Synthysis, Characterization and Conformation of Some New Macromolecules Containing Nitrone Moieties

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Abstract

Macromolecules containing Nitrone moieties were prepared by oxidation of imines formed by the reaction of terephthaldehyde with diamine compounds using a mixture of hydrogen peroxide and glacial acetic acid. The Nitrone compounds were characterized by CHN analysis, Infra-red and mass spectrometry. Geometrical optimization and calculation of heat of formation for these compounds confirm that the structure of these compounds is of the E form.

Keywords : Macromolecules, Nitrones, Conformation

1.Introduction

Nitrone compounds are very important class of compounds due to their medicinal and pharmaceutical applications. They show antifungal [Thirumalaikumar et al.,1996; Matharu et al.,2006; Kumar et al.,2006; Makkar et al.,2009; Salman et al.,2013], antibacterial [Damodrian et al.,2009; Chakraborty et al.,2010], neuroprotective [Ley et al.,2005; Chioua et al.,2012] and anticancer [Floyd et al.,2011] activities.In addition, the nitrone compounds are widely used as antioxidant agents [Ameer et al., 2006; Al-Mowali et al.,2007; Al-Mowali et al.,2014] due to their ability to scavenge free radicals quite smoothly. As far as we know, most of Nitrone compounds prepared so far contain one nitrone moiety. The present paper reports synthesis and characterization of some novel macromolecules containing three Nitrone moieties in order to increase the compounds effectiveness as therpeutic agents**.**

2. Experimental

2.1 Materials

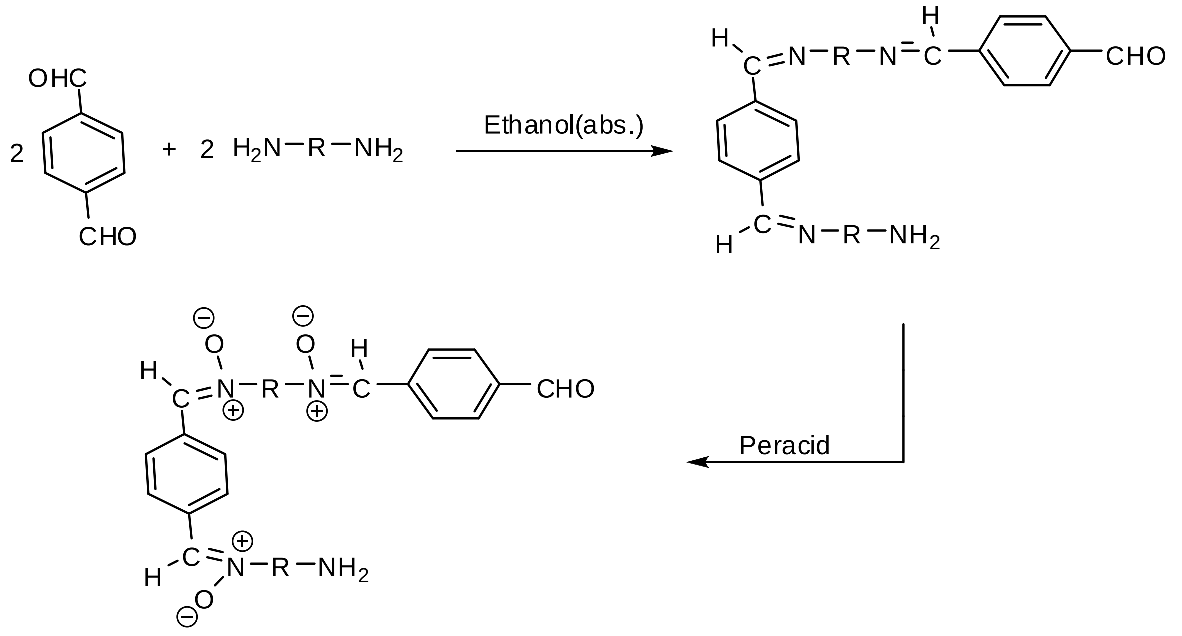
Terphthaldehyde, m-phenylenediamine, p-phenylenediamine, Benzilidene and Methylenedianiline were obtained from Aldrich. Hydrogen peroxide was obtained from G.C.C. .Potassium carbonate and dibromoethane were obtained from B.D.H. .Solvents were used after being purified according to the standard method.

2.2 Instruments

The elemental analysis was performed on Euro Vectro EA 3000 A. IR spectra was recorded on FT-IR (type Shimadzu model 4800s) as KBr disk in wave-number region 4000-400 Cm^{-1}. The mass spectra were recorded on QP 5050A Shimadzu type instrument.

2.3 Synthesis of macromolecule Nitrones

The Nitrone compounds were prepared from the oxidation of the appropriate Schiff bases with Hydrogen peroxide and glacial acetic acid. Schiff bases were prepared by addition drop by drop of 0.01 mole diamine compounds NH_2-R-NH_2 ,where R=1,4-Ph , Ph-Ph , Ph-CH_2-Ph and 1,3-Ph , in 100 ml of absolute ethanol to 0.01 mole of terphthaldehyde in 100 ml of absolute ethanol. The resulted solution was refluxed for about 20 hours and the solid product formed was filtered and washed several times with dry diethyl ether.0.004 mole of the prepared Schiff bases were added to 4.6 of 36% H_2O_2 and 10.2 ml of glacial acetic acid. The mixtuproduct was filtered and washed sere was stirred in ice bath for 6 hours and then left in refrigerator for 24 hours. The solid product was filtered and washed several times with absolute ethanol. Four Nitrone compounds we prepared in this way: N_1,redish brown, m.pt. d-136.8 c^{o}; N_2, greenish brown, m.pt. d- 159.4c^{o} ; N_3, brown, m.pt. d-169.7 c^{o} and N_4, black, m.pt. d-111.7 c^{o}



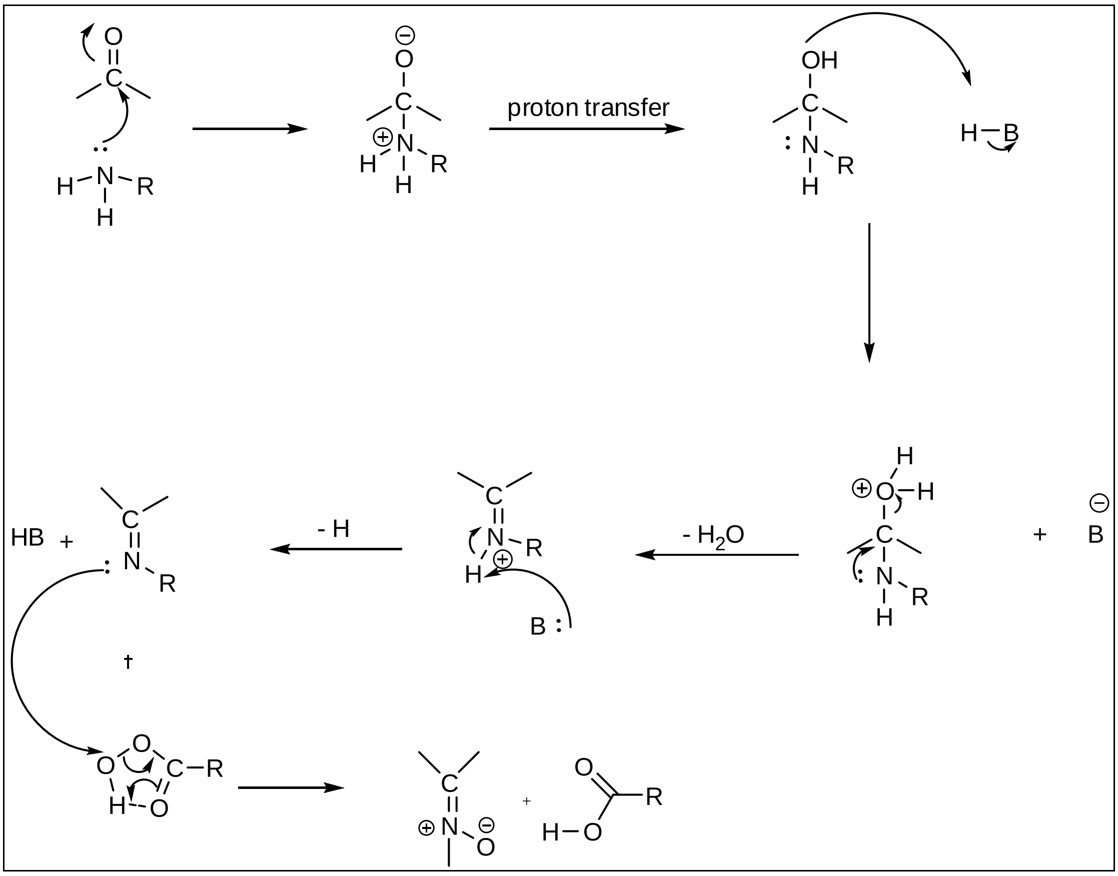
R= 1,4-Ph (N_1) ; Ph-Ph (N_2) ; Ph-CH_2-Ph (N_3) ; 1,3-Ph (N_4)

Scheme(1) Synthetic route for nitrone compounds

3.Results and discussion

3.1 Synthesis of Nitrone compounds

Synthesis of Nitrone compounds , as mentioned in experimental part , were carried out by two steps, the first is the formation of Schiff bases by reaction of 1mole of terphthaldehyde and 1mole of diamine. This reaction occurred by attacking the unpaired electron of nitrogen atom on carbon atom of carbonyl group with release of hydrogen molecule .The second step which produced Nitrone compounds involved the oxidation of amine by peracetic acid. This reaction was formed during attack of the unpaired electron of C=N¨ group on the oxygen of peracetic acid to form Nitrone compound.



Scheme(2): illustrates the mechanism of the formation of Nitrone compounds.

3.2 Elemental analysis

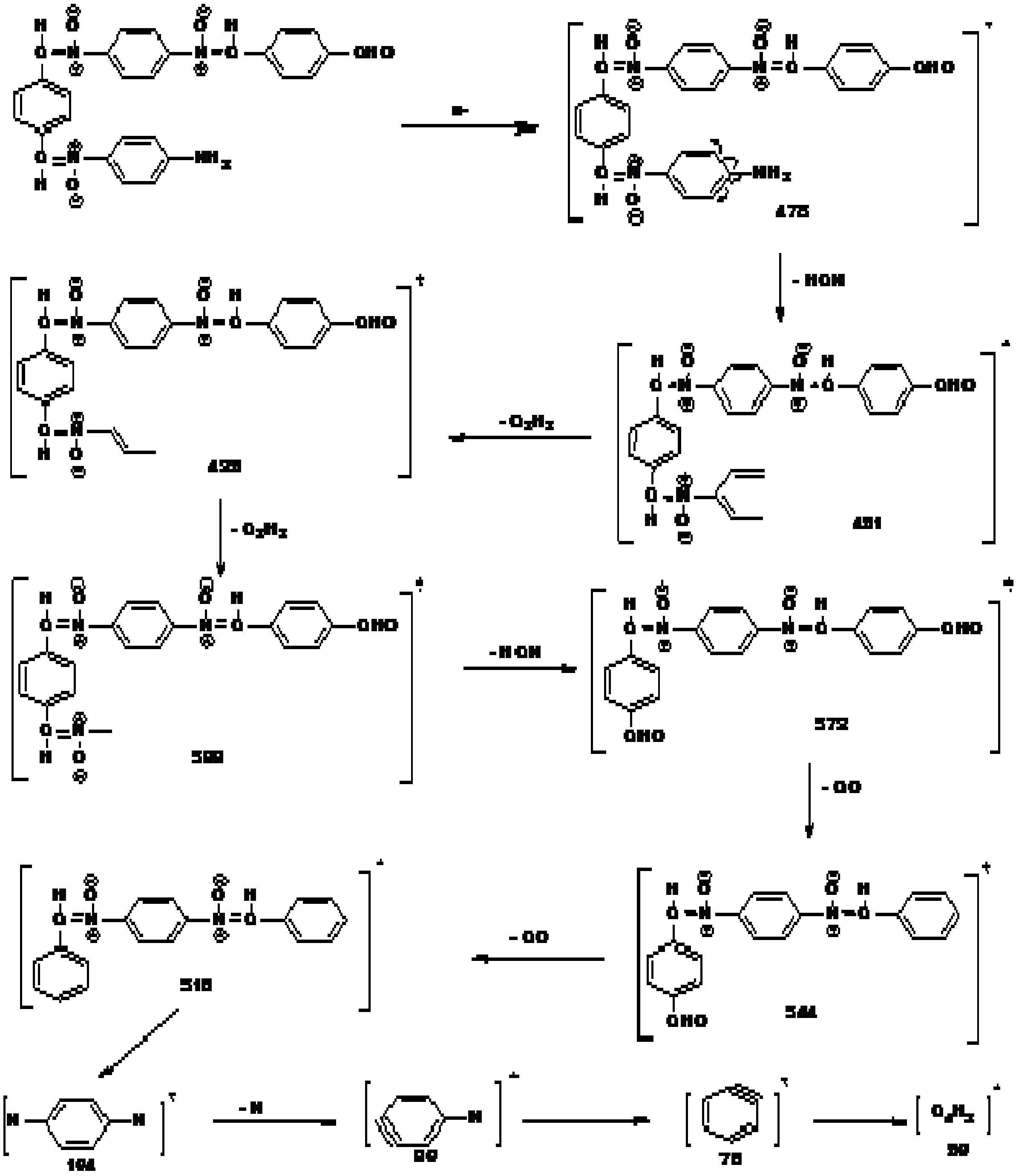
Elemental analysis of the prepared Nitrone compounds are summarized in Table (1). This table indicates that the percentges founded for CHN are in good agreement with the calculated values, which means that the reactions are successful.

3.3 Infra-red spectra

The infra-red spectra of Nitrone compounds N_1, N_2, are represent in Figures 1and 2. These figures show absorption bands in the range (1195-1207) Cm^{-1}which assigned to the stretching vibration of the bond N-O in the Nitrone group. The appearance of sharp absorption bands in the range (1616-1625) Cm^{-1} may be attributed to stretching vibration of C=N bond of Nitrone group which are quite different from the absorption of the corresponding C=N in prepared Schiff bases. In addition to the above mentioned groups, table (2) also summarized the stretching vibrations of C=C, C-H, NH_2, C-N and C=O groups.

3.3 Mass Spectra

Figure 3 shows the mass spectra of the nitrone compounds and table (3) summarized the essential fragments of the prepared nitrones. The mass spectra for all prepared compounds contain the molecular ion band (M^+) which confirm the accuracy of molecular formula for nitrones N_1-N_4. It is also observed that the compounds have the same fragments which indicate that all nitrone compounds suffered from the same symmetrical fragmentation as shown in scheme (3).



Scheme (3) Essential fragments of Nitrone compounds

3.4 Conformation analysis

Geometrical optimization of nitrone compounds was drawn by using PM3 method. Figures 4 and 5show the optimized structures for all nitrones N_1-N_4. From the geometrical optimization models of the nitrones, it was observed that all compounds have E confirmation. The semiemprical method was used to calculate the heat of formation of E and Z forms of all nitrones. The result of this calculation is represented in table (4). From the heat of formation values, it is obvious that the most stable confirmation is stand when the oxygen attached to nitrogen atom is trans to phenyl group, i.e E form.

4. Conclusion

It may be concluded that the macromolecules containing nitrones could be prepare by oxidation of macrocyclic schiff base with peracid under vigrous conditions.

References:

Thirumalaikumar M. ,Sivasubramanian S. , Ponnuswamy A. and Mohan P.(1996): Synthesis, reactions and antimicrobial studies of α –aryl-N-(nitrocarboxyl)Nitrones "Euro.J.Med.Chem." 31(11),905-908.

Matharu B.K., Sharma J.R. and Manro M.R.(2006): Synthesis and antifungal Potential of C-(4-fluorophenyl)- a–phenylnitrone and its N-phenyl derivatives "J.Ind.Council chem." 23(2),40-43.

Kumar K.R., Mallesha H. and Rangappa K.S.(2006): Isoxazolidines derived from 1,3-dipolar cycloaddition of Nitrones with olefines: studies of antibacterial and antifungal activities "Synthesis Communications" 33(9),1445-1555.

Makkar A., Sharma J.R. and Manro M.R.(2009): Synthesis and antifungal potential of C-(2-hydroxyphenyl-N-phenyl)-N-phenylnitrone and its N-phenyl derivatives "J. Ind. Council chem." 26(1),28-30.

Salman H.H. and N.N.Majeed(2013): Synthesis ,characterization and study of biological activity of some Nitrone and Isoxazolidin compounds "J. Basrah Research" 39(2),99-111.

Damodrian M., Sivakumar P.M.,Senthilkumar R., Muralidharan D., Kumar B. and Perumal P.(2009): Antibacterial activity of Isoxazolidine derivatives of Nitrone with olefine"Chemical Biology and Drug design" 74(5),495-506.

Chakraborty B., Schhetric M., Kafly S. and Samanta A.(2010): Synthesis and antibacterial activities of some novel Isoxazolidine derivatives derived from N-phenyl-a-chloronitrone in water"Indian Journal of Chemistry" 4913,209-215.

Ley J.J., Nigdorchik A., Belayev L., Zhao W., Busto K., Khoutorova L., Becker D.A. and Ginsberg M.D. (2005): Stillbazulenyl Nitrone, a second generation azulenyl Nitrone antioxidant, neurobehaviour, histopathology, and pharmacokinetics "J.pharmacology and Experimental Therapeutics" 313(3),1090-1100.

Chioua M., Sucunza D., Soriano E., Litina D.H., Alcazar A., Ayuso I., Gasque M.J., Gonzaiez P., Monjas L., Isabel M., Contelles J., and Samadi A. (2012):a-aryl-N-alkylnitrone, as potential agents for stroke treatment: Synthesis, antioxidant, neuroprotective and brain-blood barrier permeability properties "J. Med. Chem." 55(1),153-168.

Floyd R.A., Chandru H.K., Hc T. and Tower R. (2011): Anti-cancer activity of Nitrones and observations on Mechanism of Action "Anticancer Agents Med. Chem." 11(4),373-379.

Ameer Z.A., Aldain N.L., Majeed N.N. and Al-Mowali A.H. (2006): Synthesis and characterization of some new heteroaldonitrones"Basrah J. Science" 24(1),129-143.

Al-Mowali A.H., Majeed N.N. and Moussa H.K. (2007): Antioxidant properties of some new a-(p-alkoxyphenyl)-N-phenylnitrones "Iraqi J. Polymer" 11(2),1-22.

Al-Mowali A.H., Majeed N.N. and Abbas A.F. (2014): Antioxidant activity of some dibenzylidine diamine-18-crown-6 materials"Re. J. Pharm. Bio.Chem." 5(3),2119-2123.

Table (1):Elemental analysis of nitrone compounds

Comp.	**Calculated**			**Observed**		
	%C	**%H**	**%N**	**%C**	**%H**	**%N**
N_1	70.29	4.60	11.71	70.27	4.63	11.71
N_2	76.19	4.76	8.88	76.17	4.79	8.88
N_3	76.59	5.16	8.51	76.58	5.20	8.51
N_4	70.29	4.60	11.71	70.27	4.63	11.71

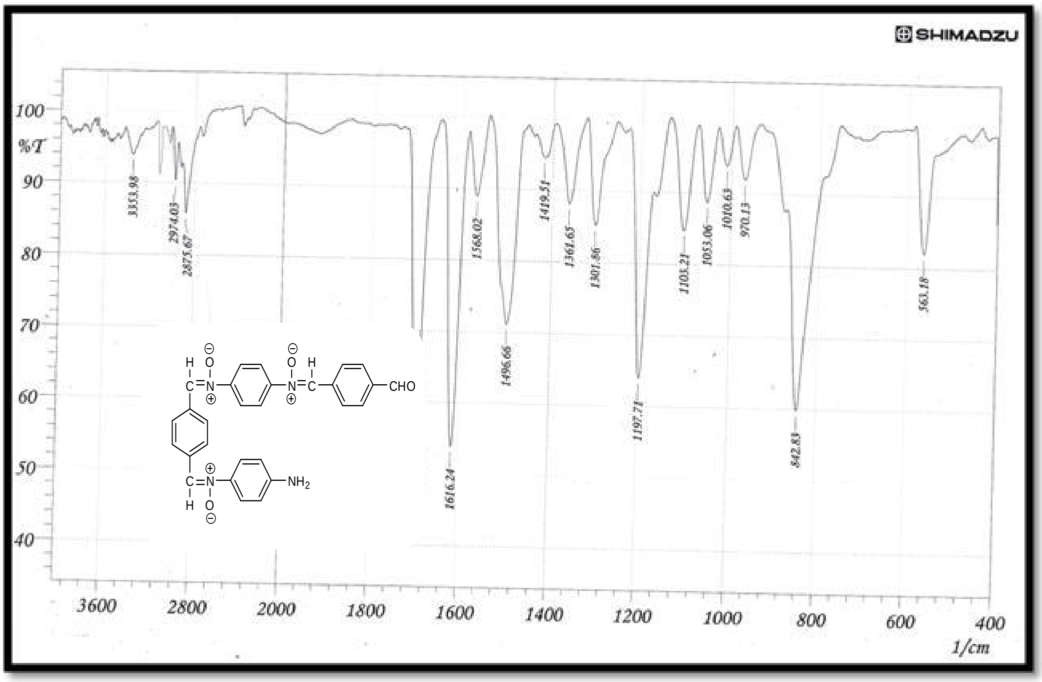


Figure (1) : FT-IR spectrum of nitrone compound (N_1)

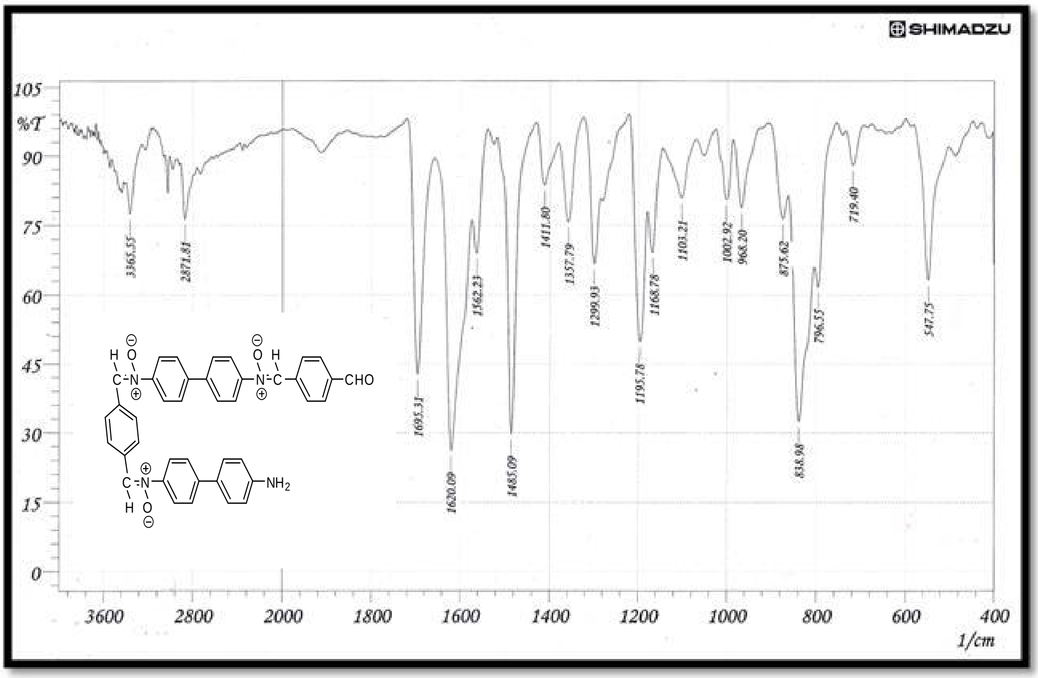


Figure (2) : FT-IR spectrum of nitrone compound (N_2)

Table (2) : Data of the FT-IR spectra of Nitrone compounds

Comp.	**C=N Str.**	**C-N Str.**	**N-O Str.**	**C=C Ar. Str.**	**C-H Ar. Str.**	**NH_2 Str.**	**NH_2 Ben.**	**C=O Str.**
N_1	1616 s	1361 w	1197 m	1496 m	3060 w	3353 w	1568 w	1697 s
N_2	1620 s	1357 w	1195 m	1485 s	3070 w	3365 w	1562 w	1695 s
N_3	1614 s	1359 w	1191 m	1558 w	3098 w	3370 w	1581 w	1693 m
N_4	1625 m	1379 w	1207 m	1496 m	3058 w	3359 s	1606 s	1697 s

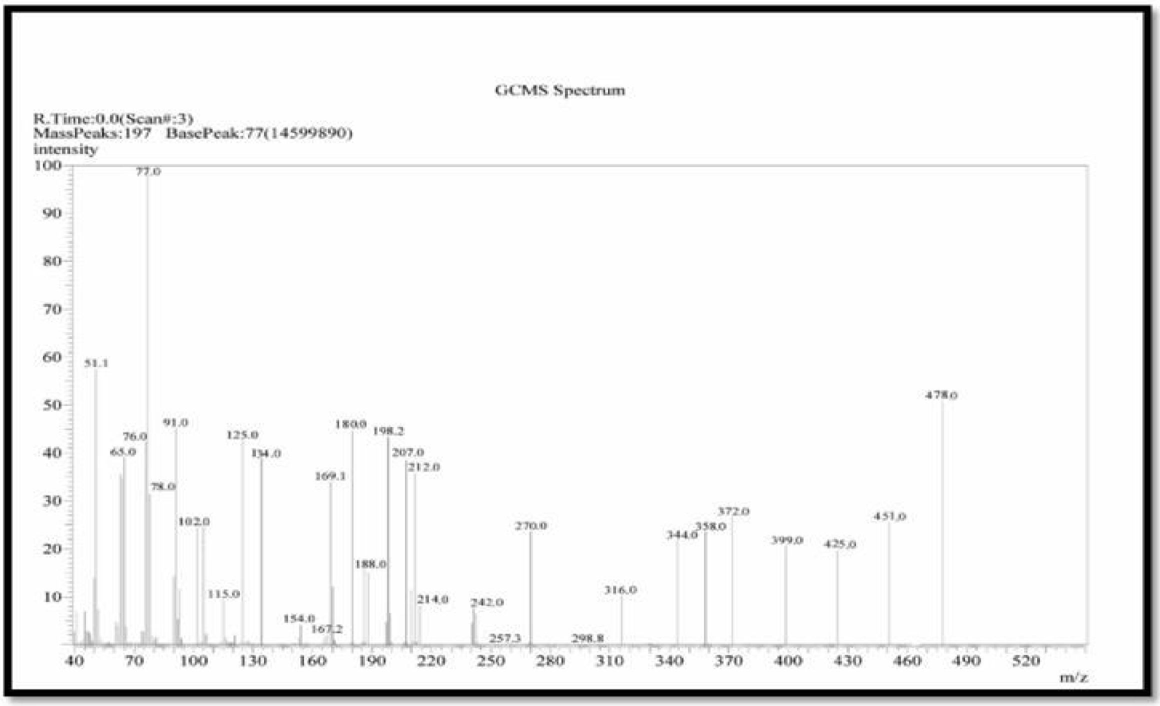


Figure (3) : GC-Mass spectrum of nitrone compound (N_1)

Table (3) : The major fragment ions of macromolecules nitrone compounds

Comp.	**Heat of formation**	
	E	**Z**
N_1	- 62.8965492	124.6730784
N_2	156.6986401	171.6919877
N_6	31.6647488	249.6098012
N_7	46.7608412	209.8520476

Table (4): Heat of formation of macromolecules nitrone compounds

Comp.	**m/z**												
	M^+	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
N_1	478	451	425	399	372	344	316	104	90	76	50		
N_2	630	603	577	537	447	419	391	106	77	51			
N_4	658	631	605	579	566	475	446	340	250	221	130	77	50

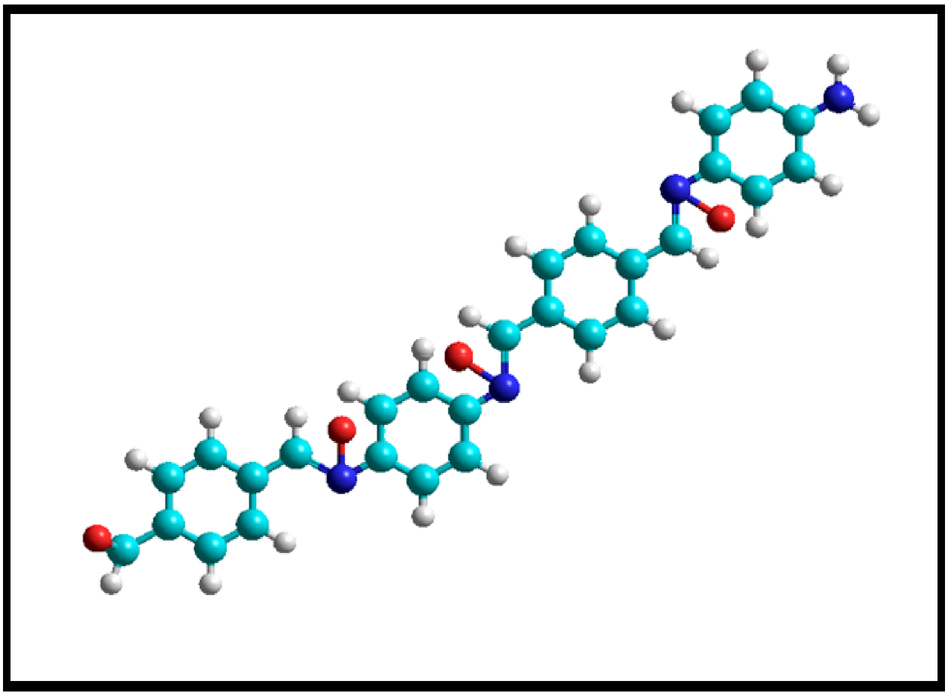


Figure (4) : Balls and cylinders model of *E*-nitrone compound (N_1)

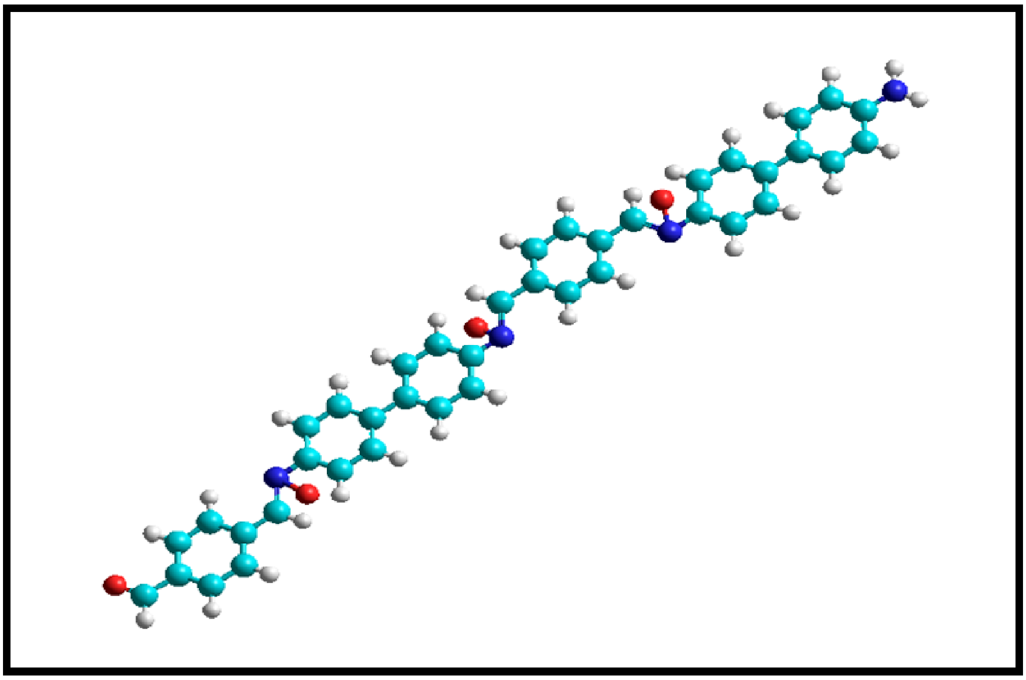


Figure (5) : Balls and cylinders model of *E*-nitrone compound (N_2)