CHAPTER - III

N-cyclohexyl methylene nitrone was prepared by the action of dry formaldehyde gas on a methanolic solution of N-cyclohexyl hydroxylamine. The dry formaldehyde gas had been prepared by heating paraformaldehyde at 140°C and was swept by a flow of nitrogen into the reaction vessel. Dry formaldehyde gas was used so that the work-out of the nitrone could be accomplished under mild condition. In scrupulous workout the monomeric nitrone was separated as a white solid (m.p. 70°C). It was found to be hygroscopic and, therefore, was crystallized from dry hexane. In dry and pure condition it could be preserved in a fridge for a week. UV absorption maxima [Fig. (UV-VIS)-1] of the nitrone in methanol is at the wave-length 233 nm (ϵ = 6730). The absorptions at 1565 cm^{-1} and 1290 cm^{-1} in IR [Fig. (IR)-1] are due to the C-N and N-O stretching modes of the nitrone. The mass and ^{1}H-NMR data are also in conformity with the proposed structure.

The nitrone on refluxing with triphenyl phosphine in dry benzene remained unchanged. This indicates that unlike the aromatic N-oxides the negative charge is not much localized on the oxygen atom of the nitrone.

Whenever during the workout of the nitrone the reaction mixture was heated to remove the solvent methanol the nitrone was found to have changed to a number of different products. Among them a white

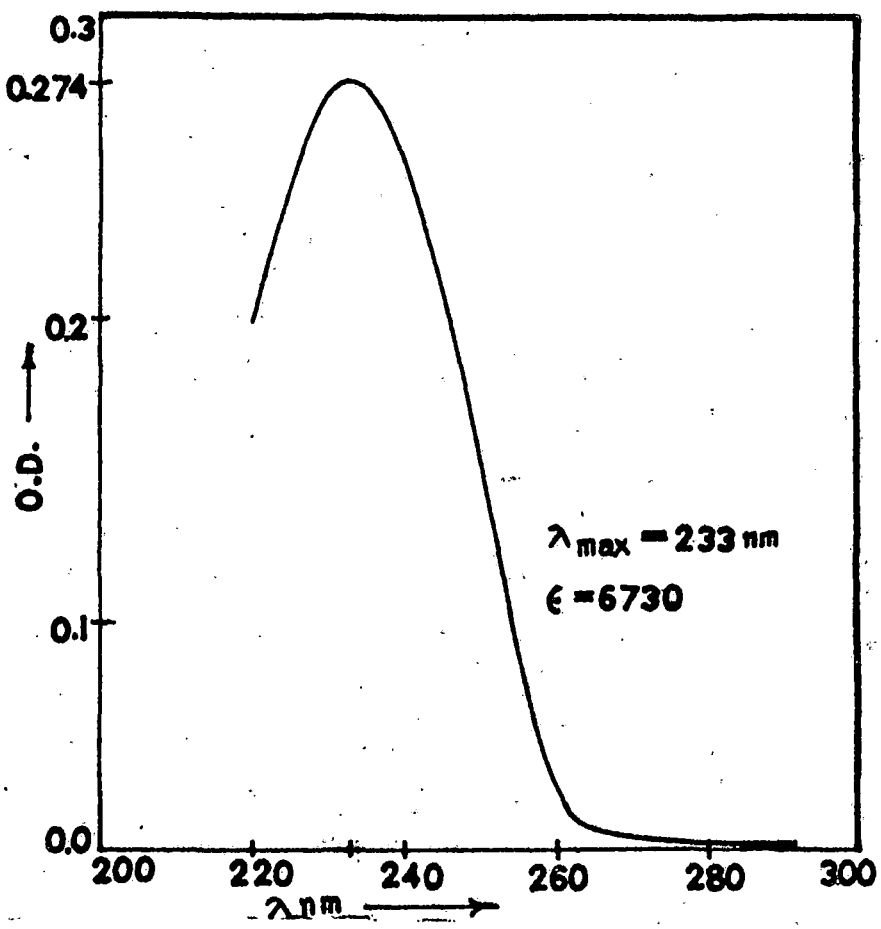
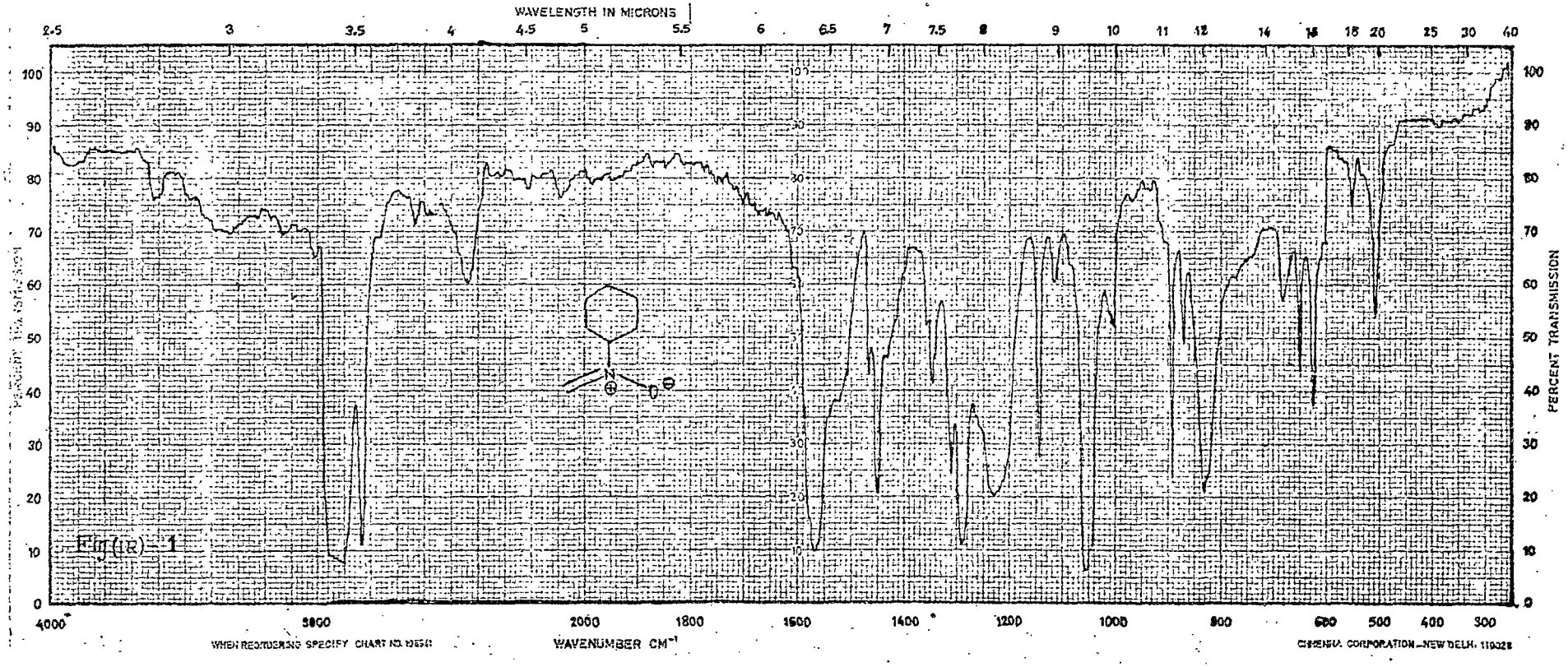


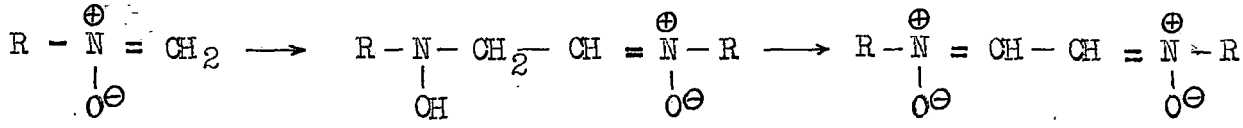
FIG. (UV-VIS) - 1. UV SPECTRUM OF N-CYCLOHEXYL METHYLENE NITRONE IN METHANOL SOLUTION.


WAVELENGTH IN MICRONS
2.5 3 3.5 4 4.5 5 5.5 6 6.5 7 7.5 8 9 10 11 12 14 15 16 20 25 30 40
100 90 80 70 60 50 40 30 20 10 0
PERCENT TRANSMISSION
4000 3600 2000 1800 1600 1400 1200 1000 800 600 500 400 300
WAVENUMBER CM⁻¹
WHEN REORDERING SPECIFY CHART NO. 10541
CESENIA CORPORATION—NEW DELHI, 110028

Fig(12) - 1

solid (m.p. 145°C) was isolated. The IR, Mass and ^{1}H-NMR spectra and elemental analyses data confirm the compound to be a dinitrone (2). In ^{1}H-NMR spectrum the olefinic proton signals are observable at δ = 7.1 ppm; the higher δ ppm range (6.35 ppm for the nitrone) is due to the effects of conjugation. The $-\overset{+}{N}(O^-)=CH-$ proton signal is at δ = 3.6 ppm and the other cyclohexyl methylene protons absorb at δ = 0.9-2.0 ppm. The characteristic IR absorptions are at 1625 cm^{-1} 1590 cm^{-1} and 1530 cm^{-1} for the different modes of stretching of the $-\overset{+}{N}=\overset{}{C}-$ bond. The mass spectrum is shown in Fig. (MASS)-1.

Utzinger et al[7] have described the dimerization in the case of N-phenyl methylene nitrone as a process of intermolecular 1,3-addition followed by the loss of hydrogen (Scheme - I).



1 2

Scheme - I

The intermediate (1) is isolated in trace amount. The IR and ^{1}H-NMR of (1) are reproduced respectively in Fig. (IR)-2 and Fig. (NMR)-1. The elemental analyses data are also in conformity with the structure.

Cycloadditions of the nitrone were studied with a wide variety of olefins and a few acetylenes. The nitrone reacted smoothly with the

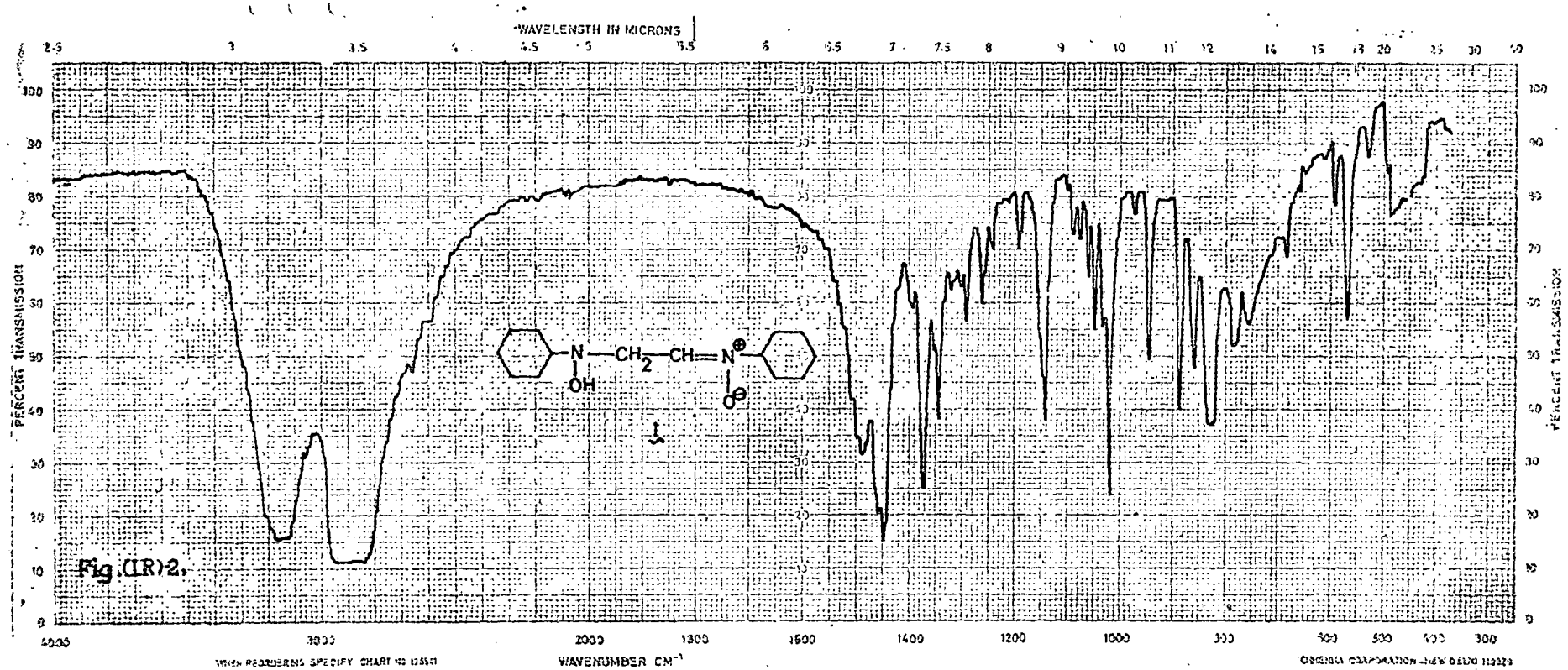
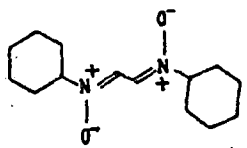
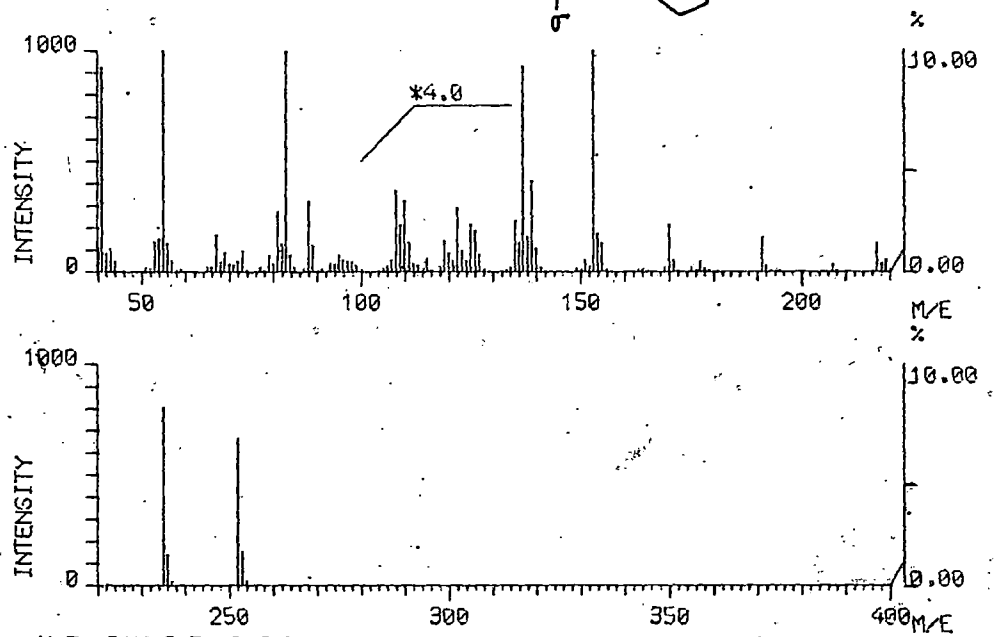

WAVELENGTH IN MICRONS
PERCENT TRANSMISSION
WAVENUMBER CM⁻¹
OH
CH2
CH
N

Fig (IR)-2.

FIG. (MASS) - 1.

MASS SPECTRUM : (5 TO 6)
SAMPLE:DR.A.K.NANDA,DARJILING
NOTE :17/6/83/ N-3
BASE PEAK : M/E 83.0 INT. 695.3





M/E	RAW INT.	R.INT.	SIGMA(%)	
151.0	10.5	15.1	1.30	
152.0	5.6	8.1	0.69	
153.0	271.4	390.4	33.55	
154.0	30.9	44.4	3.82	
155.0	23.3	33.6	2.88	
169.0	5.6	8.1	0.70	
170.0	38.3	55.1	4.74	
171.0	10.3	14.8	1.27	
175.0	5.5	7.9	0.68	
177.0	9.7	13.9	1.19	
191.0	28.6	41.2	3.54	
192.0	6.1	8.7	0.75	
207.0	7.6	11.0	0.95	
217.0	25.5	36.7	3.15	
218.0	8.3	11.9	1.02	
219.0	10.9	15.7	1.35	
235.0	142.0	204.2	17.55	
236.0	24.6	35.4	3.04	
252.0	116.1	167.0	14.36	
253.0	27.3	39.3	3.37	END

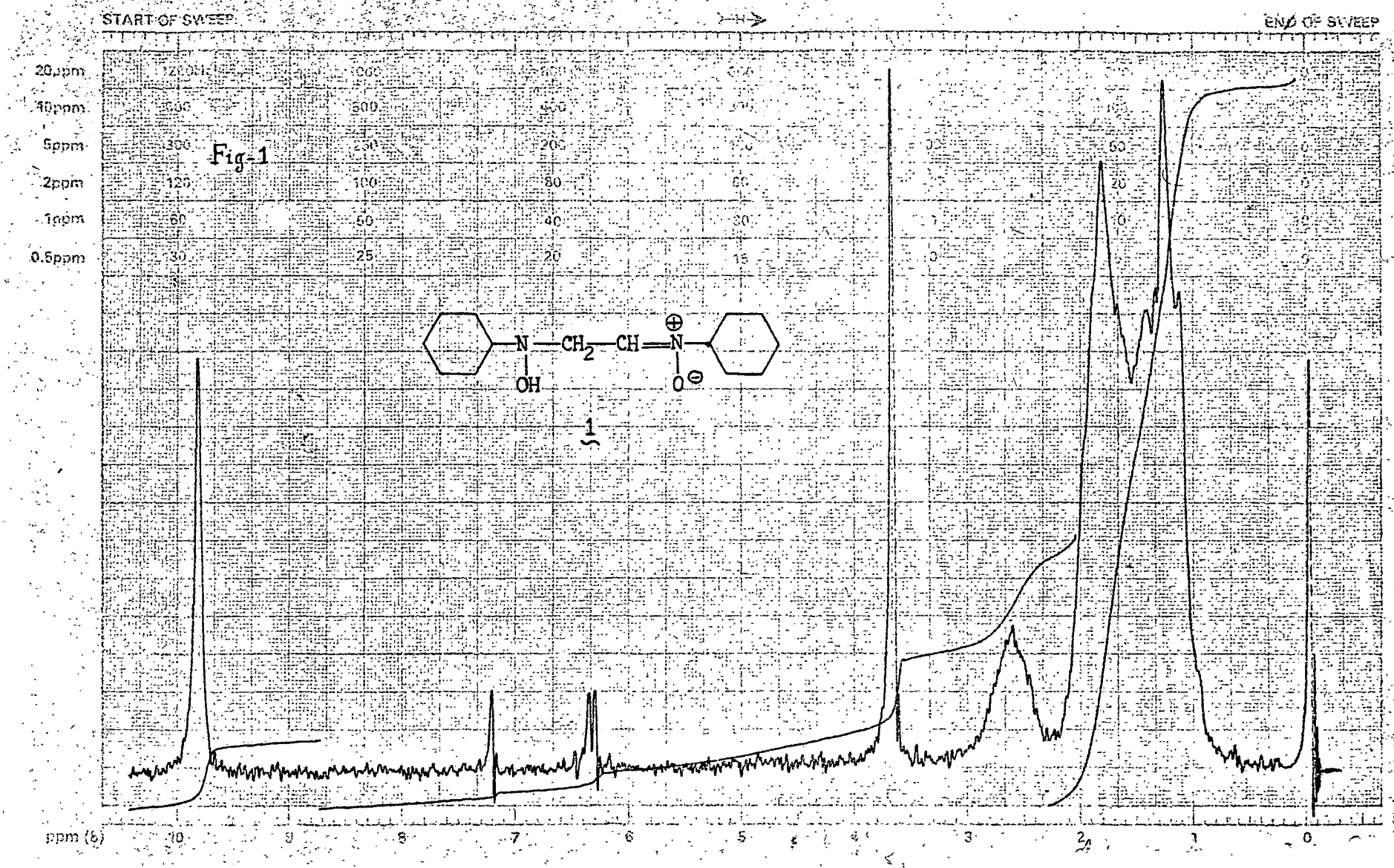
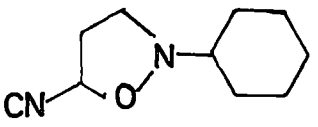

START OF SWEEP
END OF SWEEP
20ppm
10ppm
5ppm
2ppm
1ppm
0.5ppm
ppm (δ)
10
9
8
7
6
5
4
3
2
1
0
OH
O⊖

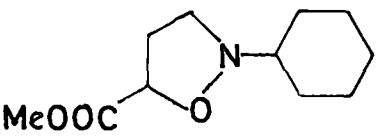
Fig-1

1

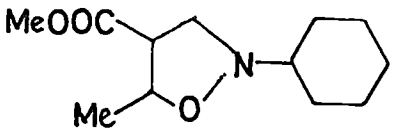
moderately electron deficient olefins at room temperature. Acrylonitrile and methyl acrylate gave exclusively 5-substituted 1,2-isoxazolidines (A and B, Fig. I). Methyl cinnamate and coumarin both gave 4- and 5-substituted products with the 4-substituted products predominating (E and G, Fig. I). In Table - I the reaction conditions, major products etc. are summarized.



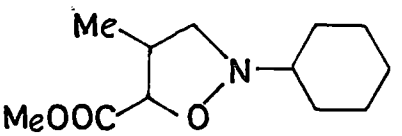
A



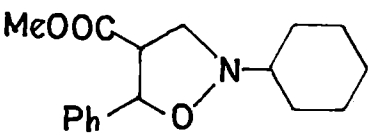
B



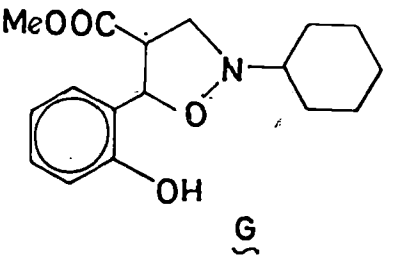
C



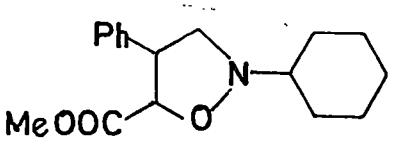
D



E



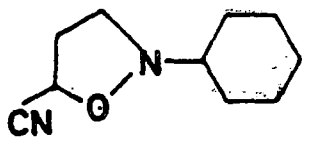
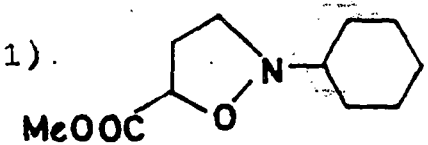
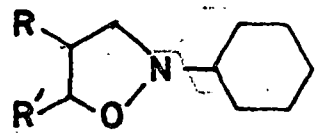
G



F

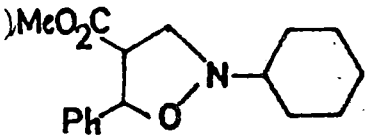
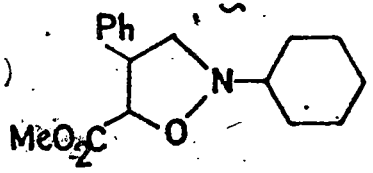
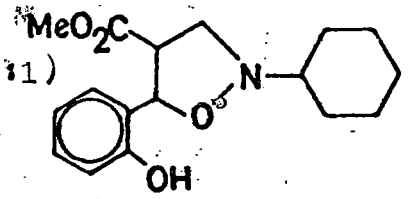
FIG-I

Table - I

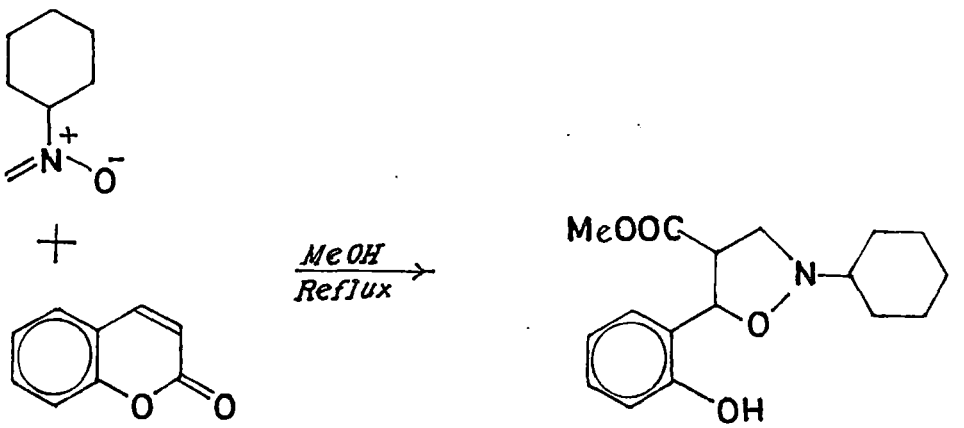
Dipolarophile	Solvent/Reaction condition	Nature of product	R_f (Benzene:Ethyl acetate)	Major product
Acrylonitrile	Acrylonitrile r.t. 24 hrs	Yellow liquid; 140°C (5 mm of Hg)	0.44 (2:1)	 A
Methyl acrylate	CH_2Cl_2, r.t.; 24 hrs	Colourless liquid; 140°C (5 mm of Hg)	0.35 (5:1)	 B
Methyl crotonate	CH_2Cl_2; r.t. 24 hrs	Colourless liquid	0.32 and 0.48 (5:1)	 R′ COOMe / Me C R Me/COOMe D

Contd...

TABLE -I. Contd.

Dipolarophile	Solvent/Reaction condition	Nature of product	R_f (Benzene:Ethyl acetate)	Major product
Methyl cinnamate	Methanol; r.t.; 2 days	Colourless viscous liquid	0.54(5:1)	 E
Methyl cinnamate	Methanol; reflux; 4 hrs.	Colourless viscous liquid	0.90(5:1)	 F
Coumarin	Methanol; Reflux 12 hrs	Yellow viscous liquid	0.74 (5:1)	 G
Coumarin	Methanol/r.t 2 days	———	———	———

Reaction of coumarin did not proceed at room temperature. In methanolic solution it reacted with the nitrone under reflux, and during the addition methanol also had reacted with coumarin and ultimately the adduct (G) was obtained (Scheme - II)



G

Scheme - II

The low reactivity of coumarin may be due to its cis geometry. Again during the isolation of the adduct (G) in column chromatography a pink coloured substance was separated in low yield which on standing lost its colour and TLC of the pink substance indicated that it gradually transformed into the product (G). Only the visible spectrum (λ_{max} = 480 nm, Fig. (UV-VIS)-2 of the coloured substance was taken. Due to its poor yield and instability no other characterizations were possible. It can be expected to be the charge transfer intermediate in the reaction. Such charge transfer intermediates were also observed during the additions of the nitrone with tetracyano ethylene and p-benzo quinone.

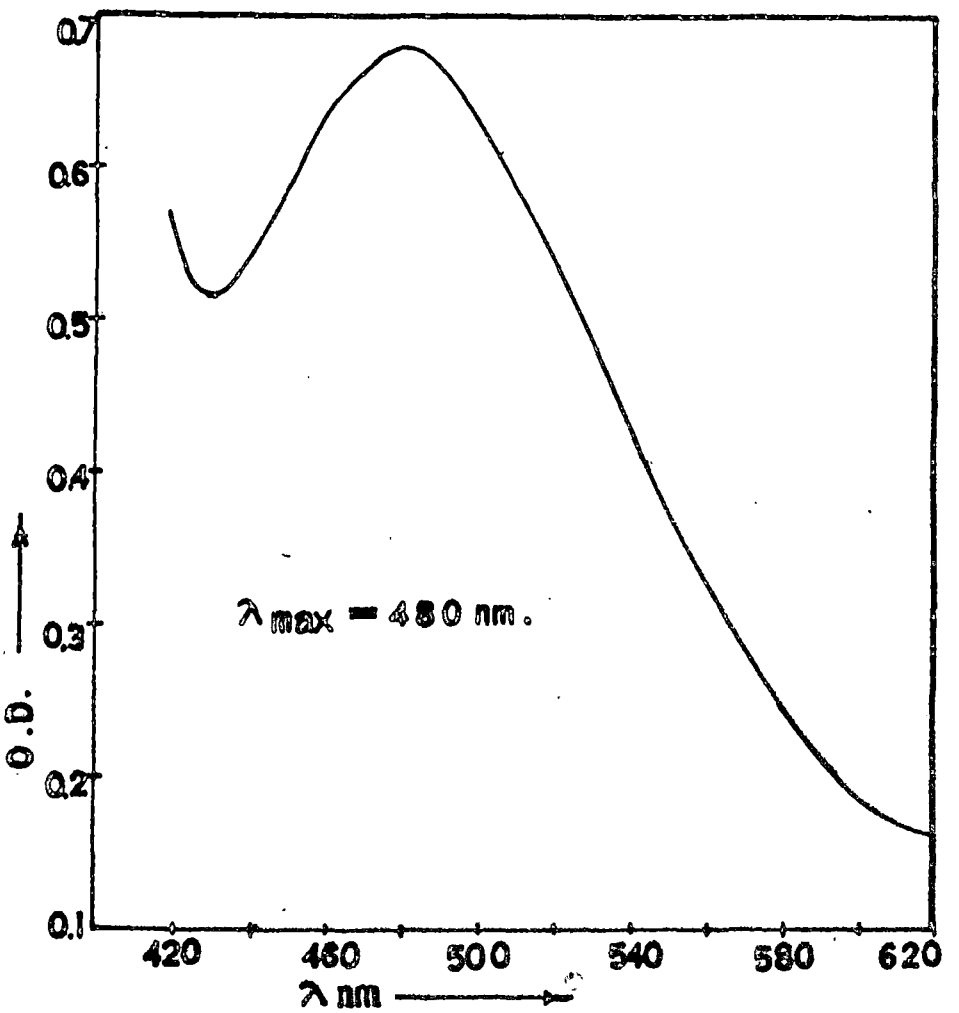
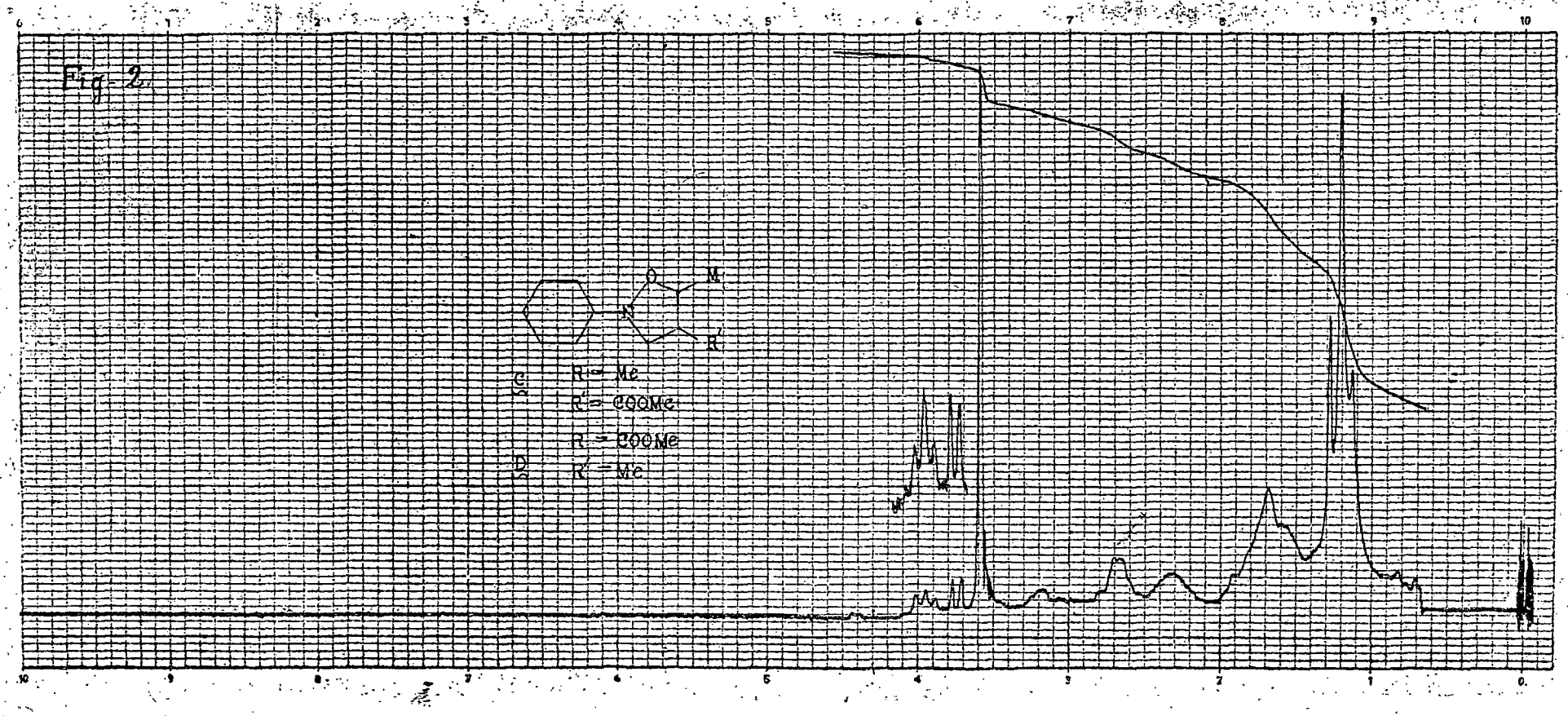


FIG. (UV-VIS) - 2. VISIBLE SPECTRUM IN METHANOL SOLUTION OF THE PINK INTERMEDIATE ISOLATED DURING THE REACTION OF COUMARIN WITH N-CYCLOHEXYL METHYLENE NITRONE.

In all cases number of products formed were examined on the basis of TLC and the major product was isolated in each case. However, for the addition of the nitrone with methyl crotonate the polarity of both the products (C and D, Fig. I) were so close that the separation was not possible. Both the adducts were isolated together from the reaction mixture by distillation and the product ratio was counted from the ^{1}H-NMR integration curve of the mixture for the respective C-5 protons of the compounds C and D. The doublet at δ= 3.75 ppm with J = 5.2 Hz and the triplet at δ= 3.95 ppm with J = 6 Hz [Fig. (NMR)-2] are assumed to be due to the C-5 protons for the compounds D and C respectively. Since in both D and C there is a single C-5 proton, the ratio (1:3) for the respective integration curve is the ratio of the two regioisomers in the mixture.

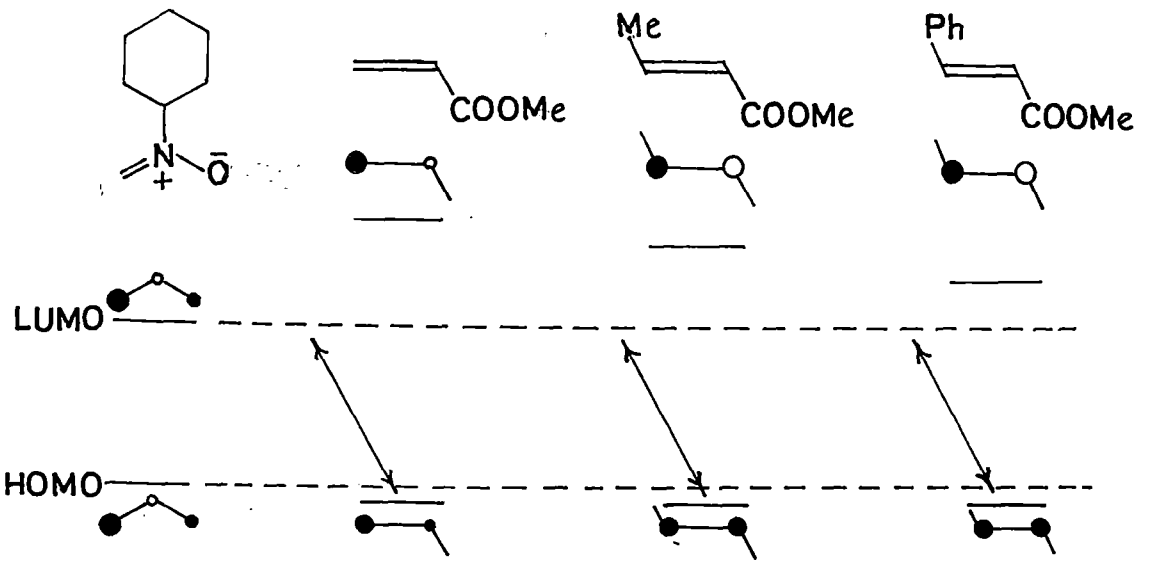
The mode of regioselections in the above cases can be well explained on the basis of qualitative frontier orbital model treatment of nitrone and the dipolarophiles. In qualitative treatment for 1,3-dipolar cycloadditions two major aspects are stressed, one is the energy levels of the dipoles and the dipolarophiles and the other is the HOMO and LUMO coefficients on the concerning atoms of the dipoles and the dipolarophiles. The HOMO-LUMO energy gap of the reactants indicates the fastness of the addition. This gap is low for the additions of the nitrone with the moderately electron deficient dipolarophiles and therefore the reactions are comparatively fast. The general principles for the regioselections for such additions

Fig. 2.


O
N
R'
R = Me
R' = COOMe
R = COOMe
R' = Me
CDCl3
0 1 2 3 4 5 6 7 8 9 10
10 9 8 7 6 5 4 3 2 1 0

has been discussed in the review part (Art. 1.6). The conugating substituents destabilise the ethylene HOMO orbitals to a greater extent than they stabilize the LUMO orbitals and 1,3-dipolar cycloadditions of nitrones are in borderline between pure HOMO and pure LUMO interactions with a little skew towards the dipole LUMO interactions. Again, the effect of the conjugating substituents in the case of the moderately electron deficient dipolarophiles further aggravate the skewness and the nitrone LUMO interactions have much choice of regioselections. As a result of these reasons, the favoured regioisomers for the nitrone additions with the mono-substituted moderately electron deficient dipolarophiles will be the 5-substituted 1,2-isoxazolidines (A and B, Fig. - I).

Now if we consider the substituent effect for the vicinal disubstituted dipolarophiles e.g. in the case of methyl cinnamate[172], the larger HOMO coefficient will be at the carbon atom attached to the ester substituent but the LUMO coefficients are about the same on both the olefinic carbon atoms. Therefore, assuming the nitrone-LUMO and the methylcinnamate-HOMO interaction is preferred, the 4-carbomethoxy substituted regioisomer will be the predominating one (Scheme - III). Actually we got such products E and G in the additions of the nitrone with methyl cinnamate and coumarin [GLC's Fig. (GLC)-6 and Fig. (GLC)-37]. Such substituent effect is also present during the addition of methyl crotonate and the mixture of C and D in 3:1 ratio was formed.



Scheme - III

Moreover, the question of regioselection is only applicable for the cases where the kinetically controlled products are considered. The thermodynamic product may be the next product as expected from the regioselection rule[93]. Such a case was observed during the addition of the nitrone with methylcinnamate. At room temperature the addition of the nitrone with the ester afforded the 4-carbomethoxy substituted product (E) in excess over the other isomer, but when the reaction was carried out under reflux the product F predominated. The C-4 and C-5 proton signals at ^{1}H-NMR for the products E and F are respectively at δ= 5.15 ppm, multiplet and δ= 2.5 ppm, multiplet and at δ= 4.5 ppm, doublet (J = 8 Hz) and δ= 4.4 ppm, doublet (J = 8 Hz).

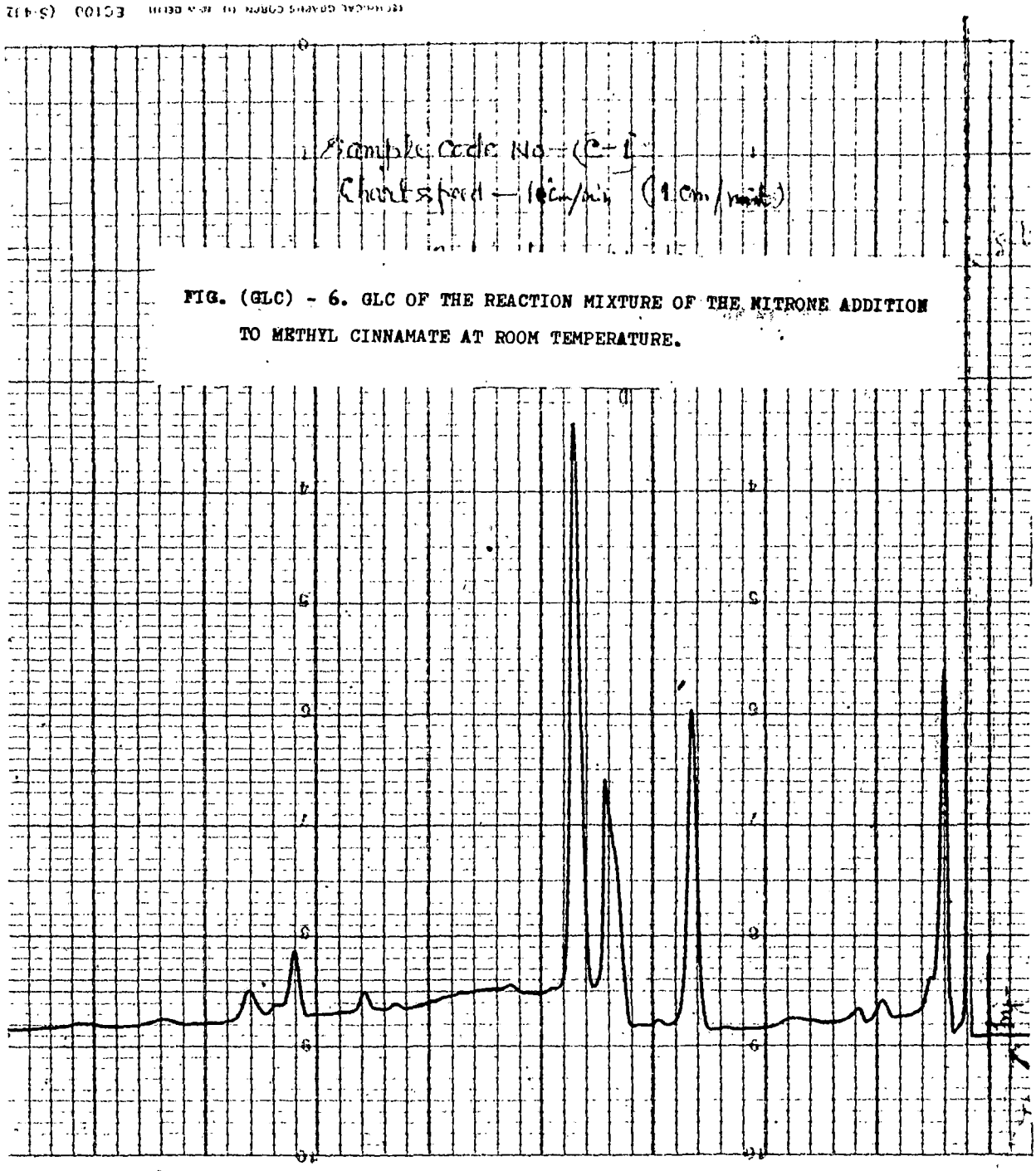
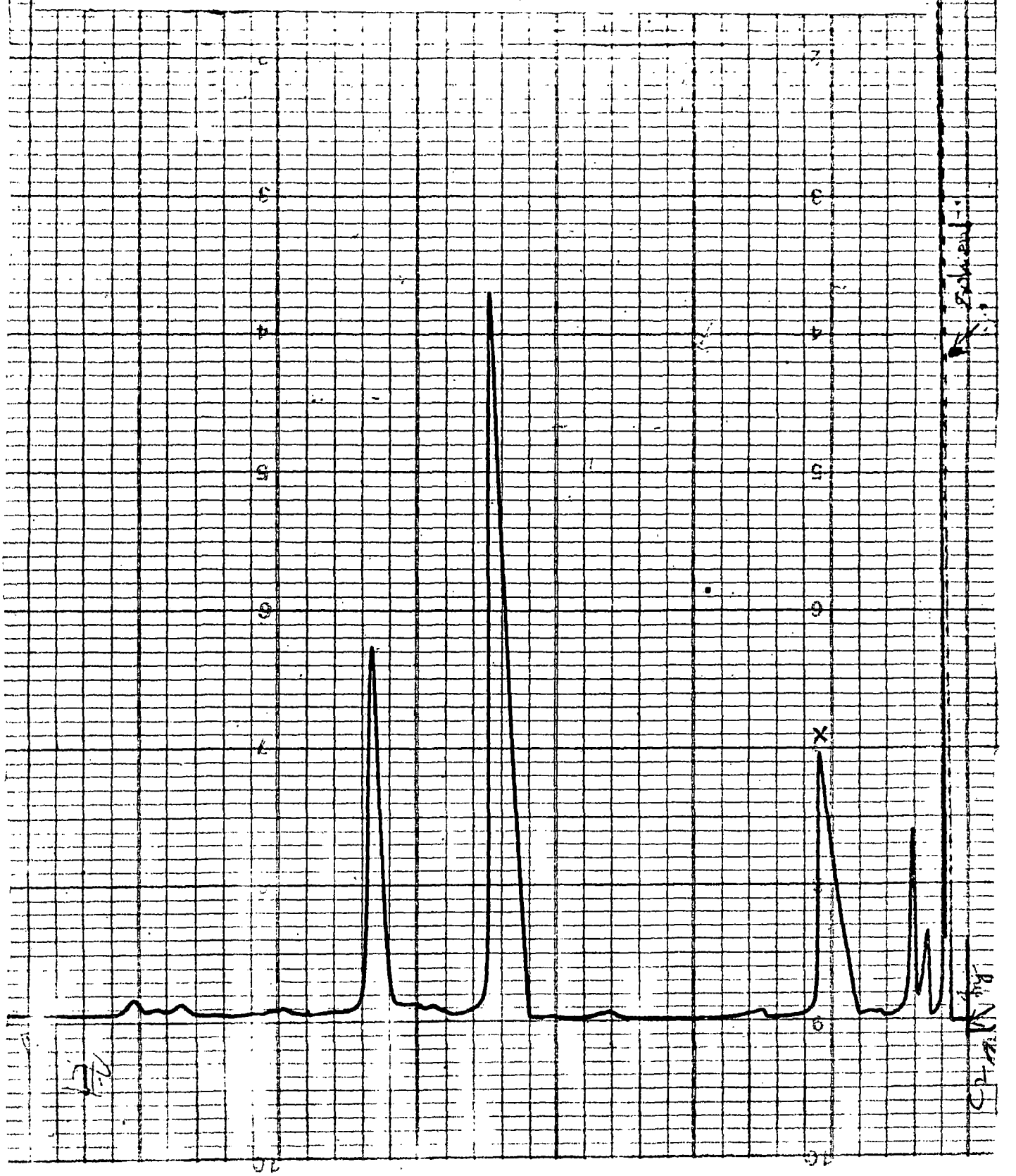


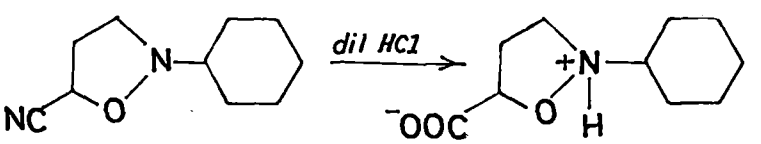
FIG. (GLC) - 6. GLC OF THE REACTION MIXTURE OF THE NITRONE ADDITION TO METHYL CINNAMATE AT ROOM TEMPERATURE.

FIG. (GLC) - 3. GLC OF THE PRODUCT MIXTURE OBTAINED FROM THE REACTION OF COUMARIN AND N-CYCLOHEXYL METHYLENE NITRONE.



GLCs of some of the reaction mixtures were carried out after removal of the product mixtures from the unreacted nitrones and solvents.

The acrylonitrile-nitrone adduct A was hydrolysed by aqueous hydrochloric acid (Scheme - IV). The product was found to be a white solid which did not melt even at 250°C. The IR and ^{1}H-NMR data of the compound suggest the zwitterionic structure of the compound. The pH-metric titration curve Fig. (T)-1 is like that of other amino acids with pK_1 = 2.1 and pK_2 = 9.65 and the isoelectric point pK_i = 5.875.



A

Scheme - IV

With so called highly electron deficient dipolarophiles like tetracyano ethylene and p-benzoquinone the nitrone additions occurred spontaneously at room temperature. In both the cases the reaction mixtures were coloured, which intensified gradually with the progress

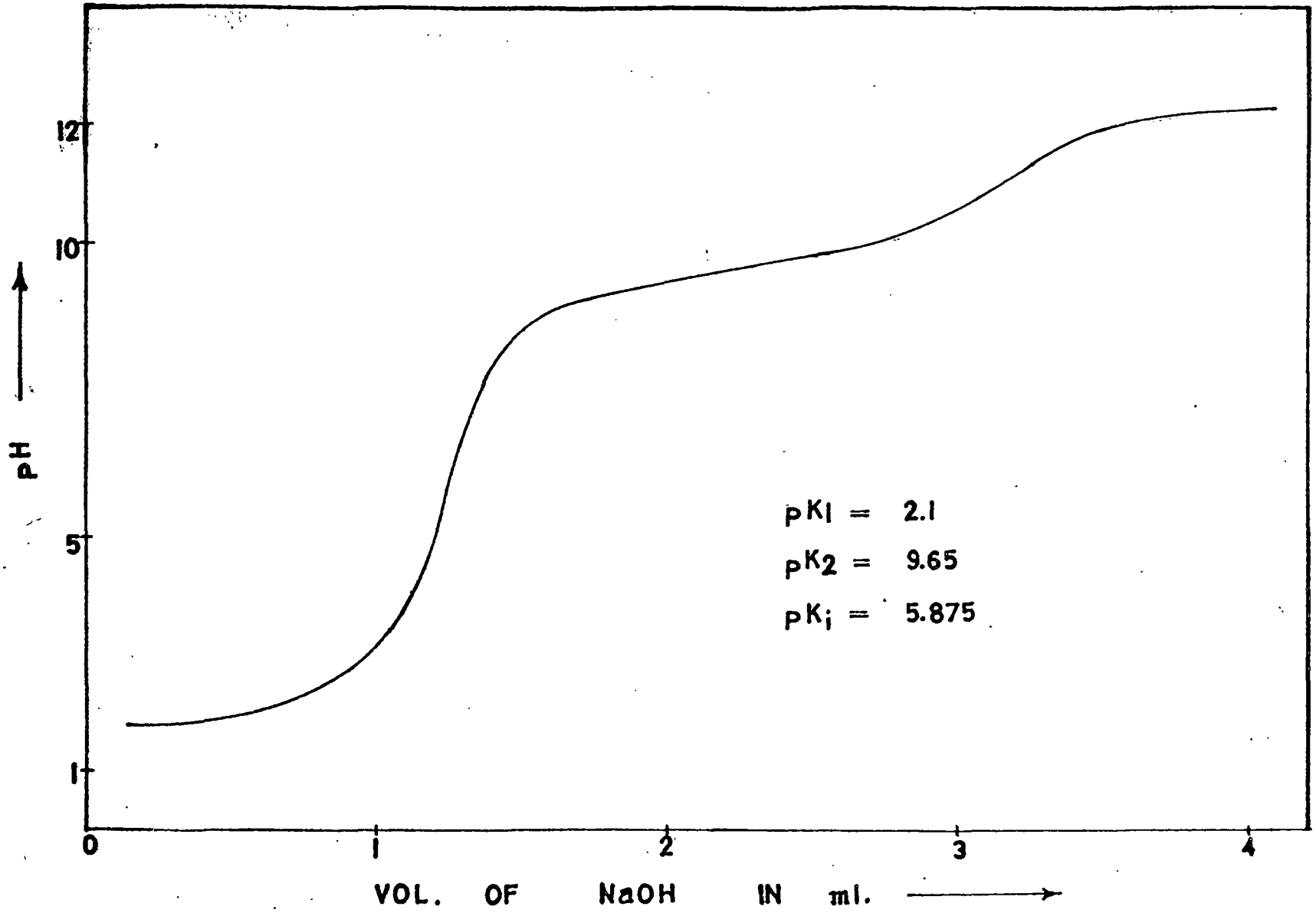
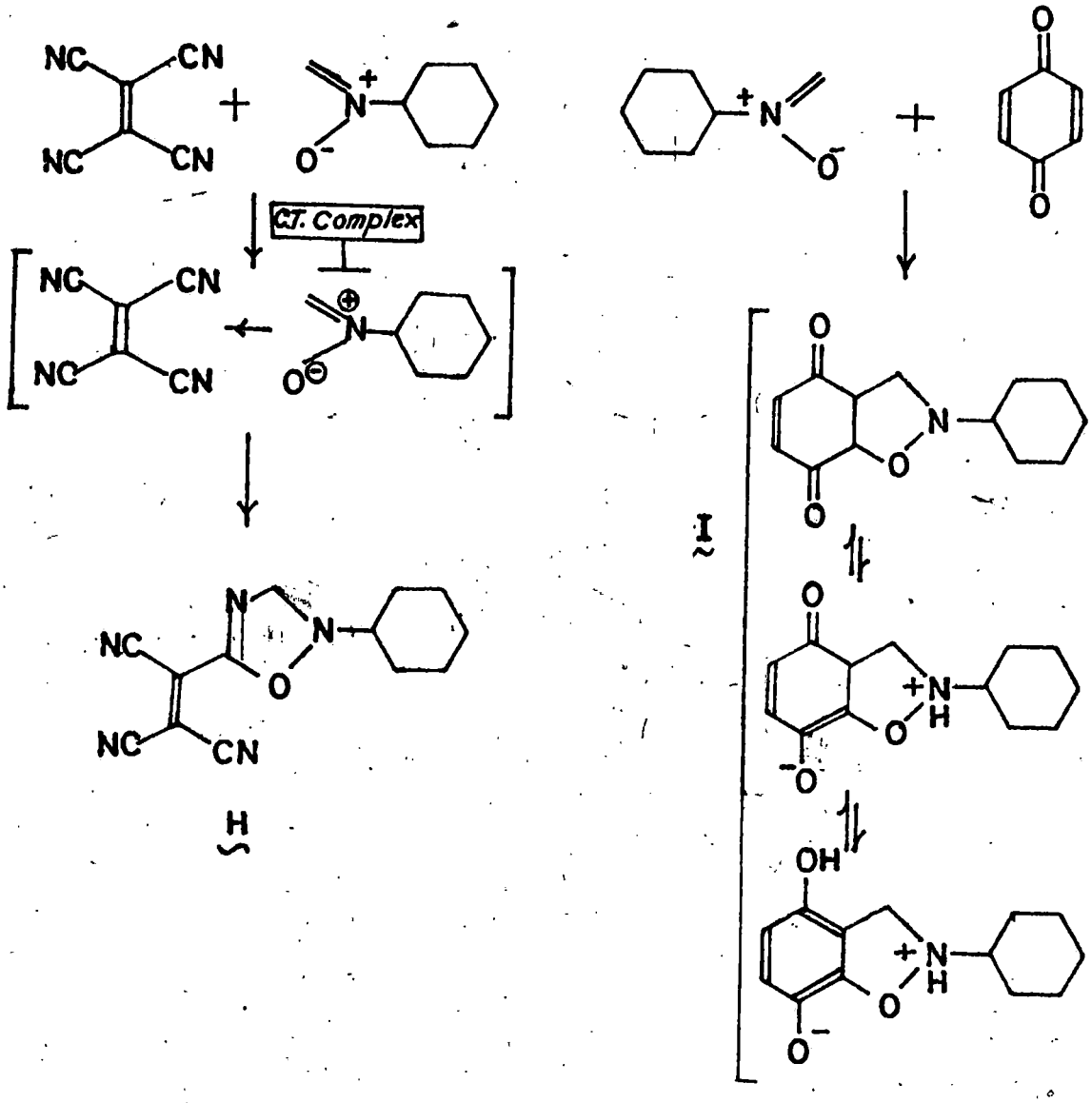


FIG. (T) - 1. pH-METRIC TITRATION CURVE OF THE HYDROLYSED PRODUCT OF THE ACRYLONITRILE-NITRONE ADDUCT.

of the reactions. Both the products are high melting solids. In one set of experiment with tetracyanoethylene, the dark red substance isolated by careful removal of the solvent methylene chloride at room temperature, underwent a vigorous exothermic reaction on being scratched with a spatula. The nature of the reaction suggests that there might be some stable charge transfer complex as the intermediate in the addition. Recently, the nature of the charge transfer between some C-aryl nitrones and TCNE, DDQ and chloranil were examined[173]. The UV-Vis spectra of the tetracyanoethylene-nitrone and p-benzoquinone-nitrone adducts show λ_{max} at 442 nm and 323 nm respectively. The IR, mass, ^{1}H-NMR spectra and elemental analyses were studied for both the compounds (H and I). Solubility of both the compounds are very low in common solvents such as chloroform, carbontetrachloride, benzene, water etc, as a result of which the ^{1}H-NMR spectra were studied in trifluroacetic acid solution.

It has been proposed that charge transfer is of importance in stabilizing the transition states of cycloadditions[176]. Identification of the dominant orbital interaction immediately provides information on the direction of charge transfer in the transition state and also provides insight into the extent and direction of non synchroneity in the cycloadditions. The degree of nonsynchroneity in the concerted cycloadditions will depend both on the inherent assymmetry of dipole and on the frontier orbital interaction which controls the addition. In extreme cases of nonsynchroneity, dipolar of diradical



SCHEME - V

intermediates may intervene in 1,3 dipolar cycloadditions. The reaction of the nitrone with tetracyanoethylene might be such a case of nonsynchroneity and the intermediate is sufficiently stable (Scheme - V). On scratching an exothermic reaction occurred furnishing the cycloadduct H.

The dark red adduct H, shows IR absorptions at 1620 cm^{-1}, 1640 cm^{-1} (-C = C-), 1680 cm^{-1}, 1720 cm^{-1} (-C = N-) and 1260 cm^{-1} (vinyl ether). The -CN absorption being at 2200 cm^{-1} indicates the presence of conjugation to the cyano group. The presence of the peak at m/e 102 [$(CN)_2C = \overset{+}{C}(CN)$] in the mass spectrum [Fig. (Mass)-2] of the compound also suggests that the adduct H has been formed by the addition of N-cyclohexyl methylene nitrone at the cyano group of the tetracyano ethylene. Colour of the compound may be due to the extensive conjugation in the adduct (H). Such type of regioselection was also observed during the 1,3-dipolar cycloadditions of benzonitrile oxide[185] and some other nitrones[186] to the TCNE. In the p-benzoquinone adduct the presence of the tert-nitrogen base and and endysable carbonyl groups might have lead to some other transformations (Scheme - V) as there is -OH absorption band at 3450 cm^{-1} region in the IR spectrum of the compound. The UV-absorption pattern [Fig. (UV-Vis)-4] is also suggestive to this type of transformation.

In order to study the nitrone addition to olefins containing latent ketene functionality we have chosen chloroacrylonitrile addition with the nitrone (Scheme - VI). When two separate solutions of the

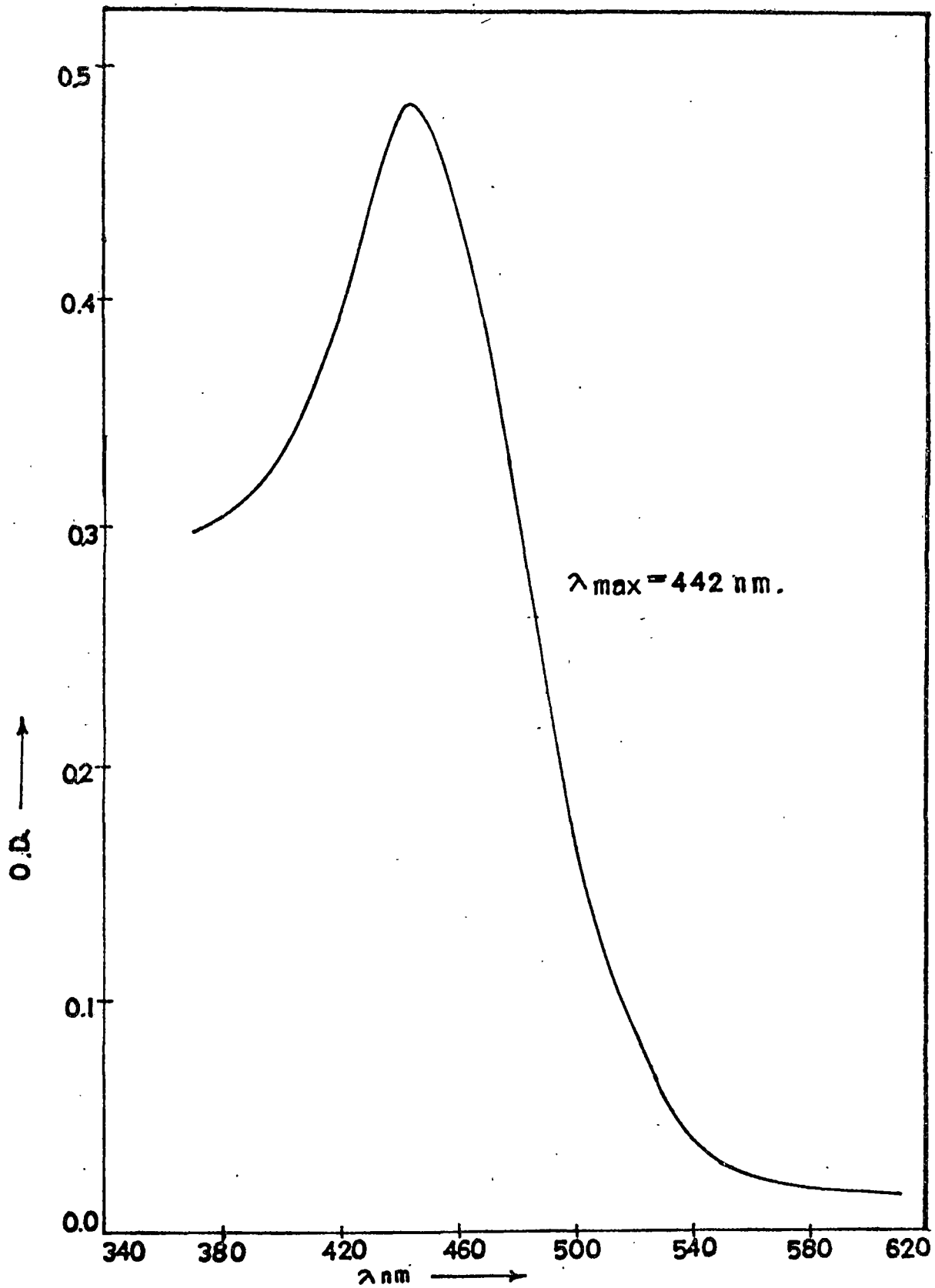


FIG. (UV-VIS)- 3. UV-VISIBLE SPECTRUM OF TCNE-NITRONE ADDUCT IN METHANOL SOLUTION.

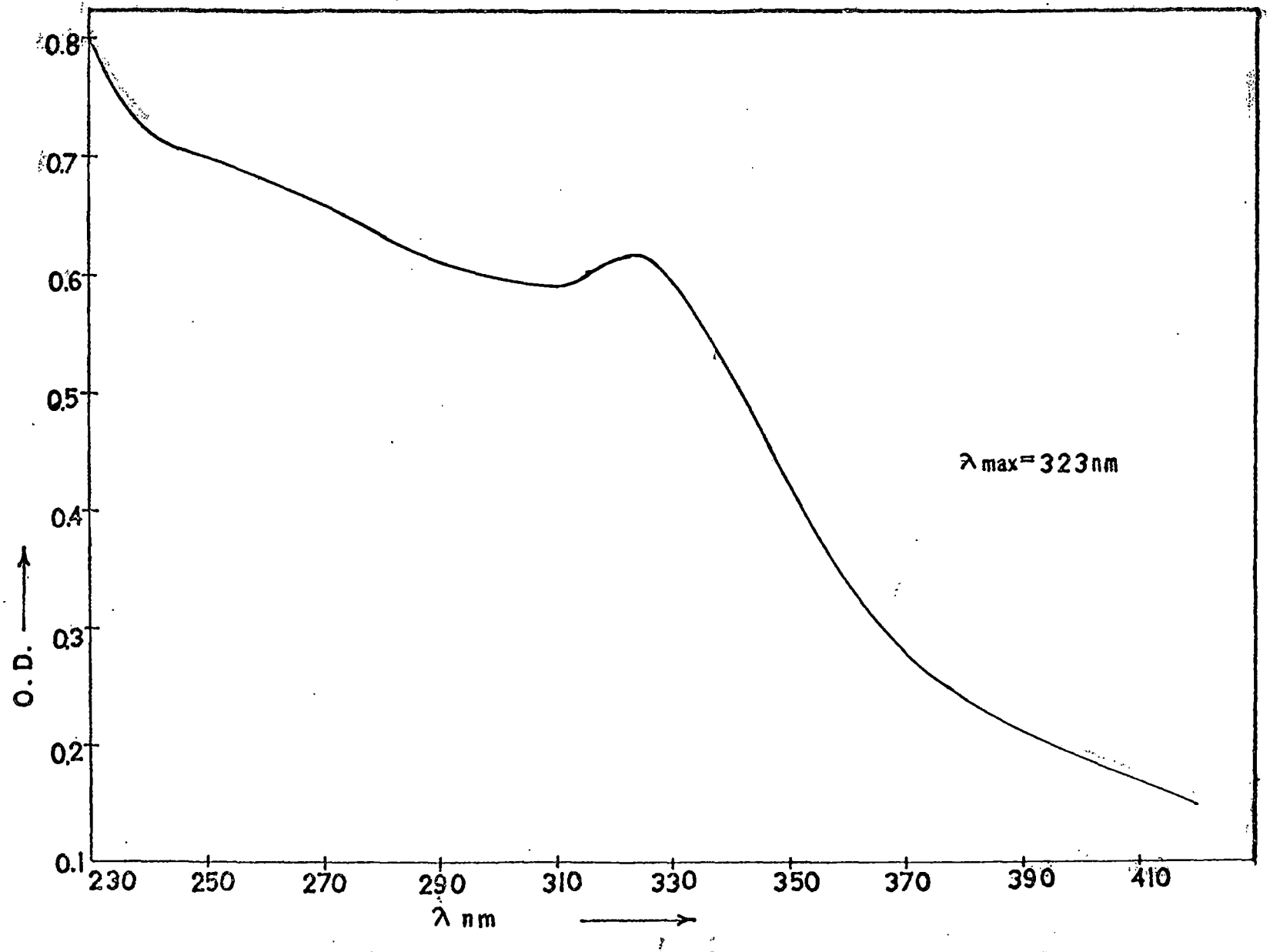
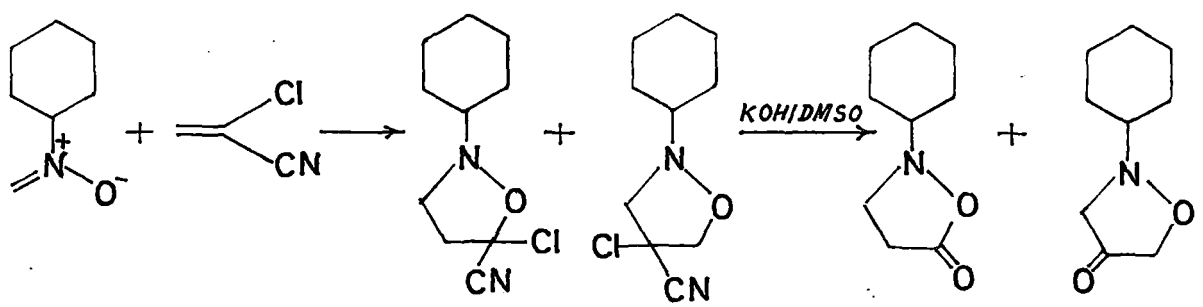


FIG. (UV-VIS) - 4. UV-VISIBLE SPECTRUM OF p-BENZOQUINONE-NITRONE ADDUCT IN METHANOL SOLUTION.

nitrone and chloroacrylonitrile in methylenechloride were mixed together, an instantaneous exothermic reaction occurred and the reaction mixture turned dark. On removal of the solvent a yellowish brown gum was obtained which could not be solidified. TLC of the reaction mixture indicated two spots at R_f 0.9 and 0.72 and also the quantitative nature of the reaction.



Scheme - VI

IR spectra of the gum was taken [Fig. (IR)-12]. An attempt was made to hydrolyse the gum with KOH/DMSO-water at room temperature. After several days, solvent extraction process was carried out with ether on the reaction mixture. The TLC of the extracted solution indicated two new spots of lower R_f values. The hydrolysed product was also

gummy. Column chromatographic method failed to separate the products. Though the IR of the new blackish gum showed carbonyl absorptions at 1665 cm^{-1} and 1700 cm^{-1} [Fig. (IR)-13] no further study was possible.

All the olefins considered so far undergo cycloadditions with the N-cyclohexyl methylene nitrone at room temperature. But the cycloadditions with normal and moderately electron rich olefins are not facile unless some drastic conditions are applied. The cycloaddition reactions are concerted in nature and possess a large negative activation volume for the formation of the adducts; therefore, under high pressure the formation of the transition state complex may be favoured. We have conducted the cycloadditions in sealed tubes. Solvents having high vapour pressures are chosen so as to generate a high pressure reaction medium in the most convenient way. Recently it has been noted that (2+3) dipolar cycloadditions of nitrones, when carried out under pressure, afforded good yields of the adducts[174]. As it would be apparent from the following discussions that the regioselectivity and stereospecificity remain unaltered during such high pressure additions.

Styrene, methylene cyclopentane, methyl-vinyl ether and 2,3-dihydropyran are unsymmetrical dipolarophiles. Hence the question of regioselections obviously arises in their cycloadditions with N-cyclohexyl methylene nitrone. In these cycloadditions the products J, K, O and P (Fig. II) have been isolated. All are the 5-substituted

adducts and the observed regioselections are in accordance with the expectations.

Cyclohexene and acenaphthalene are symmetrical specieses, therefore, the problem of regioselections during the cycloadditions with the nitrone does not arise. Nature of the products (L and M; Fig. II) obtained in these reactions indicates the cis fashion of C-5 and C-4 protons, which in turn indicates the cis additions of the reactants during the reactions.

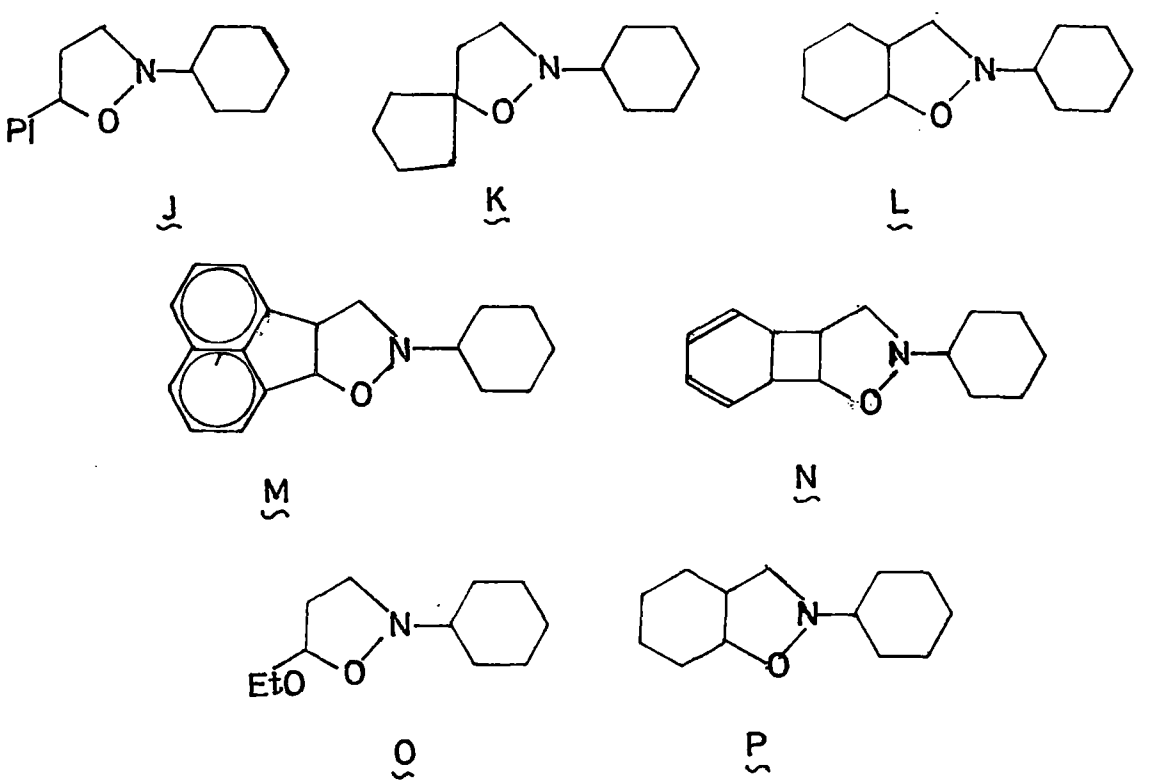
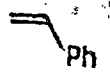
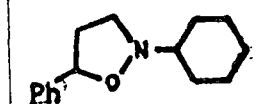
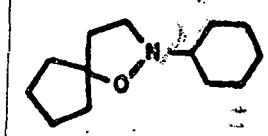
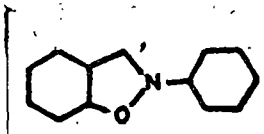


Fig. II

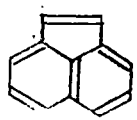
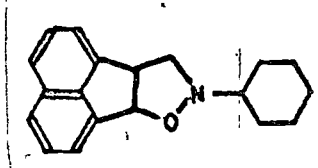
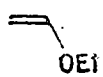
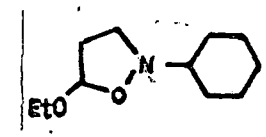
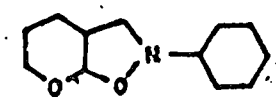
Except the acenaphthalene adduct, M, which is a white crystalline solid (m.p. 100 C) all the other products J, K, L, O and P (Fig. II) are liquids. In Table - II reaction conditions, yields and

TABLE - II.

Dipolarophile	Solvent/Reaction condition	Nature of product	R_f (Benzene:Ethyl acetate)	Major product
	$CHCl_3$, 120°C, 1 hr., sealed.	Colourless liquid, 160°C (4mm of Hg)	0.67 (5:1)	
	CH_2Cl_2, 130°C, 2hrs., sealed tube.	Colourless liquid, 120°C (4mm of Hg)	0.55 (5:1)	
	Cyclohexene, 140°C, 1½ hrs., sealed tube	Colourless liquid, 120°C (4mm of Hg)	0.82 (2:1)	

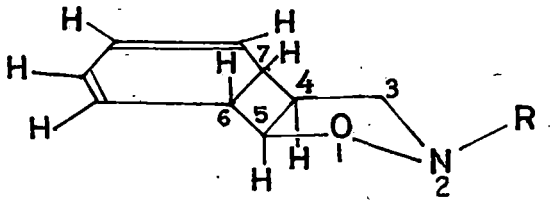
Contd...

TABLE - II. Contd.

Dipolarophile	Solvent/Reaction condition	Nature of product	R_f (Benzene:ethyl acetate)	Major product
	CH_2Cl_2, 160°C, 2 hrs, sealed tube.	White solid, 100-1°C m.p.	0.81 (5:1)	
	Ethyl vinyl ether, 150°C, 2½ hrs., sealed tube.	Colourless liquid, 130°C (4mm of Hg)	0.54 (2:1)	
	$CHCl_3$, 150°C, 3 hrs., sealed tube.	Colourless liquid, 135°C (4mm of Hg)	0.40 (4:1)	

the nature of the products are summarised. The structural assignments of the adducts as will be discussed in the next part of the chapter are mainly based on the ^{1}H-NMR and mass spectral data; IR data are not much helpful except for the assignment of functional groups. For the liquid products GLC's have been carried out.

The reaction of N-cyclohexyl methylene nitrone with cyclooctatetraene is quite interesting since both the electro cyclic ring closure of the cyclooctatetraene system and the nitrone addition have occurred to afford the product N (Fig. III)



N

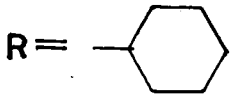
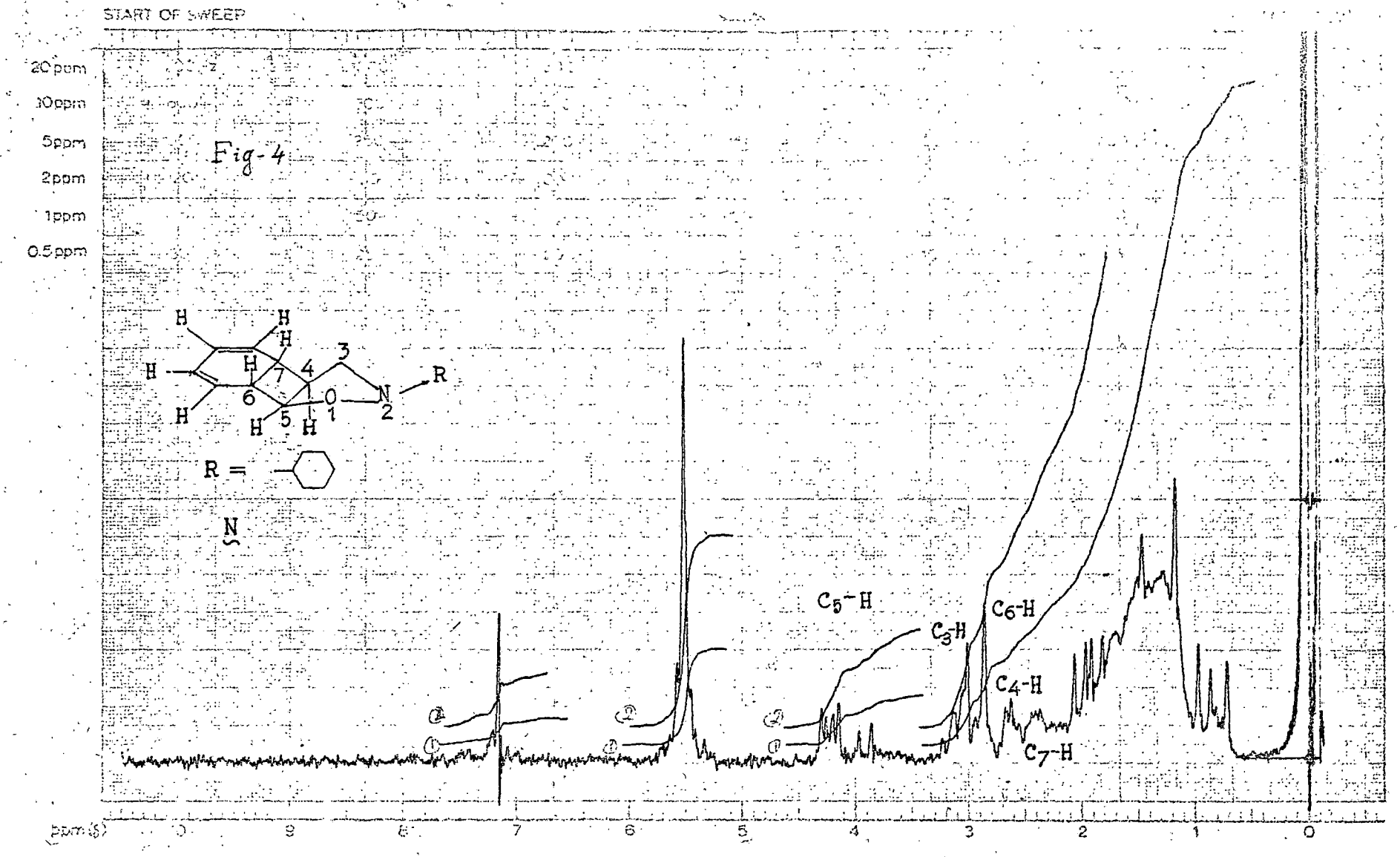


Fig. III

The ^{1}H-NMR spectrum [Fig. 'NMR)-4] of the compound, N, shows the following signals: a multiplet at 5.50 ppm (δ) for the four olefinic protons; a quartet with J = 2.5 Hz and 5.0 Hz at 4.25 ppm (δ) indicate the C-5 proton; two C-3 protons correspond to the multiplet at 3.1 ppm (δ); the C-6 proton signal is a multiplet at 2.9 ppm (δ); an unsymmetrical quartet with J = 2.5 Hz and 4.5 Hz at 2.65 ppm (δ) is for the C-4 proton; the single proton at C-7 shows a broad quartet at 2.4 ppm (δ); the cyclohexyl $-CH_2-$ proton peaks lie between 1-2 ppm (δ). It is also worth noting that the band-widths of the C-4, C-5, C-6 and C-7 proton peaks are comparable and are 14 ppm, 16 ppm, 15 ppm, and 14 ppm respectively. The anti conformar N is drawn in Fig. III. The syn adduct is not expected due to steric factors during addition. Moreover, the coupling constant values are in accordance with the proposed structure. Mass fragmentation pattern of the compound has been discussed separately. The IR spectrum is shown in Fig. (IR)-18.

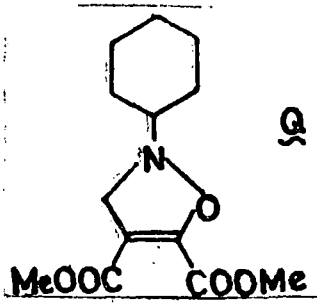
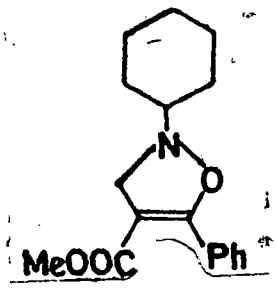
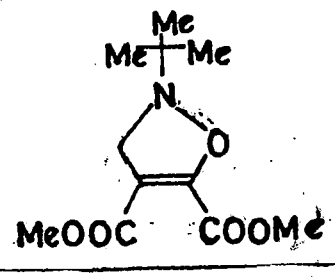
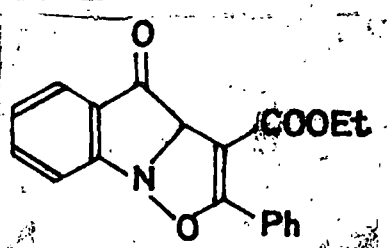
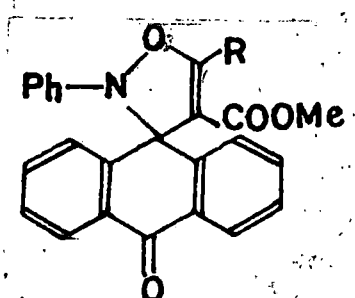
Another aspect of the cycloaddition reactions is their preference for the endo addition over the exo addition. In the present cases of cycloadditions of the N-cyclohexyl methylene nitrone the question cannot be answered from the inspection of the product structure since in such a case either the endo or the exo addition affords the same product. But, inasmuch as these cycloadditions hold all the criteria of other cycloadditions there is no reason to expect that the secondary orbital interactions will be absent in such cases.


START OF SWEEP
20ppm
10ppm
5ppm
2ppm
1ppm
0.5ppm
Fig-4
H
H
H
H
H
H
H
H
3
4
7
6
5
0
1
N
2
R
R =
N
C5-H
C3-H
C6-H
C4-H
C7-H
ppm (δ)
10
9
8
7
6
5
4
3
2
1
0

Houk et al have proposed that the preference for the endo transition state will only be large in these cycloadditions when the dipole-LUMO and dipolarophile-HOMO interaction will be important.

Reaction of the nitrone with the electron deficient acetylenes are very vigorous and exothermic in nature. Dimethyl acetylene dicarboxylate instantaneously reacted with the nitrone to give an orange-yellow gummy product, Q. An attempt to purify it by column chromatography over aluminium oxide had been unsuccessful. Even the adduct on standing for a few hours gradually decomposed to a number of products. IR spectrum [Fig. (IR)-21] of the product, Q, was taken immediately after the reaction. A relatively stable adduct, R, was isolated as a yellowish viscous liquid during the reaction of the N-cyclohexyl methylene nitrone with phenyl methyl propiolate. The product, R, did not decompose during column chromatography and remained unchanged after refluxing in benzene at 80°C for 5½ hrs. under nitrogen. But an attempt to distill it under low pressure had been unsuccessful. Structures of the adducts, Q and R, have been assigned on the basis of comparison of IR data with that of a few other reported adducts and methyl cinnamate (Table - III). Mass spectrum [Fig. (Mass)-16] of the adduct, R, shows M^+ ion peak at m/e 287 and the base peak at m/e 105 suggests the ion fragment $C_6H_5C = O$. The peak at m/e 204 originated from the aziridines, S, with the C-N bond cleavage (Scheme - VII). Thus we find that the relatively stable adduct, R, has suffered Baldwin transformation to aziridine during the mass fragmentation of the compound. The UV absorption maxima is at 252 nm. The ^{1}H-NMR spectrum of the compound,

TABLE - III.

Compound	IR (cm^{-1})	Chemical shift in (δ)ppm of C_3 methylene protons.
 Q	1750, 1710, 1655, Fig. (IR)-21.	———
 R	1700, 1625, Fig. (IR)-22.	4.16 (singlet)
	1760, 1715, 1660. (Ref. 130)	4.18 (singlet)
	1732, 1687, 1617. (Ref. 123)	———
	R = COOMe 1745, 1715, 1675, 1650, 1600, 1320. R = $-CH_3$ 1720, 1665, 1630, 1600, 1320, 1140, 1125. (Ref. 184)	———

SCHEME - VII.

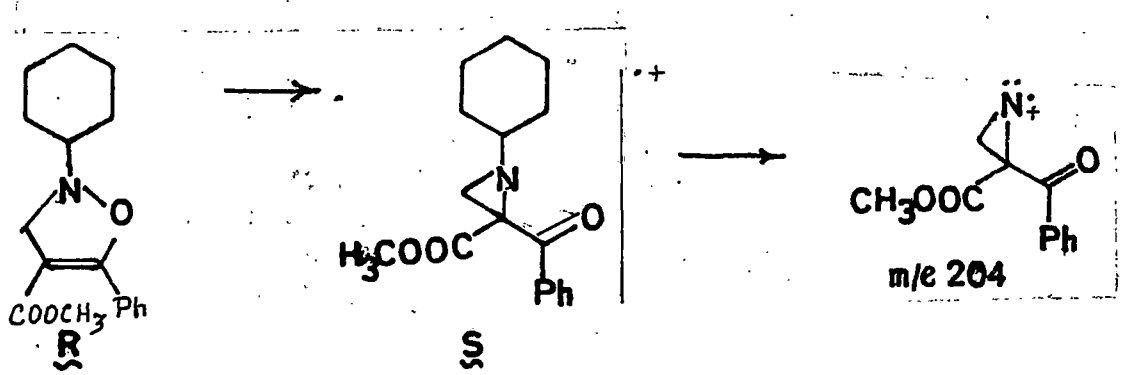
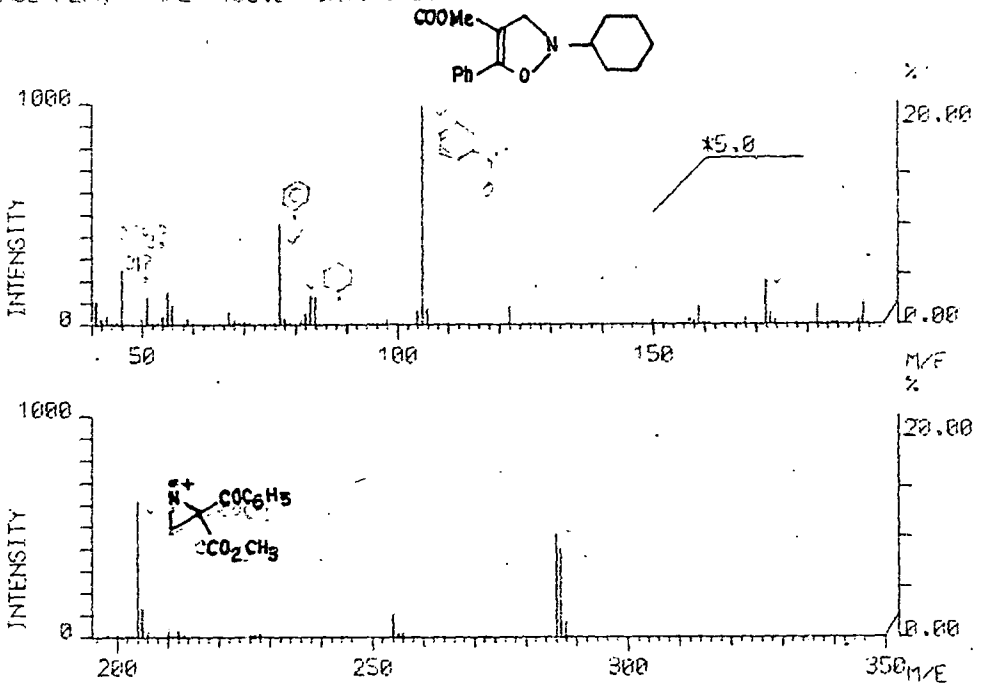


FIG. (MASS) - 16.

MASS SPECTRUM : 1 TO 37 (A)
SAMPLE:DR AK WANDA,DEPT.OF CHEM,DARJEELING.WEST BENGAL
NOTE :25-2-82
BASE PEAK : M/E 105.0 INT. 678.7



M/E	RAW INT.	R.INT.	SIGMA(%)	
41.0	78.1	115.1	3.65	
45.0	178.3	262.8	8.34	
51.0	90.7	133.5	4.24	
55.0	100.0	159.2	5.05	
56.0	61.9	91.2	2.89	
57.0	50.7	74.8	2.37	
77.0	316.3	466.0	14.78	
83.0	99.3	145.3	4.64	
84.0	93.6	137.9	4.37	
104.0	52.4	77.3	2.45	
105.0	678.7	1000.0	31.74	
106.0	55.1	81.2	2.58	
122.0	67.3	99.2	3.15	
204.0	85.5	126.0	4.00	
286.0	55.1	95.9	3.04	
287.0	56.0	82.6	2.62	END

R, shows the following signals: a multiplet at 7.7-7.2 ppm (δ) for the five aromatic protons; a singlet at 4.16 ppm (δ) for the two C-3 methylene protons; a broad multiplet at 3.3 ppm (δ) for the single N-CH- proton; a singlet at 6.45 ppm (δ) for ester protons and the ten cyclohexyl methylene proton signals lie between 1-2 ppm (δ).

Interpretation of the proton NMR spectra

During interpreting the NMR spectra of the compounds in addition to the chemical shift and coupling constant values we shall consider the band width, i.e. the distance between the first and last line of the multiplet of the signal due to a certain proton in ppm unit. Baumann et al[175] used such methods to elucidate the conformations of cis and trans cyclopentane-1-carbomethoxy-2-ol and found that for trans isomers the band width is 18 c/s and that of the cis is 11 c/s for the C-1 protons. Similarly we have measured the band width for C-5 protons of all the compounds prepared and found that for the expected cis compounds (I, M, N and P Fig. II.) the band widths are 18 ppm and that of the expected trans ones (A, B, C, E, F, J and D, Fig. - I.) are 25-27 ppm, as represented in the table - E.

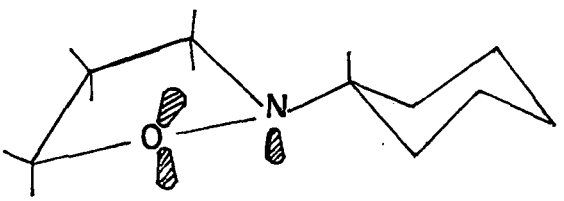
Table - E

Compound	(ppm) C-5 proton	Band width (ppm)	Coupling values
A	4.6, q	27	J = 6.75 Hz and 4.5 Hz
B	4.3, t	25	J = 7.87 & 7.87
C	3.95, t	25	J = 5.6 Hz & 6.75 Hz
E	5.15, m	27	-
F	4.5, q	24.5	J = 8 Hz and 9 Hz
L	3.9, q	18.5	J = 4.5 Hz and 7.87 Hz
J	5.0, t	26	J = 7 Hz and 7 Hz
M	5.65, d	18	J = 8 Hz
N	4.25, q	16	J = 2.5 Hz & 5.0 Hz
O	4.9, q	25	J = 3.37 Hz & 4.5 Hz
P	4.85 d	18.5	J = 4.5 Hz

From these band-width values we may conclude that the dipolarophiles with cis configurations about the double bonds give rise to cis products and therefore, the nitrone additions under normal or high pressure conditions are stereospecifically cis.

From the coupling constant values for C-5 protons of the nitrone adducts with acrylonitrile (A), methyl acrylate (B), styrene (J) and ethyl-vinyl-ether (O) we have calculated the dehedral angles between the C-5 proton and the C-4 protons from a standard graph. From these calculated values along with the assumption that 2-

cyclohexyl 1,2-isoxazolidine at normal condition will prefer the 'envelop' configuration with N-cyclohexyl group at equatorial position (Fig. – IV.), we have constructed the C_5 - C_4 projections with



envelop configuration

Fig. – IV.

the corresponding dehedral angles (Fig. – V) for the compounds A, B, J and O. From these figures it is clear that the substituents

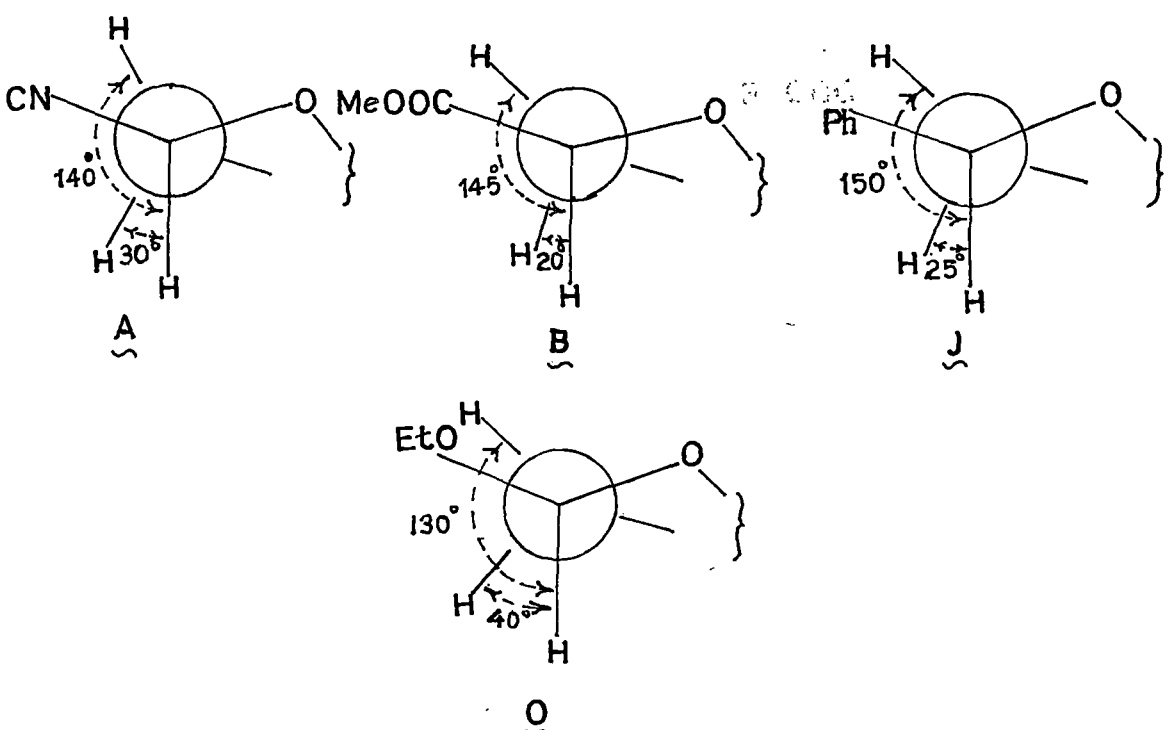
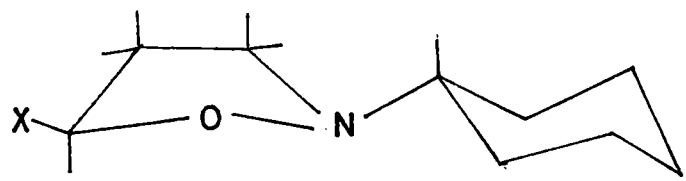


Fig. – V

at the C-5 position tries to have the equatorial position from the quasi-equatorial position of the envelop form. As a result the 1,2 isoxazolidine conformation shifts from envelop to half-chair-form depending on the bulkiness of the C-5 substituents. The conformation of A and O having less bulky groups are close to the envelop form and that of B and J are close to the half chair form. The pseudo-rotation of the five-membered ring is restricted by the substituents in all these compounds.



Half-chair form

This indicates that in each of the compounds C-5 proton and C-4 proton couple in the same way and comparison of the corresponding dehedral angle suggests that the dehedral angle of the protons is 50^{o}. The normal dihedral angles for cyclohexane in perfect chair form are 60^{o} for cis protons and 180^{o} for trans protons. The deviation is due to the strain of the five membered ring. Another coupling constant for the cyclohexane adduct viz. 7.87 Hz, suggests a dehedral angle of 155^{o} which indicates that in the compounds P and L the six membered rings are not in perfect chair form but slightly deviated

to relieve the strain of the 1,2-isoxazolidine ring.

In the case of the acenaphthalene adduct two five membered rings are fused in 1,2 positions and the planer nature of the aromatic ring brought the C_5 and C_4 protons in nearly eclipsed position with the dehedral angle 15^o corresponding to J = 8 Hz.

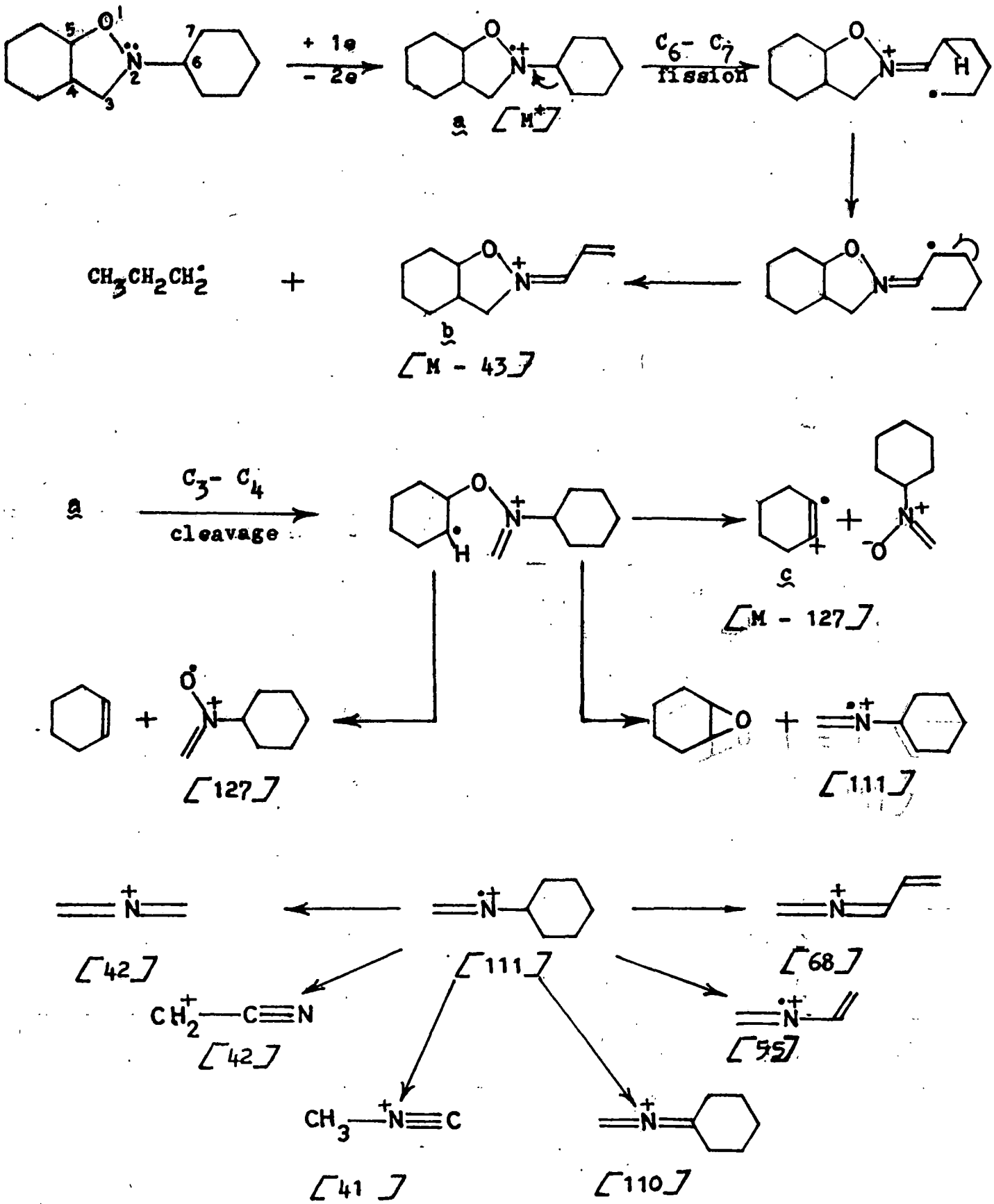
As the C_5 - protons in the other compounds are either absent or their splittings are not prominent, nothing can be inferred in such cases about the conformations of the products. Absence of any signals in the δ=3-5 ppm region for the nitrone-methylene cyclopentane adduct suggests the absence of C-5 proton. The two C-4 protons and two C-3 protons of the compound show signals at δ = 2.1 ppm with a sharp triplet with J = 6.3 Hz and at 2.8 ppm with a sharp triplet with J = 6.3 Hz respectively suggests some average environments forthe protons. C-4 and C-3 protons of all other compounds are also in the region 2.1 - 2.8 ppm but often the signals are not clear due to the broad $-\overset{|}{N} - \overset{|}{C}H-$ signal and the tail of the cyclohexyl methylene proton signals.

Mass spectral interpretation

The nitrone adducts : All the compounds considered here possess 2-cyclohexyl 1,2-isoxazolidine moiety in common. Therefore, it is very usual to expect some rationalization in the mass fragmentation patterns of the compounds. As the general basis of mass fragmentation, on impact of an electron with the molecule a radical ion will generate and expectedly one of the non-bonding electrons from the nitrogen atom of 1,2-isoxazolidine will be removed. In comparison with the fragmentation pattern of a molecular ion thus

SCHEME - I

General patterns of mass fragmentation



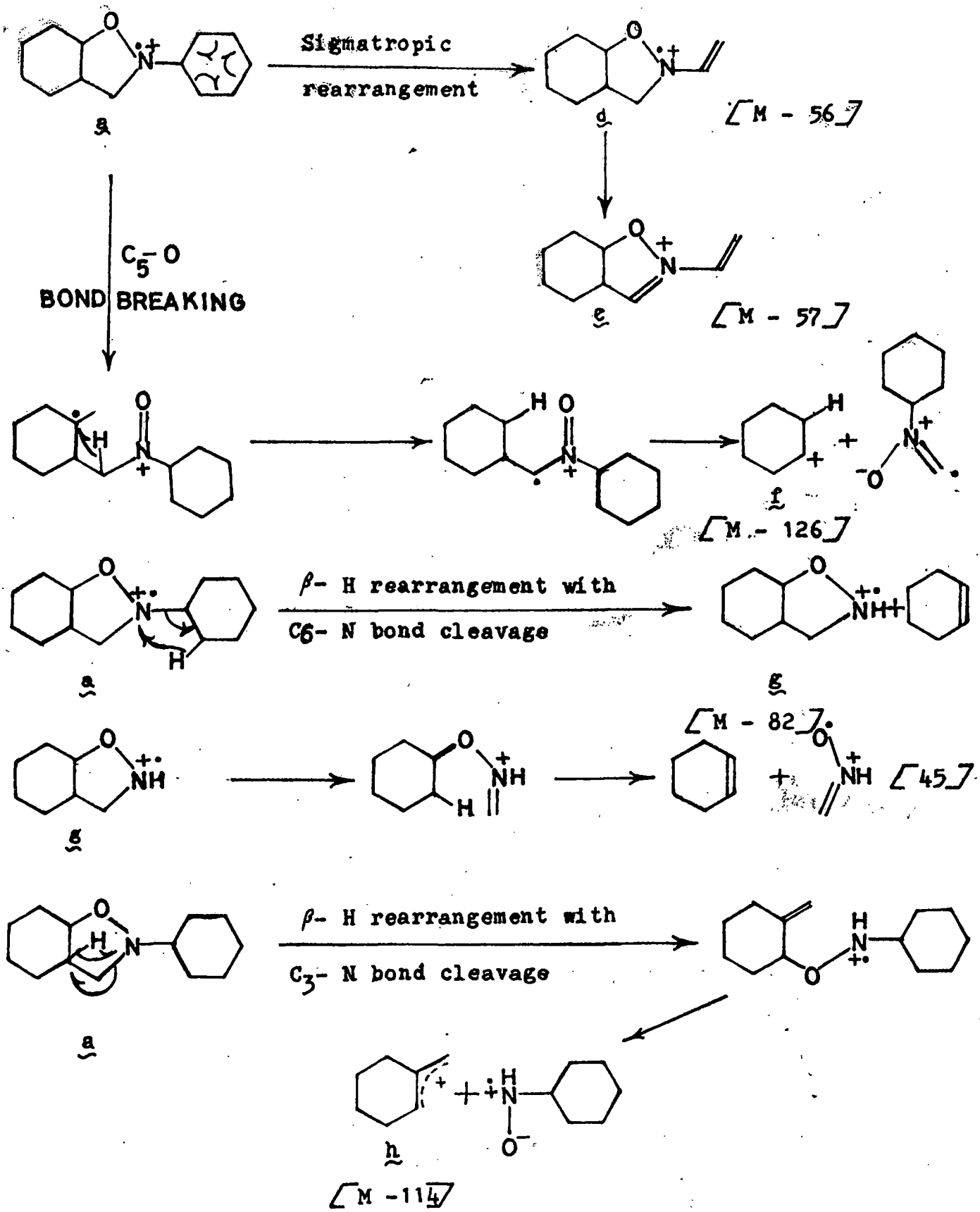

Sigmatropic
rearrangement
[M - 56]
C_5- O
BOND BREAKING
[M - 57]
[M - 126]
β- H rearrangement with
C_6- N bond cleavage
[M - 82]
[45]
β- H rearrangement with
C_3- N bond cleavage
[M -114]

TABLE - I

COMMON MASS FRAGMENTATIONS OF DIFFERENT COMPOUNDS HAVING 2-CYCLOHEXYL 1,2-ISOXAZOLIDINE MOITY IN COMMON.

The '+' sign indicates presence of the ion fragment and its number crudly indicates the Relative intensity and the '-' sign indicates absence of the ion peak in the mass spectrum.

MASS FRAGMENTS ALONG WITH THE GENERAL TYPES (SCHEME - I).

Nitrone adducts with	M^+,a	M-43,b	M-127,c	M-56,d	M-126,f	M-82,g	M6114, h	111	110	68	55	42	41	127	45
Cyclohexene (L)	209 ++	166 ++++	82 +	153 +	83 +	127 +	95 ++	-	+	+	+++	+	+++	+	+++
Metylene Cyclo-pantane (K)	209 +	166 ++	82 +	153 +	83 +	127 +	95 ++	+	+	+	+++	+	++	+	+
							117 ++++	-	+	+	-	+	++	-	-
Styrene (J)	231 +	188 +	104 ++	175 -	105 +	149 +	165 +++	-	-	-	++	-	+	-	-
Acenaphthalene (N)	273 ++	236 -	152 ++++	223 -	153 ++	197 -	117 +	+	+	+	+++	+	+	+	-
Cyclooctatetraene (N)	231 +	188 +	104 +	175 -	105 +	149 +	85 ++++	+	++	++	+++	+	++	-	+
Ethyl vinyl ether (O)	199 ++	156 +	72 +	1 43 +	73 -	117 +	97 ++++	++	++	+	+++	+	++	+	-
2:3 dihydro pyran (P)	211 +	168 ++	84 +	155 -	85 ++++	129 ++	66 +	+	+	+	++++	+	+++	+	+
Acrylonitrile (A)	180 ++	137 +++	53 +	124 +	54 +	98 +++	99 +	-	+	+	+++	+	++	-	+
Methyl acrylate (B)	213 ++	1700 ++++	86 +	157 +	87 +	131 ++	113 +	-	+	+	+++	+	+++	+	+
Methyl crotonate (C&D)	227 ++	184 ++++	100 +	171 +	101 +	145 +	175 +	-	+	+	++++	+	+++	+	+
Methyl cinnamate (E&F)	289 ++	246 ++	162 +	233 +	163 +	207 +	191 ++	-	+	+	++	-	+	-	+
Methyl coumarate (G)	305 +	262 +	178 +	249 +	179 -	223 -	121 -	+	++++	+	+	+	++	+	+
p-benzoquinone (I)	235 +	192 +	108 +	179 +	109 +	153 +									

formed from an amine a generalized scheme is produced (Scheme - I) for the nitrone-cyclohexene adduct. And the fragmentation patterns of all other types of molecules under consideration are discussed in the light of this fission pattern. Like the case with the cyclic amines the major fission pattern of such a molecular ion will be due to α-bond cleavage. Among the two probable modes of α-cleavage viz. C_3-C_4 and C_6-C_7, the C_6-C_7 cleavage will expectedly be the favoured one due to the reason that highly substituted bond breaks to the greater extent in the process of α-cleavage. The cleavages of C_3-C_4 bonds will also occur with lots of subsequent transformations leading to the fragments with m/e, [M-127 (type -e)] 111, 110, 68, 55, 42, 41 and 40. Another process of concerted homolytic fission of the cyclohexyl ring may lead to a fragment with m/e [M-56 (type - d)]. This type of fragmentation originates from the concerted homolytic fission of the N-substituted six membered ring. The ion fragment m/e [M-56] may subsequently loss a hydrogen to form the ion of the type c, with m/e [M-57].

Another mode of α-cleavage in which at first the C_3-O bond will be broken will lead to the ion of the type,f, with m/e [M-126].

The process of β-hydrogen rearrangement with C-N bond cleavage may occur in two ways leading to the types g, with m/e [M-52] and h, with m/e [M-144] (Scheme - I).

The ion radical 'g' may further split although the fragmentations have not been shown in the shheme. Among other fragments the

[M+1] peak is common. Occurrance of these expected mass fragments are tabulated in the Table - 1. The other peaks which depend on the nature of substituents at 4 and 5 positions of the 1,2-isoxazolidines are as follows.

In the fragmentation pattern of the methylene cyclopentane adduct, in addition to the common expected fragments a promient fragment m/e 140 is observed. (The m/e 140 peak is also found in the fragmentation patterns of cyclohexene adduct, 2,3-dihydropyran adduct and acenaphthalene adduct (m/e 164, R. Int. 24.6, sigma p.c. 0.84). We like to show a special cleavage pattern for the adduct so as to lead to a m/e 140 fragment [Scheme - IIA]. Another fragment at m/e 58 may be the $[CH_2 - CH_2 - N = O]^{+\cdot}$; this is the base peak in the mass fragmentation of the compound.

For the styrene adduct the base peak is at m/e 117 i.e. type 'h' and all characteristic peaks of the phenyl group are present in trace amounts, viz. m/e 91 (tropylium ion), 77 (benzyl ion), 51 $[C_3H_4]$. The peaks corresponding to the fragments of type d, as well as 45 (m/e), 155 (m/e), 111 (m/e), 127 (m/e) are absent indicating that these types of fragmentations are not favoured. M + 1 peak at m/e 232 (R. Int. 451 sigma p.c. 2.13) is also a characteristic peak of the compounds having aromatic nucleus.

The spectra of the acenaphthalene - nitrone adduct is much simple. The ions a, b, c, f, h, 55 and 41 are only present from the general pattern. The peak at m/e 166 (R. Int. 98.0 and sigma p.c. 23.82) is new . This [M-113] ion fragment might have occurred from direct C_3-N and C_5-O bond rupture of the 1,2 isoxazolidine ring.

The mass spectrum of the nitrone-cyclooctatetraene adduct

possesses some unique fragmentation patterns. The molecular peak is at m/e 231 (R. Int. 6.2, 0.37). There are two new intense peaks, at m/e 153 (M-78). (R. Int. 722.1, sigma p.c. 43.12) and at m/e 152 $\left[M - 79\right]$ (R. Int. 687.2, sigma p.c. 41.03) in addition to the pattern shown in the general scheme - I. The fragmentation patterns which lead to the ions have been tentatively formulated in scheme - II(B). The sigmatropic rearrangement which leads to the above two fragments is the preferred mode of fission of the molecule. This type of rearrangement is uncommon in all other cases. The other strong peaks at m/e 83, 71, and 70 are not found in the general mode of fragmentations, and, therefore, must have originated from the radical ion 'i' (Scheme - IIB). The base peak m/e 70 may be thought to be a isoxazolidinium ion originated from 'i' by β-hydrogen rearrangement with N - C_6 bond cleavage followed by an elimination of hydrogen (Scheme - IIB).

The nitrone - ethylvinylether adduct in its mass spectrum possesses the ions as expected from the general pattern. Only the strongest new peak at m/e 154 (R. Int. 104.2 sigma p.c. 16.46) originates from the process of α-cleavage of C_3-C_4 bond followed by C_2H_3O elimination (Scheme - IIC). This is probably the most favoured process of fragmentations of the molecular ion. Another new fragment m/e 57 is relatively strong. This fragment m/e 57 $\left[CH_2\text{-}CH_2\text{-}C = O\right]^+$ might have originated from the cleavages of the bonds N-C_3 and N-O.

The fragmentation pattern of the 2,3-dihydropyrannitrone adduct is similar to that of the general pattern (Table - I, Scheme-I).

The base peak at m/e 97 is a 'h' type ion fragment. The additional remarkable mass peaks at m/e 182, 168 and 112 have been explained in Scheme - IID.

Mass fragmentation pattern of the acrylonitrile adduct is very much like the general pattern (Scheme - I, Table - I). The base peak is m/e 55. The molecular ion peak is associated with M+1 and M - 1 peaks of much lower intensity. A very weak peak at m/e 154 (M-26) indicates CN elimination which is not much favoured. Another new peak at m/e 68 must have occurred due to the radical ion $\overset{\cdot}{\overset{+}{N}} \equiv C - C(O) - \dot{C}H_2$.

The nitrone-methyl acrylate adduct also prefers the general modes of mass fragmentations (Table - I, Scheme - I). The base peak is of type 'b' at m/e $\lceil M-43 \rfloor$. $\lceil M+1 \rfloor$ and $\lceil M - 1 \rfloor$ peaks though weak, is present along with the moderately intense molecular ion peak. Among the additional peaks, the peak with m/e 154 originates from the elimination of the radical $COOCH_3$ from the molecular ion. A peak of low intensity is also present at m/e 50 probably for the ion fragment $\lceil COOCH_3 \rfloor^+$.

The fragmentation pattern of methyl crotonate-nitrone adduct is similar to the general pattern and is very much like that of methacrylate-nitrone adduct. Here also the peak at m/e 184 $\lceil M-43 \rfloor$ is the base peak. The weak peaks at m/e 59 and $\lceil M-59 \rfloor$ i.e. 168 are also present.

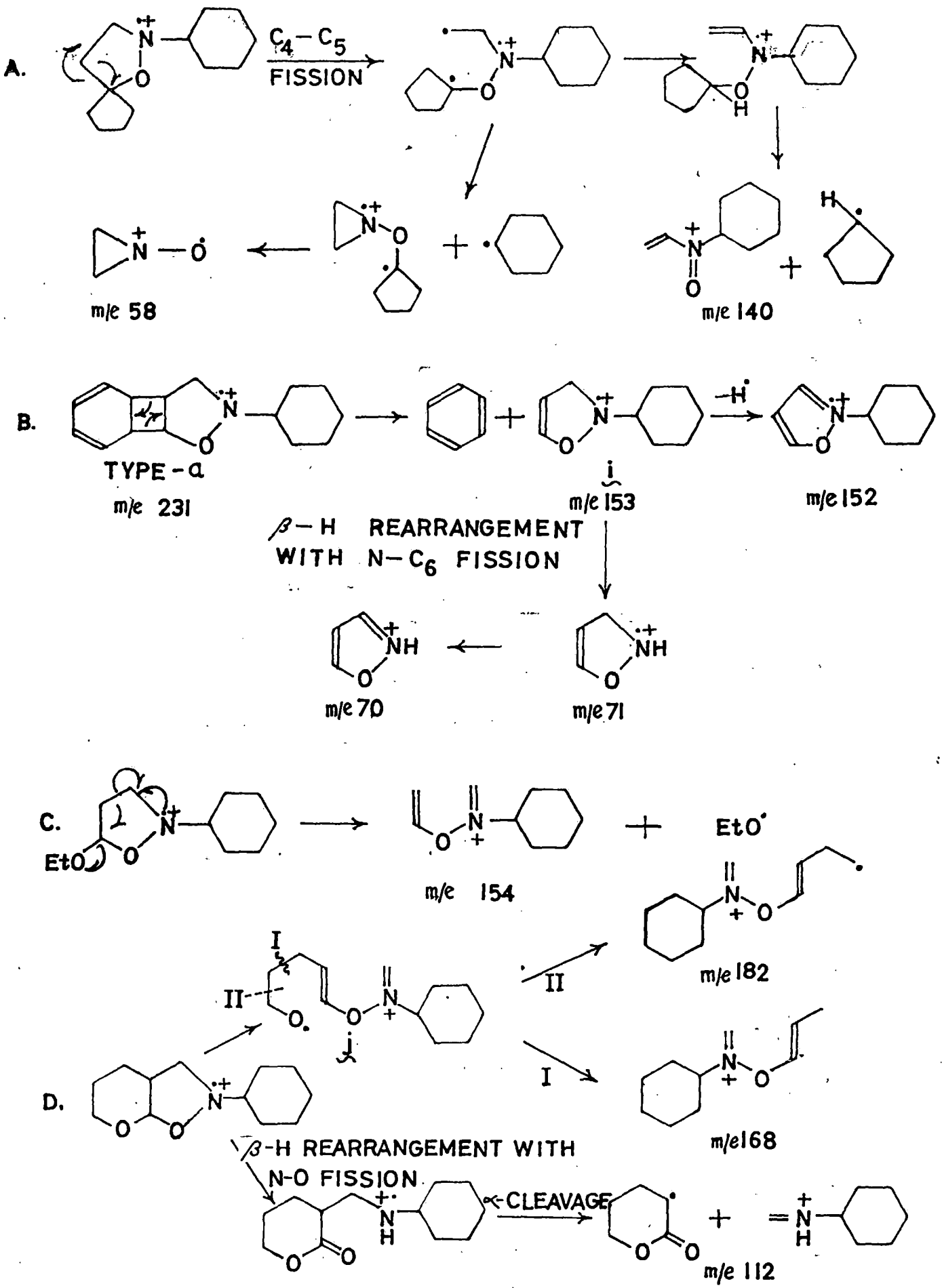
The mass fragmentation pattern of the methyl cinnamate-nitrone adduct also corresponds to the general pattern and is

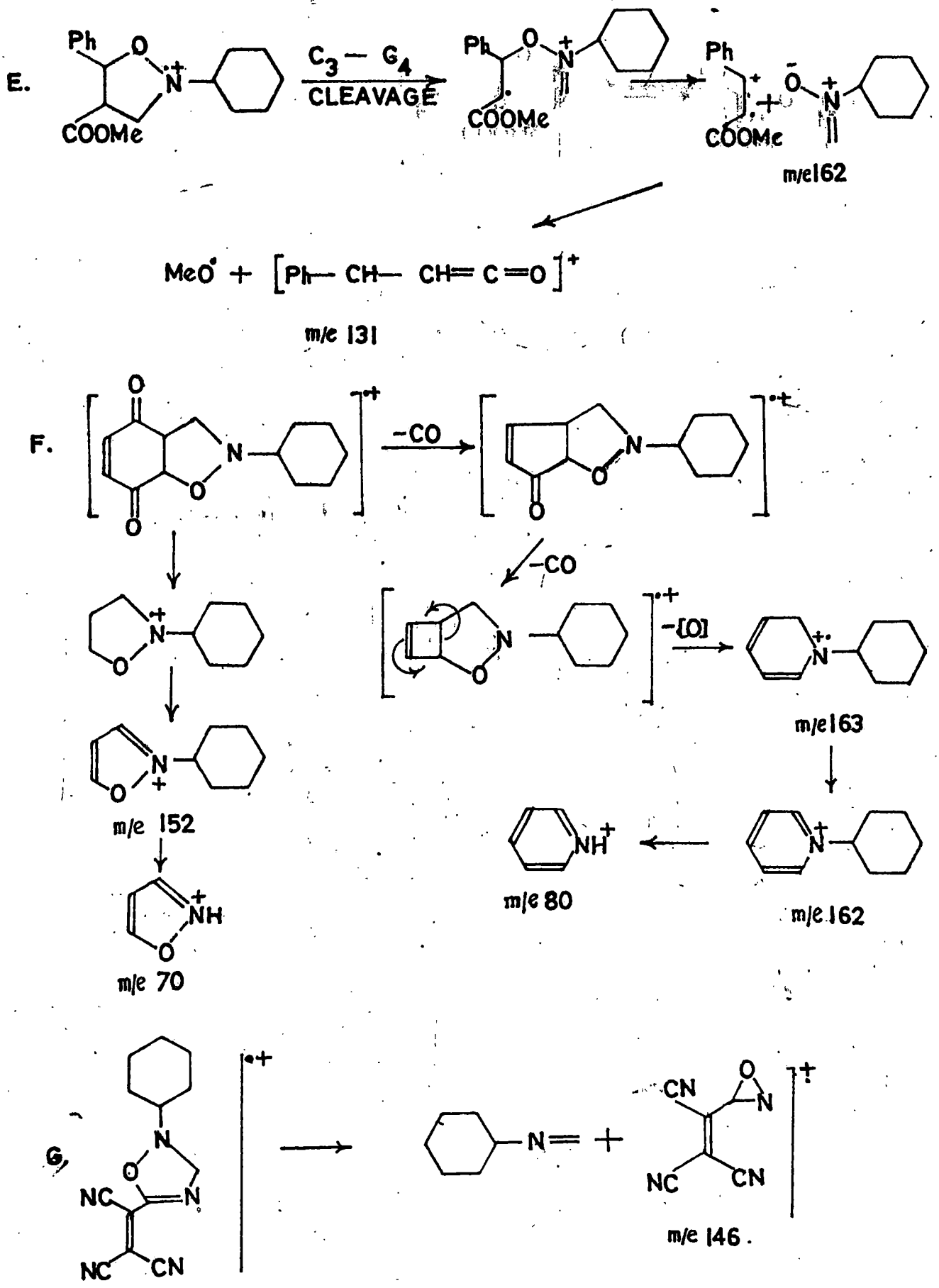
similar to those of the nitrone adducts with methyl acrylate and methyl crotonate (Table - I, Scheme - I). In this case also the weak peaks at m/e 59 and 230 (M-59) with R. Int. 22.0 and sigma p.c. 1.31 respectively are present. In addition to these peaks other peaks at m/e 77, 91, 51 and 105 characteristic of benzyl substituents are present. There is another peak at m/e 131 which corresponds to the characteristic peaks in the mass fragmentations of all cinnamates. Occurrance of the peak in the present case may be explained as in Scheme - IIE.

Fragmentation pattern of p-benzoquinone-nitrone adduct follows quite a different pattern of mass fragmentations. In its fragmentation pattern, M^+, m/e 235; M+1 and M-1 peaks are also present. There are other major peaks viz. m/e 162 (R. Int. 9.7 sigma p.c. 20.2), 161 (R. Int. 9.4 sigma p.c. 19.62) and 152. The tentative formulation of these peaks are represented at Scheme - II F. The base peak at m/e 110 might have occurred according to Scheme - I.

The mass fragmentation pattern of the nitrone - TCNE adduct also shows marked dissimilarity with the general pattern. It possesses M (m/e 255), M 1, and M-1 ion fragments and the base peak at m/e 40 which follow the general pattern. But the other intense peaks at m/e 235, 206, 174, 162, 159, 146, 118 and 90 are new and explained as in Scheme - II G.

SCHEME - II.


A.
$C_4 - C_5$ FISSION
m/e 58
m/e 140
B.
TYPE - a
m/e 231
m/e 153
m/e 152
β - H REARRANGEMENT WITH N - C_6 FISSION
m/e 70
m/e 71
C.
EtO
m/e 154
D.
II
I
m/e 182
m/e 168
β-H REARRANGEMENT WITH N-O FISSION
α-CLEAVAGE
m/e 112


E.
Ph
O
N
COOMe
C3 — C4
CLEAVAGE
COOMe
Ph
O
N
COOMe
m/e162
MeO + [Ph— CH— CH= C =O]+
m/e 131
F.
O
N
O
O
-CO
-CO
-[O]
m/e163
m/e 152
NH
m/e 80
m/e 162
m/e 70
G
N
O
NC
N
NC
CN
CN
N=
O
N
CN
NC
CN
m/e 146.