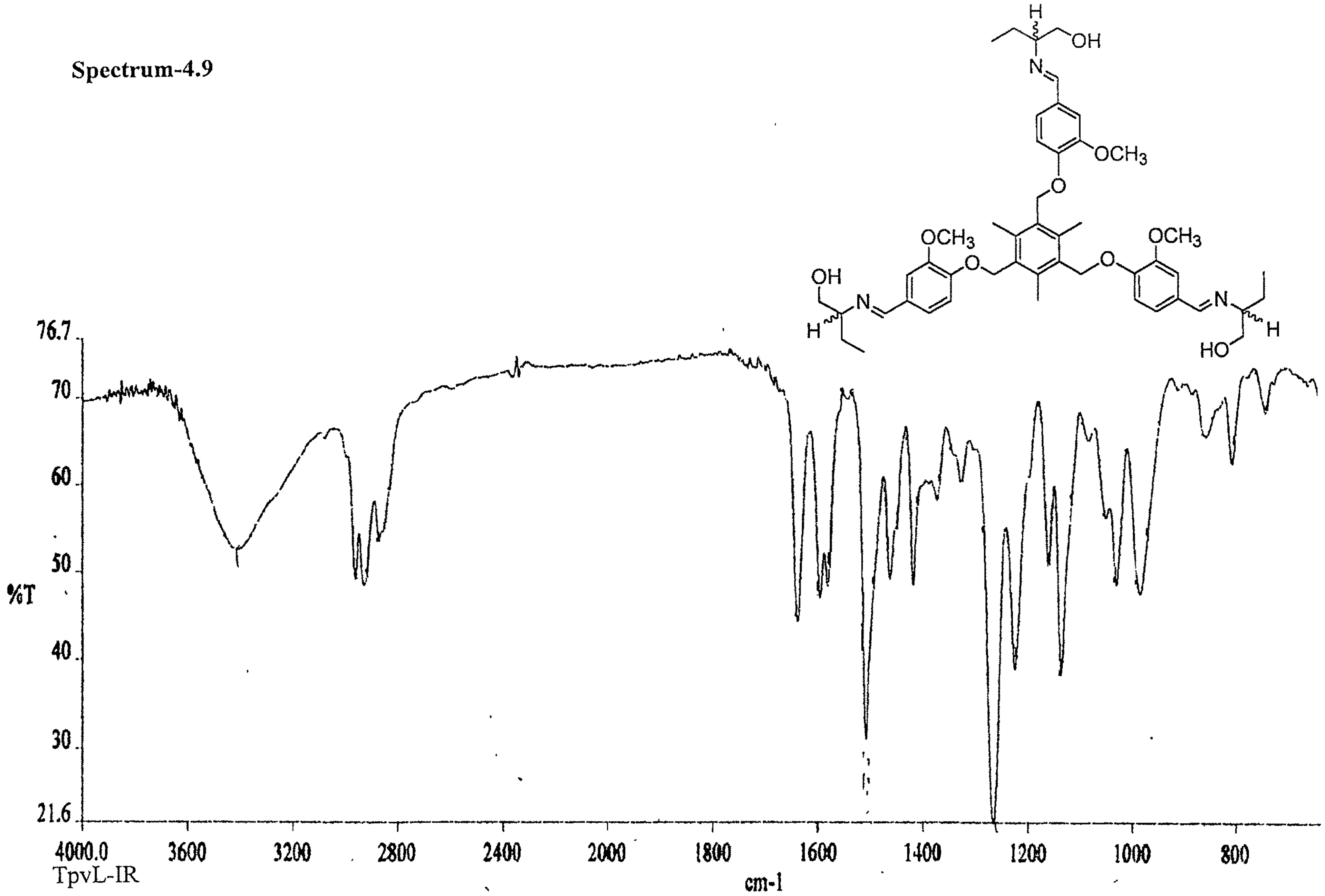
O
O
O
H
H
H

Spectrum-4.9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H
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60
50
%T
40
30
21.6
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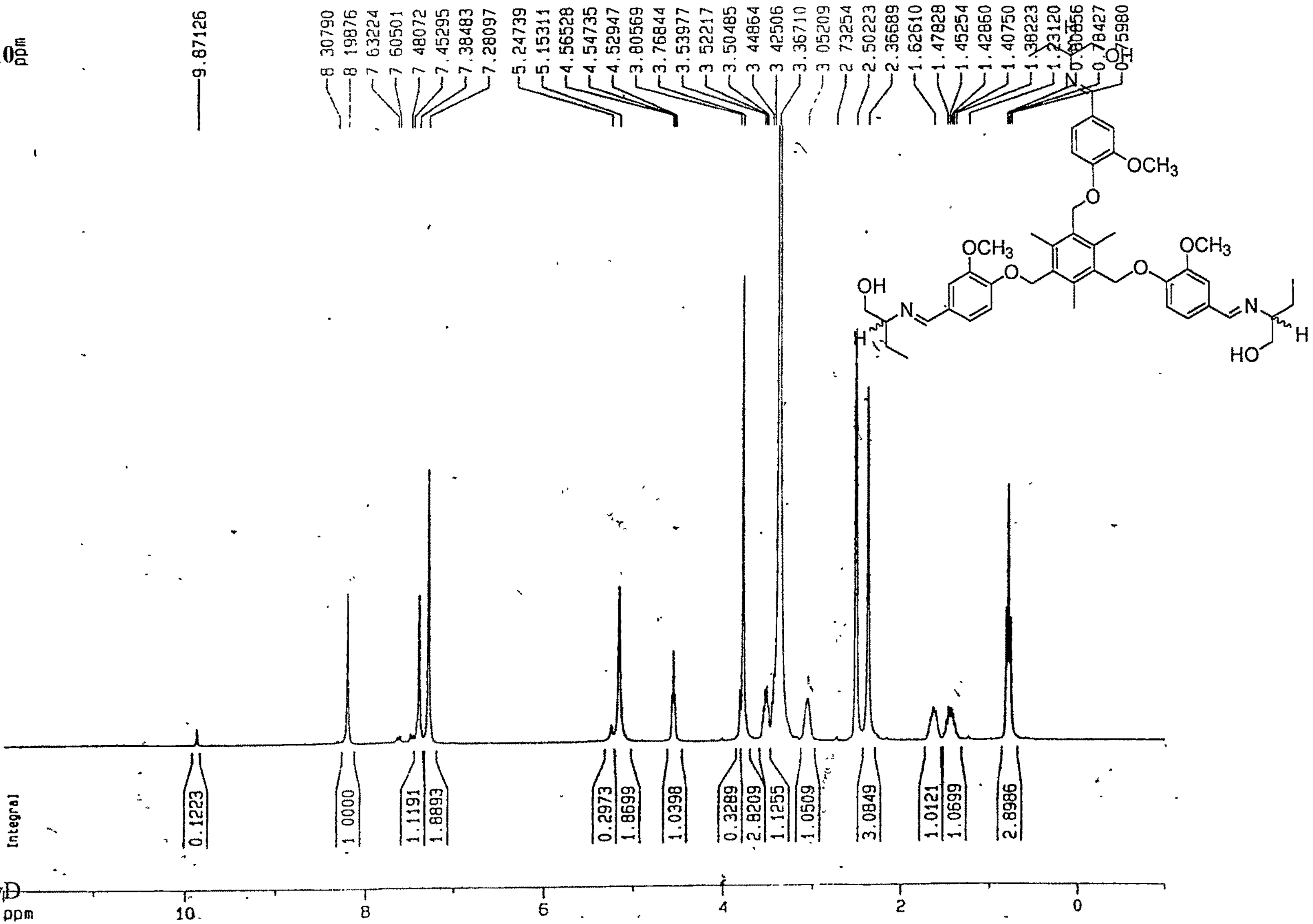
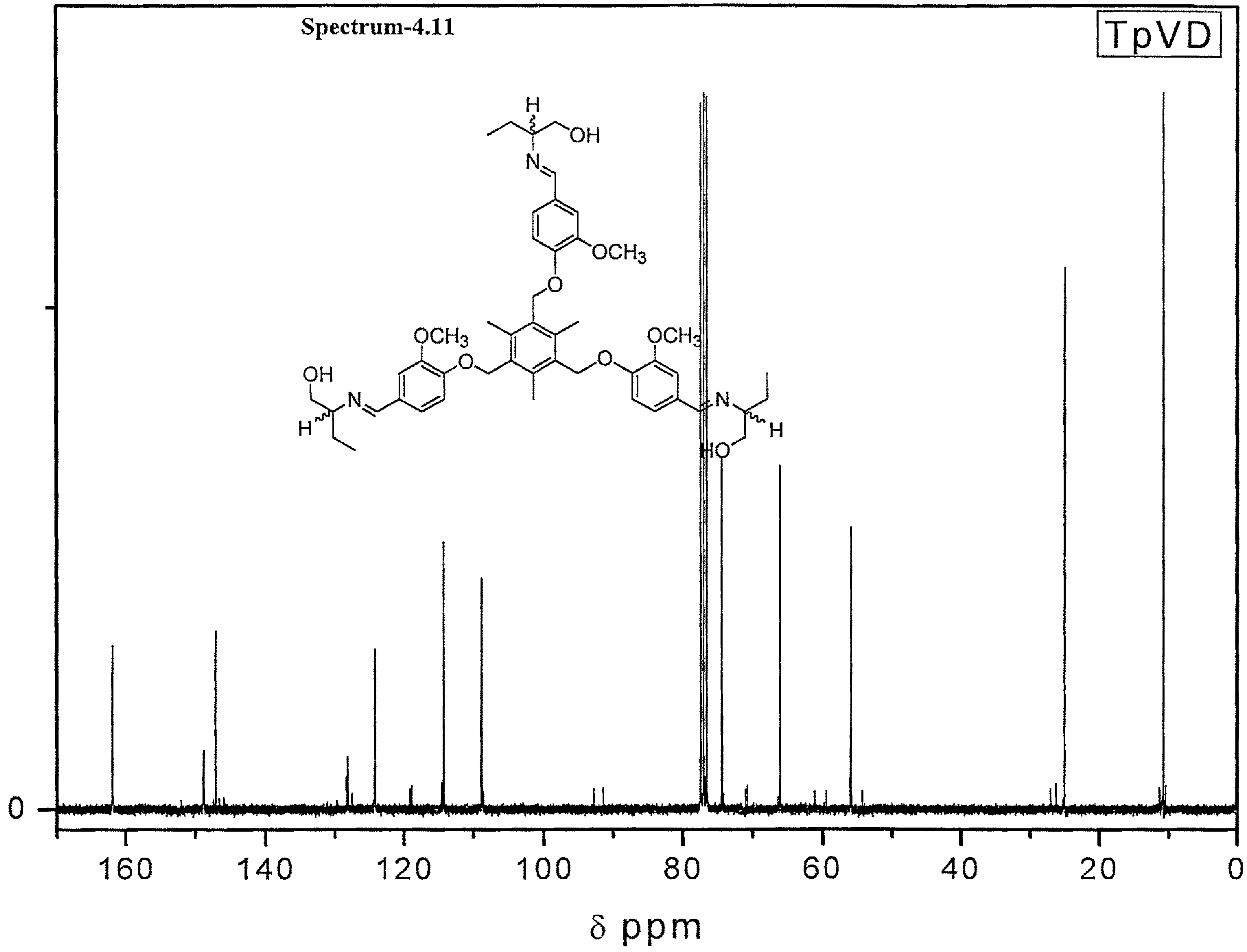
1000
800
cm-1
TpvL-IR

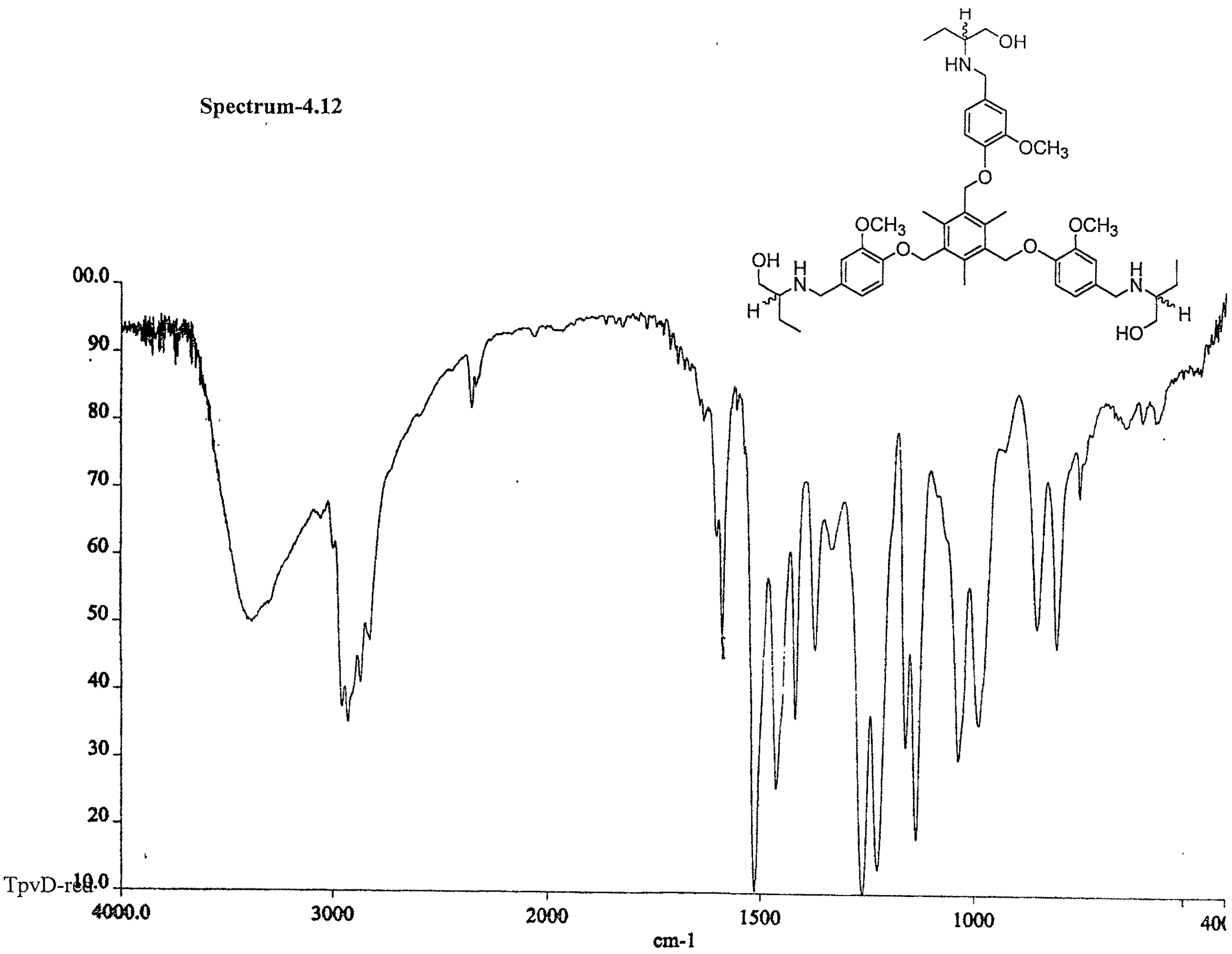
Spectrum-4.10



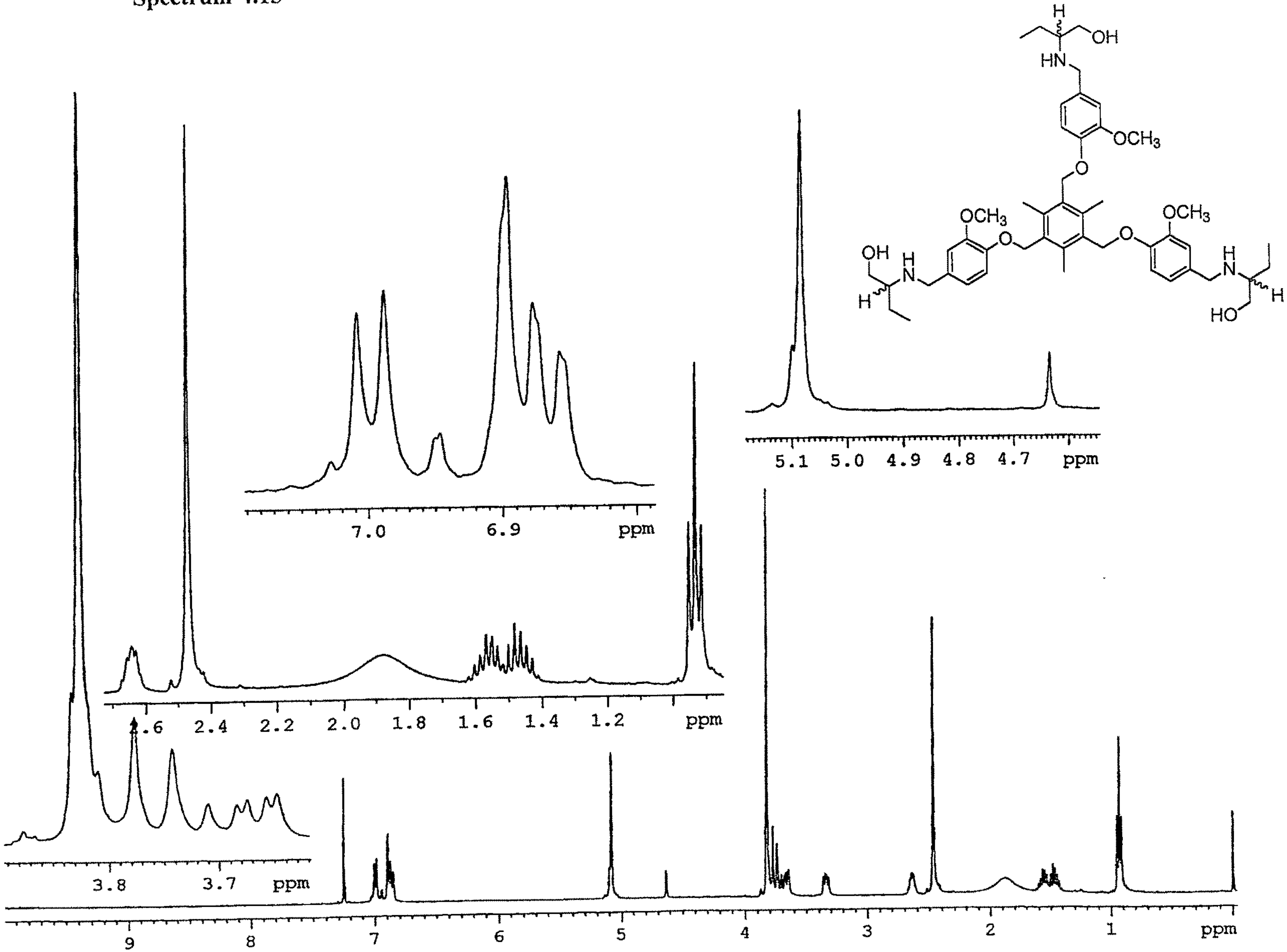


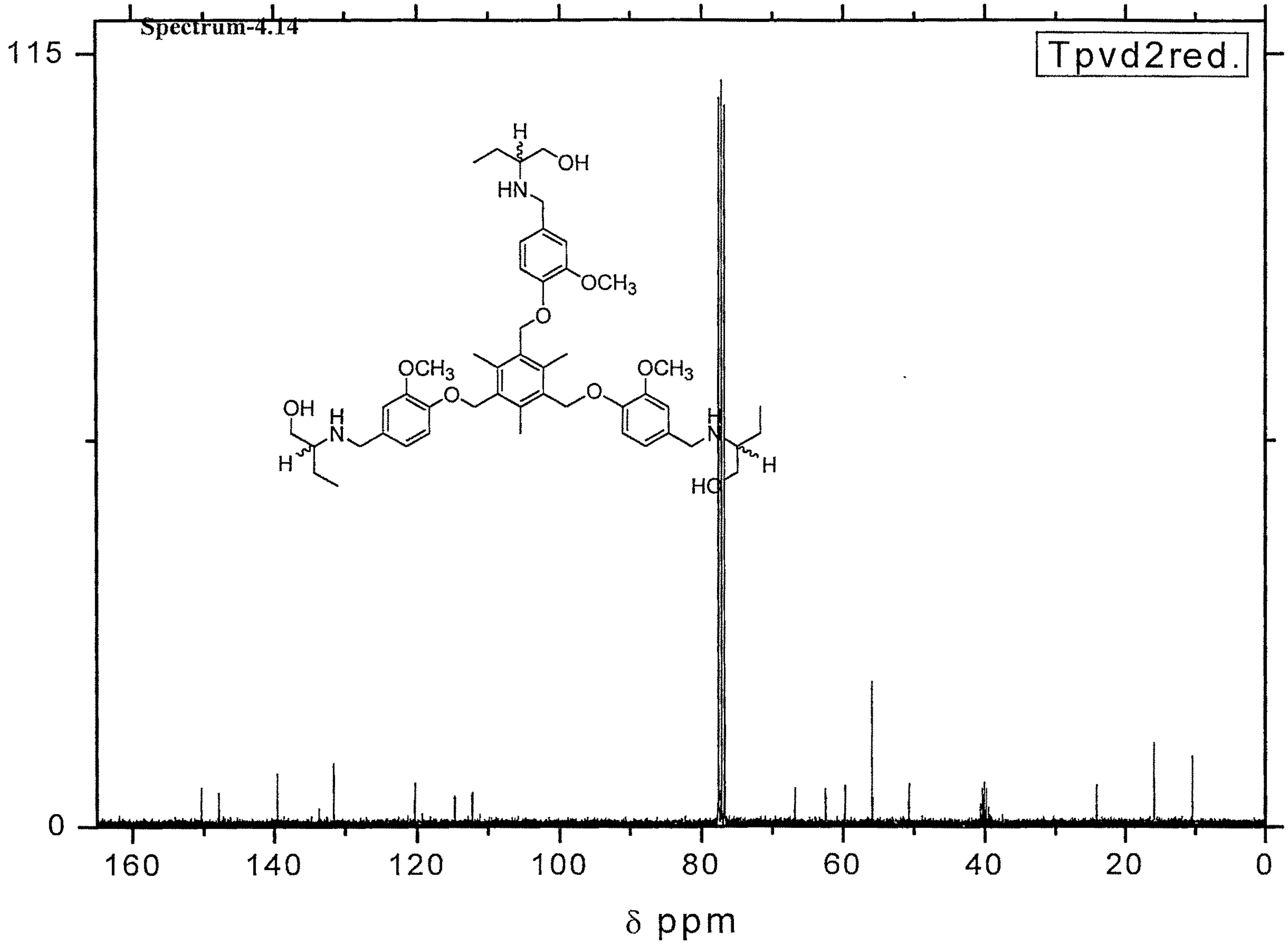
Spectrum-4.11

Spectrum-4.12

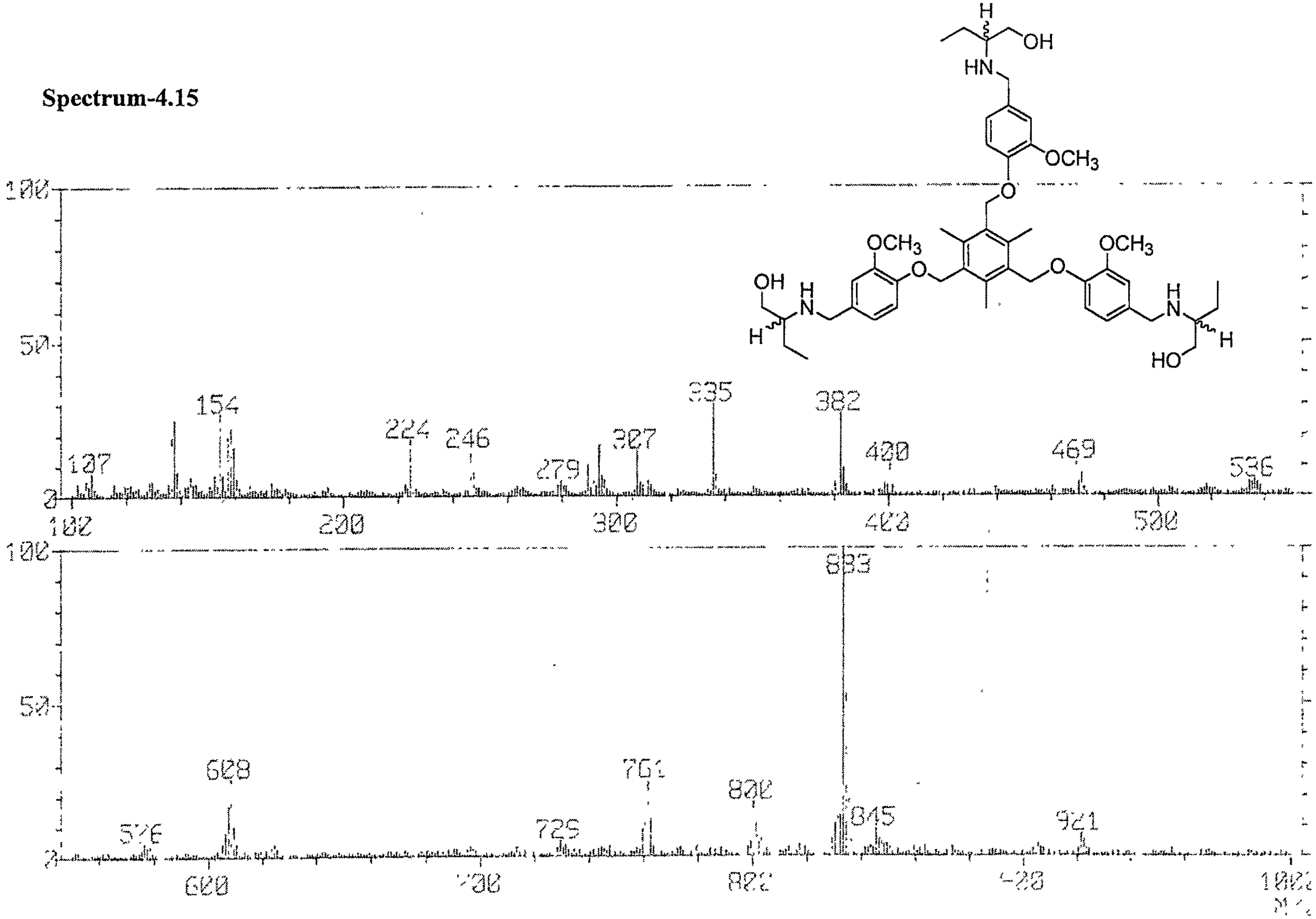


Spectrum-4.13



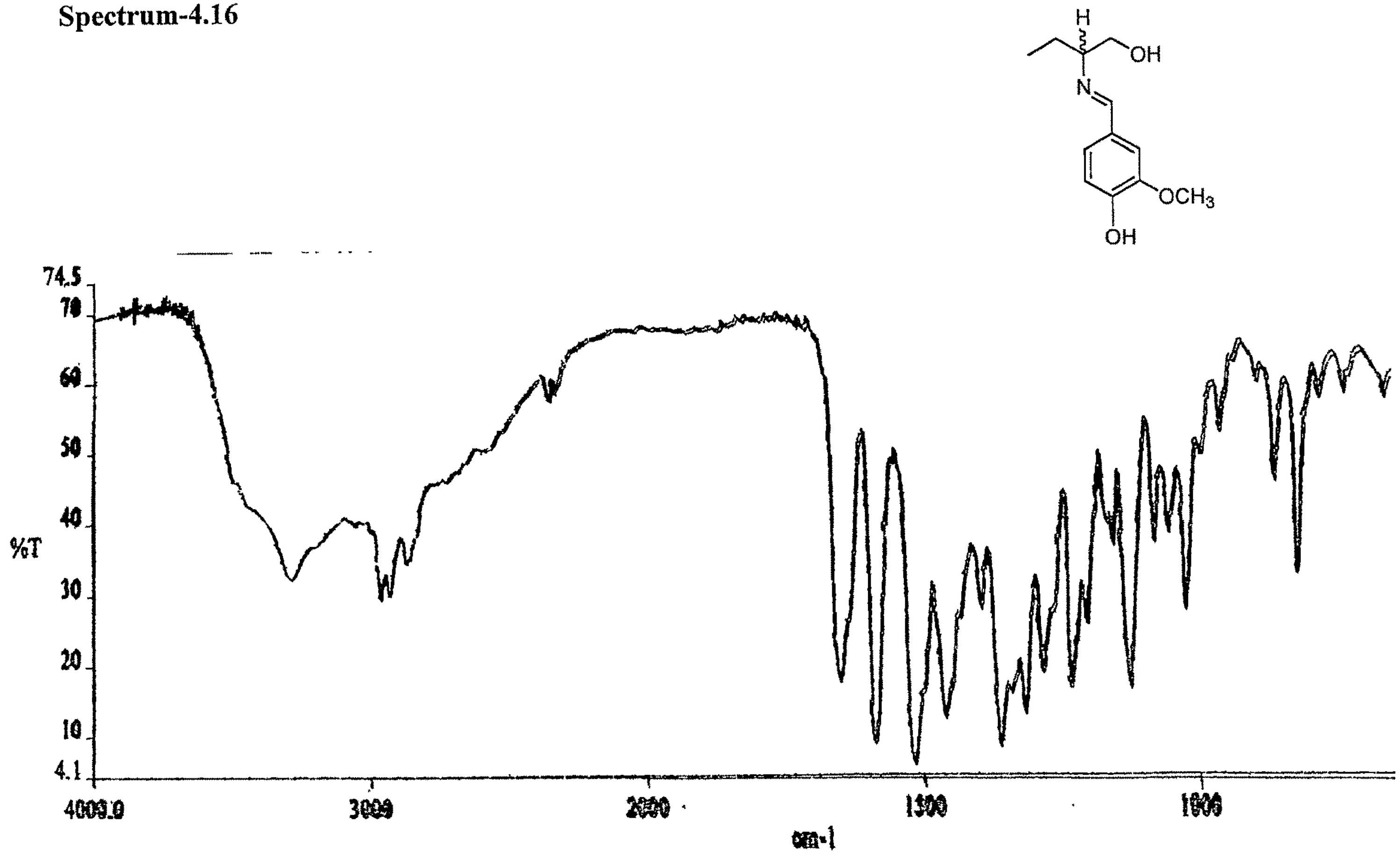

Spectrum-4.14

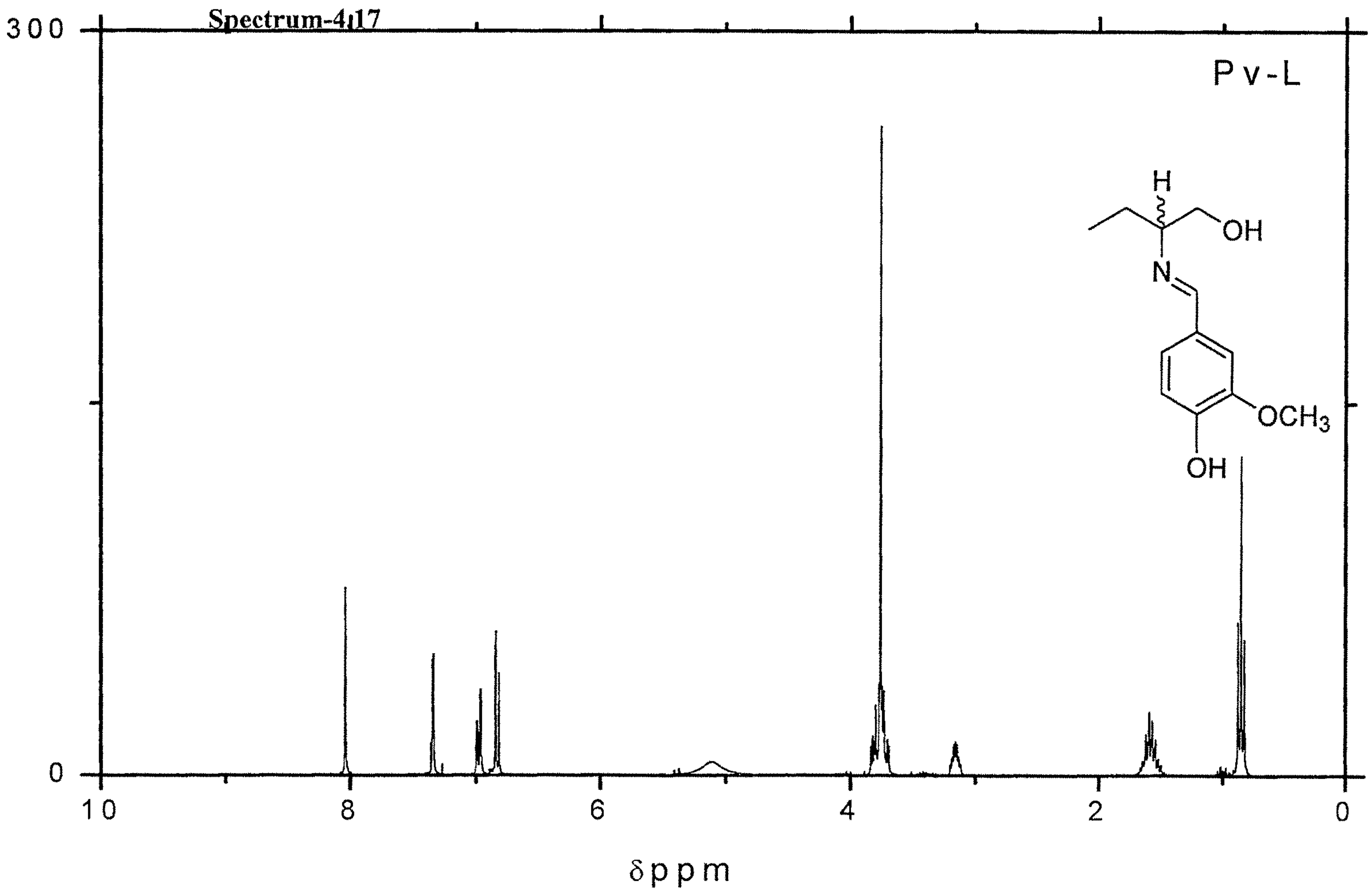
Spectrum-4.15



TpvDred

Spectrum-4.16




Spectrum-4.17
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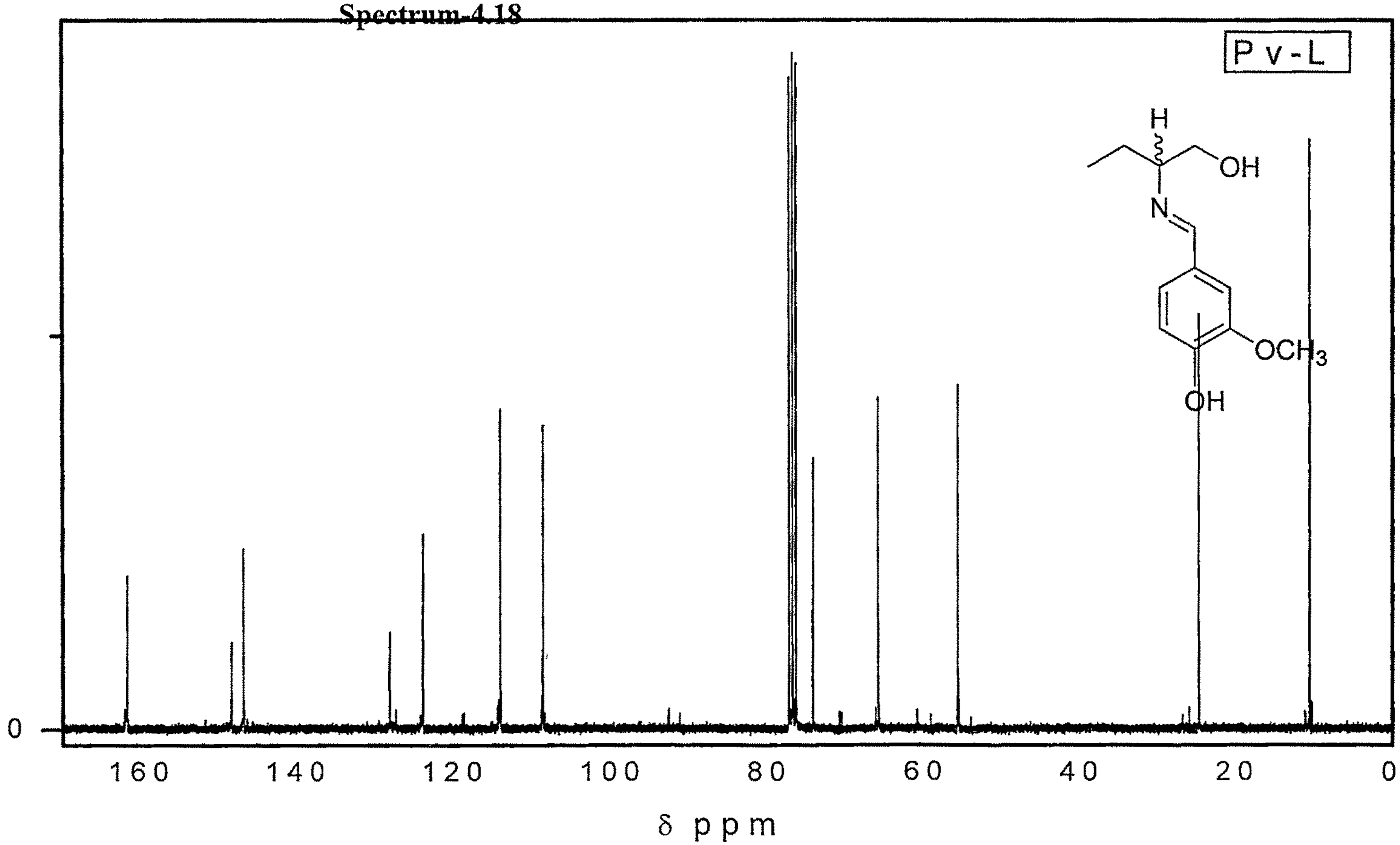
8
6
4
2
0
δppm

Spectrum-4.18



4.5 References

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