# APPROACHES TO THE SYNTHESIS OF DIAZABIPHENYLENES

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MASTER OF PHILOSOPHY

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by

TERENCE WILLIAM PACKHAM

School of Chemistry
Thames Polytechnic
London

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C O N T E N T S

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## A B S T R A C T

Cyclopent-2-enone was prepared from either dicyclopentadiene or cycopentanone, and then converted to the photodimer cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione. A limited investigation was conducted into the Beckmann rearrangement of the dioxime(s) of this diketone and polyphosphoric acid then used as a catalyst to give the expected cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane-3,9-dione as the major product. The Schmidt reaction of the diketone gave the known cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione, which was converted into its N,N'-dibenzyl derivative.

The two dilactams were reduced to the corresponding amines cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane and cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane, with diborane, the structures of which were established on the basis of their spectroscopic properties and also those of their N,N'-bis(4-nitrobenzoyl) derivatives. The N,N'-dibenzyl derivative of the latter dilactam was reduced with lithium aluminium hydride to the known tertiary amine.

The catalytic dehydrogenation of the tertiary amine with palladium on carbon gave two products, one of which was shown to be 2,3'-bipyridine, and the other tentatively identified as either 3- or 4-benzylpyridine. A repetition of this reaction, using nitrobenzene as a solvent, again gave two products, one of which was established as benzylideneaniline and the other also tentatively identified as either 3- or 4-benzylpyridine. Following initial dehydrogenation studies on piperidine as a model compound, the catalytic dehydrogenations of the above two amines was attempted, both neat and in solution. However, it appeared that polymeric material only was produced and no identifiable products were observed for any of the reactions.

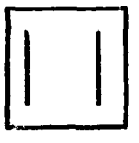
Attempts to prepare the 0,0'-dimethyl derivatives of the dilactams from the Beckmann and Schmidt reactions were unsuccessful, but following experiments with a model compound, piperazine-2,5-dione, treatment of the dilactams with triethyloxonium tetrafluoroborate gave the lactim ethers cis,trans,cis-3,9-diethoxy-4,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodeca-3,9-diene and cis,trans,cis-4,10-diethoxy-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene. A minor product cis,trans,cis-9-ethoxy-4,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodec-9-en-3-one was also isolated from the former reaction and the structures of all three compounds were established on the basis of their spectroscopic properties.

The attempted dehydrogenations of these two lactim ethers with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone did not give any diazabiphenylenes.

# I N T R O D U C T I O N

## CYCLOBUTADIENE

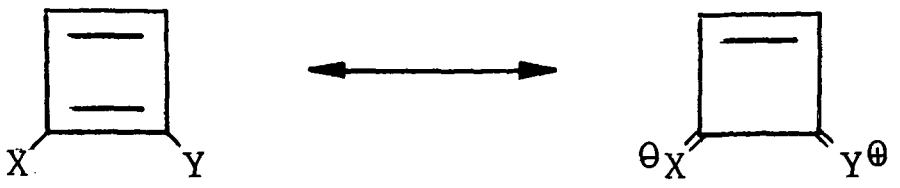
Cyclobutadiene (I) is the simplest member of the series of fully conjugated cyclic polyenes having the general composition $(C_2H_2)_n$. Before the development of molecular orbital theory, it was believed that cyclobutadiene would be a stable aromatic system with a chemistry similar to that of benzene. Various attempts [1,2,3,4] to prepare cyclobutadiene were unsuccessful until the 1960s when it was formed and shown to be a reactive unstable species [5,6].



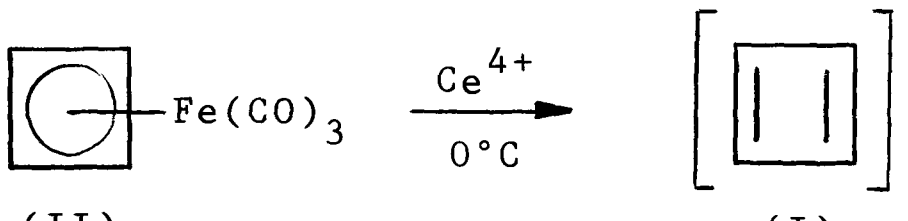
(I)

The reasons for the instability of cyclobutadiene became clear when modern molecular orbital theory was developed. Arising from this theory is the Hückel rule, which states that one of the requirements for aromaticity, and thus stability, is that the cyclic polyene should have a $(4n + 2)\pi$ electron system, where n is an integer. Since cyclobutadiene has a $4\pi$ electron system, the molecule would be expected to be highly unstable, having zero delocalisation energy. It is now known [7] that if valence-bond wave functions are constructed from all canonical structures and all configurations are included in the molecular orbital wave-functions, the two theories are completely equivalent.

Many attempts have been made to synthesise cyclobutadiene and cyclobutadienoid systems which would be stabilised by the incorporation of carefully chosen groups into the molecule. Roberts has proposed [8] that the cyclobutadiene system might be appreciably stabilised by a pair of neighbouring conjugative substitutents, one of which would be electron-releasing and the other electron-attracting.

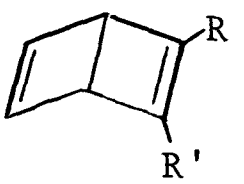



The first unambiguous formation of cyclobutadiene was in 1965, when Pettit [9] described the preparation of cyclobutadieneiron tricarbonyl (II) and its subsequent oxidation by ceric ion at 0°C. The generation of cyclobutadiene in the presence of a dienophile led to the formation of the $2\pi + 4\pi$adduct III, and the final proof for the existence of free cyclobutadiene under these conditions came a few years later [10,11,12] using either an optically active derivative of II or by supporting the dienophile on different polymers yielding products IV and V respectively.

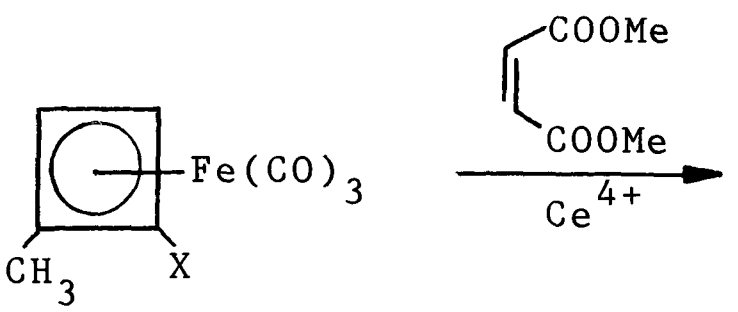



(II) (I)

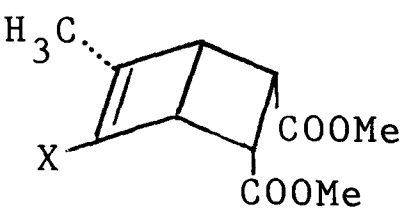
R, R' = COOMe, H | RC≡CR'



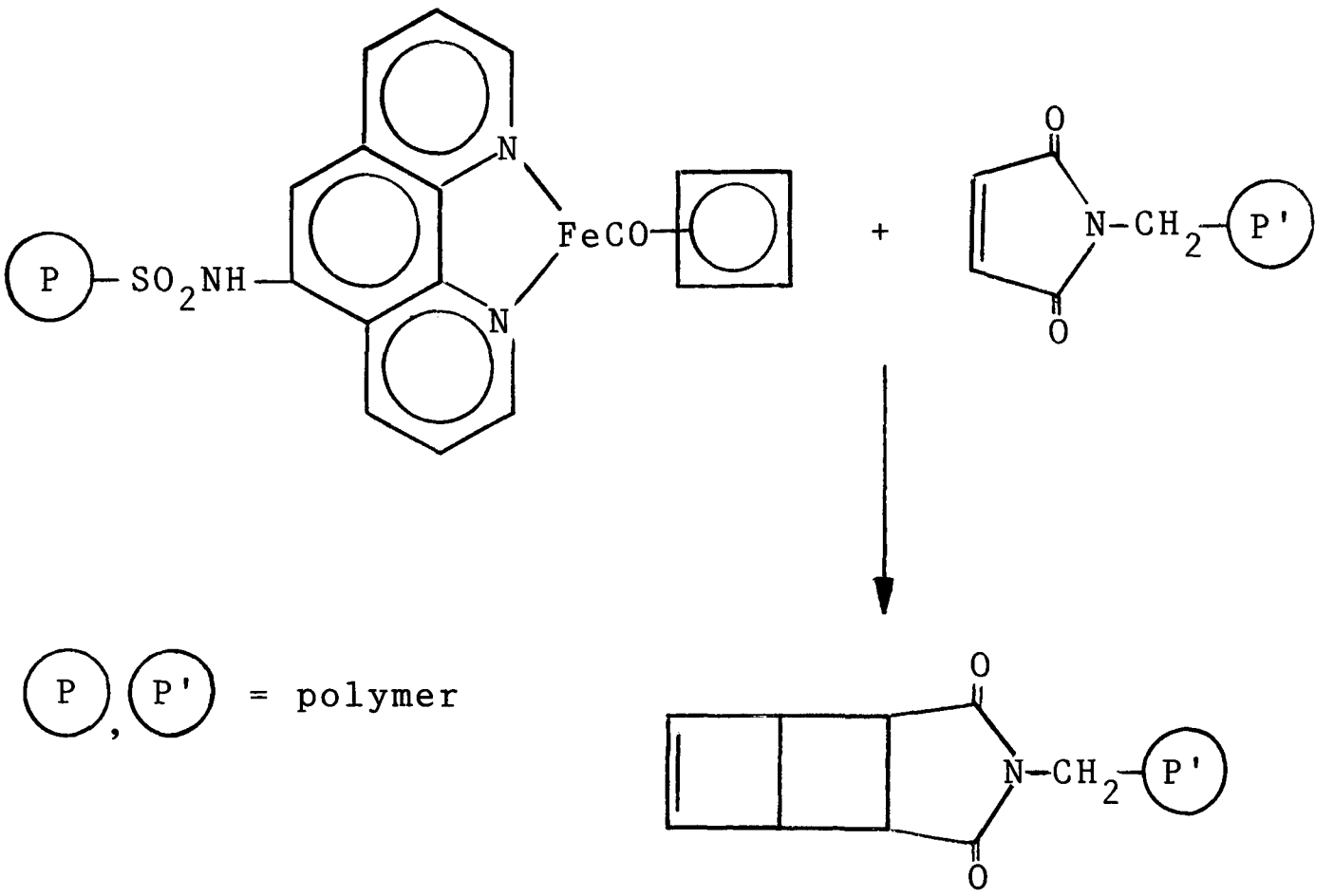

(III)




X = $CH_2OCH_3$, $CH_2CH_3$




(IV)

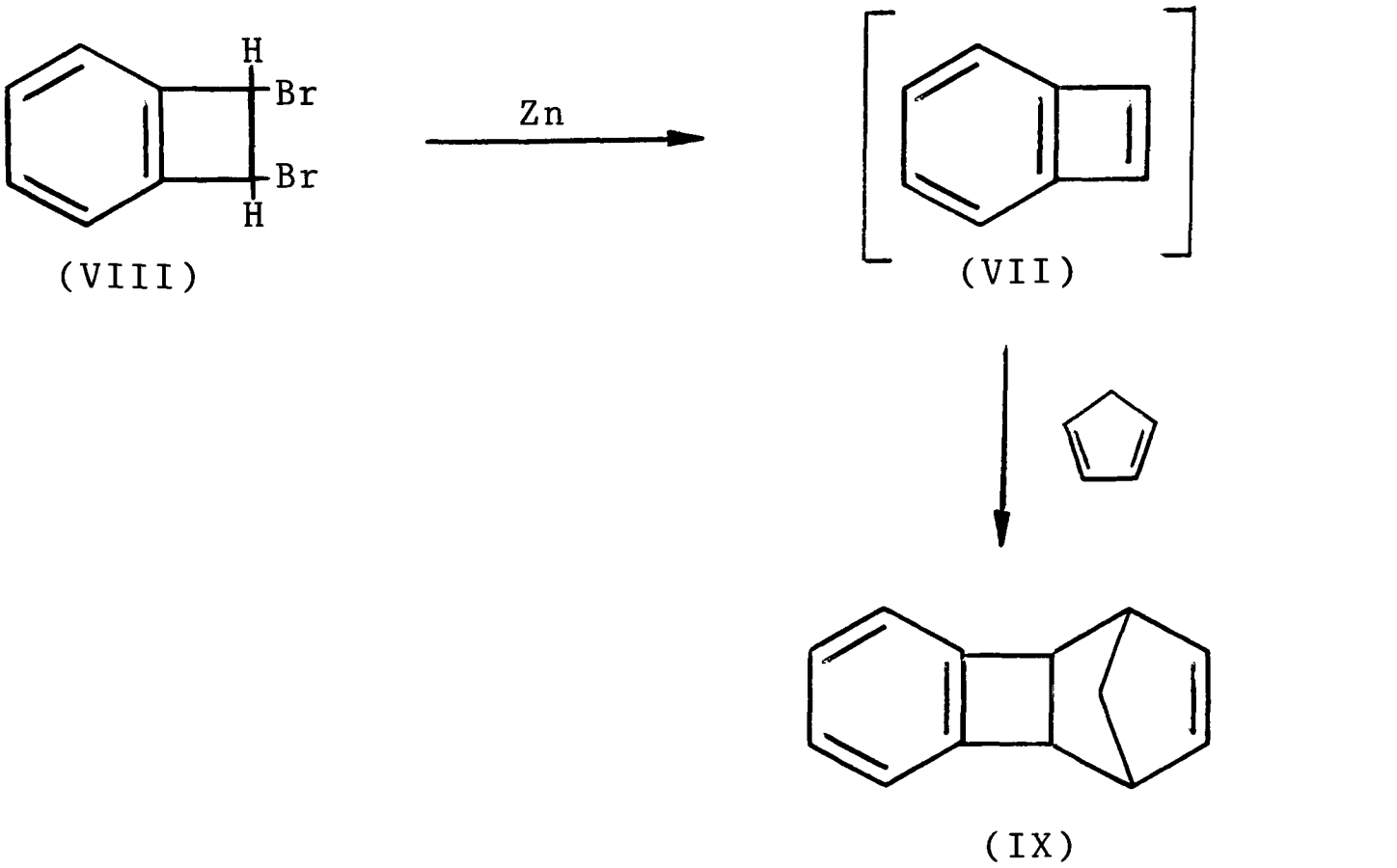



(V)

In the trapping experiments cyclobutadiene reacted in a stereospecific manner both as a diene and a dienophile, indicating that it has a singlet ground state rather than the triplet state (VI) at 0°C.

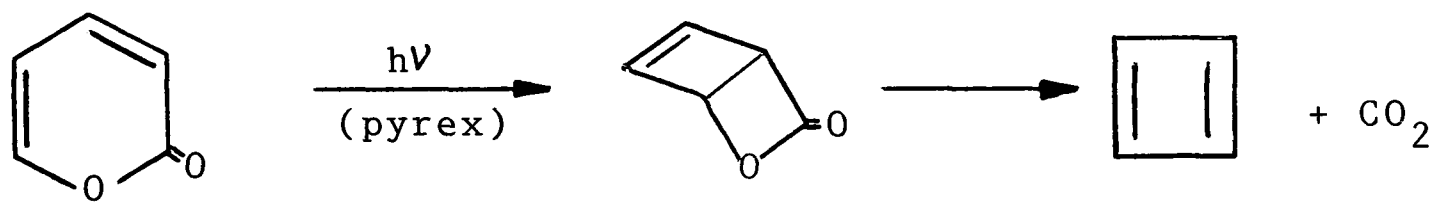
(VI)

Prior to the above work many attempts were made to synthesise compounds containing a stabilised cyclobutadienoid system [13]. All attempts to isolate the monobenzo compound benzocyclobutadiene (VII) failed although Nenitzescu et al [14] proved it exists as an intermediate in the zinc dust debromination of the dibromide VIII, by forming its adduct IX with cyclopentadiene.



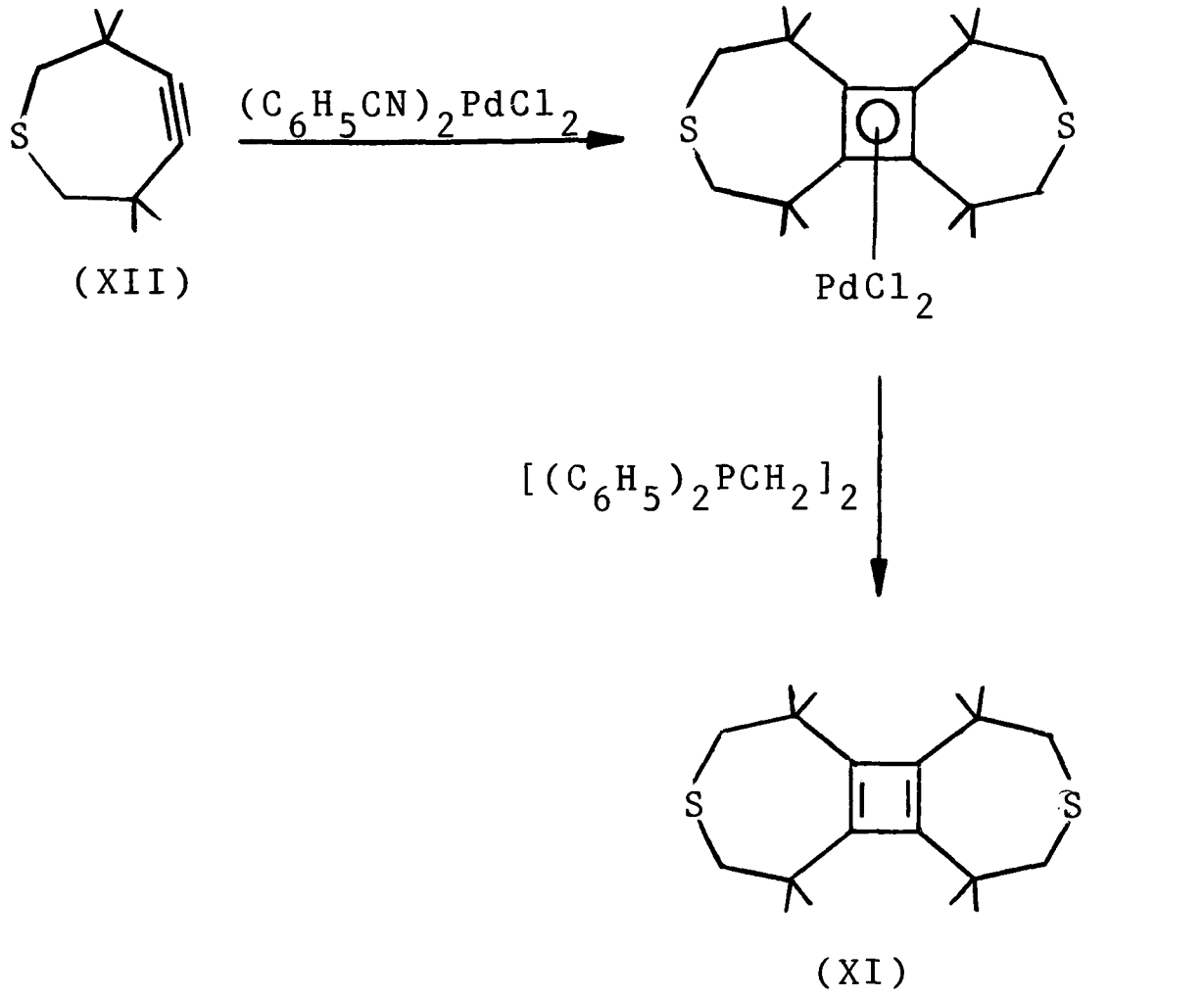

(VIII) (VII) (IX)

In contrast with its behaviour at 0°C, cyclobutadiene generated by pyrolysis of a photo-α-pyrone (X) at 800°C exhibited the characteristic reactions of diradicals. The half-life of cyclobutadiene in the gas phase, generated via this pyrolytic procedure, was shown to be 10ms at 35 mtorr, in reasonable agreement with the value of 2ms at 100 mtorr obtained in a different manner [15].




(X)

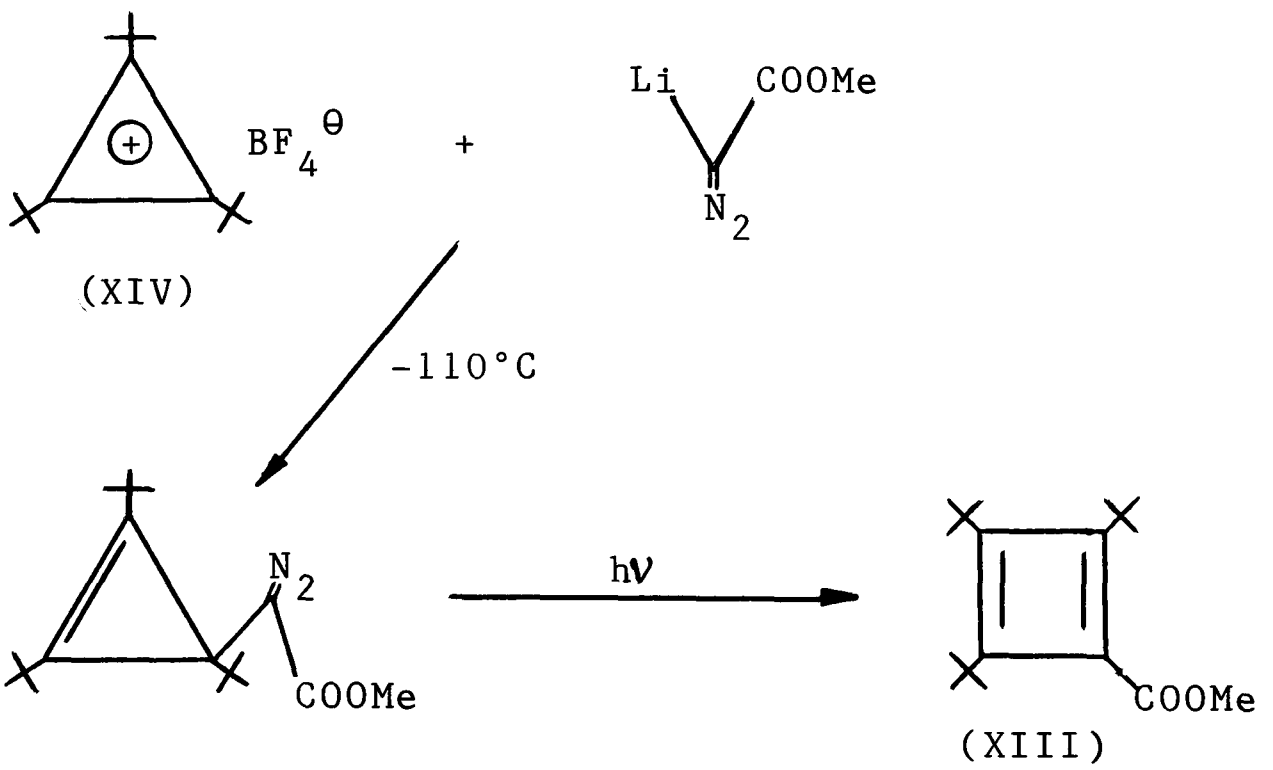
The first isolable crystalline derivative of cyclobutadiene, XI, was obtained in 1972 [16] by complexation of a palladium salt with the strained acetylene XII, followed by ligand exchange.




(XII)

(XI)

This was followed by the preparation of methyl tri-t-butylcyclobutadienecarboxylate (XIII) from the substituted cyclopropyl salt XIV as indicated below. X-ray analyses of the cyclobutadienes, XI and XIII, show that the central ring framework is completely planar and displays localised double bonds [17].

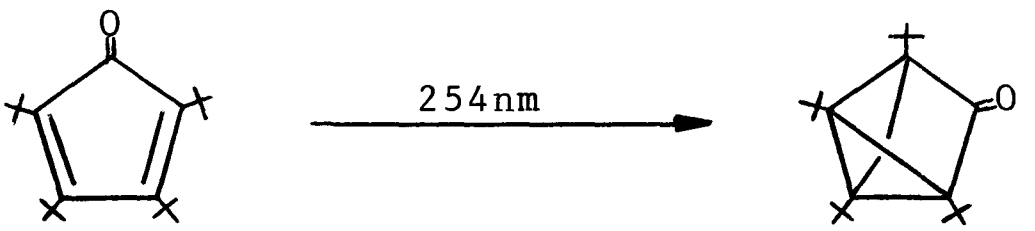



(XIV)

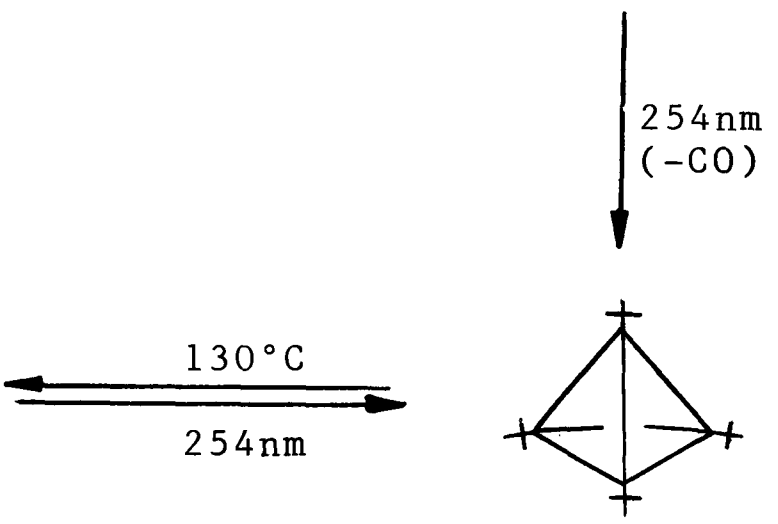
(XIII)

The first symmetrically substituted cyclobutadiene derivative (XV) has recently (1978) been prepared [18]. Irradiation of tetra-t-butylcyclopentadienone (XVI) produced the tricyclopentanone XVII, which on further irradiation rearranged to produce the highly strained tetrahedrane XVIII. On heating to 130°C, this in turn rearranged to yield tetra-t-butylcyclobutadiene (XV).

The steric repulsions between the t-butyl groups in XV distort the cyclobutadiene ring out of planarity so that the bond alternation is less than in other stable cyclobutadiene derivatives [19].



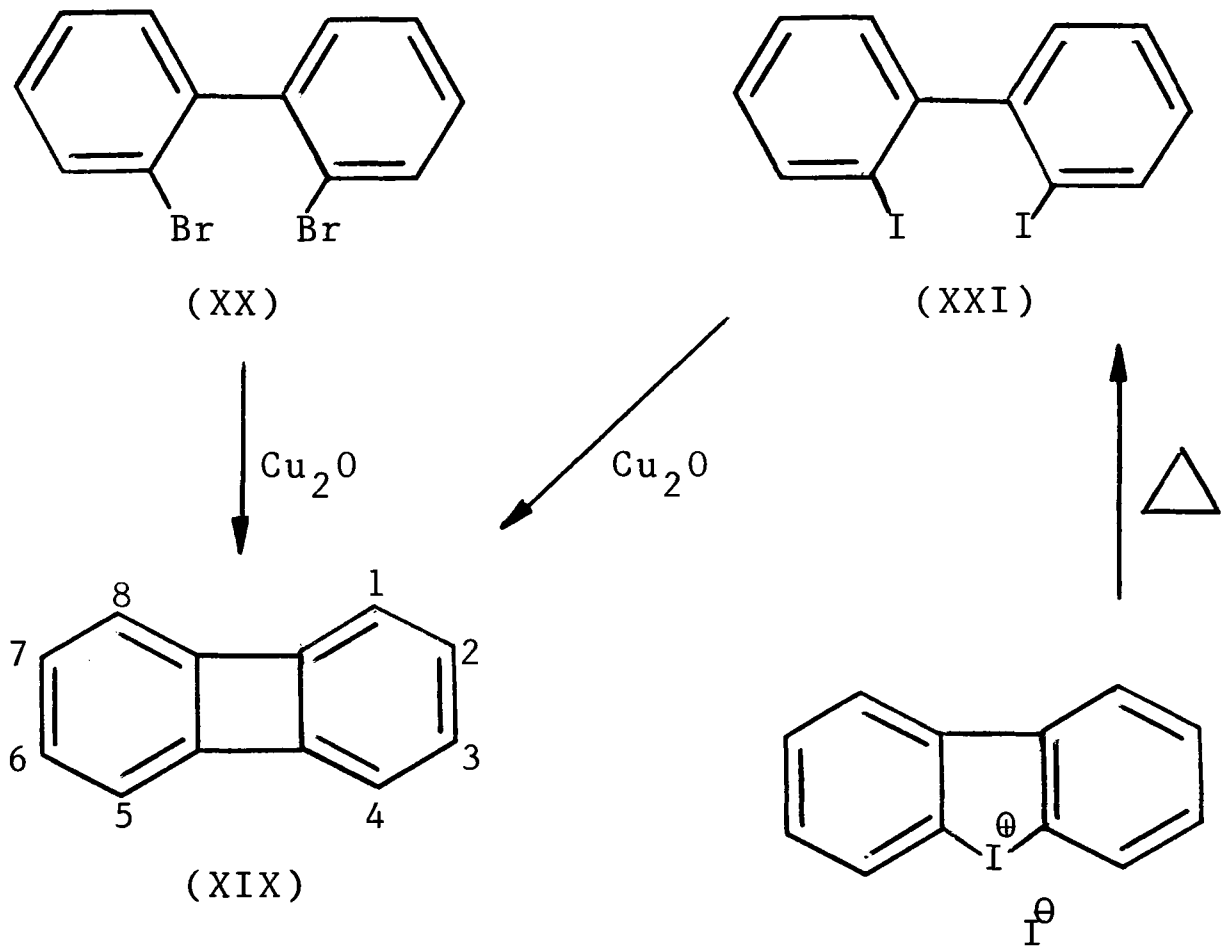

(XVI) (XVII)




(XV) (XVIII)

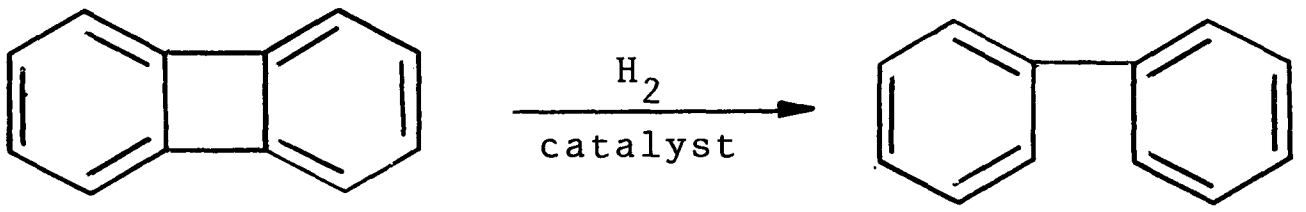
## BIPHENYLENE

Biphenylene (XIX), a formal dibenzo derivative of cyclobutadiene, is a very stable compound which has been known for over 40 years. Many attempts were made to prepare biphenylene before it was first synthesised by Lothrop [20], who obtained it by heating 2,2'-dihalobiphenyls with cuprous oxide. The poor yields which were obtained using 2,2'-dibromobiphenyl (XX) were improved by the use of either 2,2'-di-iodobiphenyl (XXI) or biphenyleneiodonium iodide (XXII), which rearranges to the di-iodo compound during the reaction.



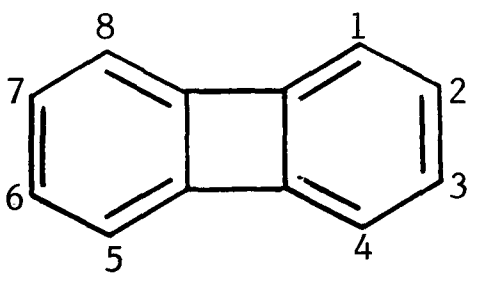

It has since been found that the reactions of several 2,2'-di-iodobiphenyls with copper gave the corresponding biphenylenes in yields superior to those obtained with cuprous oxide [21].

Biphenylene undergoes electrophilic substitution somewhat more readily than benzene and the acetoxymercuri, acetyl, benzoyl, bromo, chloro, iodo and nitro groups have been introduced by direct substitution, usually in good yield and always at the 2-position. Like benzene it is very resistant to attack by radicals, acetoxylation with lead tetra-acetate occurred in only 1.5% yield [22] and bromination with N-bromosuccinimide did not proceed at all [23]. Hydrogenation of biphenylene using either a red hot copper catalyst [20] or activated Raney nickel [22,24] at room temperature to yield biphenyl, (XXIII) is a useful method for determining the orientation of substituents in substituted biphenylenes.

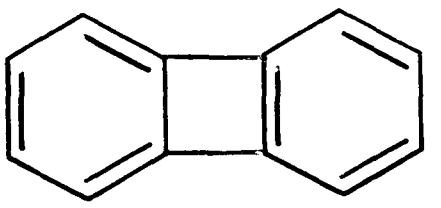



(XIX) (XXIII)

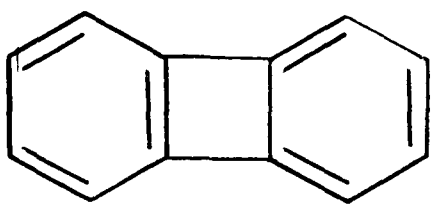
Biphenylene has 5 canonical forms (XXIV), (XXV), (XXVI), (XXVII), (XXVIII) and simple resonance theory leads to the erroneous conclusion that the 1,2 bond has more double-bond character than the 2,3 bond. However, if it is assumed that the high-energy cyclobutadienoid resonance forms XXVII and XXVIII only contribute very little to the resonance hybrid, the calculated bond orders and bond lengths are in accord with the experimentally determined values, as are those calculated from molecular orbital theory.



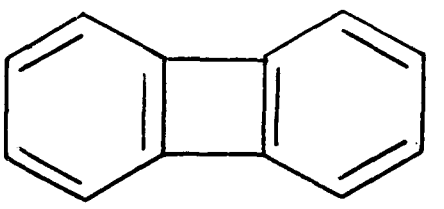

(XXIV)



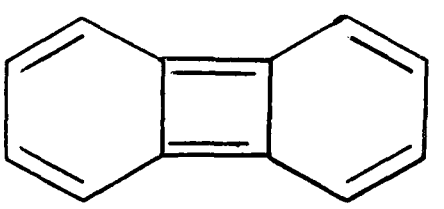
(XXV)



(XXVI)



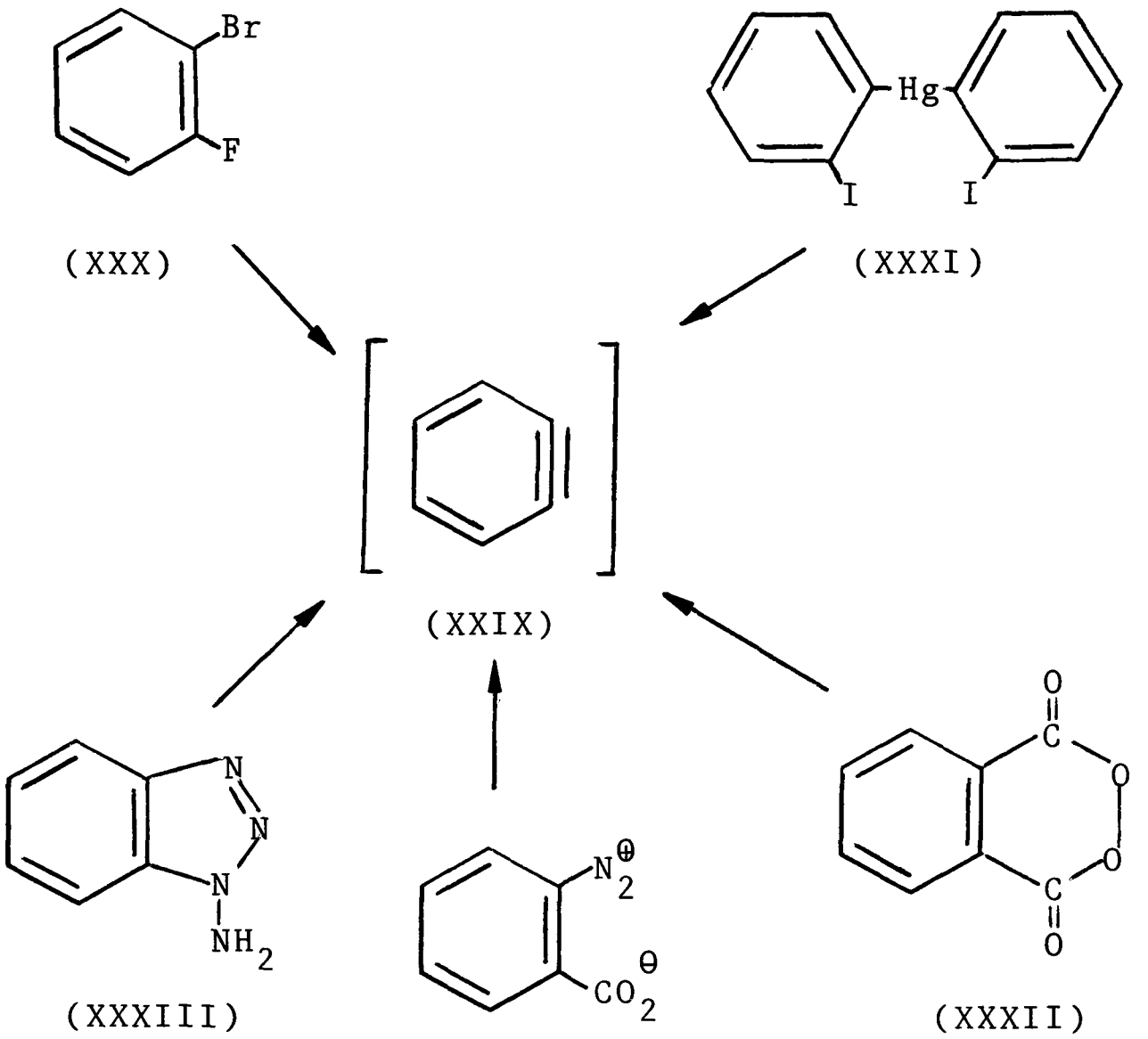
(XXVII)



(XXVIII)

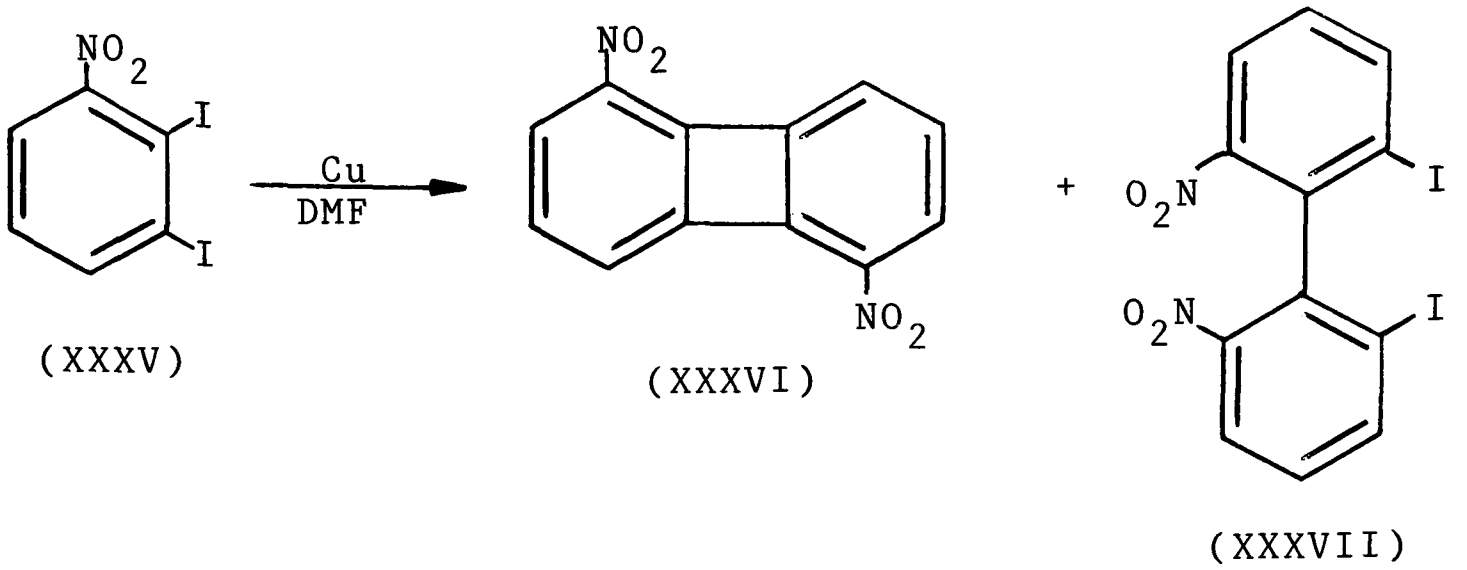
A number of theoretical studies have predicted that nucleophilic, electrophilic and radical substitution [25] will occur exclusively at the 2-position. This has been confirmed experimentally for electrophilic substitution and to some extent for radical substitution. If the substituent is electron-donating further substitution occurs at the 3-position, but for an electron-withdrawing substituent subsequent substitution takes place at the 6-position.

The dimerisation of benzyne (XXIX) is a useful synthetic method for the generation of biphenylene. Benzyne may be generated from a variety of precursors, such as the dehalogenation of 2-fluorobromobenzene (XXX) with lithium amalgam in ether [26,27], which afford biphenylene in a 24% yield, and the low-pressure, gas-phase, flash pyrolysis of either bis(2-iodophenyl)mercury (XXXI) or phthaloyl peroxide (XXXII) at 600°C which give biphenylene in yields of 54% and 27% respectively [28]. Biphenylene may also be obtained in an 83% yield by the oxidation of 1-aminobenzotriazole (XXXIII) with lead tetra-acetate [29] and in 21-30% yield by the rapid decomposition of benzenediazonium carboxylate (XXXIV) in boiling 1,2-dichloroethane [30]. Benzenediazonium carboxylate may be easily obtained by the aprotic diazotisation of readily available anthranilic acid.




(XXXIV)

Several substituted biphenylenes have been prepared by treatment of the appropriately substituted o-dihalobenzenes with dehalogenating agents. The reaction between 2,3-di-iodonitrobenzene (XXXV) and copper-bronze in dimethylformamide gave the dinitrobiphenylene XXXVI in 43% yield, other products being the di-iodonitrobiphenyl XXXVII and the tetranitrophenylene XXXVIII [31]. It has been suggested that this reaction proceeds via formation and dimerisation of the substituted benzyne.

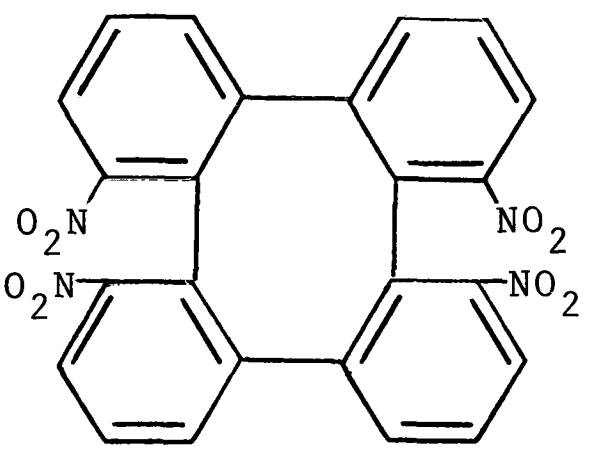


(XXXV)

(XXXVI)

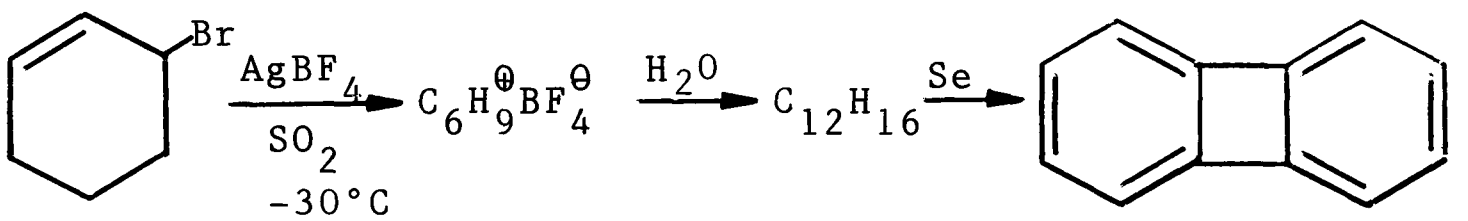
(XXXVII)

+



(XXXVIII)

It is of interest to note that only one synthesis of biphenylene by a dehydrogenation procedure appears to have been reported; Olah and Tolgyesi [32] found that addition of water to the carbonium ion salt XXXIX obtained by reaction of 3-bromocyclohexene with silver fluoroborate gave, among other products, a small amount of hydrocarbon $C_{12}H_{16}$ which they called octahydrobiphenylene as dehydrogenation with selenium gave biphenylene.



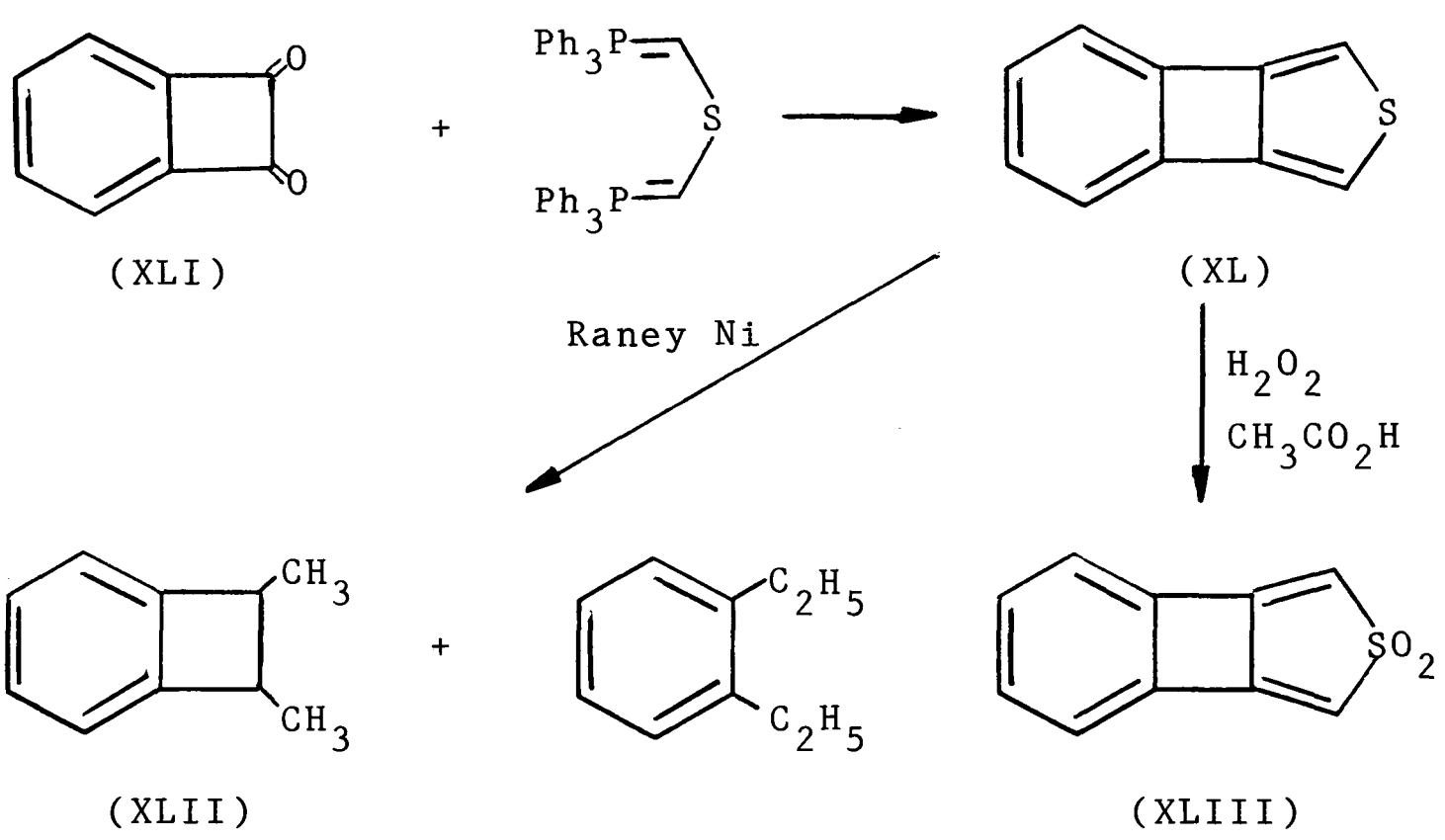
(XXXIX)

## Heterocyclic Analogues of Biphenylene

The study of the heterocyclic analogues of biphenylene would be of particular interest in connection with the influence of the hetero atoms on bond structure and the stability of the four-membered ring. An increasing number of investigations on the synthesis and reactions of such compounds are being reported.

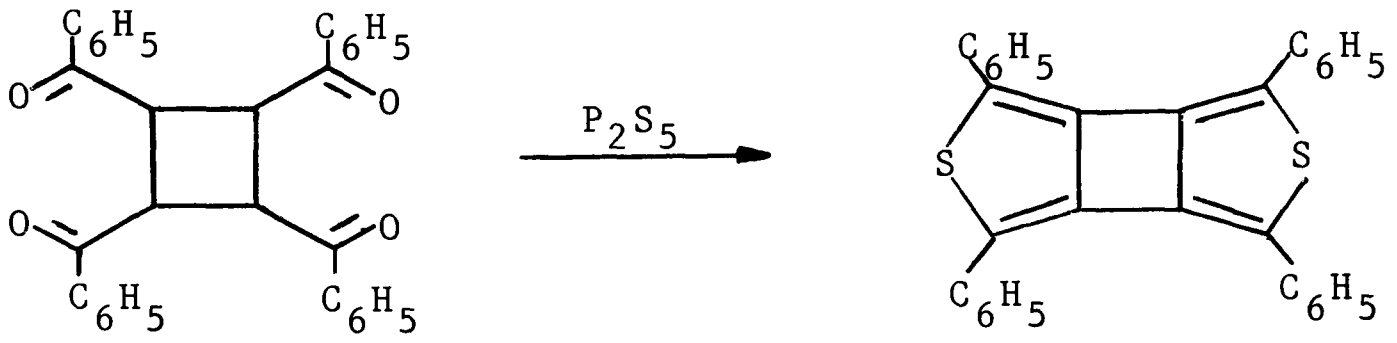
## Sulphur Analogues

In 1970, Garratt and Vollhardt [33] obtained benzo [3,4]-cyclobuta[1,2-c]thiophene (XL) by the Wittig reaction of 1,2-benzocyclobutadienoquinone [34] (XLI) with a sulphur triphenylphosphorane in dry ether under nitrogen.



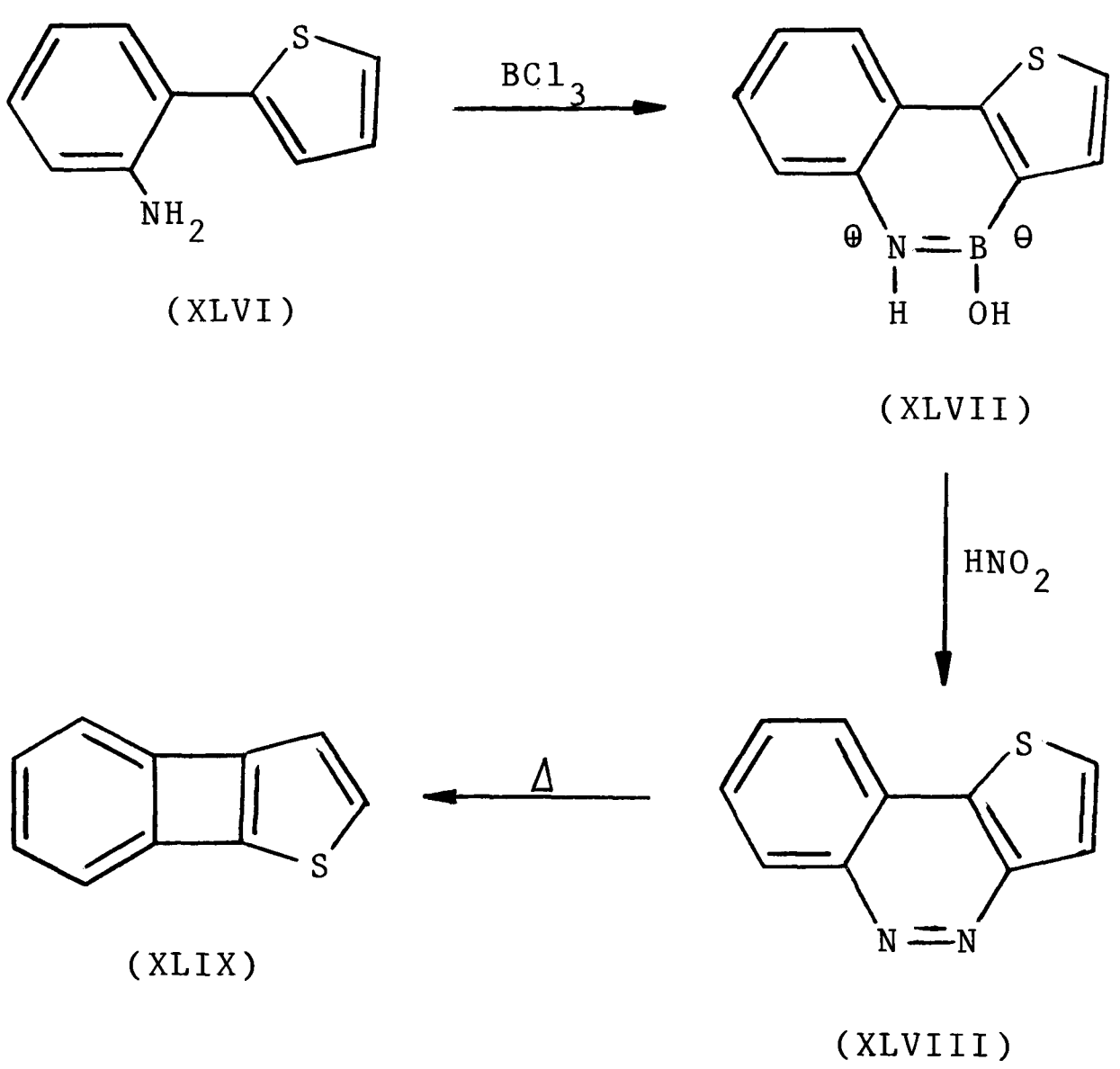

The compound was obtained as a crystalline solid in 14% yield m.p. 98-98.5°C. Desulphurisation with Raney nickel gave 1,2-dimethylbenzocyclobutene (XLII) and 1,2-diethylbenzene. Oxidation of the compound with hydrogen peroxide in acetic acid yielded benzo[3,4]cyclobuta-[1,2-c]thiophene 2,2-dioxide (XLIII), m.p. 213-215°C.

More recently, Garrat and Neoh [35] prepared a biphenylene analogue containing two five-membered heterocycles. Thus, treatment of cis, trans, cis-1,2,3,4-tetrabenzoylcyclobutane [36] (XLIV) with phosphorus pentasulphide in boiling pyridine gave a low yield of tetraphenyl-2,5-dithiabisnorbiphenylene (XLV), m.p. 194-194.5°C.




(XLIV) (XLV)

The isomer of the thiophene XL has been prepared by Barton and Lapham [37] using the thermal extrusion of nitrogen technique, which has also been used to prepare several diazabiphenylenes (see later).

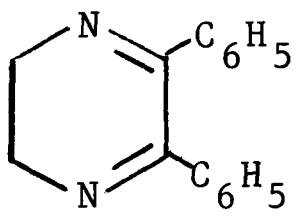



(XLVI) (XLVII) (XLVIII) (XLIX)

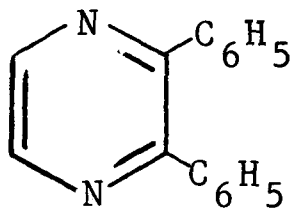
Aprotic diazotisation of 2-nitroaniline dissolved in thiophene gave 2-(2-nitrophenyl)thiophene, which was reduced to the amine XLVI with sodium hydrosulphide. Cyclisation of XLVI with boron trichloride in refluxing xylene, followed by hydrolysis gave the benzo[e]thieno-[3,2-c]azaborine (XLVII), which, on treatment with nitrous acid, was converted into thieno[3,2-c]cinnoline (XLVIII). Passage of this compound through a silica tube at 830°C and 0.005 torr gave, after purification, benzo[3,4]cyclo-buta[1,2,-b]thiophene (XLIX) as a pale yellow oil. This compound is much less stable than either biphenylene or the isomer XL, undergoing extensive decomposition within a few hours at room temperature. This can readily be accounted for by the fact that the four-membered ring in biphenylene and XL contains very little cyclobutadiene character, whereas in the thiophene XLIX the four-membered ring has a much higher bond order and is therefore correspondingly less stable.

Nitrogen Analogues

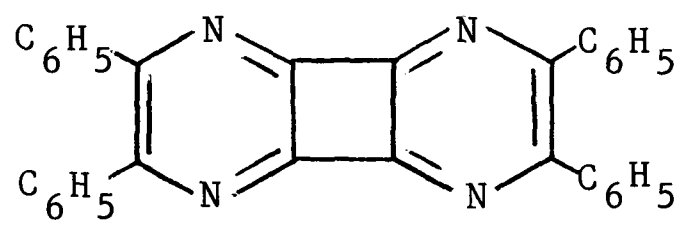
A tetra-azabiphenylene was postulated as early as 1893 by Mason and Dryfoos [38], who reported that the reaction of 2,3-dihydro-5,6-diphenylpyrazine (L) with alcoholic potassium hydroxide gave mainly 2,3-diphenylpyrazine (LI) together with a compound called "tetraphenyldipiazine". They assigned the structure LII to this compound on the basis of its elemental analysis and molecular weight determination, although no attempt was made to confirm the structure.



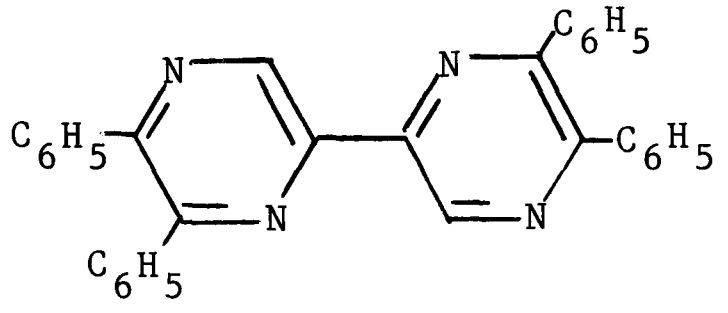

(L)



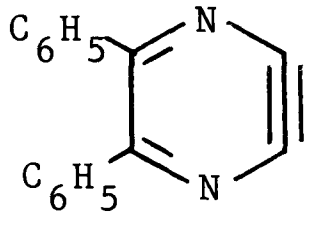

(LI)



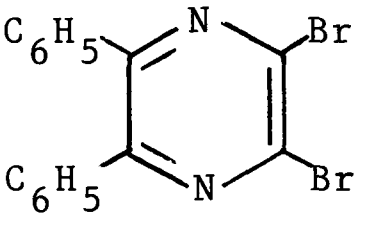

(LII)



(LIII)



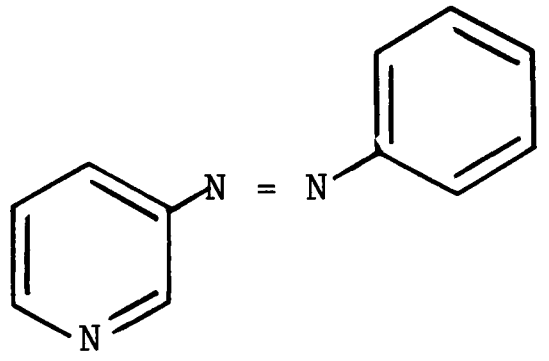
(LIV)



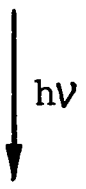
(LV)

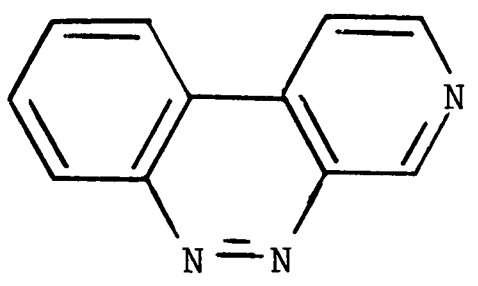
Recently, England and McDougall reinvestigated this reaction and showed that "tetraphenyldipiazine" was in fact 5,5',6,6'-tetraphenyl-2,2'-bipyrazinyl (LIII) [39]. An attempt to prepare a 3,3'-dihalogeno derivative of this compound as a possible precursor of the tetra-azabiphenylene LII was unsuccessful and an alternative route, the possible generation and subsequent dimerisation of a pyrazyne (LIV) by treatment of 2,3-dibromo-5,6-diphenylpyrazine (LV) with copper in dimethylformamide (cf. ref. 31) gave much intractable material and a small amount of compound LIII, formation of which need not have involved the pyrazyne as an intermediate.

The first two monoazabiphenylenes to be prepared were recently reported by Barton and Walker [40].

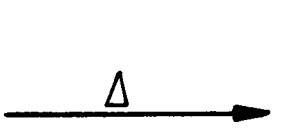


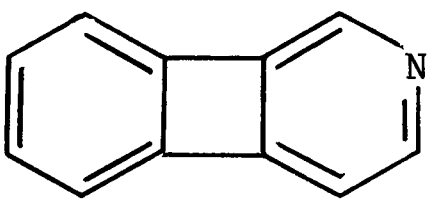
(LVI)



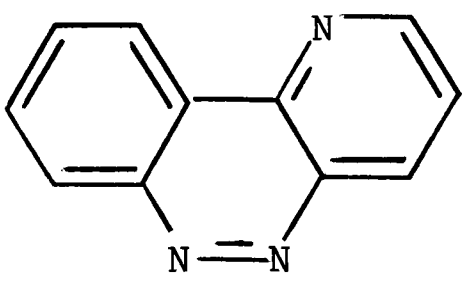
(LVII)



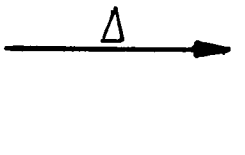



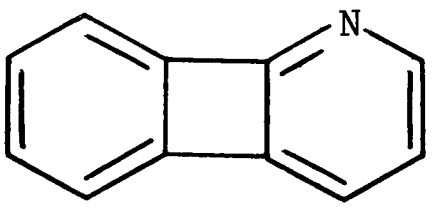
(LVIX)

+



(LVIII)

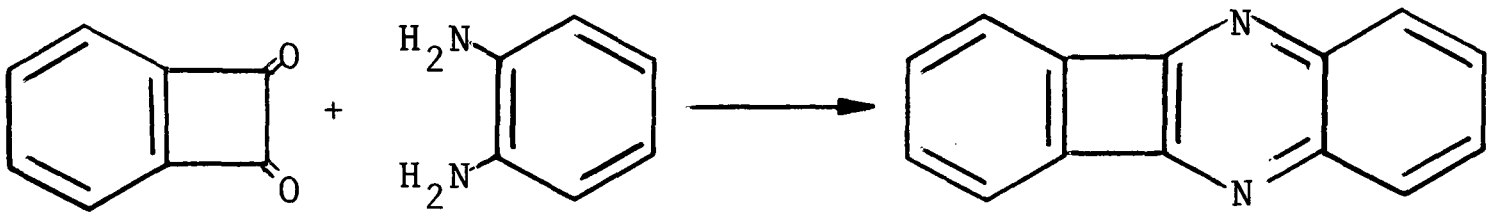


(LX)

Irradiation of a 1% solution of 3-phenylazopyridine (LVI) in concentrated sulphuric acid yielded mainly 2,9,10-triaza-phenanthrene (LVII), together with a smaller quantity of 4,9,10-triazaphenanthrene (LVIII). Vacuum thermolysis of the 2,9,10-isomer (LVII) gave 2-azabiphenylene (LVIX), m.p. 88.5-89.5°C, whilst the minor isomer (LVIII) gave 1-azabiphenylene (LX), m.p. 70-71°C, after similar treatment.

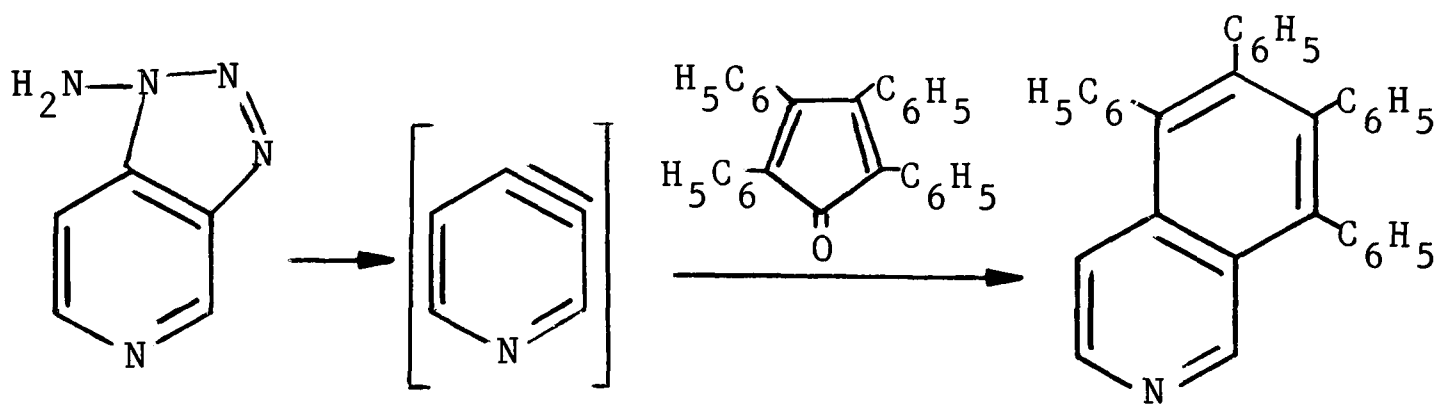
The first successful synthesis of a diaza analogue of biphenylene was reported in 1963 by Cava and associates [34], who found that treatment of 1,2-benzocyclobutadienoquinone (XLI) with an equimolar quantity of 1,2-diaminobenzene gave 5,10-diazabenzo[b]biphenylene (LXI) as long white needles, m.p. 238-239°C.



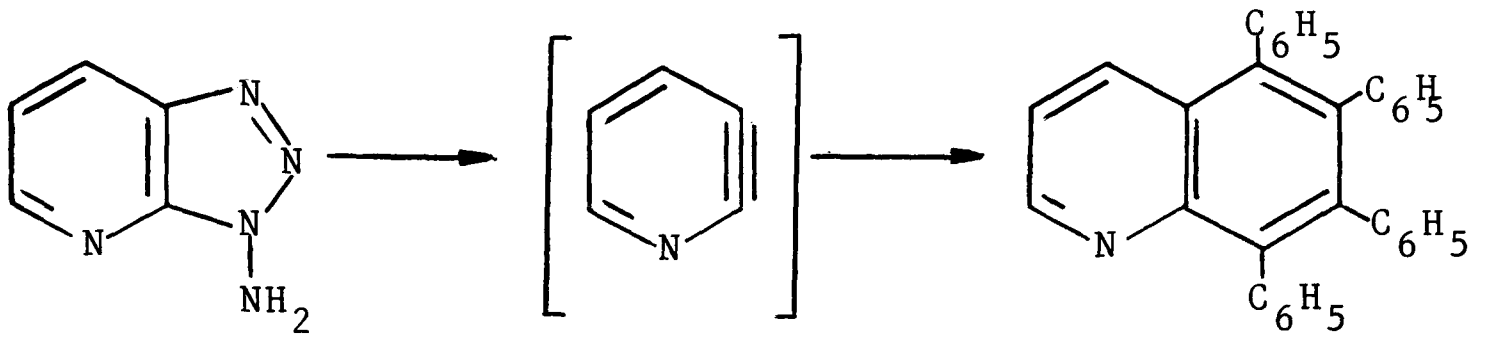
(XLI) (LXI)

Since the dimerisation of benzyne is a useful synthetic route for the preparation of biphenylene, several workers have attempted to prepare diazabiphenylenes with the nitrogen in different rings by the generation and subsequent dimerisation of pyridynes.

Fleet and Fleming [41] prepared 1-aminotriazolo[4,5-c]-pyridine (LXII) and 3-aminotriazolo[4,5-b]pyridine (LXIII) as potential precursors of diazabiphenylenes; they also prepared the corresponding aminotriazoloquinolines. Lead tetra-acetate oxidation of the above aminotriazoles in the presence of tetraphenylcyclopentadienone gave products consistent with the intermediacy of 3,4- and 2,3- pyridynes.

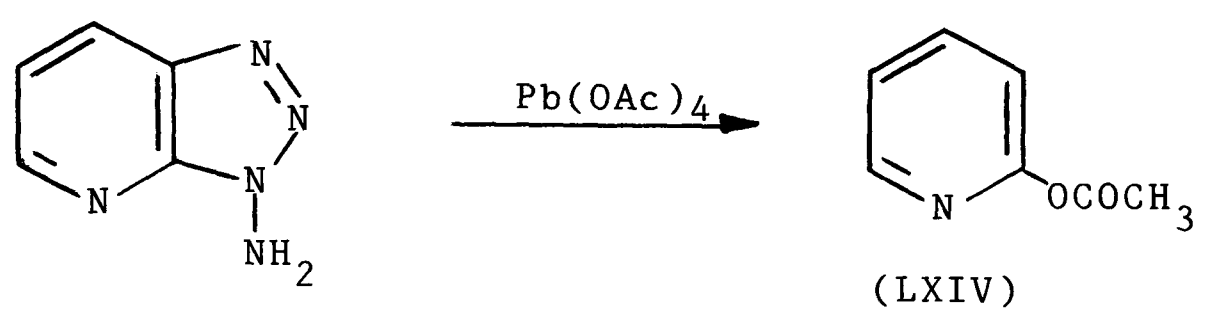


(LXII)



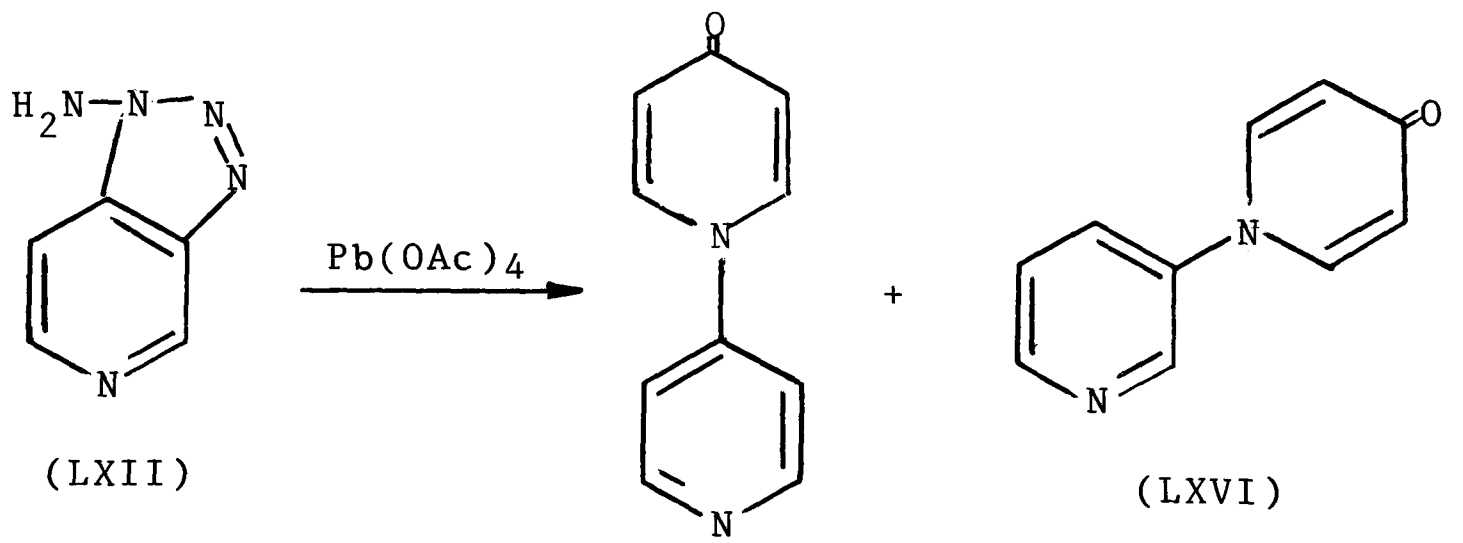
(LXIII)

Attempts to prepare diazabiphenylenes by the oxidation of LXIII in the absence of tetraphenylcyclopentadienone yields mainly 2-acetoxypyridine (LXIV) resulting from the addition of acetic acid to 2,3-pyridyne. However, in the case of the 3,4-pyridyne precursor LXII the main products were N-4'-pyridyl-4-pyridone (LXV) and another compound which was tentatively identified as N-3'-pyridyl-4-pyridone (LXVI). No evidence for the dimerisation of pyridynes could be found.



(LVII)

(LXIV)



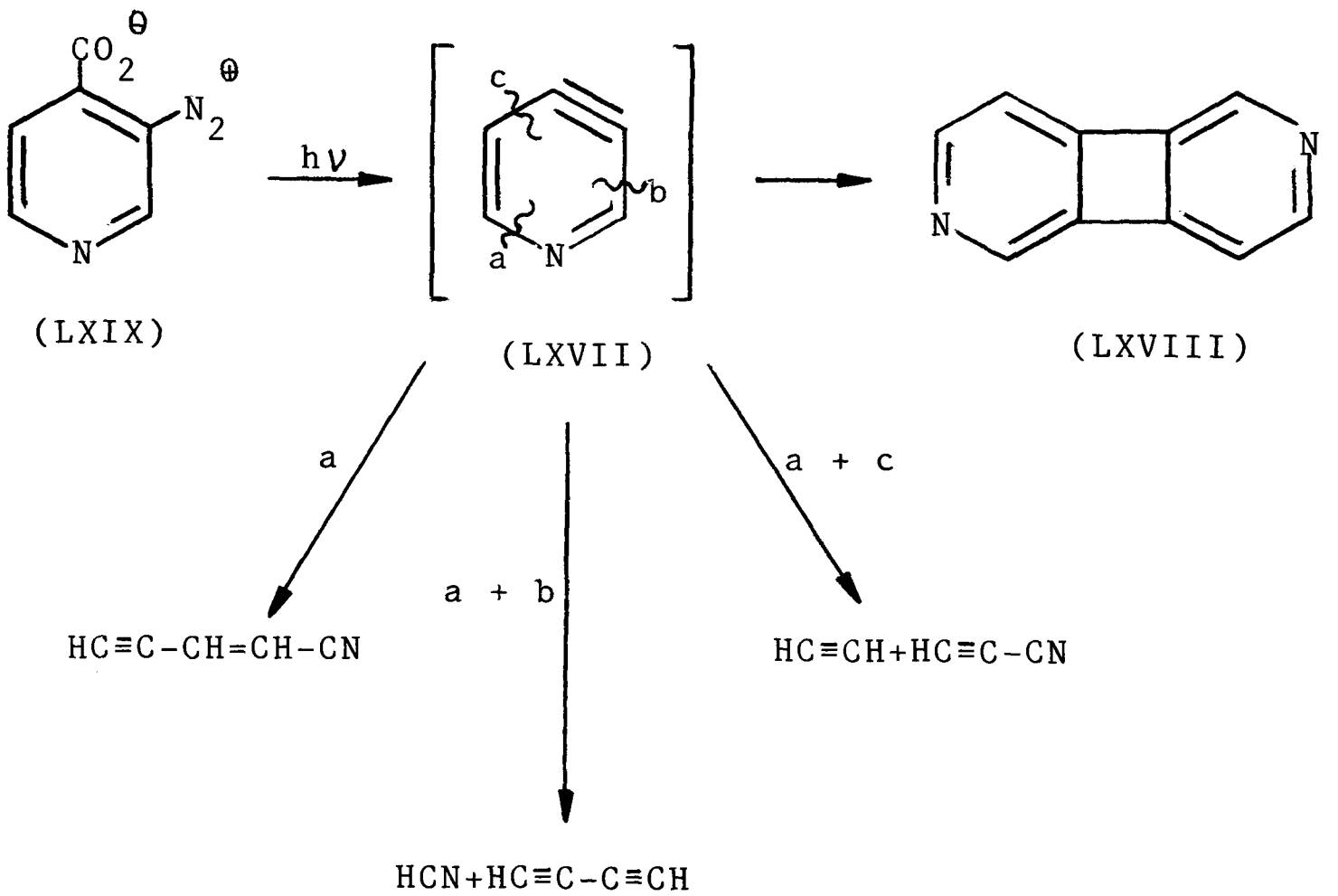
(LXII)

(LXV)

(LXVI)

The corresponding 2,3- and 3,4-quinolyne precursors gave analogous results.

In 1972 Kramer and Berry [42] reported a study of the unimolecular decomposition of gaseous 3,4-pyridyne [43] (LXVII) and its dimerisation to 2,6-diazabiphenylene (LXVIII). The method consisted of photolysing solid pyridine-3-diazonium-4-carboxylate [44] (LXIX) and monitoring the reaction products by time-of-flight mass spectrometry. From the results of mass spectrometry, the authors concluded that 3,4-pyridyne (LXVII) underwent unimolecular decomposition as shown below as well as dimerisation to 2,6-diazabiphenylene.

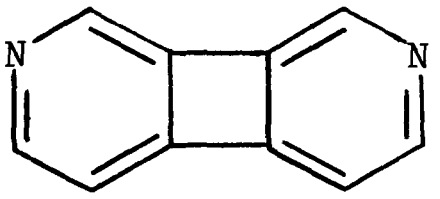



Dimerisation occurred in poor yield (5%) in contrast to benzyne which dimerises to biphenylene in good yield (35%) under similar conditions and shows no unimolecular decay [45]. The authors have explained this difference in the chemistry on the basis of the energy contents of the two species (3,4-pyridyne and benzyne). The resonance energy of pyridine is $\triangleq$ 15Kcal $mol^{-1}$ less than benzene, a C-N bond is $\triangleq$ 10Kcal $mol^{-1}$ weaker than a C-C bond and a C≡N bond is

≙ 13Kcal $mol^{-1}$ stronger than a C≡C bond. This net difference of ≙ 38Kcal $mol^{-1}$ it was suggested, opens many bond breaking possibilities in LXVII. The authors demonstrated that the unimolecular reaction could be inhibited by the addition of an inert gas, and the yield of 2,6-diazabiphenylene consequently increased to 12%.

The dimer (LXVIII) was isolated as a white solid, m.p. 169-169.5°C and high resolution mass spectrometry confirmed its molecular weight. The strongest band in the infra-red spectrum was at 838$cm^{-1}$ characteristic of a 1,2,4-trisubstituted benzene; and C≡N stretching vibrations were absent. The ultraviolet spectrum indicated extended conjugation with maxima at 338, 325, 312, 297, 283, 241 and 234nm. The NMR spectrum consisted of three sets of protons in the ratio of 1:1:1.

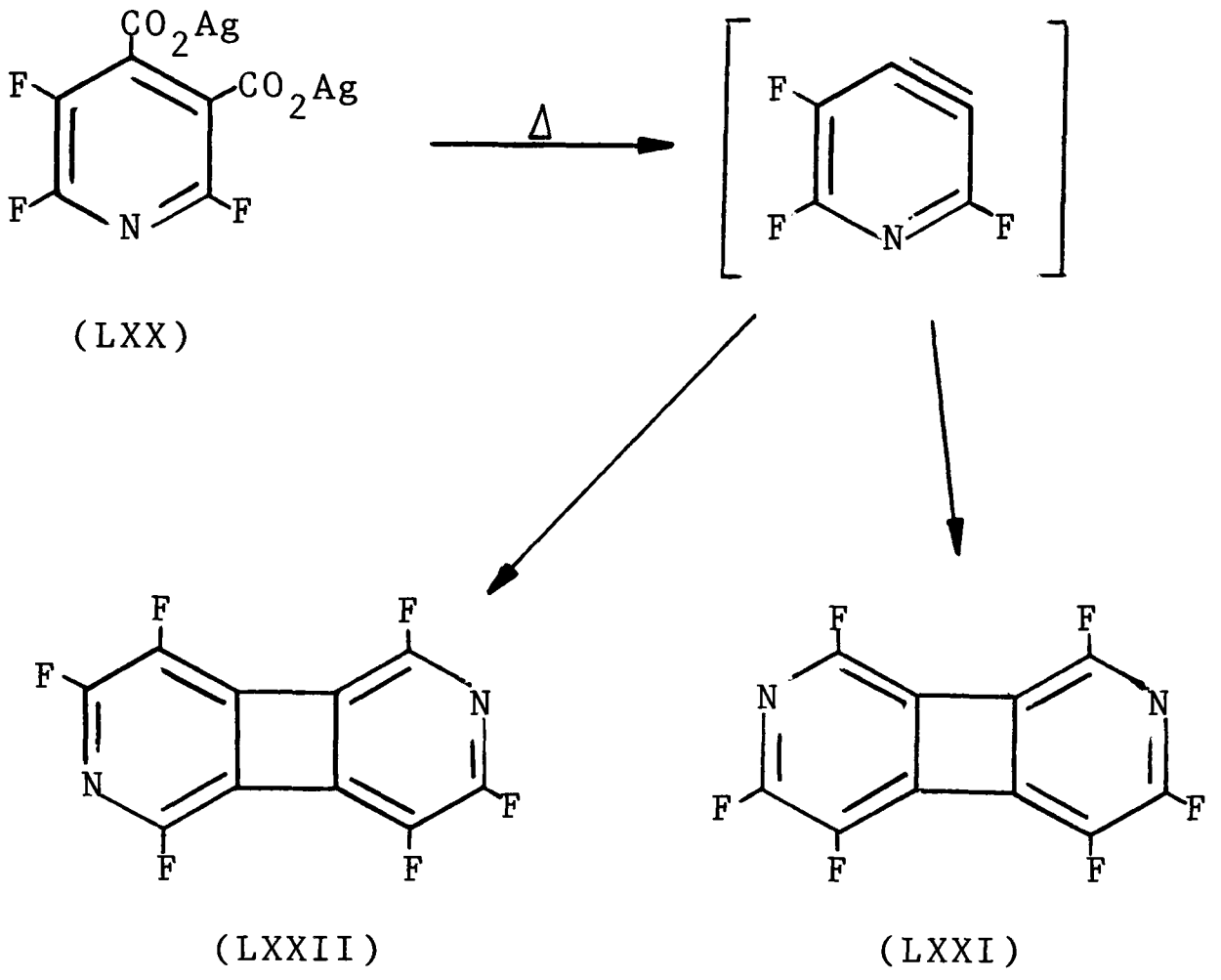
The authors were uncertain whether they had prepared the 2,6-isomer (LXVIII) or 2,7-diazabiphenylene (LXIX). However,




(LXIX)

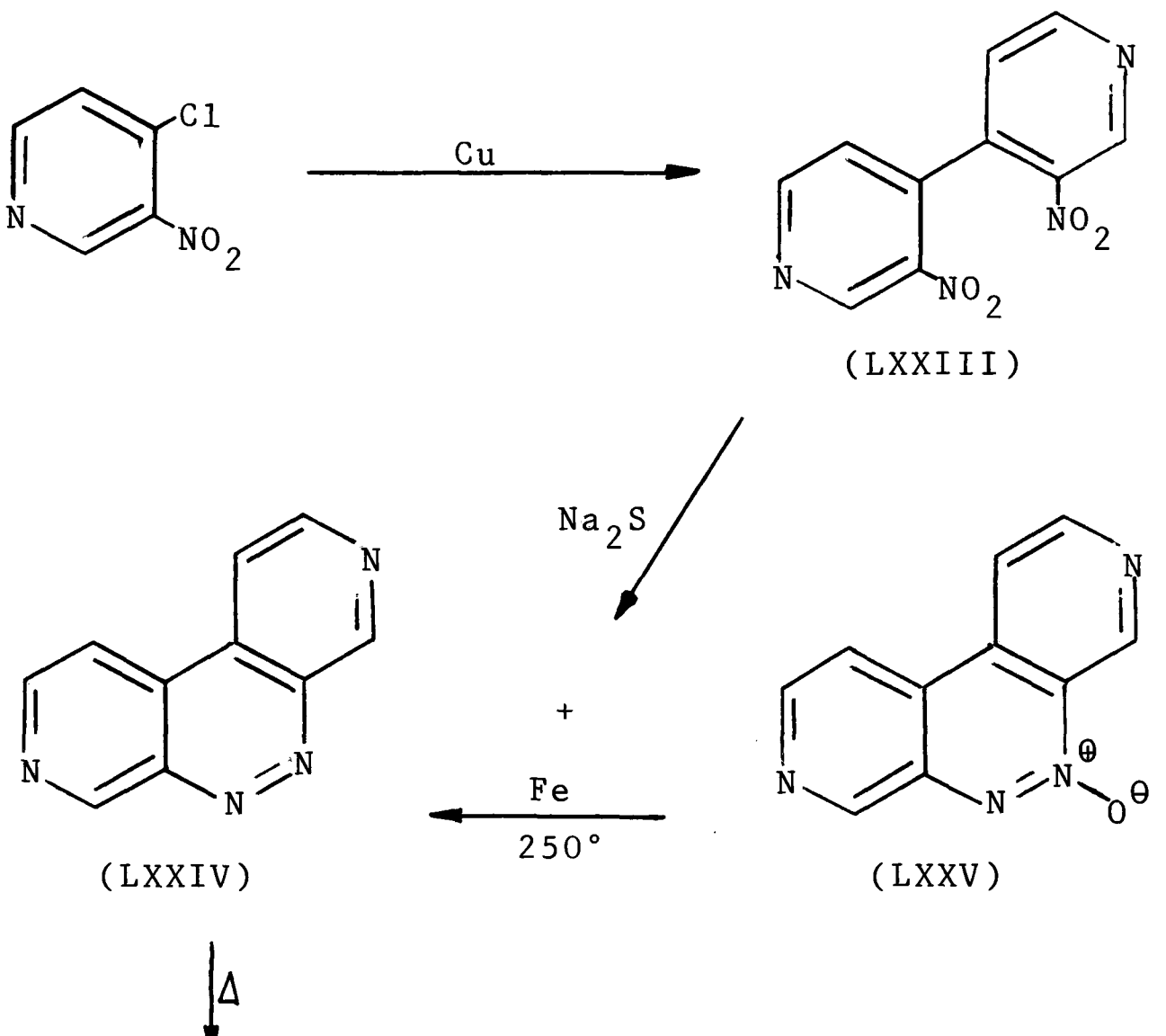
the later preparation of the 2,7-isomer by MacBride [46] confirmed that Kramer and Berry had indeed prepared 2,6-diazabiphenylene.

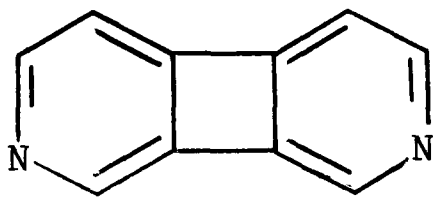
The dimerisation of a pyridyne has also been reported by another group of workers [47]. Thus, pyrolysis of the di-silver salt of 2,5,6-trifluoropyridine-3,4-dicarboxylic acid (LXX) gave a mixture of the two perfluorodiazabiphenylenes (LXXI) and (LXXII).




The thermal extrusion of nitrogen from tetra-azaphenanthrenes has proved to be a useful synthetic route to diazabiphenylenes,[46,48,49] and is similar to that used to prepare the monoazabiphenylenes,[40] octachlorobiphenylene[50] and biphenylene itself[50].

Thus, MacBride[46] converted 4-chloro-3-nitropyridine into 3,3'-dinitro-4,4'-bipyridyl (LXXIII), which upon reduction with aqueous sodium sulphide yielded a mixture of 2,7,9,10-tetra-azaphenanthrene (LXXIV) and its N-oxide (LXXV). After deoxygenation of the N-oxide with iron powder at 250°C, the tetra-azaphenanthrene (LXXIV) was pyrolysed by passing through a silica tube at 900°C and 0.04 torr to give 2,7-diazabiphenylene (LXXVI) as pale yellow crystals, m.p. 192-192.5°C.



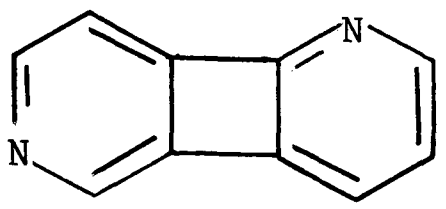




(LXXVI)

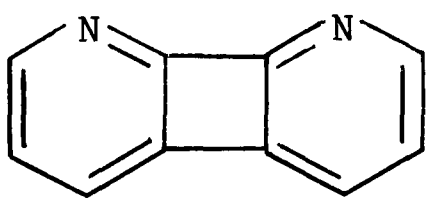
The strongest band in the infra-red spectrum of LXXVI was at 834cm$^{-1}$ and the ultraviolet spectrum exhibited maxima at 326.5, 312, 297.5, 284, 242 and 234.5nm. The molecular weight was confirmed by mass spectrometry and the NMR spectrum showed three sets of protons in the ratio of 1:1:1. The melting points and ultraviolet spectra of 2,7-diaza-biphenylene and the 2,6-isomer (LXVIII) differ, although the infra-red, NMR and mass spectra are similar.

1,6-diazabiphenylene [48] (LXXVII) has been similarly prepared, as have the 1,8-isomer [40] (LXXVIII), the 1,4-isomer [51] (LXXIX) and similar compounds such as the

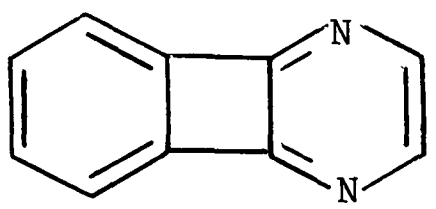
biquinoxalylene [51] (LXXX) and 5,10-diazabenzo [b] biphenylene [49] (LXI), which had been previously prepared from 1,2-benzocyclobutadienoquinone by Cava and associates [34]. The halogenated compounds hexachloro- (LXXXI) and hexafluoro-1,8-diazabiphenylene (LXXXII) have also been synthesised [52] by this method.



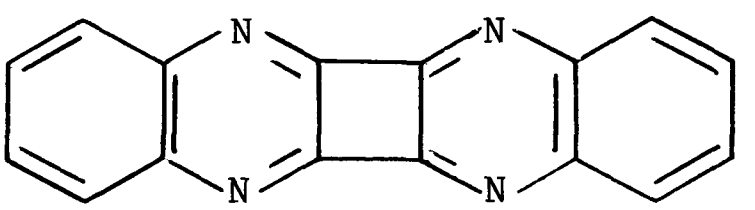
(LXXVII)



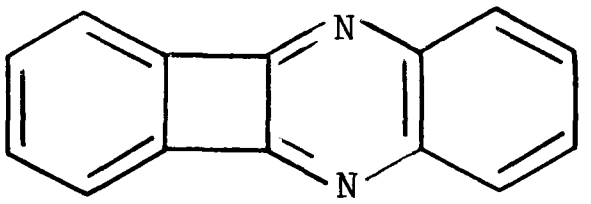
(LXXVIII)



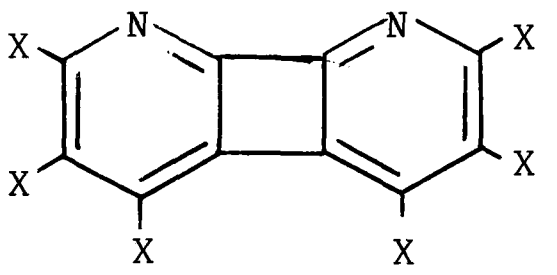
(LXXIX)



(LXXX)

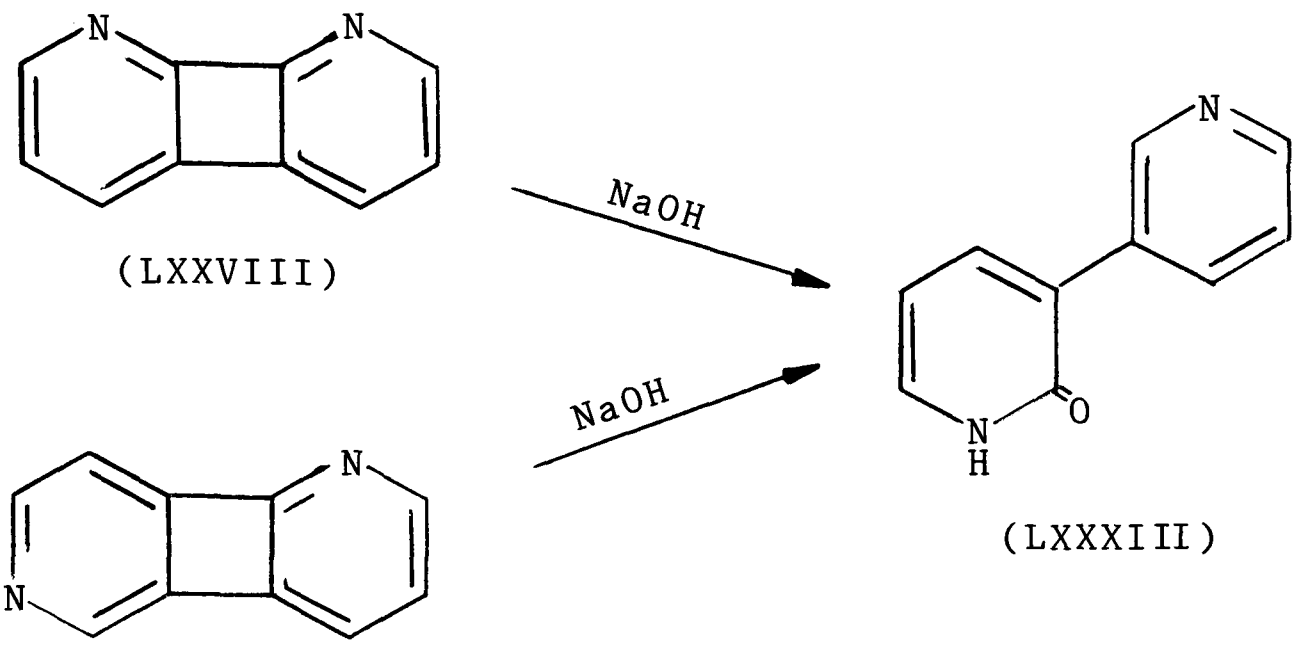


(LXI)

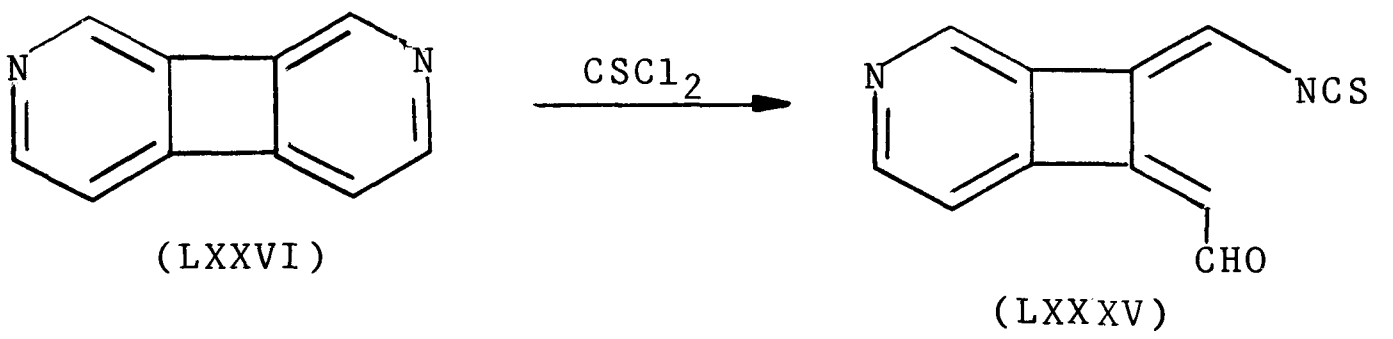


X= Cl (LXXXI)
X = F (LXXXII)

Besides undergoing the expected quaternisation reactions with alkyl halides [53], hydrolysis of diazabiphenylenes with aqueous sodium hydroxide solutions leads to the formation of pyridones and opening of the four-membered ring [54]. Thus, 1,8-diazabiphenylene (LXXVIII) and the 1,6-isomer (LXXVII) both give good yields of 1H-3(pyrid-3'-yl)pyrid-2-one (LXXXIII), m.p. 195-196°C, while the 2,7-isomer (LXXVI) gives a 45% yield of 1H-3(pyrid-3'-yl)pyrid-4-one (LXXXIV), m.p. 222-226°C.

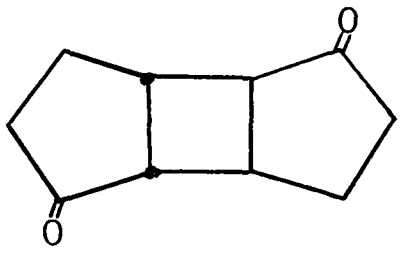



In contrast, however, treatment of a solution of 2,7-diazabiphenylene in dichloromethane with thiophosgene [55] leads to opening of the 6-membered ring giving the aldehyde (LXXXV).

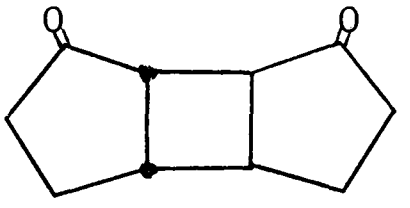



An alternative approach to the synthesis of diazabiphenylenes would be by the construction of the heterocyclic rings on suitably functionalised cyclobutanes. An attractive route to such systems would be the insertion of

a nitrogen atom in each of the cyclopentanone rings of the known cis, trans, cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione (LXXXVI) and cis, trans, cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,10-dione (LXXXVII) [56].

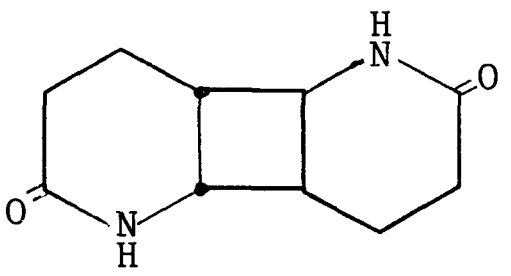


(LXXXVI)

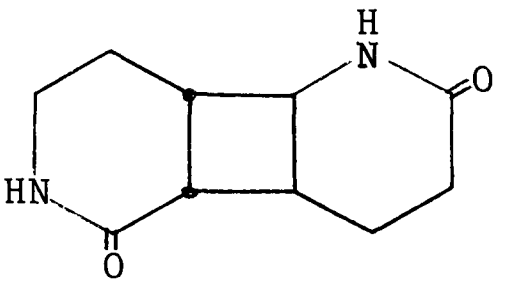


(LXXXVII)

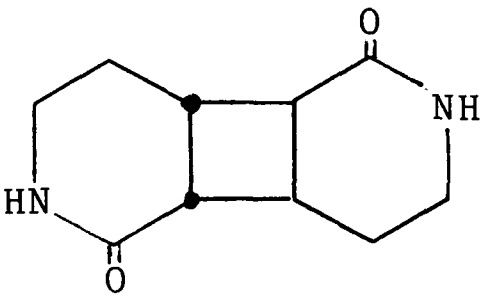
S Mendonca [57] has prepared these two diketones, subjected the 3,8-dione (LXXXVI) to the Schmidt reaction and identified the products as the dilactams LXXXVIII and LXXXIX. He also found that the Beckmann rearrangement of the dioximes of diketone LXXXVI gave the dilactams LXXXIX and XC.



(LXXXVIII)

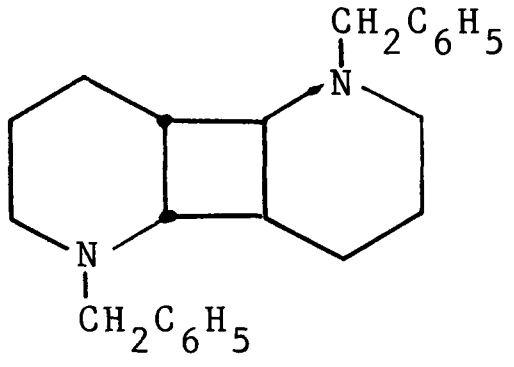


(LXXXIX)



(XC)

Reduction of the N,N'-dibenzyl derivative of dilactam LXXXVIII gave the diamine XCI, which on dehydrogenation with palladium on carbon gave a mixture of four compounds. However, this mixture was not fully investigated.



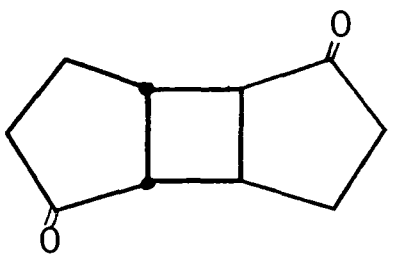

(XCI)

The following work continues this approach to the synthesis of diazabiphenylenes and describes the reduction and dehydrogenation of the dilactams LXXXVIII and XC, derived from the Schmidt and Beckmann reactions of the diketone LXXXVI.

# D I S C U S S I O N

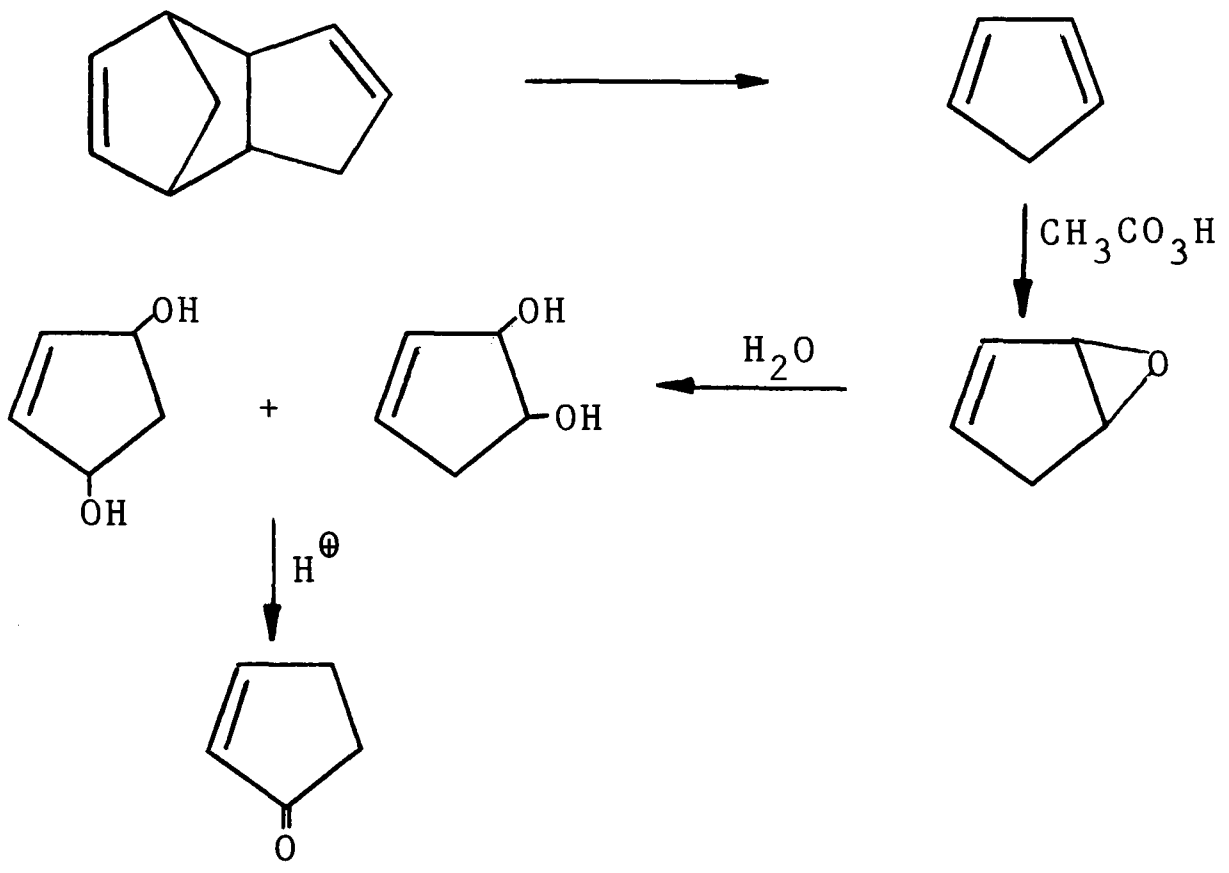
## SYNTHESIS OF CIS,TRANS,CIS-TRICYCLO[5,3,0,$0^{2,6}$]DECANE-3,8-DIONE

The synthesis of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]-decane-3,8-dione (I), required for these investigations, involved the preparation of cyclopent-2-enone as the immediate precursor.

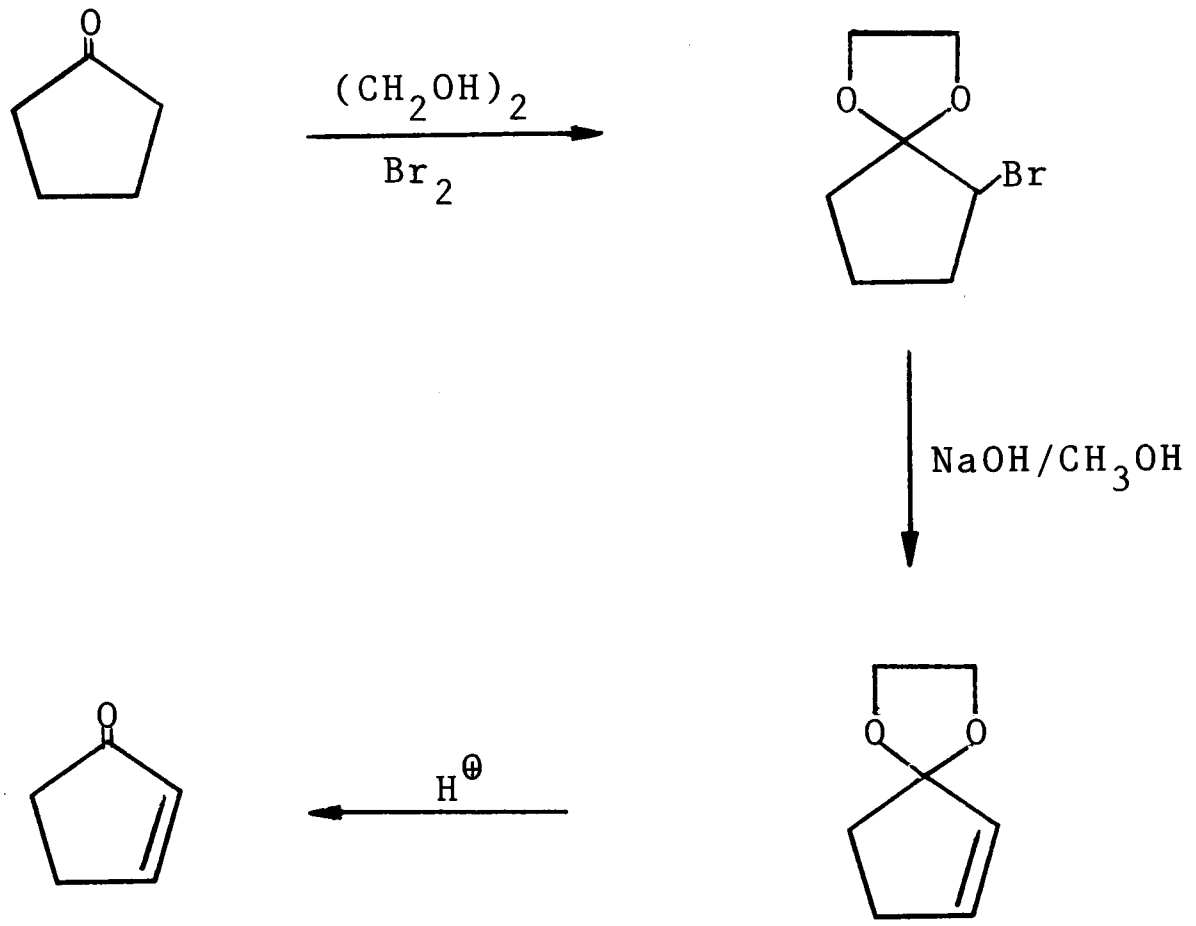


(I)

Cyclopentadiene, obtained by thermolysis of dicyclopentadiene, was converted into a mixture of cyclopentendiol isomers by oxidation with peracetic acid and subsequent hydrolysis of the intermediate epoxide, as described in the method of Korach, Nielsen and Rideout [58]. The authors claimed that this procedure produced two isomers in the ratio 4:1, although in the present work several repetitions of this procedure each gave a mixture of three compounds in the approximate ratio of 2:4:5. This isomer mixture was in turn dehydrated by heating with toluene-4-sulphonic acid to yield pure cyclopent-2-enone, using the procedure described by De Puy and Eilers [59].

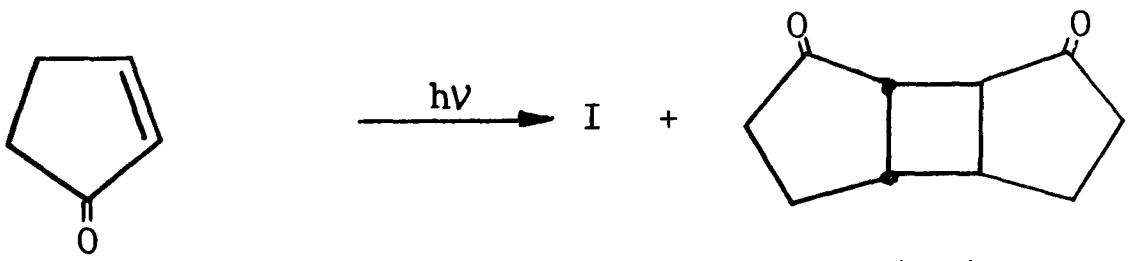


An alternative preparation of cyclopent-2-enone [60], starting from readily available cyclopentanone involves bromination of the ketone in ethanediol to give the corresponding bromoketal, which is dehydrobrominated with base, and the resulting unsaturated ketal hydrolysed with dilute acid. Following this sequence of reactions, the expected yield of cyclopent-2-enone ethylene ketal was obtained, however, hydrolysis with dilute sulphuric acid gave a low yield of product, possibly due to either the rather high solubility of the ketone in water or its acid catalysed polymerisation.



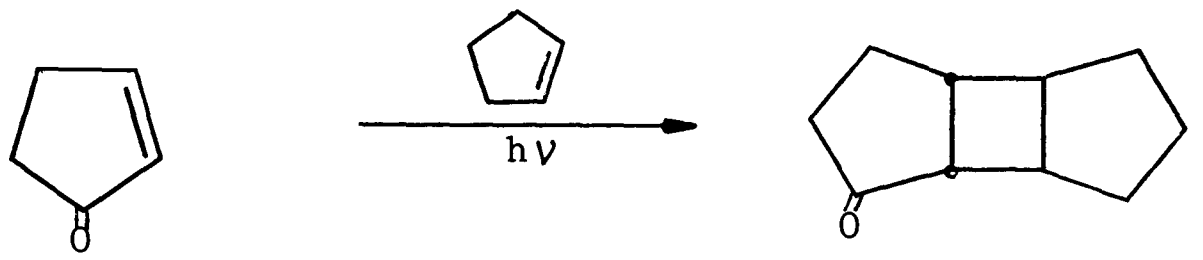

Eaton reported that photolysis of cyclopent-2-enone itself or in solution in a variety of solvents with light of wavelength >300nm, gave an approximately equal mixture of diketone (I) and cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]-decane-3,10-dione (II) in high yield [56].

The mechanism has been represented as the attack of a photo-excited molecule on a non-excited substrate [61], the initial excited species being formed by promotion of an electron from one of oxygen non-bonding orbitals to an antibonding $\pi$ orbital.




(II)

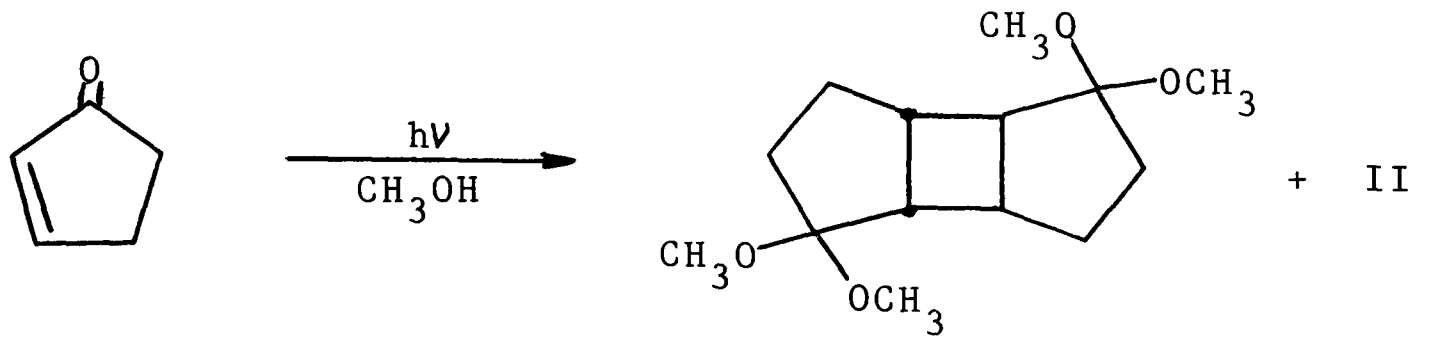
Since the original publication by Eaton, further work on this and similar reactions has been published by several authors [62,63,64]. Thus it was found [61] that irradiation of a 10% solution of cyclopent-2-enone in cyclopentene, gave cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decan-3-one (III).




(III)

The above mixed addition was regarded as supporting the hypothesis that the mechanism of these cycloadditions involves attack of a photo-excited cyclopent-2-enone molecule on a non-excited substrate, as the simple olefins are not excited by light of wavelength greater than 300nm.

In the present work, photolysis of cyclopent-2-enone was effected in methanol solution giving the diketal (IV) as a white precipitate, as found by Mendonca [57]. The solid was collected by filtration at regular intervals and the course of the reaction was monitored by gas-liquid chromatography (glc).




(IV)

The diketal (IV) was converted into the diketone (I) by heating in the two phase system of dichloromethane and dilute hydrochloric acid, a method described by Janot and associates [65] for the hydrolysis of ketals. Recrystallisation from carbon tetrachloride gave the diketone (I), m.p. 126-127°C in 26% yield.

Concentration of the methanol liquors from the reaction, treatment of the residue with dichloromethane-hydrochloric acid as before, followed by vacuum distillation gave a small quantity of a white solid. Recrystallisation from a large volume of hexane gave the diketone (II), m.p. 66-67°C, which was contaminated with a trace of diketone (I), the head-to-tail isomer.

It has been reported by Ruhlen and Leermakers [63] that photolysis of a 1.2M solution of cyclopent-2-enone in cyclohexane gave double the yield of the required diketone (I), compared with the use of methanol as a solvent, and this observation was confirmed in the present work.

Irradiation of cyclopent-2-enone in this solvent gave a mixture of the diketones (I) and (II) as a brown solid. Dissolution of this solid in methanol afforded the diketal (IV) as a white solid, and conversion to the diketone as before, followed by recrystallisation from carbon tetrachloride gave the required diketone as a white solid, m.p. 126-127°C in 47% yield.

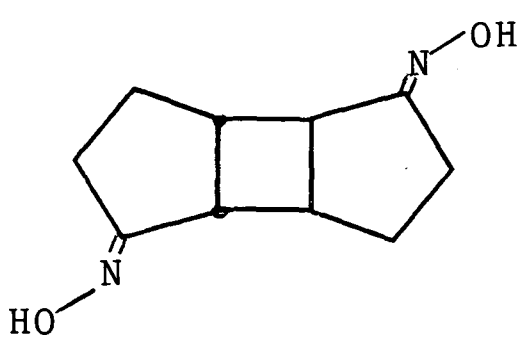
Concentration of the methanol liquors, treatment with dichloromethane-hydochloric acid, followed by vacuum distillation gave impure diketone (II) as a pale yellow solid. Two recrystallisations from hexane gave the diketone, m.p. 59-62°C, which was still contaminated with ca. 12% of the head-to-tail isomer.

The ultraviolet spectrum of an isolated carbonyl group exhibits an intense $\pi \rightarrow \pi^*$ band at 185nm ($\varepsilon \doteq 10^4$), together with a weaker $n \rightarrow \pi^*$ band at 280nm ($\varepsilon < 50$); conjugation with a double bond shifts these bands to 220-260nm and 300-350nm respectively. It is of interest to note that whereas the spectrum of cyclopentanone shows the expected

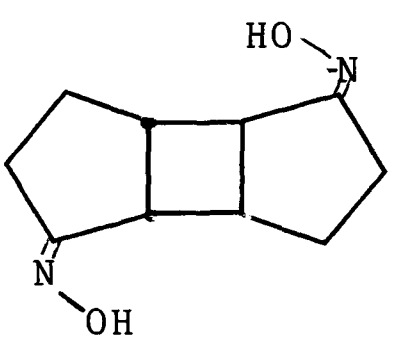
$n \rightarrow \pi^*$ band at 286nm ($\varepsilon$=19), in the spectra of the diketones (I) and (II) (uv 1 and 2) this band is intensified and shifted to longer wavelengths, giving bands at 293nm ($\varepsilon$=68) and 305nm ($\varepsilon$=133) respectively. These spectra also exhibit more intense bands at 210nm ($\varepsilon$=355) and 215nm ($\varepsilon$=1892) respectively. These spectral shifts are typical of those caused by homoconjugation [66], which is taking place due to cross-wise p-orbital overlap of the carbonyl double bonds. This is confirmed by the facts that firstly this effect is more pronounced for diketone (II), where the carbonyl groups are closer together than in (I), and secondly that the infra-red carbonyl stretching frequencies for both I and II (1730$cm^{-1}$) (ir 1 and 2) are almost the same as that for cyclopentanone (1740$cm^{-1}$).

## BECKMANN REARRANGEMENT OF THE DIOXIME(S) OF CIS,TRANS,CIS-TRICYCLO[5,3,0,$0^{2,6}$]DECANE-3,8-DIONE (I)

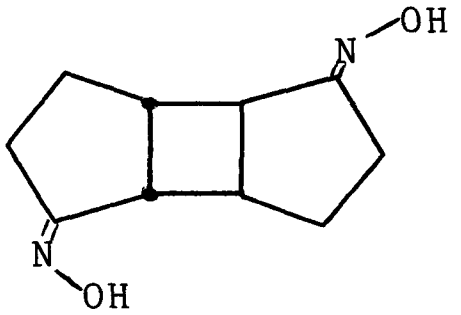
A useful method of inserting nitrogen in both the five-membered rings of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]-decane-3,8-dione (I) is the formation of its dioxime followed by a Beckmann rearrangement. Thus treatment of diketone (I) in ethanol with hydroxylamine hydrochloride and either sodium hydroxide or sodium acetate gave a 1:1 mixture of isomeric dioxime(s), m.p. 225-227°C (decomp.), as found by Mendonca [57]. The product was a mixture of two or more of the possible isomeric dioximes (V),(VI),(VII).




(V)



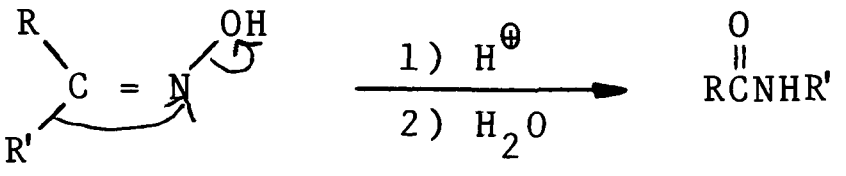

(VI)

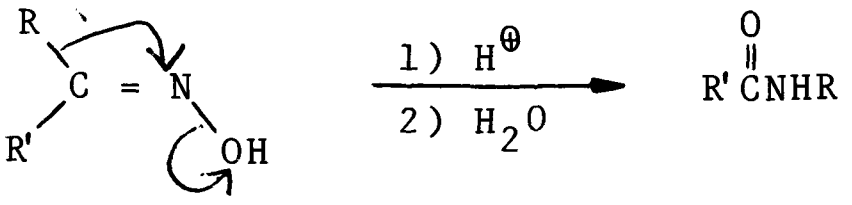



(VII)

No attempt was made to separate the mixture of dioxime(s), which was used directly for the subsequent Beckmann rearrangement.

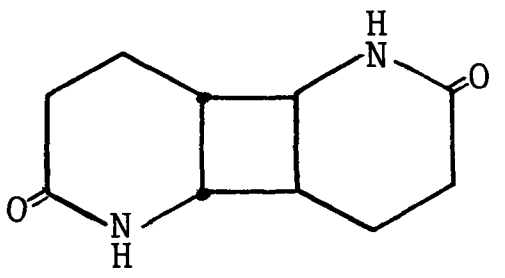
The Beckmann rearrangement of oximes is known to proceed generally via the acid catalysed formation of an electron deficient nitrogen atom by the partial ionisation of the oxygen-nitrogen bond with a simultaneous migration of the group anti to the departing group as shown:



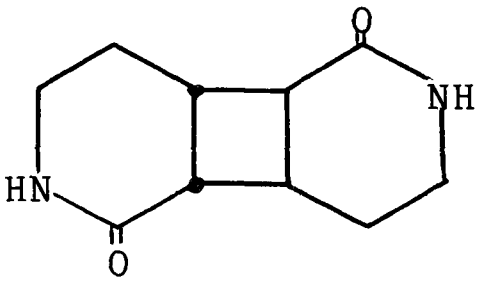




However, there are some instances where the anti-migration rule does not appear to hold and it is known that when the catalyst used is a Bronsted acid, the syn and anti forms of the oxime are readily interconverted prior to the actual Beckmann rearrangement [67].

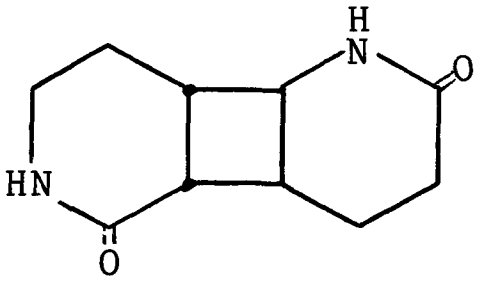
On this basis three possible dilactams (VIII), (IX) and (X) may be expected from the Beckmann rearrangement of the isomeric dioxime(s) obtained from diketone (I).




(VIII)




(IX)




(X)

This reaction has been studied by Mendonca, using polyphosphoric acid as a catalyst, and he obtained two isomeric dilactams which were shown to have the structures (IX) and (X), largely by pmr studies on the dilactams and their N,N'-dimethyl derivatives. However, the isomers were

difficult to separate and hence the Beckmann rearrangement was studied under different conditions to investigate the possibility of the preferential formation of only one isomer.

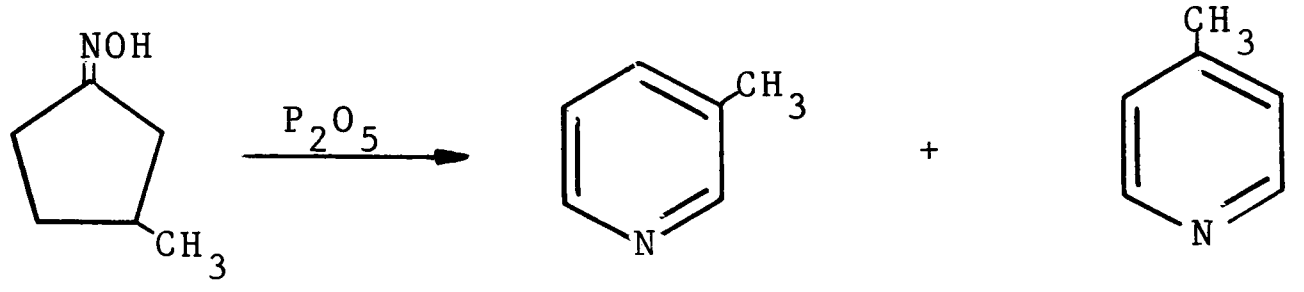
The Beckmann rearrangement has been effected with many different catalysts [68]. The classical methods involve treating the oxime with phosphorus pentachloride in ether, with strong sulphuric acid or with hydrogen chloride in acetic acid-acetic anhydride. Newer procedures include the use of polyphosphoric acid, benzenesulphonyl chloride and its derivatives, phosphorus oxychloride, boron trifluoride, iodine pentafluoride, thionyl chloride, trifluoroacetic anhydride or formic acid [69]. More recently ethyl polyphosphate [70] and trimethylsilyl polyphosphate [71] have been employed.

A limited study was therefore undertaken, to determine the effect of various catalysts on the dioxime(s) of the diketone (I). The reaction mixtures were generally treated with water, adjusted to pH 8.5, and continuously extracted with chloroform for several days. The products were analysed by thin layer chromatography (tlc).

The best reaction conditions were found to be concentrated sulphuric acid at 125°C which gave, after work-up, solely the dilactam (IX). Conversely the use of thionyl chloride at 5-10°C yielded mainly dilactam (X), together with some of the dilactam (IX). Only the recovered dioxime(s) were obtained when either boron trifluoride etherate at 50°C or phosphorus pentachloride in ether at 0°C were used. This failure to react was probably due to the insolubility of the dioxime(s) in ether. It has been reported that when a mixture of benzenesulphonyl chloride and sodium hydroxide at 0°C was employed for the rearrangement of cyclopentanone oxime, a high yield of valerolactam was obtained [72]. However, the use of this mixture with the present dioxime(s) gave a complex mixture of products, as indicated by tlc. This was possibly due to fragmentation of the reaction inter-

mediate and examples of these fission reactions are quite common [73,74]. A similar reaction occurred when the dioxime(s) were refluxed with a solution of trifluoro-acetic anhydride in dimethoxyethane, as tlc again showed a mixture of at least three unknown compounds. Poly-phosphoric acid, as expected [57], gave a mixture of the dilactams (IX) and (X).

It has been reported by Wallach and Rath [75] that the Beckmann reaction between 3-methylcyclopentanone oxime and phosphorus pentoxide yielded a mixture of compounds containing 3-methylpyridine and 4-methylpyridine.




This reaction, should it occur with the tricyclic diketone, could result in the direct formation of the diazabiphenylene system. Accordingly, following extraction of the dilactams with chloroform, the neutral aqueous solution from each experiment was made strongly basic with sodium hydroxide and extracted with ether. However, evaporation of the extracts gave no material.

Since the dilactam (IX) was required as the potential precursor of 2,6-diazabiphenylene, further Beckmann rearrangements were conducted using sulphuric acid. Some samples of the dioxime(s) of diketone (I) dissolved in cold concentrated sulphuric acid to give a colourless solution, but others reacted violently resulting in a black solution. This violent reaction was not due to any impurities in the dioxime(s) and may possibly have been related to the particle size of the various dioxime samples. A similar occurrence has been reported using cyclopentanone oxime and 85% sulphuric acid [76].

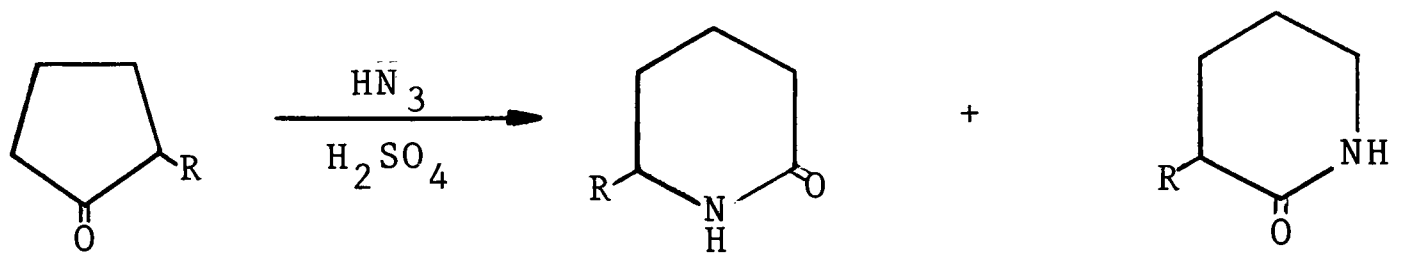
Following these result, polyphosphoric acid was used as a catalyst for subsequent preparations of the dilactam (IX).

Treatment of the mixture of dioxime(s) in polyphosphoric acid at 120°C, followed by continuous chloroform extraction of the neutralised aqueous reaction mixture gave a white solid, m.p. 300°C (decomp.) in high yield. Fractional crystallisation from water gave white needles of the major product cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-3,9-dione (IX), m.p. 320°C (decomp.), as found by Mendonca [57]. The mother liquors from the recrystallisation contained mainly the minor product cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione (X), by tlc, but no attempt was made to purify this compound.

The aqueous solution from the chloroform extractions was made alkaline with sodium hydroxide and extracted with ether. Concentration of the ether extracts did not give any residue.

## SCHMIDT REACTION OF CIS,TRANS,CIS-TRICYCLO[5,3,0,$0^{2,6}$]DECANE-3,8-DIONE

Together with the Beckmann rearrangement of ketoximes, the Schmidt reaction has been used extensively for the conversion of ketones to amides. Cyclic ketones give rise to lactams; thus α-substituted cyclopentanones yield a mixture of isomeric lactams [77].

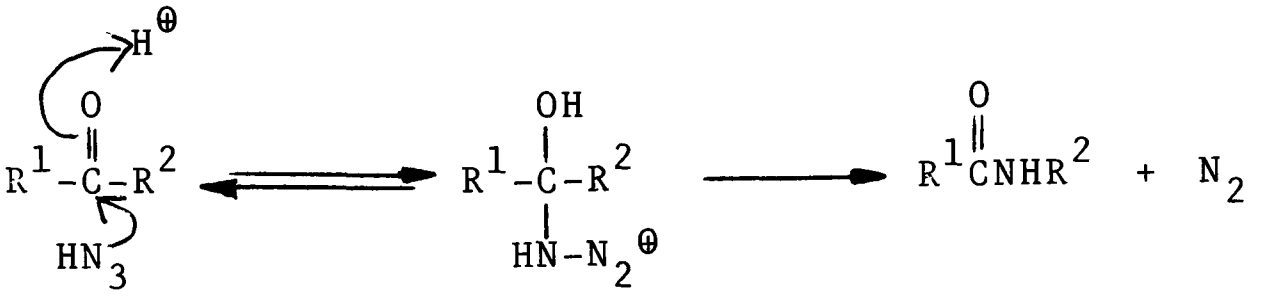



(XI) (XII)

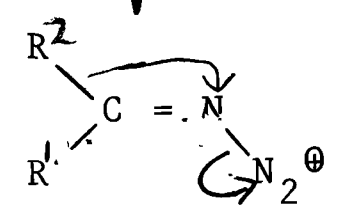
The application of this reaction to diketone (I) would be expected to yield a tricyclic dilactam or mixture of dilactams having a basic carbon-nitrogen skeleton which could possibly be further elaborated to diazabiphenylenes.

The reaction usually involves treatment of the ketone with hydrazoic acid in the presence of an acidic catalyst. Chloroform or benzene may be used as solvents and the catalyst is commonly concentrated hydrochloric acid, sulphuric acid or polyphosphoric acid. Hydrazoic acid may be generated in situ from sodium azide in the acid medium. For aliphatic ketones, concentrated hydrochloric acid appears to be a useful solvent and the preferred catalyst [78].

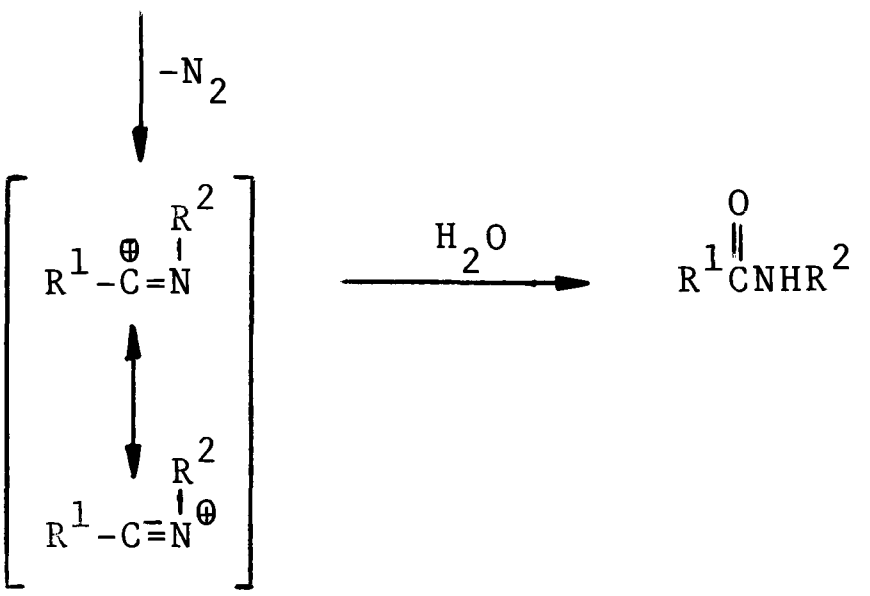
It is now generally conceded [79] that the reaction mechanism involves two closely related but distinct pathways, both of which include alkyl or aryl migration to an electron-deficient nitrogen atom, as in the Beckmann rearrangement. The two routes diverge from a common intermediate (XIII), formed by acid catalysed addition of hydrogen azide to the carbonyl group.



(XIII)

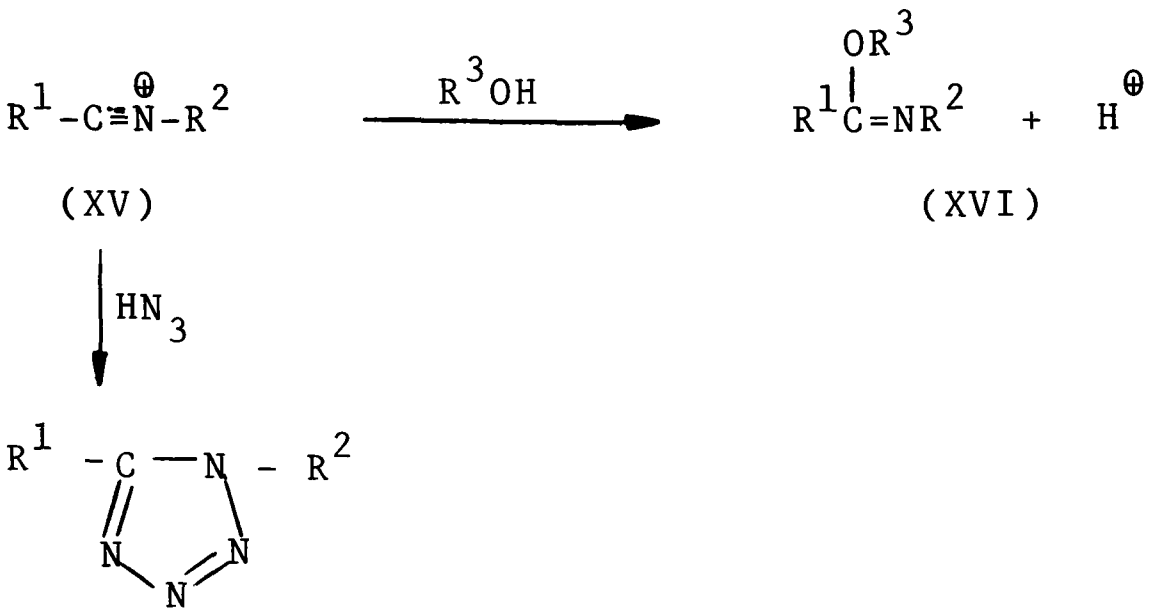


(XIV)



(XV)

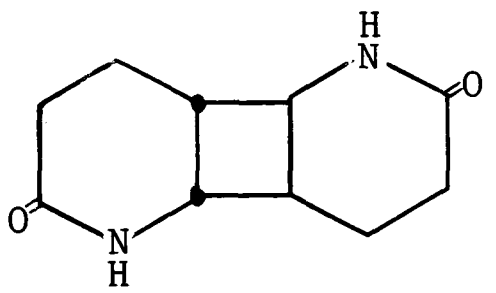
As in the Beckmann rearrangement the intermediate iminium ion (XV) may be intercepted by suitable nucleophiles. Thus the Schmidt reaction sometimes affords imino-ethers (XVI) when conducted in the presence of alcohols or tetrazoles (XVII) when an excess of hydrazoic acid is employed.



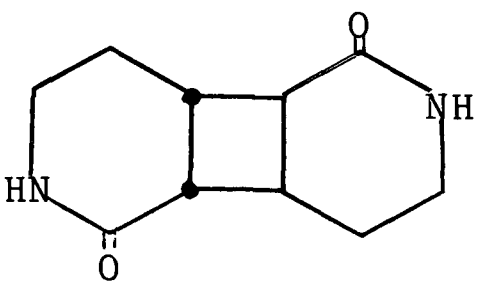
(XV) (XVI) (XVII)

In the case of unsymmetrical ketones, two diazoketimine ions (XIV, syn and anti) are possible and should lead to two different amides. It has been shown that, in general, the group which migrates to the electron deficient nitrogen atom is the one with the greater bulk. Thus, Schechter and Kirk found that α-substituted cyclopentanones give predominantly lactams of type (XI) rather than (XII) [77]. Similarly the work of Fusco and Rossi [80] and Conley [81] appear to strengthen the case for the above rule.

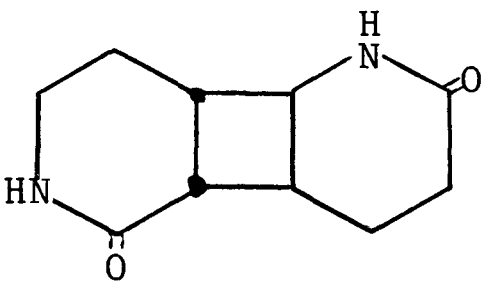
On the basis of the mechanism discussed above, the Schmidt reaction of diketone (I) would be expected to give mainly dilactam (VIII) together with the dilactams (IX) and (X) and this was substantiated by Mendonca [57], who found that dilactam (VIII) was the major product, together with a small amount of dilactam (X).



(VIII)



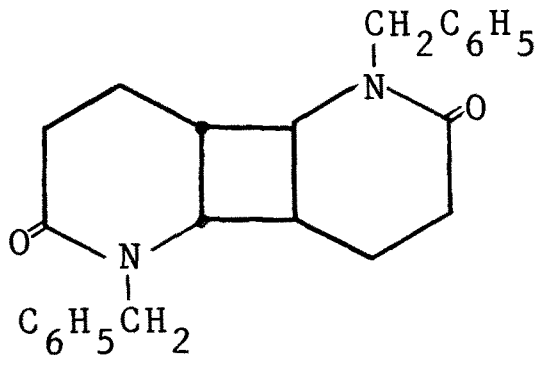
(IX)



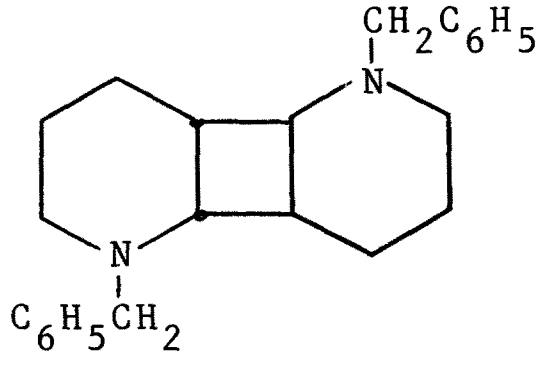
(X)

Treatment of diketone (I) with 2.2 molar equivalents of sodium azide in concentrated hydrochloric acid, followed by continuous chloroform extraction of the slightly basified (pH 8.5) aqueous reaction mixture gave a pale brown solid, m.p. 250-310°C (decomp.) in good yield. Fractional crystallisation from water gave the major product cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione (VIII), m.p. 349-350°C (decomp.). The mother liquors from the recrystallisation contained mainly the minor product cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane-4,9-dione (X), by tlc, but no attempt was made to purify this compound.

S Mendonca [57] had converted the dilactam (VIII) into the N,N'-dibenzyl derivative (XVIII) and also reduced this compound to the corresponding diamine (XIX). The dehydrogenation of this diamine with palladium on carbon had not been fully investigated, and it was intended to repeat this work and identify the products from the dehydrogenation.




(XVIII)




(XIX)

Thus, treatment of the dilactam (VIII) with a suspension of sodium hydride in N,N-dimethylformamide, followed by benzyl chloride gave the N,N'-dibenzyl derivative (XVIII) in rather poor yield.

## THE REDUCTION OF CIS,TRANS,CIS-4,10-DIAZATRICYCLO[6,4,0,$0^{2,7}$]DODECANE-3,9-DIONE AND CIS,TRANS,CIS-3,9-DIAZATRICYCLO[6,4,0,$0^{2,7}$]DODECANE-4,10-DIONE

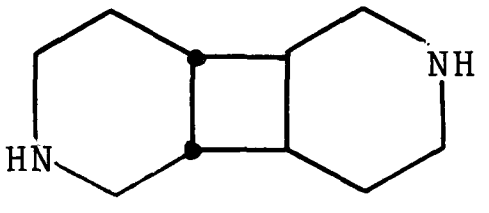
Earlier attempts by S Mendonca [57] to reduce the dilactams from the Beckmann and Schmidt reactions using either lithium aluminium hydride or sodium in ethanol proved fruitless, largely due to the insolubilities of the lactams in appropriate solvents. It was thus decided to investigate alternative methods of reduction. Boron hydrides have been extensively used as reducing agents [82] and borane itself has been stabilised by complexing with various electron donor compounds such as ethers [83,84], dimethyl sulphide [85] or amines [86] such as the very reactive and highly stable diphenylamine·borane complex [87].

The commercially-available tetrahydrofuran·borane complex converts primary, secondary and tertiary amides to the corresponding amines [88]. In the case of secondary amides a total of six "active hydrides" are required for the reduction: one for reaction with active hydrogen present in the molecule, two for the reduction, and the remaining three for the complex formation with the resulting amine. Thus, one mole of a secondary amide requires two moles of borane for its complete reduction.

Treatment of a slurry of dilactam (IX), derived from the Beckmann rearrangement, in tetrahydrofuran with borane at 5-10°C, followed by acidification, basification and extraction with ether gave a pale brown gum, which was stored under nitrogen. Both tlc and glc showed the gum to be largely one component with none of the starting dilactam present. The structure of this compound was assigned on the basis of chemical and spectroscopic data.

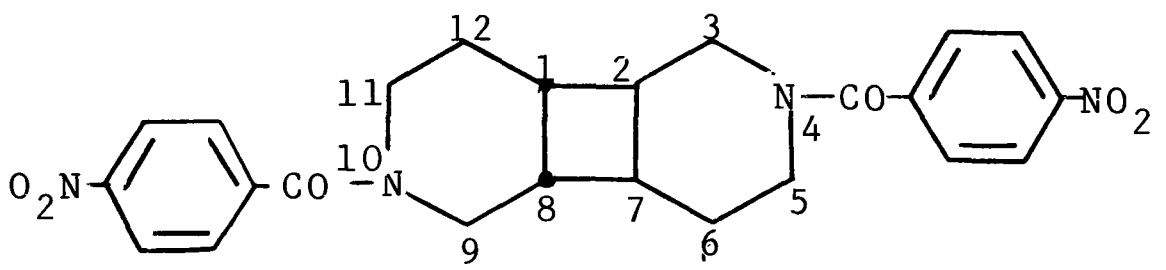
A consistent elemental analysis could not be obtained, probably due to the absorption of atmospheric moisture by the gum. The infrared spectrum (ir 3) showed a charac-

teristic band for the N-H group. The medium-weak band at $1650cm^{-1}$ was probably due to water. The proton magnetic resonance (pmr) spectrum (pmr 1) showed the absence of the amide hydrogen at δ9.0 and the presence of a complex multiplet at δ1.2-3.7 with a signal at δ2.3 being exchangeable with $D_2O$. The spectra were regarded as being consistent with the formulation of the compound as cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane (XX).




(XX)

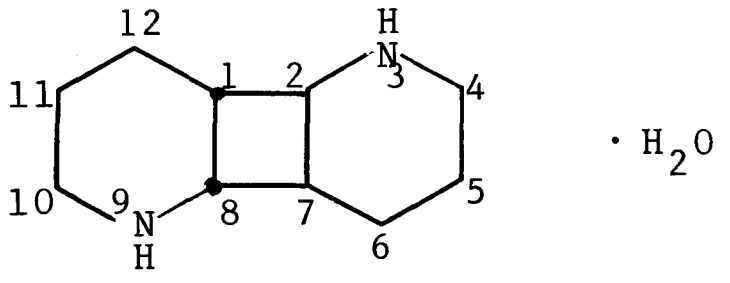
More definitive evidence was obtained by converting the diamine to its bis(4-nitrobenzoyl) derivative with 4-nitrobenzoyl chloride and sodium carbonate in pyridine. Elemental analysis indicated the molecular formula as $C_{24}H_{24}N_4O_6$ and the infrared spectrum (ir 4) showed characteristic bands for aliphatic and aromatic hydrogens and the tertiary amide carbonyl group. Apart from the eight aromatic protons at δ7.5-8.7, the pmr spectrum (pmr 2) showed two broad signals integrating for eight protons each, giving the expected ratio of aliphatic:aromatic protons of 2:1. These spectra are consistent with the formulated compound N,N'-bis(4-nitrobenzoyl)-cis,trans,-cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane (XXI).




(XXI)

The signal at δ1.7-3.1 was assigned to the eight hydrogens at C-6, C-12 and the four cyclobutyl protons, whilst the signal at δ3.1-4.4 was assigned to the eight hydrogens at C-3, C-5, C-9 and C-11 adjacent to nitrogen. The AB quartet at δ7.5-8.7 was due to the eight aromatic protons.

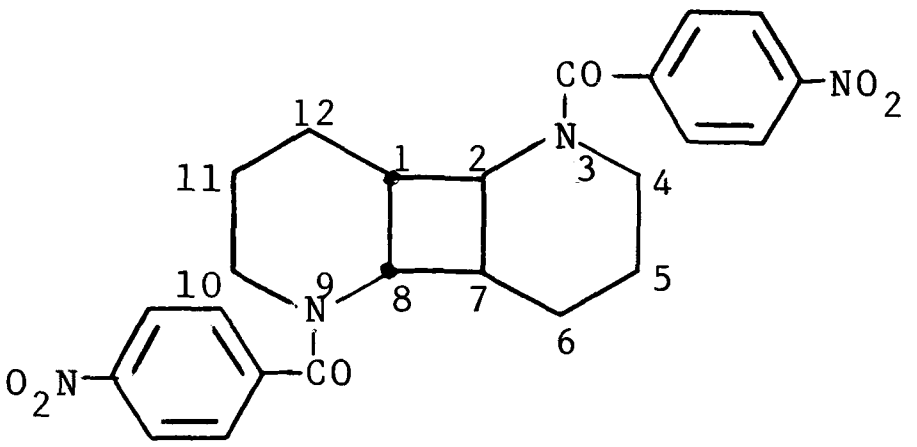
Treatment of dilactam (VIII), from the Schmidt reaction, with borane in a manner similar to that for dilactam (IX) afforded a pale brown gum, which was stored under nitrogen. Tlc and glc indicated that the gum was essentially one component, with no starting dilactam present. Attempts to obtain a satisfactory elemental analysis of this compound were unsuccessful, since inconsistent results were obtained probably due to the rapid absorption of moisture and carbon dioxide from the atmosphere. The infrared spectrum (ir 5) was very similar to that for the diamine (XX), showing a band at 3300cm$^{-1}$, characteristic of the N-H and O-H groups, and a band at 1640cm$^{-1}$ due to water. The pmr spectrum (pmr 3) showed two groups of signals, at δ1.2-3.8 and 4.4 respectively. The latter signal disappeared with $D_2O$, and is assigned to the water of hydration. No signals characteristic of amide protons were observed at δ9.1. This evidence was regarded as being consistent with the formulation of the compound as cis,trans,cis-3,9-diazatricyclo[6,4,0,0$^{2,7}$]dodecane monohydrate (XXII).




$\cdot H_2O$

(XXII)

This compound was also characterised as its bis(4-nitrobenzoyl) derivative. Elemental analysis indicated a molecular formula of $C_{24}H_{24}N_4O_6$ and the ir and pmr were consistent with the compound being N,N'-bis(4-nitrobenzoyl)-cis,trans,cis-3,9-diazatricyclo[6,4,0,0$^{2,7}$]dodecane (XXIII).



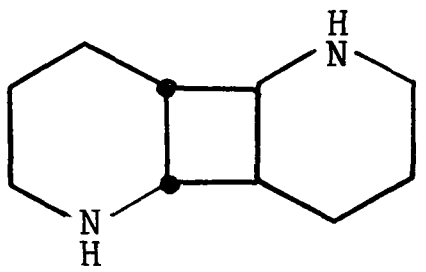

(XXIII)

The infrared spectrum (ir 6) showed characteristic bands for aromatic hydrogens and the tertiary amide carbonyl group. The pmr spectrum (pmr 4) showed the aliphatic and aromatic protons in the expected ratio of 2:1. The signal at $\delta$1.1-2.3 was due to the protons at C-5, C-6, C-11 and C-12, the broad doublet at $\delta$2.6-3.7 was assigned to the six hydrogens at C-1, C-4, C-7 and C-10, and the broad singlet at $\delta$4.4 was due to the cyclobutyl protons on C-2 and C-8. The aromatic hydrogens were again present as an AB quartet at $\delta$7.5-8.5. It is noteworthy that although this compound was readily soluble in deuterochloroform, the previous bis(4-nitrobenzoyl) derivative (XXI) could only be dissolved in trifluoroacetic acid, being insoluble in most common organic solvents.

In spite of precautions to exclude air, the diamine (XXII) rapidly absorbed water and carbon dioxide from the atmosphere to form the carbonate (XXIV) as an off-white solid, m.p. mainly 290-295°C (decomp.).

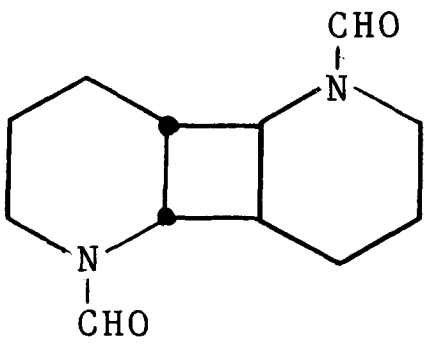
Elemental analysis indicated a molecular formula of $C_{10}H_{18}N_2 \cdot CO_2 \cdot 2H_2O$ and the infrared spectrum (ir 7) showed $NH_2^{\oplus}$ and N-H groups at 3400, 2800-2700, 2390 and 1580cm$^{-1}$ and $H_2O$ at 1640cm$^{-1}$.

The diamine (XX), derived from the Beckmann dilactam (IX) did not rapidly form the carbonate and was stable when stored under nitrogen.



$\cdot CO_2 \cdot 2H_2O$

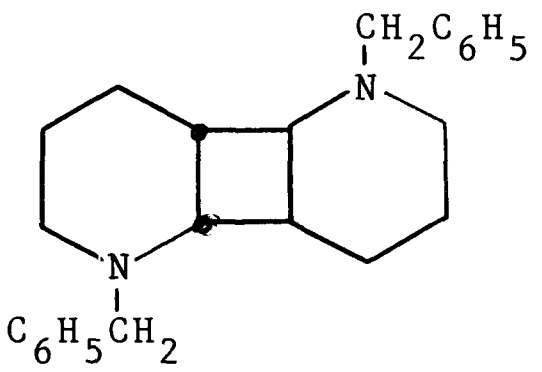
(XXIV)



(XXV)

A solution of the diamine (XXII), in 100% formic acid was heated on a steam bath in an attempt to form the N,N'-diformyl derivative (XXV). However, work-up of the solution gave a brown oil, which was essentially the starting diamine.

The N,N'-dibenzyl diamine (XIX) was also required for dehydrogenation studies and this was obtained by lithium aluminium hydride reduction of the corresponding dilactam (XVIII) as described by Mendonca [57]. The product was shown to be one component by glc and tlc.



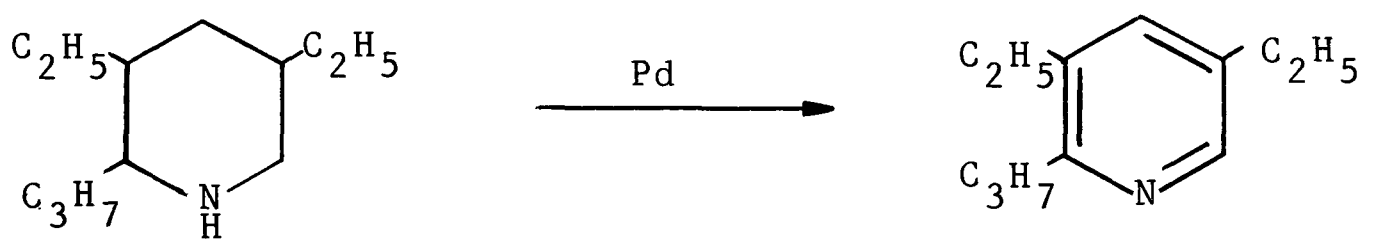
(XIX)

## DEHYDROGENATION STUDIES

The diamines (XX) and (XXII) and the N,N'-dibenzyl derivative (XIX) appeared to be promising precursors of diazabiphenylenes, since it was possible that they could be dehydrogenated to the corresponding diazabiphenylenes.

The dehydrogenation of piperidines to pyridines has been carried out quite extensively [89]. As early as 1927, pyridine was obtained [90] by passing piperidine vapour over manganous oxide at 600°C. Reagents such as concentrated sulphuric acid at 300°C, nitrobenzene at 260°C and silver acetate in acetic acid have been employed [91], as well as palladium, platinum, selenium, sulphur and nickel [89]. Homogeneous dehydrogenation has been effected with palladous chloride [92], or more recently (1970) by complexes of the platinum group [93].

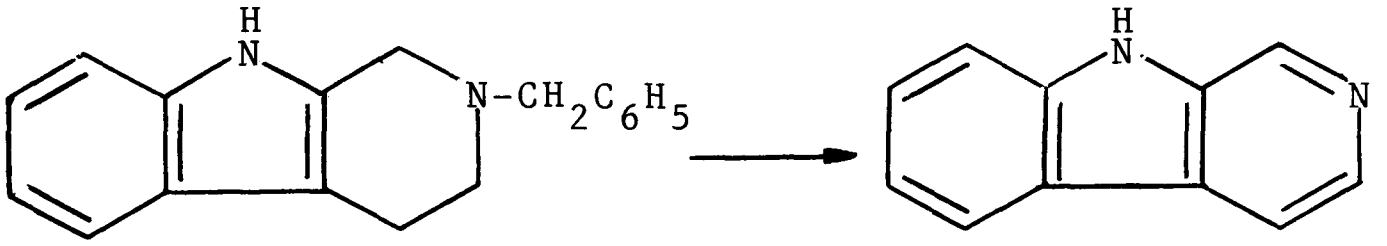
Palladium on carbon has been used extensively as a catalyst, in particular for the dehydrogenation investigation of complex nitrogenous compounds such as alkaloids. The piperidine is heated with the catalyst at 200-300°C, and usually gives good yields. Thus, treatment of 3,5-diethyl-2-propylpiperidine (XXVI) with 5% palladium on carbon at 236°C gives 3,5-diethyl-2-propylpyridine (XXVII) in a 62% yield [94].




(XXVI) (XXVII)

Similarly, the complex Ormosia alkaloids which contain piperidine rings have been dehydrogenated with 5% palladium on carbon at 250°C [95], and 2-benzyl-1,2,3,4-tetrahydro-β-carboline (XXVIII) has been converted into β-carboline (XXIX) [96] by heating with palladium on carbon above 200°C.

The latter reaction illustrates the general rule that N-alkyl groups are lost during aromatisation.




(XXVIII) (XXIX)

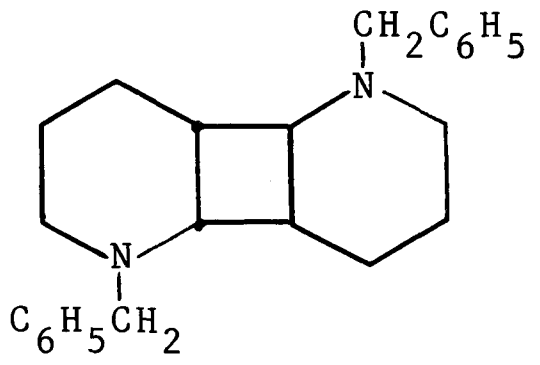
Nitrobenzene has been employed for the dehydrogenation of hydroaromatic compounds [97] and has also been used by Schmidle and co-workers [98] as a solvent for the palladium catalysed dehydrogenation of 4-p-tolyl-1,2,3,6-tetrahydropyridine (XXX) to 4-p-tolylpyridine (XXXI). A similar reaction has been carried out on substituted piperidines by Julia et al [99].


(XXX) (XXXI)

S Mendonca [57] had heated the N,N'-dibenzyl diamine (XIX) with 10% palladium on carbon and obtained a mixture of four compounds by glc. This reaction was not fully investigated and it was decided to repeat this work, identify the products from the reaction, and also attempt the dehydrogenation of the tricyclic diamines (XX) and (XXII).

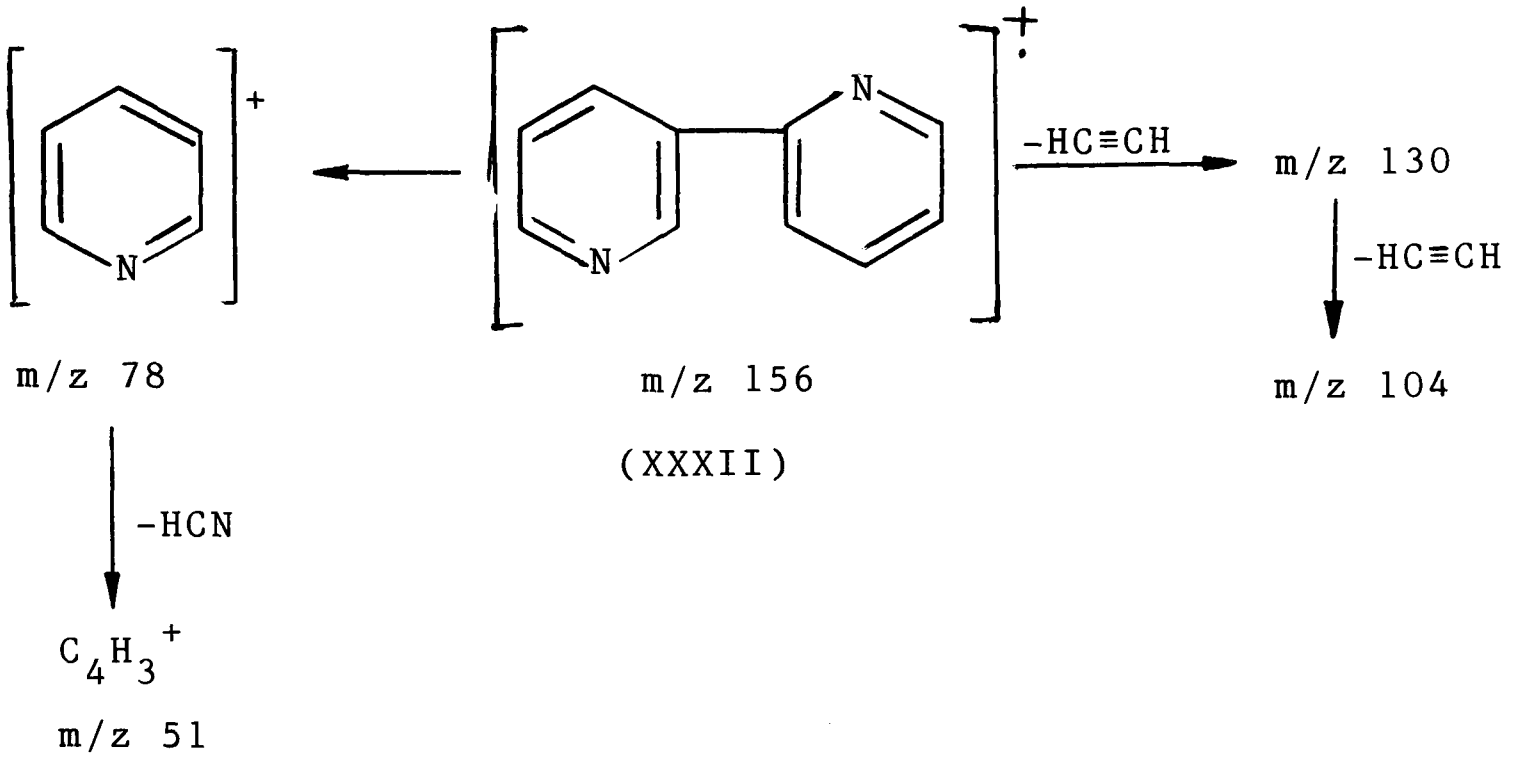
Dehydrogenation of the N,N'-dibenzyl diamine

In the present work, N,N'-dibenzyl-*cis*,*trans*,*cis*-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane (XIX) was heated with 10% palladium on carbon at 225°C, cooled and extracted with benzene.



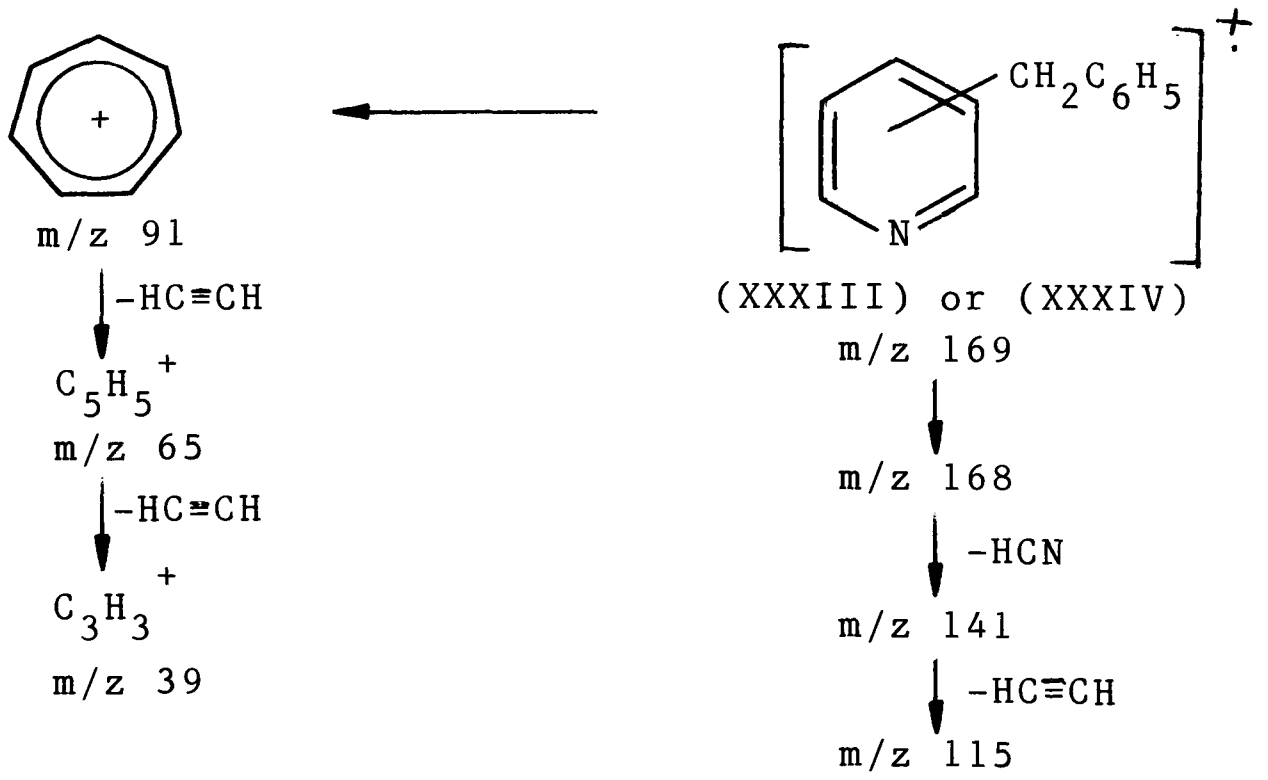
(XIX)

The benzene extract was shown to contain toluene (by glc) due to elimination of the benzyl groups, but pyridine was absent indicating that the cyclobutane ring had not undergone complete fission. Evaporation of the benzene extract gave a brown liquid which was shown by glc (glc 1) to contain mainly two compounds in the ratio 2:3, which were examined by glc-mass spectrometry (glc-ms ). The mass spectrum of the major component (ms 1) gave a molecular ion at m/z 156 and principal fragments at m/z values 155, 130, 104, 78 and 51. This data suggested that the compound was a bipyridine and this was established to be 2,3'-bipyridine (XXXII) by comparison with an authentic specimen on glc. A possible mode of fragmentation which would account for the ions observed is shown overleaf:



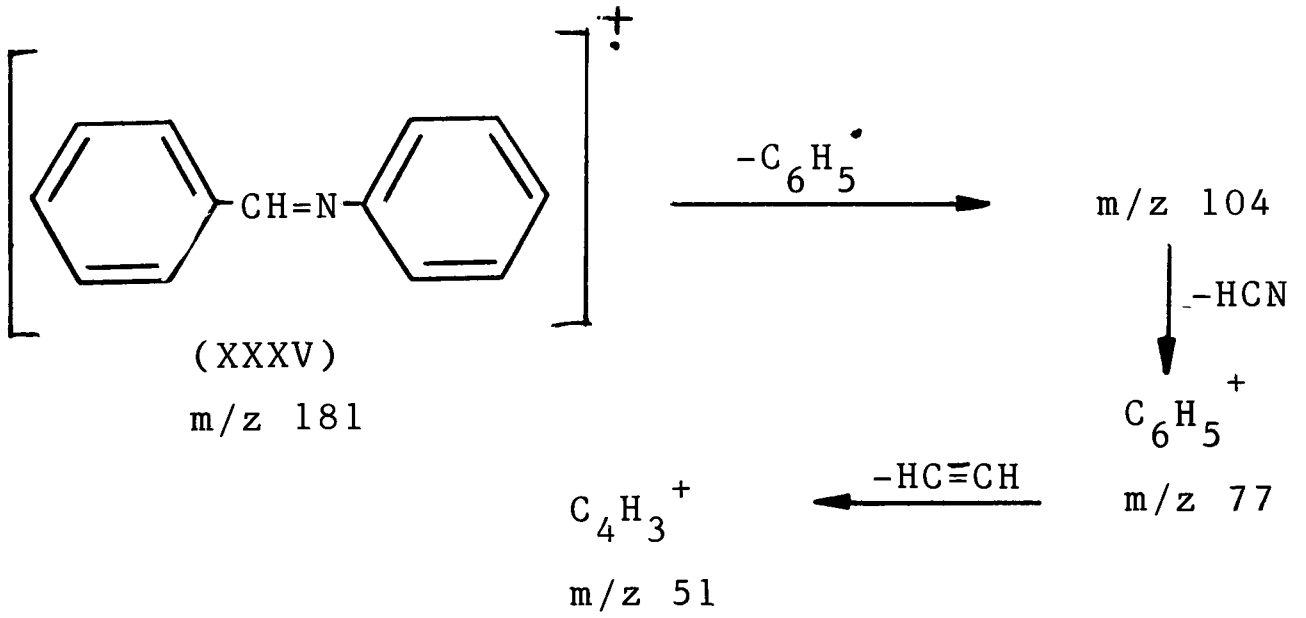

This compound possibly arises from elimination of the benzyl groups, from the diamine (XIX), fission of the four membered ring and dehydrogenation of the two heterocyclic rings.

The minor component was similarly examined and the mass spectrum (ms 2) gave a molecular ion at m/z 169 and principal fragments at m/z 168, 167, 141, 115, 91, 65 and 39. These results suggested that the compound was a benzylpyridine and by comparisons with authentic specimens on three glc columns it was tentatively identified as either 3-benzylpyridine (XXXIII) or 4-benzylpyridine (XXXIV). A possible fragmentation pattern is given below:



The dehydrogenation of the N,N'-dibenzyl diamine (XIX) was repeated using a mixture of nitrobenzene and palladium on carbon at reflux. The cooled mixture was extracted with benzene and glc of the extract showed the presence of toluene and absence of pyridine, as before, as well as the presence of aniline from the reduction of the nitrobenzene in the reaction.

Evaporation of the benzene extract gave a black tar, which still contained some nitrobenzene. Examination of the tar by glc (glc 2) and later glc-ms showed two compounds in the ratio 1:2, neither of which was 2,3'-bipyridine. The minor component had the same retention time on glc and mass spectrum as the minor product from the previous dehydrogenation, and was therefore also tentatively identified as either 3-benzylpyridine or 4-benzylpyridine. The mass spectrum (ms 3) of the major component gave a strong molecular ion at m/z 181, with principal fragments at m/z 180, 104, 77 and 51. This data suggested that the compound may be benzylideneaniline (XXXV), and this was confirmed by comparison with an authentic sample on glc. A possible mode of fragmentation is given below:




(XXXV)
m/z 181

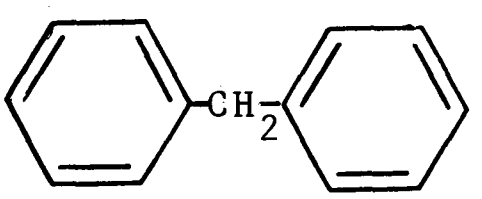
This compound may well arise by reaction of aniline, formed by reduction of the nitrobenzene, with benzaldehyde, that could itself be formed by oxidation of either toluene or a benzyl radical with nitrobenzene (under the reaction conditions).

Attempted dehydrogenation of cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

The catalytic dehydrogenation of complex piperidines has been carried out in various solvents such as p-xylene [100], biphenyl [101], 1-methylnaphthalene [102] and pseudocumene [96]. Some workers [102] have used an inert gas flow over the surface of the reaction mixture to remove the hydrogen formed.

Since it was possible that the dehydrogenation of the tricyclic diamines (XX) and (XXII) would lead to the formation of diazabiphenylenes, the effect of various dehydrogenation procedures in several solvents was investigated, using piperidine as a model compound.

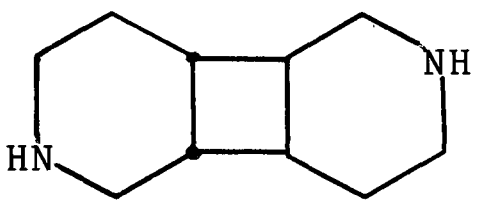
Piperidine, 10% palladium on carbon and the solvent were refluxed for 4-24 h, cooled and the conversion of piperidine to pyridine estimated by glc. In some of the experiments either nitrogen or carbon dioxide was passed over the surface of the reaction mixture. The use of m-xylene, either with or without a nitrogen purge, gave poor yields of pyridine after 20-24 h (4-8%), although changing to the higher boiling p-cymene gave a significant increase in yield (25%) when a nitrogen purge was used. Paradoxically, when the reaction temperature was increased by employing 1-methylnaphthalene no conversion to pyridine occurred at all, either with or without purging with nitrogen. An attempt to replace nitrogen with carbon dioxide was unsuccessful, leading to the rapid precipitation of white crystals of piperidine carbonate. A complete dehydrogenation could only be obtained with the highest boiling solvent, diphenylmethane (XXXVI), which gave a complete conversion to pyridine after the reaction mixture was refluxed for 5 h.



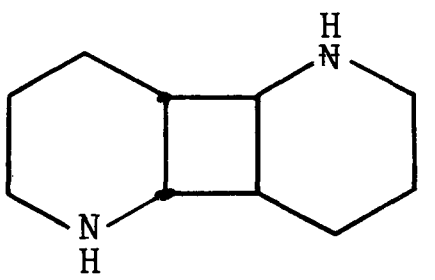

(XXXVI)

Although pure pyridine was obtained by distilling the reaction mixture, the isolated yield was low (31%). The low yield cannot have been due to evaporation of either piperidine or pyridine during the reaction, since the use of a dry-ice condenser led to a lower yield (21%), but may have been due to side reaction of piperidine with the active methylene group of diphenylmethane.

In the light of these results the dehydrogenation of the diamines (XX) and (XXII) was attempted neat and also in solution in diphenylmethane.




(XX)




(XXII)

The diamine, derived from the Beckmann reaction, cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane (XX), was heated with palladium on carbon at 220°C, under nitrogen, for 1 h, then extracted with a mixture of benzene and ethanol. Evaporation of the extract gave a brown oil (95%) which was shown to be the starting material by tlc and glc.

The reaction was therefore repeated at 300°C, and the mixture extracted with methanol, followed by ethanol. Concentration of the combined extracts gave a small quantity of a brown gum, the odour of which was similar to that of pyridine. This gum appeared to be polymeric, since no compounds could be eluted after injection onto several glc columns and tlc showed mainly baseline material. The pmr signals were mainly in the aliphatic region, with only a trace of aromatic protons present, showing the presence of only a small quantity of aromatic material, hence the reaction was not further studied.

The dehydrogenation of the diamine (XX) was further

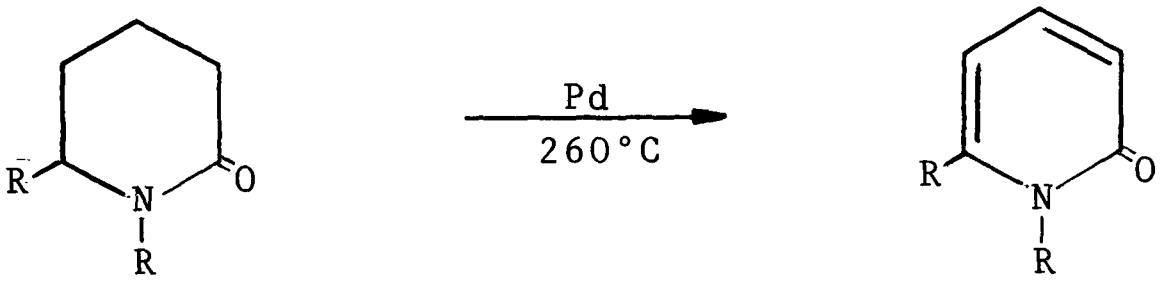
investigated by heating a solution of the compound in diphenylmethane with palladium on carbon at 220°C. The cooled mixture was extracted with methanol; the extract showed only the starting material on glc. Evaporation of the solution and isolation of basic material *via* acid extraction gave a gum, which was shown (by glc) to be starting material; the pmr spectrum indicated the presence of aliphatic protons only.

Attempted dehydrogenation of *cis,trans,cis*-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

The dehydrogenation of the diamine derived from the Schmidt reaction, *cis,trans,cis*-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane (XXII), was attempted in a similar manner. Thus, the compound was heated with palladium on carbon at 230°C, extracted with a mixture of benzene and ethanol, then filtered and the solvent removed by distillation leaving a brown oil. The distillate contained a small quantity of pyridine, indicating that complete opening of the cyclobutane ring and dehydrogenation had occurred. The brown oil again appeared to be polymeric, since it was insoluble in most organic solvents and no compounds could be eluted after injection onto several glc columns. Additionally, it showed only baseline material on tlc and only aliphatic protons in the pmr spectrum.

The attempted dehydrogenation of the diamine (XXII) in diphenylmethane with palladium on carbon at 230°C gave similar results. The cooled reaction mixture was diluted with methanol and filtered. The filtrate did not contain pyridine, 2,3'-bipyridine or the starting material (by glc). Concentration of this solution followed by acid extraction and work-up as before gave a brown gum, which showed mainly baseline material on tlc and only signals for aliphatic protons in the pmr spectrum.

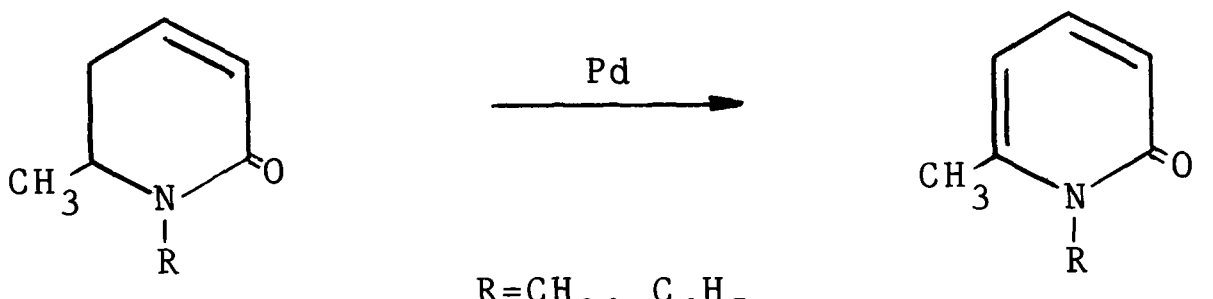
Saturated lactams, such as piperidones (XXXVII), have been dehydrogenated by treatment with palladium at 260°C to give the corresponding pyridones (XXXVIII) [103].




R=H, $CH_3$

(XXXVII) (XXXVIII)

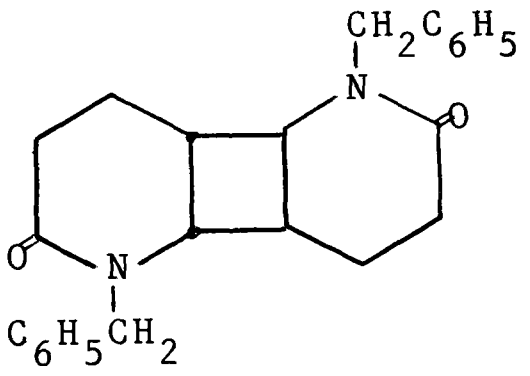
The unsaturated lactams (XXXIX) were similarly dehydrogenated to the pyridones (XL) on treatment with palladium on carbon in various solvents at reflux [104].




R=$CH_3$, $C_6H_5$

(XXXIX) (XL)

Accordingly, in the present work, a mixture of N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane-4,10-dione (XVIII), nitrobenzene and palladium on carbon was stirred under reflux for 3 h. Concentration




(XVIII)

of the filtrate gave only a small quantity of starting material. Extraction of the catalyst with methanol gave a further quantity of starting material (82% recovery).

It was evident from the foregoing results that this approach to the formation of diazabiphenylenes was not promising. It was therefore decided to investigate an alternative route *via* chemical dehydrogenation of appropriate derivatives of the dilactams from the Beckmann and Schmidt reactions. With this objective in view it was decided to investigate the conversion of the dilactams to the O-alkyl ethers, and attempt to dehydrogenate these compounds with high potential quinones.

## O-Alkylation of the dilactams from the Beckmann and Schmidt reactions

The O-alkylation of amides has been effected using several reagents [105] such as dialkyl sulphates, alkyl benzenesulphonates, alkyl halides at elevated temperatures, diazoalkanes, ethyl chloroformate or a mixture of an alkyl halide and a silver salt under basic conditions.

The most useful reagents, however, are the trialkyloxonium salts (XLI) [106]. These reagents were discovered

$$[R_3O]^{\oplus}\ X^{\ominus}$$

(XLI)

R = methyl, ethyl, propyl, butyl

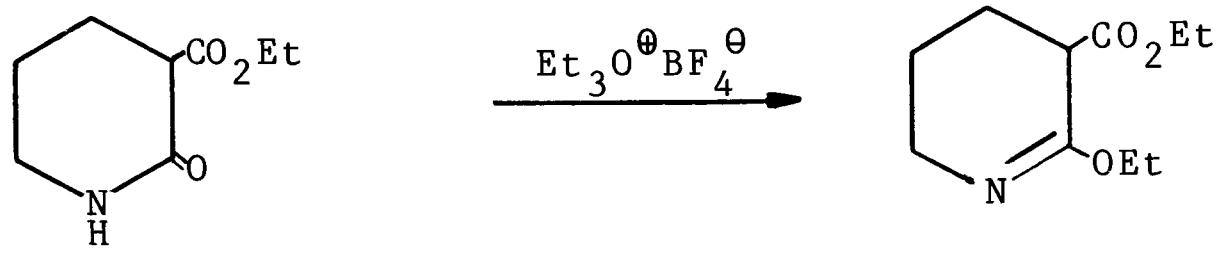
X = tetrafluoroborate, hexachloroantimonate, 2,4,6-trinitrobenzenesulphonate

by Meerwein [107], who also investigated much of their chemistry. The commonest of these salts are trimethyloxonium tetrafluoroborate [108] (XLII) and triethyloxonium tetrafluoroborate [109] (XLIII), which are prepared from boron trifluoride etherate, epichlorohydrin and the appropriate dialkyl ether.

$(CH_3)_3O^{\oplus}BF_4^{\ominus}$ (XLII)

$(C_2H_5)_3O^{\oplus}BF_4^{\ominus}$ (XLIII)

Treatment of lactams with trialkyloxonium fluoroborates gives lactim ethers [110] in high yield. Thus, the alkylation of the piperidone (XLIV) gave the tetrahydropyridine (XLV).




(XLIV) (XLV)

In general, a mixture of the lactam and alkylating agent is stirred in dichloromethane for 4-24 h at ambient temperature, treated with aqueous sodium bicarbonate and the organic phase separated and concentrated to afford the product.

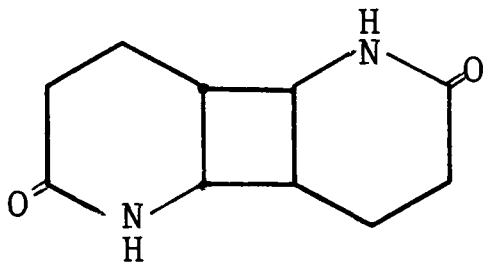
However, treatment of the dilactam (IX) with a suspension of trimethyloxonium tetrafluoroborate in dichloromethane for an extended reaction period of 39 days at ambient temperature gave, after treatment with sodium bicarbonate, mainly recovered dilactam (by tlc) rather than the expected lactim ether (XLVI).


(IX) (XLVI)

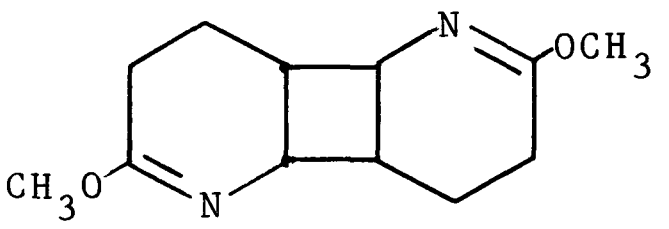
Concentration of the organic phase from the reaction gave a small quantity of a yellow oil, which was shown to be a mixture of two components by tlc and was not investigated further.

The dilactam (VIII) was similarly treated with a suspension of trimethyloxonium tetrafluoroborate in

dichloromethane for 39 days at ambient temperature giving after work-up a small quantity of a yellow oil. Tlc showed essentially one component, but the material was not investigated further because of the small amount which had been isolated. Continuous extraction of the aqueous solution did, however, afford a high yield of the starting dilactam showing that the lactim ether (XLVII) had not been formed to any extent.



(VIII)



(XLVII)

It was suspected that trimethyloxonium tetrafluoroborate probably failed to react with either of the dilactams (IX) or (VIII) because of the low solubilities of both the dilactams and the alkylating agent in dichloromethane. In both experiments there was a substantial quantity of undissolved solid despite the extended reaction period.

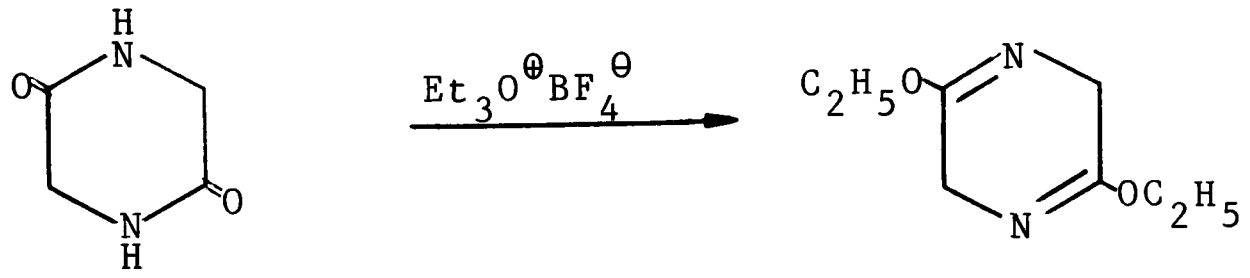
Further support for this was obtained by attempting the alkylation of another amide, piperazine-2,5-dione (XLVIII), which is also sparingly soluble in dichloromethane.

A mixture of piperazine-2,5-dione, trimethyloxonium tetrafluoroborate and dichloromethane was stirred for 3 h, further quantities of the alkylating agent and dichloromethane added and the reaction mixture stirred at ambient temperature for 24 h. Work-up as in the previous experiments gave only a small quantity of a yellow gum, which was not investigated further.

The formation of lactim ethers using the more soluble triethyloxonium tetrafluoroborate was then ivestigated.

A suspension of piperazine-2,5-dione in dichloromethane was treated with a solution of triethyloxonium

tetrafluoroborate in dichloromethane using the method of Sammes and co-workers [111]. Treatment with aqueous sodium bicarbonate and dichloromethane extraction gave the expected yield of 2,5-diethoxy-3,6-dihydropyrazine (XLIX).

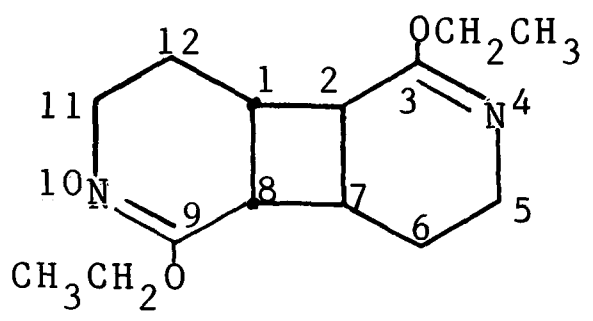



(XLVIII) (XLIX)

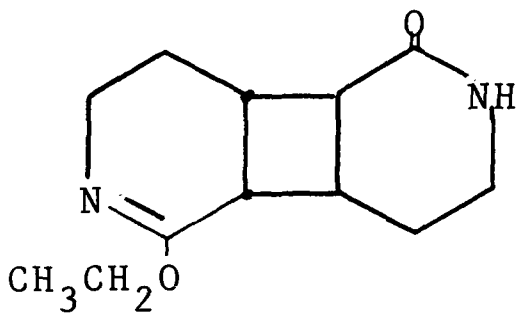
The infrared spectrum (ir 8) showed intense C=N and =C-O bands at 1700 and 1260cm$^{-1}$ respectively and the pmr spectrum (pmr 5) showed a triplet at δ1.2 (J=6Hz) for the two methyl groups, and a multiplet centred on δ4.2 comprising a quartet for the two $OCH_2$ groups and a singlet at δ4.1 for the two ring methylene groups.

Following this result the O-ethylation of the tricyclic dilactams was investigated. A suspension of the dilactam, cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane-3,9-dione (IX), in dichloromethane was similarly reacted with a solution of triethyloxonium tetrafluoroborate in dichloromethane for 18 h at ambient temperature. Work-up in the usual manner afforded a sticky yellow solid in good yield. Tlc showed mainly one component, and glc indicated that the material was pure. A sample of the crude product was sublimed to give a white solid, which was pure by glc and showed essentially one component on tlc. The material melted partly at 41-43°C and then completely at 70-75°C.

Elemental analysis indicated the molecular formula $C_{14}H_{22}N_2O_2$, and the infrared spectrum (ir 9) showed characteristic bands for the C=N and C-O groups. The pmr spectrum (pmr 6) was consistent with the expected cis,-trans,cis-3,9-diethoxy-4,10-diazatricyclo[6,4,0,$0^{2,7}$]-dodeca-3,9-diene structure (L).



(L)



(LI)

The triplet at δ1.3 was assigned to the two methyl groups; the multiplet at δ1.7 to the four cyclobutyl protons; the multiplet at δ2.6 to the four protons at C-6 and C-12; the triplet at δ3.6 to the four protons at C-5 and C-11; and the quartet at δ4.4 was assigned to the two $OCH_2$ groups. The coupling constant for the ethyl protons (6Hz) and the chemical shift values were the same as those for the ethyl protons in 2,5-diethoxy-3,6-dihydropyrazine.

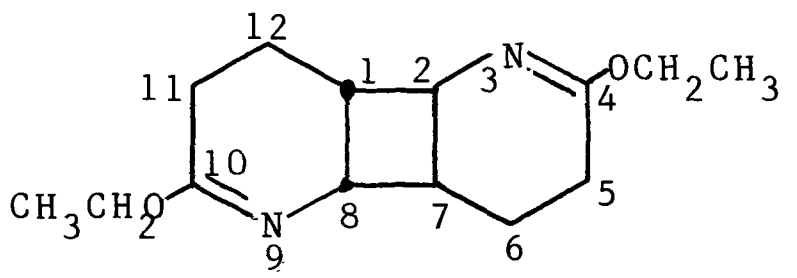
An attempt to recrystallise a sample of the crude lactim ether from cyclohexane resulted in the isolation of a small quantity (23mg) of a white solid, m.p. 130-133°C. The tlc showed only one component, and although the elemental analysis figures were rather poor, they indicated the molecular formula $C_{12}H_{18}N_2O_2$, consistent with the formulation of the compound as cis,trans,cis-9-ethoxy-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodec-9-en-3-one (LI). This was supported by the infrared spectrum (ir 10) which showed characteristic bands due to amide, C=N and $OCH_2$ absorptions. Evidently this arises from incomplete reaction of the dilactam with the alkylating agent, or possibly by hydrolysis of a small amount of the diethoxy compound (L).

O-Ethylation of the dilactam (VIII) derived from the Schmidt reaction was then effected in the same way.

Treatment of a suspension of cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione in dichloromethane with triethyloxonium tetrafluoroborate and work-up as above gave an off-white solid, m.p. 63-65°C (partly) and 93-98°C (completely). Both tlc and glc showed that

the material was essentially a single compound. A sample of the crude material was sublimed to give a white powder, which was pure by glc, but contained a trace impurity on tlc. The material melted partly at 64-65°C and completely at 95-100°C [cf. (L)].

Elemental analysis showed a molecular formula $C_{14}H_{22}N_2O_2$; the infrared spectrum (ir 11) exhibited bands for the C=N and C-O groups; and the pmr spectrum (pmr 7) was consistent with the formulation cis,trans,cis-4,10-diethoxy-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene (LII).

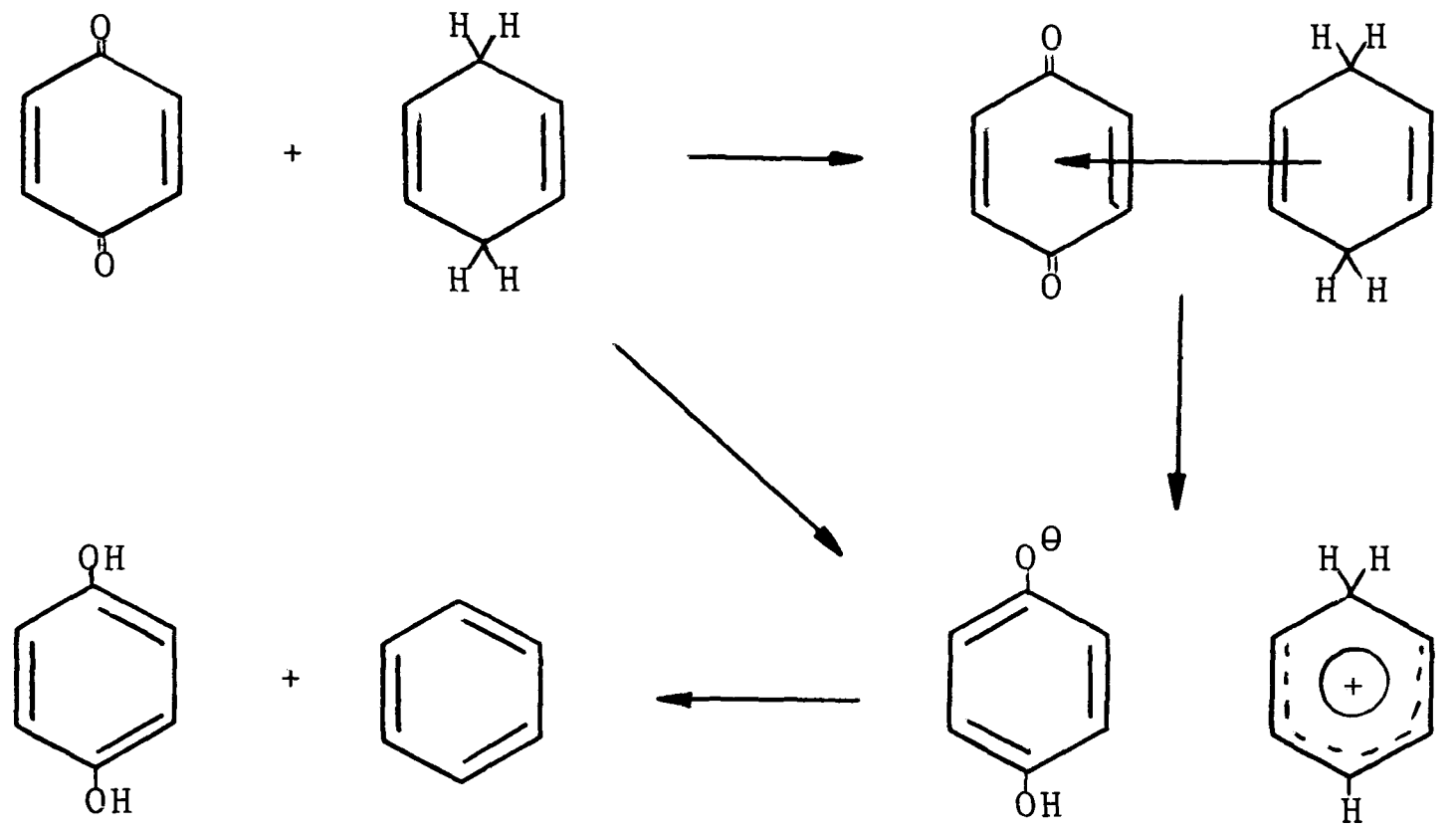



(LII)

A triplet at δ1.3 was assigned to the two methyl groups; a ten proton multiplet at δ2.1 was assigned to the hydrogens at carbons 1, 5, 6, 7, 11 and 12; and the multiplet at δ4.1 was a combination of the signals from 2-H, 8-H and the quartet from the two $OCH_2$ groups. The coupling constant (7Hz) and chemical shift values for the ethyl protons were very similar to those for the ethyl protons in the previous lactim ether (L).

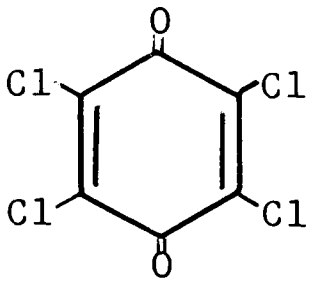
Attempted dehydrogenations with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone

The use of a quinone for the dehydrogenation of hydroaromatic compounds was first reported by Clar and John [112] in 1930, and has since found considerable application in organic synthesis, particularly in the steroid field. The mechanism of the reaction is a two stage ionic process, as shown below. Charge transfer complexes are probably formed in the initial step of the over-all reaction sequence [113].

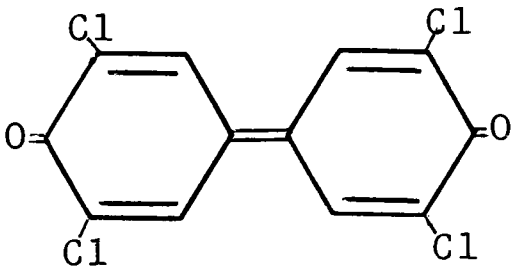


A study of the mechanism shows that electron-withdrawing substituents should increase the dehydrogenating power of quinones and such changes in substitution also affect the oxidation-reduction potential of the quinone.

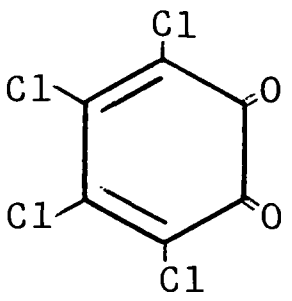
Thus, although many reactions have been carried out using chloranil (LIII), this is not the most effective reagent, and in the dehydrogenation of 1,2-dihydronaphthalene it was found that 3,3',5,5'-tetrachloro-4,4'-diphenoquinone (LIV), tetrachloro-1,2-benzoquinone (LV), and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (LVI) all reacted several thousand times faster than chloranil [114].



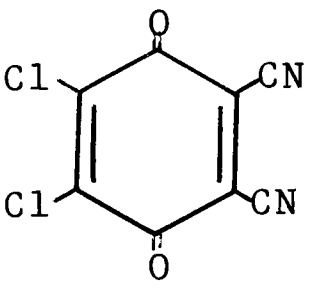
(LIII)



(LIV)



(LV)

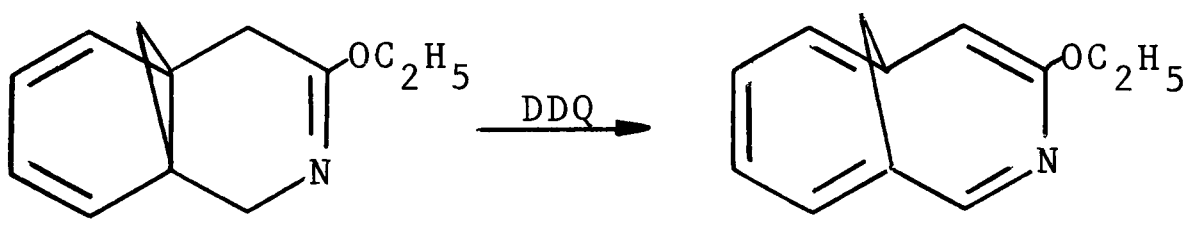


(LVI)

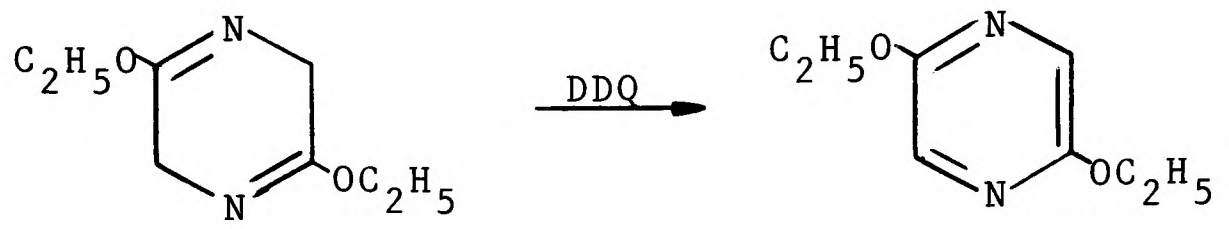
The most common side reactions of quinones are diene addition (Diels-Alder reaction), nucleophilic addition in the case of unsubstituted quinones, and nucleophilic substitution with halogenated quinones.

One of the most useful of these reagents is DDQ [106], which was first reported by Thiele and Günther [115] in 1906, and found to be a superior dehydrogenation reagent of hydroaromatic compounds by Linstead and co-workers [116].

Of relevance to the present work are the DDQ dehydrogenations of the lactim ether (LVII) to the aza [10]-annulene (LVIII) [117] and the conversion of the dihydropyrazine (XLIX) to the pyrazine (LIX) [111].

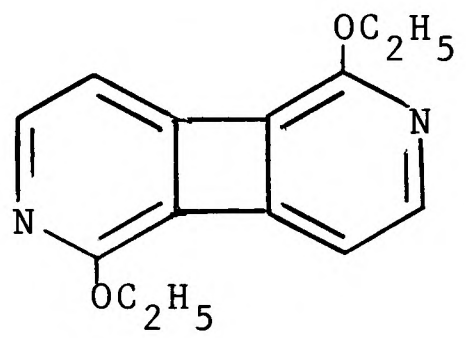


(LVII) (LVIII)

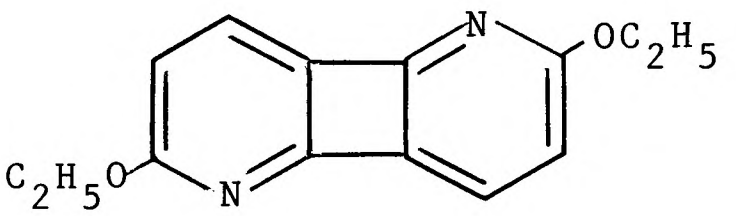


(XLIX) (LIX)

It was hoped that similar dehydrogenations of the lactim ethers could be effected; thus compounds (L) and (LII) could give rise to (LX) and (LXI) respectively. It was decided to attempt the dehydrogenation of the lactim ethers with the preferred quinone, DDQ.



(LX)



(LXI)

A solution of cis,trans,cis-3,9-diethoxy-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene (L) and DDQ in benzene was heated at reflux; a vigorous reaction occurred during the initial heating period. The solid which separated was removed by filtration; glc of the filtrate indicated absence of starting material, hence the material was concentrated and chromatographed on alumina. However, no material could be eluted from the column with either benzene or ethyl acetate. The pmr spectrum of the solid from the reaction showed a benzene signal at δ7.4, and several weak signals in the range δ1.3-4.5 due to aliphatic protons but no signals in the range expected for the diethoxydiazabiphenylene.

Similarly, a benzene solution of cis,trans,cis-4,10-diethoxy-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene (LII)

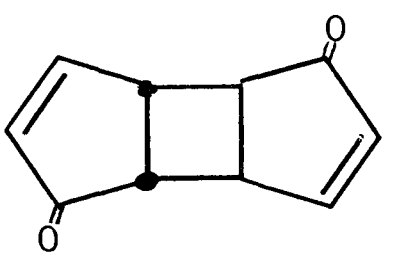
was refluxed with DDQ with similar results. A vigorous reaction again occurred during the initial heating period and after filtration, the benzene solution was free of starting material (by glc), but when chromatography on alumina was attempted, no material could be eluted from the column with either benzene or ethyl acetate.

The pmr spectrum of the solid from the reaction showed a singlet at δ7.4 due to benzene, and several signals in the range δ1.3-4.5 due to aliphatic protons; but again there was no evidence for aromatic signals corresponding to a diazabiphenylene.

The work described above further extends the investigations into the synthesis of diazabiphenylenes which were begun by Mendonca [57]. Milder methods of dehydrogenation of the tricyclic diamines (XX) and (XXII), by the use of reagents such as silver acetate, may be worth pursuing. Also the dehydrogenation of the lactim ethers (L) and (LII) should be further investigated as it was evident that the compounds had reacted with DDQ, but lack of time prevented a full study of the reactions.

Piperid-2-one may be converted into 2,3,3-trichloro-1-piperideine [118], and a similar transformation of the dilactams from the Beckmann and Schmidt reactions, followed by dehydrochlorination and dehydrogenation may be a possible route to diazabiphenylenes.

A different approach, which it would be worthwhile to investigate, is the Beckmann or Schmidt reactions of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-4,9-diene-3,8-dione [56,119], which may result in the formation of unsaturated lactams. The O-alkylation of these dilactams,




followed by dehydrogenation, may result in the formation of substituted diazabiphenylenes.

# E X P E R I M E N T A L

## GENERAL TECHNIQUES

Infrared (ir) spectra were determined as potassium bromide discs, using a Perkin Elmer 397 or Unicam SP200 spectrophotometer, the intensities of the bands being indicated by vs (very strong), s (strong), m (medium) and w (weak).

Proton magnetic resonance (pmr) spectra were obtained for the appropriate compounds in either deutero-chloroform or trifluoroacetic acid (TFA) at 60MHz on a Varian EM-360 spectrometer; tetramethylsilane was used as an internal standard. Mass spectra (ms) were determined on a Vacuum Generators 7070 spectrometer, and ultraviolet spectra (uv) on a Unicam SP800 spectrophotometer.

Thin layer chromatography (tlc) was run on silica gel 60F-254 (Merck pre-coated plates) for all mobile phases except chloroform-ammonia, when alumina F-254 (type E) plates were used; components were detected by ultraviolet light or with iodine vapour. Melting points were determined either on a Reichert, a Büchi 510 or an Electrothermal melting point apparatus.

High performance liquid chromatography (hplc) was carried out on a Bondapak carbohydrate column with a flow rate of $1.0 ml min^{-1}$ for the mobile phase. Gas-liquid chromatography (glc) was carried out on a Pye-Unicam GCD with a carrier gas flow rate of $30 ml min^{-1}$; the columns were packed with Chromosorb W containing 10% of the stationary phase.

A Bellingham and Stanley refractometer was used to obtain refractive indices. Column chromatography was carried out on neutral alumina, Brockmann grade 1.

When appropriate, solvents were dried over molecular sieves (4A) and filtered before use.

## SYNTHESIS OF CYCLOPENT-2-ENONE

### (a) From Cyclopentadiene

#### Cyclopentadiene [58]

Liquid paraffin (400ml) was heated to 240-270°C in a flask fitted with a stirrer, dropping funnel, thermometer and fractionating column. Dicyclopentadiene (1 kg) was added slowly *via* the dropping funnel and the cyclopentadiene b.p. 38-42°C which formed was collected (860g). The cyclopentadiene, which is *ca*. 95% pure, dimerizes at room temperature and hence was stored in dry-ice.

#### Cyclopentenediols [58]

Cyclopentadiene (56g, 0.81 mol), sodium carbonate (106g, 1.0 mol) and dichloromethane (500ml) were stirred in a round bottomed flask fitted with a thermometer and dropping funnel. A solution of sodium acetate (2.0g) in 40% w/w peracetic acid (76.0g, 0.4 mol) was added at 20°C with cooling over 1.25 h. After stirring for a further 1 h, the mixture was filtered and the solid washed with dichloromethane (3 x 75ml). The dichloromethane solution was slowly added during 1 h to water (250ml) at 5-10°C, with stirring and cooling. After stirring for 1 h, the two layers were separated and the organic phase extracted with water (2 x 25ml). The total aqueous solution was concentrated *in vacuo* to yield a mixture of cyclopentenediol isomers (20g, 50%). Glc on Silar 10C at 135°C showed three peaks (19%, 34% and 47%) with retention times 7.0, 16.0 and 19.5 min respectively.

#### Cyclopent-2-enone [59,60]

A mixture of cyclopentenediol isomers (150g, 1.5 mol) was placed in a 500ml flask and warmed to 50°C. Toluene-4-sulphonic acid monohydrate (3g) was added and the cyclopent-2-enone formed was distilled as rapidly as possible, to prevent polymerisation, and collected in the range b.p. 40-90°C/15 mmHg. The distillate was dissolved in

dichloromethane (230ml), the aqueous layer discarded, and the dichloromethane solution concentrated and distilled to give cyclopent-2-enone (61.5g, 50%) b.p. 151-156°C (lit.[59], b.p. 151-154°C) as a colourless liquid. Glc on OV17 at 85°C showed one peak, $R_t$ 6.1 min. $\nu_{max}$ 1710vs (C=O) $cm^{-1}$.

(b) From Cyclopentanone

2-Bromocyclopentanone ethylene ketal

A solution of cyclopentanone (33.6g, 0.4 mol) in ethanediol (500ml) was stirred and bromine (70g, 0.44 mol) added during 20 min, whilst the reaction mixture was maintained at 30-35°C by cooling in ice-water. After stirring for a further 5 min, the solution was poured onto a mixture of sodium carbonate (100g) and pentane (400ml), then water (500ml) was added. The organic phase was separated, dried ($MgSO_4$) and evaporated to yield the bromo-ketal as a green liquid (67.6g).

Cyclopent-2-enone ethylene ketal

The above crude bromoketal was added to a solution of sodium hydroxide (50g) in methanol (200ml), and refluxed with stirring for 3 h, then poured into a mixture of saturated sodium chloride solution (400ml) and pentane (400ml). After filtering through Celite, the aqueous layer was separated and extracted with pentane (2 x 400ml). The combined organic extracts were evaporated and the residue distilled to afford the ethylene ketal of cyclo-pent-2-enone as a colourless liquid (30.07g, 60%) b.p. 57°C/10 mmHg (lit.[60], b.p. 64-65°C/22 mmHg); $n_D^{19}$ 1.4695 (lit.[120], $n_D^{18}$ 1.4675).

Cyclopent-2-enone

The ketal was shaken with 0.6M sulphuric acid (30ml) for 5 min and the mixture extracted with ether (3 x 50ml). The combined extracts were washed with 0.6M sodium bicarbonate (30ml) and distilled to give cyclopent-2-enone (6.82g, 21%) b.p. 45°C/10 mmHg (lit.[60], b.p. 68.5-69°C at 23 mmHg); $n_D^{29}$ 1.4680 (lit.[60], $n_D^{29}$ 1.4739). Glc on OV17 at 85°C showed one peak, $R_t$ 6.1 min.

## CIS,TRANS,CIS-TRICYCLO[5,3,0,$0^{2,6}$]DECANE-3,8-DIONE

(a) Photolysis of cyclopent-2-enone in methanol [57]

Cyclopent-2-enone (50g, 0.61 mol) in methanol (800ml) was placed in the chamber of a 1 litre Hanovia photochemical reactor and exposed to the output of a 100 watt medium pressure mercury arc lamp through Pyrex, under an atmosphere of nitrogen, for 3 days. The white precipitate was filtered and the solution irradiated again for 24 h. This procedure was repeated until all of the cyclopent-2-enone had reacted (as indicated by glc) to yield cis,trans-cis-3,3,8,8-tetramethoxytricyclo[5,3,0,$0^{2,6}$]decane (33.2g) as a white solid, m.p. 164-168°C (lit.[57], m.p. 173-174°C).

The solid was refluxed with a stirred mixture of dichloromethane (400ml) and 2M hydrochloric acid (60ml) for 1 h, and the dichloromethane solution separated and evaporated to dryness to yield a brown solid (17.7g), m.p. 120-124°C. This was recrystallised from carbon tetrachloride to yield cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione as a white solid (13.0g, 26%), m.p. 126-127°C (lit.[56], m.p. 125-126°C). Glc on XE60 at 190°C showed one peak $R_t$ 5.6 min; tlc (50% ethyl acetate in toluene) showed one component at $R_F$ 0.52; $\lambda_{max}$ (uv 1) (95% EtOH) 210, 293nm ($\varepsilon$355, 68 $dm^3\ mol^{-1}\ cm^{-1}$); $\nu_{max}$ (ir 1) 1730vs (C=O) $cm^{-1}$.

The methanol liquors from the photolysis were evaporated to dryness and the red oil (29.7g) was refluxed with a stirred mixture of dichloromethane (358ml) and 2M hydrochloric acid (54ml) for 1 h. After cooling, the dichloromethane solution was evaporated to dryness and the red oil (30.6g) distilled quickly at 120-125°C/0.05 mmHg and the distillate then redistilled slowly to give a white solid (1.8g) b.p. 116°C/0.04 mmHg; m.p. 52-59°C. A portion of this solid (1.0g) was recrystallised from a large volume of hexane to yield cis,trans,cis-tricyclo-[5,3,0,$0^{2,6}$]decane-3,10-dione (0.75g) m.p. 66-67°C (lit.[56], m.p. 66-67°C). Glc on XE60 at 180°C showed one peak $R_t$ 17.4 min with a small amount of the 3,8-isomer. Tlc

(50% ethyl acetate in toluene) showed one component $R_F$ 0.57, together with a trace of the 3,8-isomer; $\lambda_{max}$ (uv 2) (95% EtOH) 215, 305nm ($\varepsilon$ 1892, 133 $dm^3$ $mol^{-1}$ $cm^{-1}$); $\nu_{max}$ (ir 2) 1730vs (C=O) $cm^{-1}$.

(b) Photolysis of cyclopent-2-enone in cyclohexane [63]

Cyclopent-2-enone (64.0g, 0.78 mol) in redistilled cyclohexane (640ml) was placed in the chamber of a 1 litre Hanovia photochemical reactor and exposed to the output of a 100 watt medium pressure mercury arc lamp, through Pyrex, under an atmosphere of nitrogen. The irradiation was continued at room temperature for a total of 7 days, with the lamp being periodically scraped free of product. The combined solids were dried to afford pale brown crystals (49.60g, 78%). The cyclohexane liquors were evaporated to dryness to give an orange oil (12.1g). The solid and the oil were combined, dissolved in methanol (615ml), stirred overnight, and the precipitate filtered and dried to yield cis,trans,cis-3,3,8,8-tetramethoxytricyclo[5,3,0,$0^{2,6}$] decane (38.1g) as a white solid m.p. 167-169°C (lit.[57], m.p. 173-174°C). Concentration of the methanol liquors afforded a further quantity (17.8g) of the diketal.

The total diketal was refluxed with a stirred mixture of dichloromethane (695ml) and 2M hydrochloric acid (105ml) for 1 h. After cooling, the dichloromethane solution was separated, concentrated in vacuo, and the product recrystallised from carbon tetrachloride to give cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione (30.11g, 47%) as a white solid, m.p. 126-127°C (lit.[56], m.p. 125-126.5°C); glc on XE60 at 190°C showed one peak, $R_t$ 5.6 min. Tlc (50% ethyl acetate in toluene) showed only one component $R_F$ 0.52.

The methanol solution from the diketal formation was concentrated and the residue (29.8g) stirred and heated under reflux with a mixture of dichloromethane (370ml) and 2M hydrochloric acid (55ml) for 1 h. After cooling, the organic phase was separated, evaporated and the

resulting oil (22.48g) distilled rapidly at 102-140°C/0.03 mmHg to afford a pale yellow solid (12.66g). Two recrystallisations from hexane gave almost pure cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,10-dione (5.94g) as a white solid m.p. 59-62°C (lit.[56], m.p. 66-67°C). Glc on XE60 at 180°C showed the presence of ca. 12% of the 3,8-isomer.

## BECKMANN REARRANGEMENT OF THE DIOXIME(S) OF CIS,TRANS,CIS-TRICYCLO[5,3,0,$0^{2,6}$]DECANE-3,8-DIONE

### Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione dioxime(s) [57]

(a) With sodium hydroxide

Hydroxylamine hydrochloride (50.8g, 0.73 mol), cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione (20g, 0.122 mol), ethanol (200ml), water (200ml) and 2.5M sodium hydroxide solution (200ml, 0.50 mol) were stirred together and refluxed for 30 min. The mixture was cooled to 0-10°C for 30 min and the crude product collected by filtration, washed with water (400ml) and dried to give a pale brown solid (21.4g, 90%). Recrystallisation from a large volume of ethanol gave cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione dioxime(s) as a white crystalline solid (17.6g, 74%) m.p. 225-227°C (decomp.) [lit.[57], m.p. 224.5-225.5°C (decomp.)]. Tlc (ethyl acetate) showed two components, $R_F$ 0.51 and 0.63, in equal quantities.

(b) With sodium acetate

Hydroxylamine hydrochloride (25g, 0.36 mol), cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione (10g, 0.061 mol), ethanol (150ml), water (100ml) and anhydrous sodium acetate (24.2g, 0.30 mol) were stirred together and refluxed for 1 h. The solution was left to stand overnight, then cooled in ice. The crude product was filtered, washed with water (200ml) and dried to give an off-white solid (9.8g, 83%). Recrystallisation from a large volume of ethanol gave cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione dioxime(s) as a white crystalline solid (7.6g, 64%) m.p. 225-227°C (decomp.) [lit.[57], m.p. 220-223°C (decomp.)]. Tlc (ethyl acetate) showed two components, $R_F$ 0.51 and 0.63, in equal quantities.

Investigation of the Beckmann rearrangement of cis,trans,-cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione dioxime(s) using various catalysts

The dioxime(s) (0.5g, 2.6 mmol) was added to the various catalysts and reacted as outlined in Table 1. The mixture was then treated with ice (40g), adjusted to pH8.5 with either sodium carbonate or hydrochloric acid and continuously extracted with chloroform for several days. The chloroform solution was evaporated to dryness to obtain the products, as listed in Table 1, which were analysed by tlc [ethanol-water (9:1)]. The aqueous solution was made strongly alkaline by the addition of sodium hydroxide (25g) and extracted with ether (2 x 50ml). The ether extracts were evaporated to dryness, but in all cases there were no residues.

Beckmann rearrangement of cis,trans,cis-tricyclo-[5,3,0,$0^{2,6}$]decane-3,8-dione dioxime(s)

(a) With polyphosphoric acid

The dioxime(s) (2.5g, 12.9 mmol) was added in portions over 5 min to polyphosphoric acid (63g) at 50°C. The stirred mixture was heated at 120°C for 15 min, then poured onto ice-water (400g). The solution was adjusted to pH 8 with sodium carbonate (ca. 60g), continuously extracted with chloroform for 6 days and the extract concentrate in vacuo to yield a white solid (2.29g, 92%), m.p. 330°C (decomp.). Tlc [ethanol-water (9:1)] showed two spots $R_F$ 0.31 and 0.35; hplc [acetonitrile-water (9:1)] Bondapak carbohydrate column showed two equal peaks $R_t$ 7.9 min and 9.0 min. The aqueous solution was made strongly alkaline by the addition of sodium hydroxide (250g) and extracted with ether (2 x 300ml). Evaporation of the ether extract gave no residue.

Repetition of this reaction with a further quantity of the dioxime(s) (7.5g) gave a mixture of the two products (7.2g) as above. Recrystallisation of the combined solids

Table 1

Beckmann rearrangements using various catalysts

| Catalyst | Reaction temperature (°C) | Reaction time | Product | M.p. (°C) | Identity of Product |
|---|---|---|---|---|---|
| Conc sulphuric Acid (15ml) | 120-130 | 10 min | white solid (0.40g, 80%) | >340 (decomp) | A |
| Thionyl chloride (10ml) | 5-10 | 30 min | pale brown solid (0.50g, 100%) | partly 250 and >350 | A + B (major) |
| Boron trifluoride etherate (10ml) | 50 | 15 min | white solid (0.50g) | 216 | starting dioxime(s) |
| Phosphorus pentachloride (1.25g) in ether (10ml) | 0-5 | 60 min | white solid (0.50g) | 170 | starting dioxime(s) |
| Benzenesulphonyl chloride (2.3g) in 3.3M sodium hydroxide (4ml) | 0-5 | 18 h | brown gum (1.3g) | - | complex mixture of seven products |
| Trifluoroacetic anhydride (2.4g) in dimethoxyethane (10ml) | reflux | 60 min | dark brown liquid (2.5g) (a) | - | mixture of three products |
| Polyphosphoric acid (13g) | 120 | 15 min | white solid (0.50g, 100%) | 290-340 | A (major) + B |

A = cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-3,9-dione

B = cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione

(a) Reaction mixture evaporated to dryness to obtain product

(9.49g) from water gave the major constituent cis,trans,-cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-3,9-dione (4.70g) as colourless needles, m.p. >320°C (decomp.) [lit.[57], m.p. >300°C (decomp.)]. Tlc [ethanol-water (9:1)] showed one compound $R_F$ 0.31.

The mother liquor contained mainly cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione (3.11g) by tlc, but this was not further purified.

(b) With concentrated sulphuric acid

Concentrated sulphuric acid (60ml) was stirred at ambient temperature and portions of the dioxime(s) (3.0g, 15.5 mmol) added slowly. Addition of the solid resulted in a very vigorous reaction giving a brown solution and the evolution of a small cloud of smoke from the reaction mixture. After a little of the dioxime(s) had been added to the sulphuric acid, the addition was stopped and the reaction mixture discarded.

## THE SCHMIDT REACTION OF CIS,TRANS,CIS-TRICYCLO[5,3,0,$0^{2,6}$]DECANE-3,8-DIONE

### Cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane-4,10-dione

Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione (10.0g, 61 mmol) was dissolved in concentrated hydrochloric acid (100ml) and the solution cooled to 5°C in an ice bath. Sodium azide (8.72g, 134.2 mmol) was added in portions over 10 min at 5-13°C with stirring. The solution was stirred at 10°C for 30 min, then at ambient temperature overnight. The mixture was diluted with water (500ml), adjusted to pH 8.5 with sodium carbonate (ca. 55g) and continuously extracted with chloroform for 8 days. The chloroform extract was evaporated to dryness to yield a pale brown solid (10.17g, 86%), m.p. 250-310°C (decomp.) [lit.[57], m.p. 245-310°C (decomp.)]. Tlc [ethanol-water (9:1)] showed two main components, $R_F$ 0.35 and 0.30, together with a minor compound at $R_F$ 0.67.

Repetition of this reaction and re-extraction of the above aqueous solution yielded a further quantity of product [11.32g, total wt. 21.49g, (91%)].

Fractional crystallisation of the combined solids from water gave the major constituent cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione (7.54g) as a cream solid, m.p. 349-350°C (decomp.) [lit.[57], chars from 338°C (sealed tube)]. Tlc [ethanol-water (9:1)] showed one compound $R_F$ 0.35.

The mother liquor contained mainly cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione (by tlc), but was not further purified.

N-Benzylation of cis,trans,cis-3,9-diaza-tricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione [57]

Cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione (3.0g, 15.5 mmol) was added in portions over 7 min to a stirred mixture of sodium hydride (1.63g, 34.0 mmol, 50% dispersion in oil, washed with light petroleum) in dry N,N-dimethylformamide (60ml). The mixture was stirred at 70-75°C for 1 h, cooled to 20°C and benzyl chloride (12ml) added. After stirring at 70-75°C for 4 h, the mixture was cooled to 30°C and treated with water (240ml). The mixture was stirred overnight and the solid filtered, washed with water (30ml) and dried to give an off-white solid (2.98g, 51%), m.p. 230-234°C. TLC (ethanol) showed one component $R_F$ 0.52. Recrystallisation from methanol gave N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione as a white sold, m.p. 233-235°C (lit.[57], m.p. 232-234°C).

The reaction liquors were continuously extracted with chloroform for 3 days. The chloroform solution was evaporated to dryness to give a brown semi-solid (2.03g). Tlc (ethanol) showed four main components $R_F$ 0.0, 0.19 (starting material), 0.46, 0.52 (N,N'-dibenzyl dilactam).

## REDUCTION OF THE DILACTAMS FROM THE BECKMANN AND SCHMIDT REACTIONS

### cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

An ice-cooled mixture of cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-3,9-dione (0.97g, 5 mmol) in dry tetrahydrofuran (15ml) was stirred under an atmosphere of nitrogen, and a 1M solution of borane in tetrahydrofuran (40ml, 40 mmol) added at 5-10°C over 10 min. The mixture was stirred at 5°C for 20 min, cautiously refluxed for 0.5h, then cooled to 20°C. There was considerable foaming during the heating period. After the careful addition of 6M hydrochloric acid (10ml), the tetrahydrofuran was removed by distillation, the solution cooled and ether (25ml) added, followed by sodium hydroxide (4g). The organic phase was separated and the aqueous solution extracted with ether (2 x 25ml). The combined ether extracts were evaporated to dryness and the residue dissolved in benzene (25ml). The dried ($K_2CO_3$) benzene solution was evaporated to afford cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane (0.653g, 79%) as a pale brown gum. The gum was stored under nitrogen. Glc on SP1000/2% KOH at 170°C showed mainly one component $R_t$ 17.9 min; tlc (chloroform saturated with 0.880 ammonia) showed mainly one compound $R_F$ 0.41; $\nu_{max}$ (ir 3) 3330m (NH str.); $\delta$(pmr 1, $CDCl_3$) 1.2-3.7 ppm (peak at 2.3ppm exchanges with $D_2O$).

The diamine was characterised as its bis(4-nitrobenzoyl) derivative using the following procedure.

Pyridine (14ml), cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane (0.374g, 2.25 mmol) and anhydrous sodium carbonate (2.4g, 22.6 mmol) were stirred and 4-nitrobenzoyl chloride (2.00g, 10.8 mmol) added over 5 min. The mixture was refluxed for 1 h, cooled and diluted with water (200ml). The water was extracted with chloroform (3 x 50ml) and the combined chloroform extracts

washed successively with 1M hydrochloric acid (300ml), 1M sodium carbonate (100ml), and water (300ml). The dried chloroform solution was evaporated to dryness to give a yellow solid (0.66g, 63%). Tlc [ethanol-water (9:1)] showed mainly two compounds at $R_F$ 0.73 and 0.77. The crude product was refluxed with ethanol (40ml) for 2 h, cooled, filtered and the dried solid recrystallised from glacial acetic acid, followed by a recrystallisation from N,N-dimethylformamide to yield N,N'-bis(4-nitrobenzoyl)-cis,-trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane as a white solid, m.p. 256-257°C. Tlc [ethanol-water (9:1)] showed a pure compound at $R_F$ 0.73. (Found: C, 62.39; H, 5.47; N, 12.08. $C_{24}H_{24}N_4O_6$ requires C, 62.07; H, 5.17; N, 12.07%); $\nu_{max}$ (ir 4) 3100w (aromatic CH), 1650s (tertiary amide C=0), 1600m (aromatic C=C) 1540, 1350m $cm^{-1}$ ($NO_2$); δ(pmr 2, T.F.A.) 1.7-3.1 (8H,m, 1-H, 2-H, 2x6-H, 7-H, 8-H, 2x12-H) 3.1-4.4 (8H, m, 2x3-H, 2x5-H, 2x9-H, 2x11-H), 7.5-8.7 (8H, q, Ph) ppm.

Cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

An ice-cooled mixture of cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione (970mg, 5 mmol) and dry tetrahydrofuran (15ml) was stirred under nitrogen, and a 1M solution of borane in tetrahydrofuran (40ml, 40 mmol) added at 5-10°C over 15 min. After stirring at 5°C for 20 min, the reaction mixture was refluxed for 30 min, cooled and 6M hydrochloric acid (10ml) added with care. The tetrahydrofuran was removed by distillation, and the aqueous solution cooled in ice and ether (25ml) added, followed by sodium hydroxide (4.0g). The aqueous phase was separated, extracted with ether (2 x 25ml) and the combined ether extracts evaporated to dryness. The residue was dissolved in benzene (25ml), dried ($K_2CO_3$) and the solution evaporated to give cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane monohydrate as a pale brown gum (930mg, 100%) which was stored under nitrogen. Glc on SP1000/2% KOH at 170°C showed mainly one component $R_t$ 13.6 min; tlc (chloroform saturated with 0.880 ammonia) showed

one component $R_F$ 0.35; $\nu_{max}$ (ir 5) 3300m (NH, OH str.), 1640m $cm^{-1}$ ($H_2O$); δ(pmr 3, $CDCl_3$) 1.2-3.8 (17H, m), 4.4 (2H, s, $H_2O$) ppm. (Peak at δ4.4 disappears on treatment with $D_2O$).

The diamine was characterised as its bis(4-nitrobenzoyl) derivative as outlined below.

A mixture of cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane (840mg, 5.06 mmol), pyridine (32ml) and anhydrous sodium carbonate (5.39g, 50.8 mmol) was stirred and 4-nitrobenzoyl chloride (4.50g, 24.3 mmol) added over 5 min. After refluxing for 1 h, the reaction mixture was cooled and treated with water (450ml). The water was extracted with chloroform (3 x 110ml) and the combined organic extracts washed successively with 2.5M hydrochloric acid (340ml), 1M sodium carbonate solution (225ml) and water (670ml). The dried ($MgSO_4$) solution was concentrated to afford a sticky yellow solid (1.11g, 47%). Tlc [ethanol-water (9:1)] showed two components at $R_F$ 0.73 and 0.48. Several recrystallisations from ethanol yielded N,N'-bis(4-nitrobenzoyl)-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane as a cream solid (0.31g), m.p. 242-246°C (decomp.). Tlc [ethanol-water (9:1)] showed one spot $R_F$ 0.73. (Found C, 61.23; H, 5.31; N, 12.00. $C_{24}H_{24}N_4O_6$ requires C,62.07; H,5.17; N,12.07%); $\nu_{max}$ (ir 6) 3100w (aromatic CH str.), 1630s (tertiary amide C=O), 1500m (aromatic C=C), 1520s and 1350s $cm^{-1}$ ($NO_2$); δ(pmr 4, $CDCl_3$) 1.1-2.3 (8H, br s,2x5-H, 2x6-H, 2x11-H, 2x12-H), 2.6-3.7 (6H, br d, 1-H, 2x4-H, 7-H, 2x10-H). 4.4 (2H, br s, 2-H, 8-H), 7.5-8.5 (8H, q, Ph)ppm.

A sample of the diamine which had been prepared previously was found to rapidly absorb moisture and carbon dioxide from the air to form the carbonate as an off-white solid, m.p. 290-295°C (decomp.) (mainly). (Found, C, 54.20; H, 8.73; N, 11.18. $C_{10}H_{18}N_2 \cdot CO_2 \cdot 2H_2O$ requires C, 53.67; H, 8.94; N, 11.38%); $\nu_{max}$ (ir 7) 3400m (NH str.), 2930s (aliphatic CH str.), 2800-2700s and 2390m ($NH_2^{\oplus}$,NH), 1640m ($H_2O$), 1580m ($NH_2^{\oplus}$), 1170m $cm^{-1}$ (C-N).

Attempted formylation of cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane

A solution of cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane (202mg, 1.2 mmol) in 100% formic acid (4.0ml) was heated on a steam bath for 4 h. After cooling, the solution was made alkaline by the addition of 2.5M sodium hydroxide solution (40ml) and extracted with chloroform (4 x 20ml). The organic extracts were combined, dried and concentrated to afford a brown oil (195mg), which was shown by pmr to be essentially the starting diamine.

Reduction of N,N'-dibenzyl-cis,trans,cis-3,9-diaza-tricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione [57]

A mixture of dry tetrahydrofuran (75ml), lithium aluminium hydride (1.20g, 31.6 mmol) and N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione (1.50g, 4.0 mmol) was stirred and refluxed for 4 h. The slurry was cooled in an ice bath and water (3ml) cautiously added, followed by ether (225ml). After vigorous stirring for 10 min, the inorganic salts were filtered, washed with ether (3 x 75ml) and the combined ether extracts evaporated to dryness to give N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane as a colourless gum (1.44g, 104%). Tlc (ethyl acetate) showed essentially one component $R_F$ 0.33; glc on OV210 at 230°C showed only one peak $R_t$ 10.3 min.

The amine was stored under nitrogen in the dark, but still darkened slowly on standing.

## DEHYDROGENATION STUDIES

### Catalytic dehydrogenation of N,N'-dibenzyl-*cis*,*trans*,*cis*-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

(a) An intimate mixture of N,N'-dibenzyl-*cis*,*trans*,*cis*-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane (414mg, 1.2 mmol) and 10% palladium on carbon (200mg) was placed in a 50ml round bottom flask fitted with a condenser. The reaction mixture was heated at 225°C for 1 h, cooled and extracted with benzene (100ml). The extract was filtered and glc on Carbowax 20M at 50°C showed the presence of toluene, but absence of pyridine. Evaporation of the benzene extract gave a brown liquid (73mg). Glc on Carbowax 20M at 175°C (glc 1) showed two peaks in the ratio 2:3 with retention times 7.5 and 11.3 min respectively.

The use of glc-ms (OV210 or Carbowax) and the addition of authentic samples enabled the major component to be identified as 2,3'-bipyridine (ms 1) m/z 156 ($M^+$, 100%),155(71), 130(30), 104(30), 78(35), 51(63), 44($CO_2$). The minor component was tentatively identified as either 3- or 4-benzylpyridine (ms 2) m/z 169 ($M^+$, 98%), 168(100), 167(30), 141(21), 115(36), 91(33), 65(30), 39(74).

Glc of the product on OV210 at 230°C showed the presence of only a trace of the starting diamine.

(b) A mixture of N,N'-dibenzyl-*cis*,*trans*,*cis*-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane (849mg, 2.45 mmol), nitrobenzene (3.74g, 30.5 mmol) and 10% palladium on carbon (100mg) was stirred and refluxed for 3 h. After cooling, the mixture was extracted with benzene (50ml) and filtered. Glc on OV17 at 40°C for 15 min $\xrightarrow{16°/min}$ 110°C indicated the presence of toluene and aniline, but absence of pyridine. Half of the benzene solution was evaporated at 70°C at 0.1 mmHg to afford a black tar (260mg). Glc on OV17 at 180°C (glc 2) showed that the sample contained some nitrobenzene and two other compounds in the ratio 1:2,

with retention times 8.4 min and 13.4 min respectively. The first component was again tentatively identified as either 3- or 4-benzylpyridine by glc-ms (OV17, OV210 or Carbowax), having a similar mass spectrum to the compound in (a) above.

The second compound was shown to be benzylidene-aniline (ms 3) m/z 181 ($M^+$, 81%), 180(100), 104(14), 77(84), 51(40).

Glc of the black tar on OV210 at 230°C indicated only a trace of the starting diamine.

Catalytic dehydrogenation of piperidine

A slurry of 10% palladium on carbon (0.85g) in the solvent (85ml) was stirred, piperidine (8.5g, 0.10 mole) added and the mixture reacted as listed in Table 2. In some of the experiments the reaction was purged with either nitrogen or carbon dioxide after first refluxing the catalyst with the solvent for 10 min, with the gas passing through the mixture. At the end of the reaction period, the slurry was cooled, filtered and the solution analysed by glc on OV210 at 35°C. If piperidine was absent, the solution was distilled into an ice-cooled receiver to yield pure pyridine, b.p. 24°C/10 mmHg, $n_D^{20}$ 1.5081 (lit.[121], $n_D^{20}$ 1.5095).

Catalytic dehydrogenation of cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

(a) Without solvent

(i) A mixture of cis,trans,cis-4,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane (286mg, 1.72 mmol) and 10% palladium on carbon (29mg) was heated at 220°C for 1 h in a round bottom flask fitted with a condenser. A very slow stream of nitrogen was passed over the surface of the reaction mixture during this heating period. After cooling, the reaction was extracted with a refluxing mixture of benzene (25ml) and ethanol (25ml) for 30 min. Evaporation of the

Table 2

Catalytic dehydrogenations of piperidine

| Solvent | Reaction temperature (°C) | Reaction period (h) | Purging gas | % conversion | % yield |
|---|---|---|---|---|---|
| m-xylene | 132 | 24 | none | 8 | - |
| m-xylene | 132 | 20 | $N_2$ | 4 | - |
| p-cymene | 150 | 19 | none | 8 | - |
| p-cymene | 150 | 4 | $N_2$ | 25 | - |
| 1-methylnaphthalene | 186 | 24 | none | 0 | - |
| 1-methylnaphthalene | 186 | 4 | $N_2$ | 0 | - |
| 1-methylnaphthalene | 186 | 4 | $CO_2$ | 0 (b) | - |
| Diphenylmethane | 194 | 24 | none | 100 | 31 |
| Diphenylmethane | 194 | 5 | none | 100 (a) | 21 |

(a) Dry-ice condenser used during the reflux period

(b) White crystals were precipitated during the reaction

filtered extract gave a brown oil (270mg), which was shown to be the starting diamine by tlc (chloroform saturated with 0.880 ammonia) and glc on SP1000/2% KOH at 170°C.

(ii) A mixture of cis,trans,cis-4,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane (210mg, 1.27 mmol) and 10% palladium on carbon (105mg) was placed in a flask and heated at 295-305°C for 30 min, in a bath of Woods metal, with a slow stream of nitrogen passing over the reaction surface. After being allowed to cool, the solid was extracted with boiling methanol (2 x 25ml) and the extract filtered and concentrated to afford a brown gum (51mg)with a pyridine-like odour. The catalyst was re-extracted with ethanol (2 x 25ml) to yield a further quantity of oil (6mg). Tlc (50% ethyl acetate in ethanol) showed mainly baseline material and two minor components at $R_F$ 0.47 and 0.75; no compounds were eluted from the glc columns Carbowax 20M, OV210 or OV17 at 220°C; the pmr spectrum showed a trace of aromatic protons, but mainly only aliphatic hydrogen.

(b) In diphenylmethane

A solution of cis,trans,cis-4,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane (249mg, 1.50 mmol) in diphenylmethane (2.5ml) was heated with 10% palladium on carbon (25mg) in a 50ml flask at 220°C for 1 h, under nitrogen. The mixture was cooled, extracted with refluxing methanol (25ml) and filtered. Glc of the methanol extract on SP1000/2% KOH at 170°C showed only the presence of the starting diamine.

The methanol extract was concentrated, the residue dissolved in ether (25ml) and the solution extracted with 2.5M hydrochloric acid (10ml). The aqueous phase was separated, washed with ether (2 x 25ml), and sodium hydroxide (2g) added. The aqueous solution was saturated

with sodium chloride (5g) and extracted with ether (3 x 25ml). The combined organic extracts were evaporated to give a brown gum (114mg). Glc on SP1000/2% KOH at 170°C showed the gum to be the starting diamine; there were no signals in the aromatic region of the pmr spectrum.

Catalytic dehydrogenation of cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

(a) Without solvent

An intimate mixture of cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane (390mg, 2.35 mmol) and 10% palladium on carbon (39mg) was placed in a round bottom flask fitted with a condenser. The reaction mixture was heated in an oil bath at 230°C for 1 h, with a very slow stream of nitrogen passing over the surface of the reaction mixture. The cooled solid was extracted with a mixture of refluxing benzene (25ml) and ethanol (25ml) for 30 min. The extract was filtered and evaporated to afford a brown oil (319mg). Glc of the benzene-ethanol distillate on Carbowax 20M at 70°C showed the presence of pyridine.

Glc of the brown oil on either OV210 at 130°C or SP1000/2% KOH at 170°C indicated the absence of 2,3'-bipyridine and the starting material since no compounds could be eluted from either column. Tlc (ethyl acetate) or [ethanol-water (9:1)] or (chloroform saturated with 0.880 ammonia) of the brown oil showed only baseline material; the pmr spectrum showed only aliphatic protons.

(b) In diphenylmethane

A solution of cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane (390mg, 2.35 mmol) in diphenylmethane (3.9ml) was added to 10% palladium on carbon (39mg) in a flask fitted with a condenser. After heating in an oil bath at 230°C for 1 h, under nitrogen, the mixture was cooled and extracted with refluxing methanol (25ml) for 30 min, filtered and the methanol removed by distillation. Glc of the distillate on Carbowax 20M at 70°C showed the absence of pyridine, and glc of the residue on either OV210 or SP1000/2% KOH showed the

absence of 2,3'-bipyridine and the starting diamine.

Half of the residue was dissolved in ether (25ml) and extracted with 2.5M hydrochloric acid (10ml). The aqueous phase was separated, washed with ether (2 x 25ml), basified by the addition of sodium hydroxide (2g) and extracted with chloroform (3 x 25ml). The organic extracts were combined and concentrated to yield a brown gum (127mg). Tlc [ethanol-water (9:1)] showed mainly baseline material with traces of other components at $R_F$ 0.07, 0.13, 0.16, 0.59, 0.72; there were no signals in the aromatic region of the pmr spectrum.

Attempted dehydrogenation of N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione

A mixture of N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione (0.45g, 1.2 mmol) and 10% palladium on carbon (49mg) in nitrobenzene (1.83g, 14.9 mmol) was stirred and refluxed for 3 h, cooled, and benzene (25ml) was added. After refluxing for 30 min, the slurry was cooled and filtered. The solid was stirred with refluxing methanol (90ml) for 30 min, the hot slurry filtered and the solution evaporated. The resulting solid was triturated with methanol (10ml), filtered and dried to yield the starting dilactam (0.30g), m.p. 233-235°C, mixed m.p. 233-235°C.

Evaporation of the combined benzene and methanol liquors afforded a further quantity (0.07g) of the starting dilactam.

Attempted O-methylation of cis-trans,cis-4,10-diazatricyclo[6,4,0,0,$^{2,7}$]dodecane-3,9-dione

Finely divided cis,trans,cis-4,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-3,9-dione (970mg, 5.0 mmol) was added to dry dichloromethane (15ml), followed by trimethyloxonium tetrafluoroborate (2.96g, 20 mmol). After stirring under nitrogen at ambient temperature for 39 days, the reaction mixture was treated with dichloromethane (50ml) and 5%

sodium bicarbonate solution (100ml). The organic phase was separated and evaporated to dryness to give a yellow oil (130mg). Tlc (methanol) showed equal quantities of two components at $R_F$ 0.59 and 0.53. The oil was not investigated further.

The aqueous phase from the reaction was continuously extracted with chloroform for 4 days. The extract was evaporated to give starting material (820mg, 85%), by tlc.

Attempted O-methylation of cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione

Finely ground cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-4,10-dione (970mg, 5.0 mmol) was added to dry dichloromethane (15ml), followed by trimethyloxonium tetrafluoroborate (2.96g, 20 mmol). After stirring under nitrogen at ambient temperature for 39 days, the reaction mixture was treated with dichloromethane (50ml) and 5% sodium bicarbonate solution (100ml). The organic phase was separated and evaporated to afford a yellow oil (49mg). Tlc (methanol) showed essentially one component, but the oil was not investigated further.

The aqueous phase from the reaction was continuously extracted with chloroform for 4 days and the extract evaporated to yield the starting dilactam (880mg, 91%).

Attempted O-methylation of piperazine-2,5-dione

A slurry of piperazine-2,5-dione (4.25g, 37 mmol) in dry dichloromethane (45ml) was stirred and trimethyloxonium tetrafluoroborate (10.9g, 74 mmol) added. After stirring under nitrogen for 3 h, further quantities of trimethyloxonium tetrafluoroborate (10.9g) and dry dichloromethane (20ml) were added. The reaction mixture was stirred for a further 24 h at room temperature, and then treated with 5% sodium bicarbonate solution (100ml). The two phases were separated and the aqueous solution extracted with dichloromethane (50ml). The combined organic extracts were dried ($K_2CO_3$) and evaporated to yield a yellow gum (0.43g) which was not investigated further.

O-Ethylation of piperazine-2,5-dione [111]

A slurry of piperazine-2,5-dione (2.13g, 18.9 mmol) in dry dichloromethane (15ml) was stirred and a solution of triethyloxonium tetrafluoroborate (6.5g, 34.2 mmol) in dry dichloromethane (10ml) added. The mixture was stirred under nitrogen for 3 h, a further solution of triethyloxonium tetrafluoroborate (6.5g) in dry dichloromethane (10ml) was added, and the slurry stirred at ambient temperature for 24 h. After treatment with 5% sodium bicarbonate solution (100ml), the organic phase was separated and evaporated to dryness to give a light brown solid (2.08g, 65%), m.p. 82-83°C. Recrystallisation from petroleum ether (b.p. 60-80°C) gave 2,5-diethoxy-3,6-dihydropyrazine as white needles (1.40g), m.p. 83-84°C (lit.[111], m.p. 84°C); $\nu_{max}$ (ir 8) 1700vs (C=N), 1260vs $cm^{-1}$ (=C-O); δ(pmr 5, $CDCl_3$) 1.2 (6H, t, J 6Hz, 2x$CH_3$), 3.9-4.3 (4H, q, J 6Hz, 2x$OCH_2$) 4.1 (4H, s, 2x3-H, 2x6-H)ppm.

O-Ethylation of cis,trans,cis-4,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-3,9-dione

A slurry of cis,trans,cis-4,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-3,9-dione (0.97g, 5 mmol) in dry dichloromethane (15ml) was stirred at ambient temperature under nitrogen, and a solution of triethyloxonium tetrafluoroborate (1.90g, 10 mmol) in dry dichloromethane (5ml) added. After 3 h a further solution of triethyloxonium tetrafluoroborate (1.90g) in dry dichloromethane (5ml) was added and the reaction mixture stirred for 18 h, by which time most of the solid had dissolved. The mixture was treated with dichloromethane (50ml) followed by 5% sodium bicarbonate solution (100ml). The organic phase was separated, dried ($K_2CO_3$) and concentrated to afford a pale yellow sticky solid (1.03g, 83%). Tlc (ethanol) indicated one main component at $R_F$ 0.51, together with slight impurities on the baseline and at $R_F$ 0.32, 0.45; glc on OV210 at 140°C showed only one peak $R_t$ 11.4 min.

A portion of this solid (449mg) was sublimed at 130°C/

0.01 mmHg to give cis,trans,cis-3,9-diethoxy-4,10-diaza-tricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene (367mg) as a white solid, m.p. 41-43°C (partly) and 70-75°C (completely). Glc on OV210 at 140°C showed one component $R_t$ 11.4 min, tlc (ethanol) indicated essentially one component at $R_F$ 0.51, together with traces of other material at $R_F$ 0.32, 0.45. (Found: C, 67.50; H, 9.03 ; N, 11.31. $C_{14}H_{22}N_2O_2$ requires C, 67.17; H, 8.86; N, 11.19%); $\nu_{max}$ (ir 9) 1660s (C=N), 1380m ($CH_3$ def.), 1220 $cm^{-1}$ (=C-O); δ(pmr 6, $CDCl_3$) 1.0-1.5 (6H, t, J 6Hz, 2x$CH_3$), 1.5-1.8 (4H, m, 1-H, 2-H, 7-H, 8-H), 2.3-2.8 (4H, m, 2x6-H, 2x12-H), 3.5-3.8 (4H, t, 2x5-H, 2x11-H), 3.8-4.4 (4H, q, J 6Hz, 2x$OCH_2$) ppm.

An attempt to recrystallise another sample of the crude diethoxy compound (821mg) from cyclohexane (4ml) resulted in the crystallisation of cis,trans,cis-9-ethoxy-4,10,diazatricyclo[6,4,0,$0^{2,7}$]dodec-9-en-3-one as a white solid (23mg), m.p. 130-133°C. Tlc (ethanol) showed one component $R_F$ 0.35. (Found: C, 63.32; H, 8.09; N, 11.92. $C_{12}H_{18}N_2O_2$ requires C, 64.86; H, 8.16; N, 12.61%); $\nu_{max}$ (ir 10) 3180s (NH str.), 1650vs (C=N, C=0), 1420m (CONH cis str.), 1380m ($CH_3$ def.), 1210s $cm^{-1}$ (=C-O).

O-Ethylation of cis,trans,cis-3,9-diaza-tricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione

A slurry of cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-4,10-dione (0.97g, 5 mmol) in dry dichloromethane (15ml) was stirred at ambient temperature under nitrogen, and a solution of triethyloxonium tetra-fluoroborate (1.90g, 10 mmol) in dry dichloromethane (5ml) added. After 3 h a further quantity of triethyloxonium tetrafluoroborate (1.90g) in dichloromethane (5ml) was added and the reaction mixture stirred for 18 h. The mixture was treated with 5% sodium bicarbonate solution (100ml) and dichloromethane (50ml). The organic phase was separated, dried ($K_2CO_3$) and evaporated to dryness to yield an off-white solid (0.77g, 62%), m.p. 63-65°C (partly) and 93-98°C (completely). Tlc (ethanol) showed one main

component $R_F$ 0.57, and trace impurities on the baseline and at $R_F$ 0.40; glc on OV210 at 140°C showed only one component $R_t$ 10.7 min.

A portion of this solid (320mg) was sublimed at 130°C/0.01 mmHg to afford cis,trans,cis-4,10-diethoxy-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene as a white powder (288mg), m.p. 64-65°C (partly) and 95-100°C (completely). Glc on OV210 at 140°C showed one component $R_t$ 10.7 min; tlc (ethanol) showed essentially one compound $R_F$ 0.57, together with a trace impurity at $R_F$ 0.40. (Found: C, 66.56; H, 8.78; N, 11.59. $C_{14}H_{22}N_2O_2$ requires C, 67.17; H, 8.86; N, 11.19%); $\nu_{max}$ (ir 11) 1660s (C=N), 1380m ($CH_3$ def.), 1230s $cm^{-1}$ (=C-O); δ(pmr 7, $CDCl_3$) 1.1-1.5 (6H, t, J 7Hz, 2x$CH_3$), 1.7-2.6 (10H, m, 1-H, 2x5-H, 2x6-H, 7-H, 2x11-H, 2x12-H) 3.7-4.4 (6H, m, 2x$OCH_2$, 2-H, 8-H) ppm.

Attempted oxidations with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone

(a) Cis,trans,cis-3,9-diethoxy-4,10-diaza-tricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene

A solution of cis,trans,cis-3,9-diethoxy-4,10-diaza-tricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene (400mg, 1.6 mmol) in dry benzene (26ml) was stirred and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1.74g, 7.68 mmol) added. The solution was heated to reflux and when the vigorous reaction had subsided, the mixture was refluxed for a further 1 h, then allowed to cool overnight. The reaction mixture was filtered, the solid washed with benzene (20ml) and the total benzene solution concentrated to a volume of 10ml. Glc of the benzene solution on OV210 at 140°C showed the absence of the starting diethoxy compound.

The benzene solution was chromatographed on neutral alumina (25g) and eluted with benzene, followed by ethyl acetate. No residues were obtained when either of the eluates were evaporated.

The pmr spectrum of the solid from the reaction showed a benzene signal at δ7.4 and several weak aliphatic signals at δ1.3-4.5ppm.

(b) Cis,trans,cis-4,10-diethoxy-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene

A stirred solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1.42g, 6.42 mmol) and cis,trans,cis-4,10-diethoxy-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene (325mg, 1.3 mmol) in dry benzene (20ml) was warmed carefully and, when the initial reaction had subsided, refluxed for 1 h then allowed to stand overnight. The mixture was filtered and the solid washed with benzene (20ml). Glc of the combined solutions on OV210 at 140°C showed the absence of the diethoxy compound.

The benzene solution was evaporated to a volume of 10ml, then chromatographed on neutral alumina (20g) and eluted with benzene, followed by ethyl acetate. No residues were obtained when either of the eluates were evaporated.

The pmr spectrum of the reaction solid showed a benzene singlet at δ7.4 and several weak signals at δ 1.3-4.5ppm due to aliphatic protons.

# SPECTRA AND CHROMATOGRAMS

ULTRAVIOLET SPECTRA

uv 1 Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione

uv 2 Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,10-dione

## INFRARED SPECTRA

ir 1 Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,8-dione

2 Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane-3,10-dione

3 Cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

4 N,N'-Bis(4-nitrobenzoyl)-cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

5 Cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane monohydrate

6 N,N'-Bis(4-nitrobenzoyl)-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

7 Cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane carbonate

8 2,5-Diethoxy-3,6-dihydropyrazine

9 Cis,trans,cis-3,9-diethoxy-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene

10 Cis,trans,cis-9-ethoxy-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodec-9-en-3-one

11 Cis,trans,cis-4,10-diethoxy-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene

## PROTON MAGNETIC RESONANCE SPECTRA

pmr 1 Cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

2 N,N'-Bis(4-nitrobenzoyl)-cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

3 Cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane monohydrate

4 N,N'-Bis(4-nitrobenzoyl)-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane

5 2,5-Diethoxy-3,6-dihydropyrazine

6 Cis,trans,cis-3,9-diethoxy-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene

7 Cis,trans,cis-4,10-diethoxy-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodeca-3,9-diene

## MASS SPECTRA

ms 1 2,3'-Bipyridine

2 Benzylpyridine (tentatively assigned)

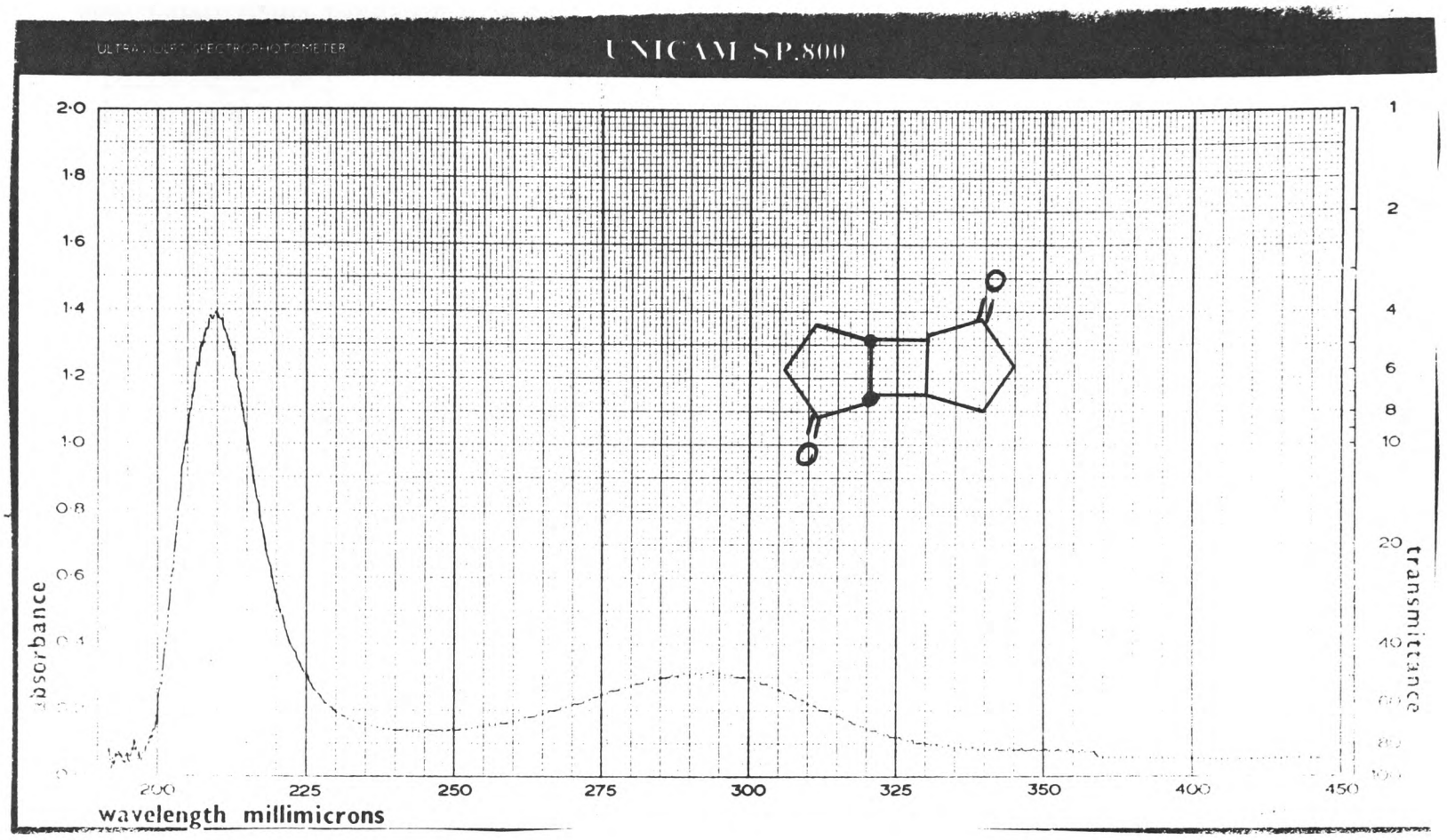
3 Benzylideneaniline

## CHROMATOGRAMS

glc 1 Mixture of compounds from the dehydrogenation of N,N'-dibenzyl-*cis*,*trans*,*cis*-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane with palladium on carbon.

2 Mixture of compounds from the nitrobenzene/palladium on carbon dehydrogenation of N,N'-dibenzyl-*cis*,*trans*,*cis*-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane.

UV 1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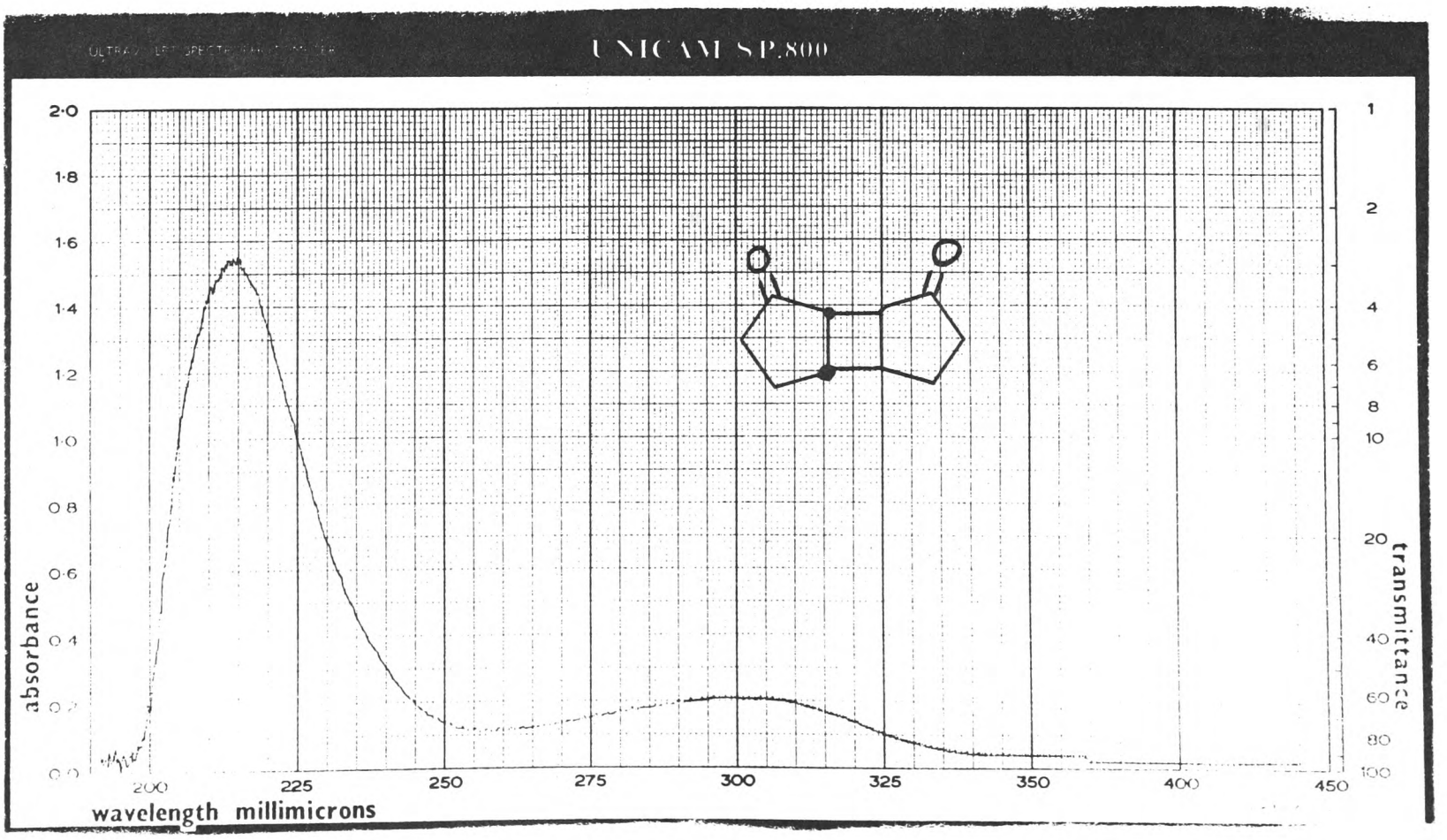
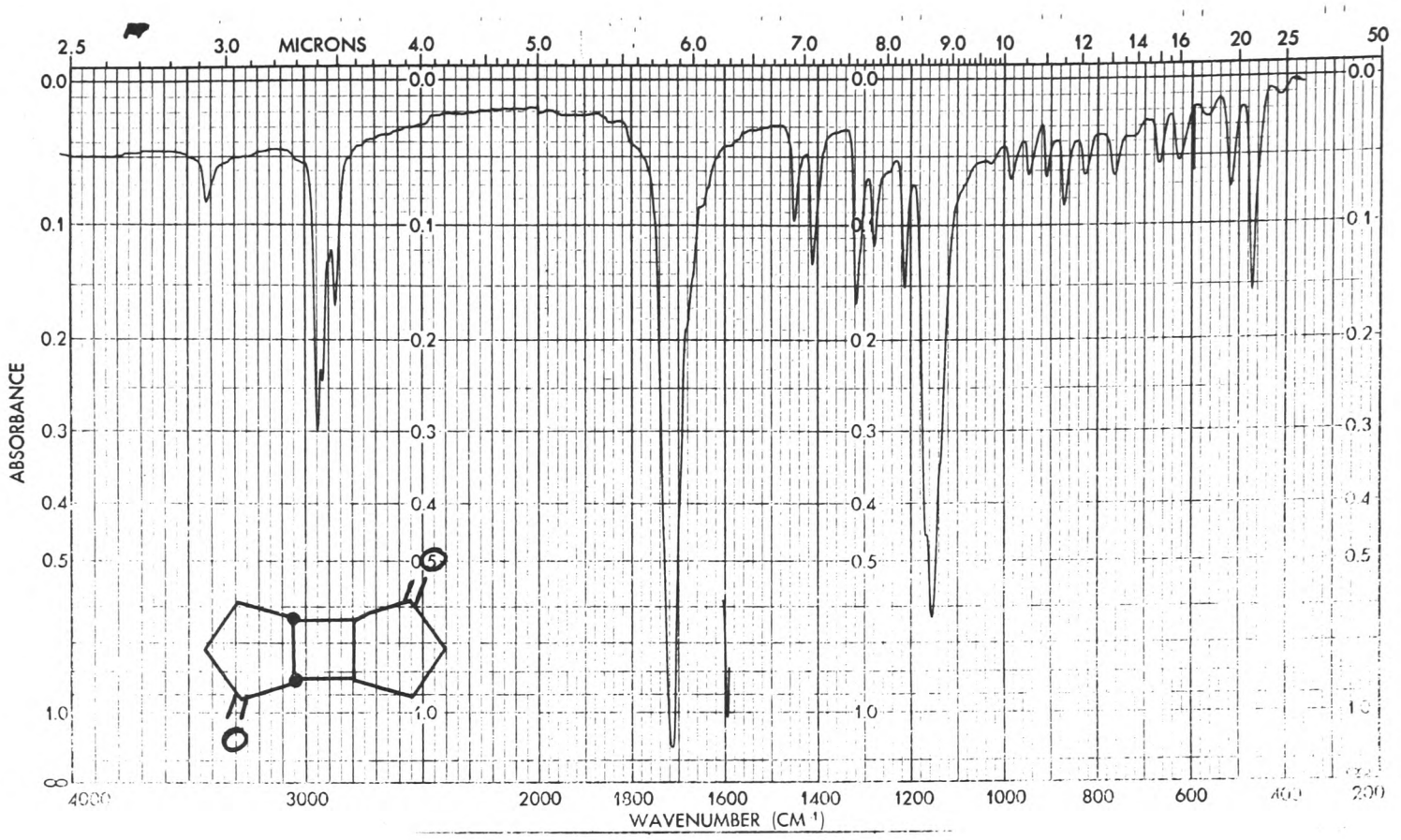
absorbance
transmittance
wavelength millimicrons
200
225
250
275
300
325
350
400
450

UV 2


UNICAM SP.800
absorbance
transmittance
wavelength millimicrons
200
225
250
275
300
325
350
400
450

IR 1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4.0
5.0
6.0
7.0
8.0
9.0
10
12
14
16
20
25
50
ABSORBANCE
0.0
0.1
0.2
0.3
0.4
0.5
1.0
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2000
1800
1600
1400
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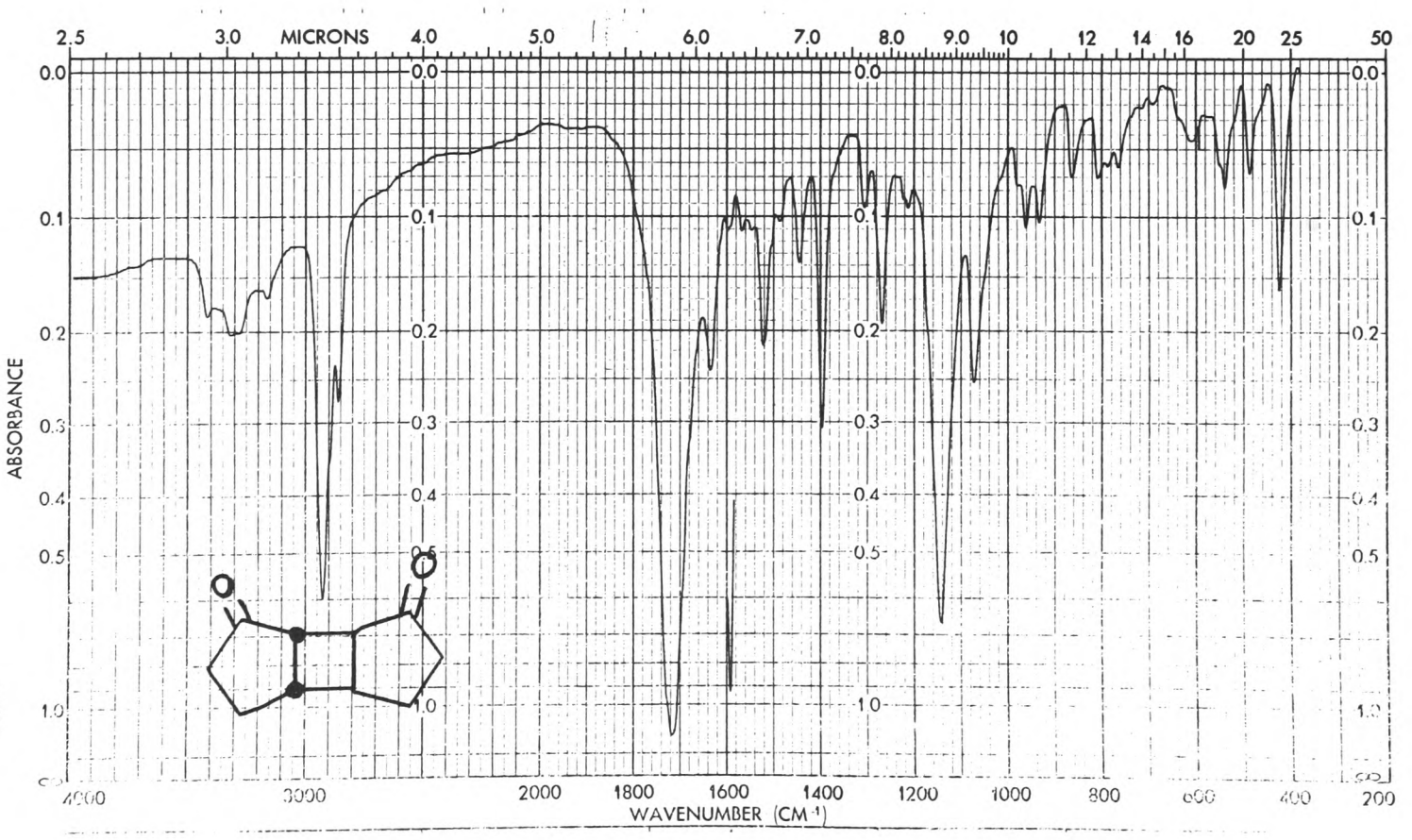
1000
800
600
400
200
WAVENUMBER (CM-1)

IR 2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5.0
6.0
7.0
8.0
9.0
10
12
14
16
20
25
50
ABSORBANCE
0.0
0.1
0.2
0.3
0.4
0.5
1.0
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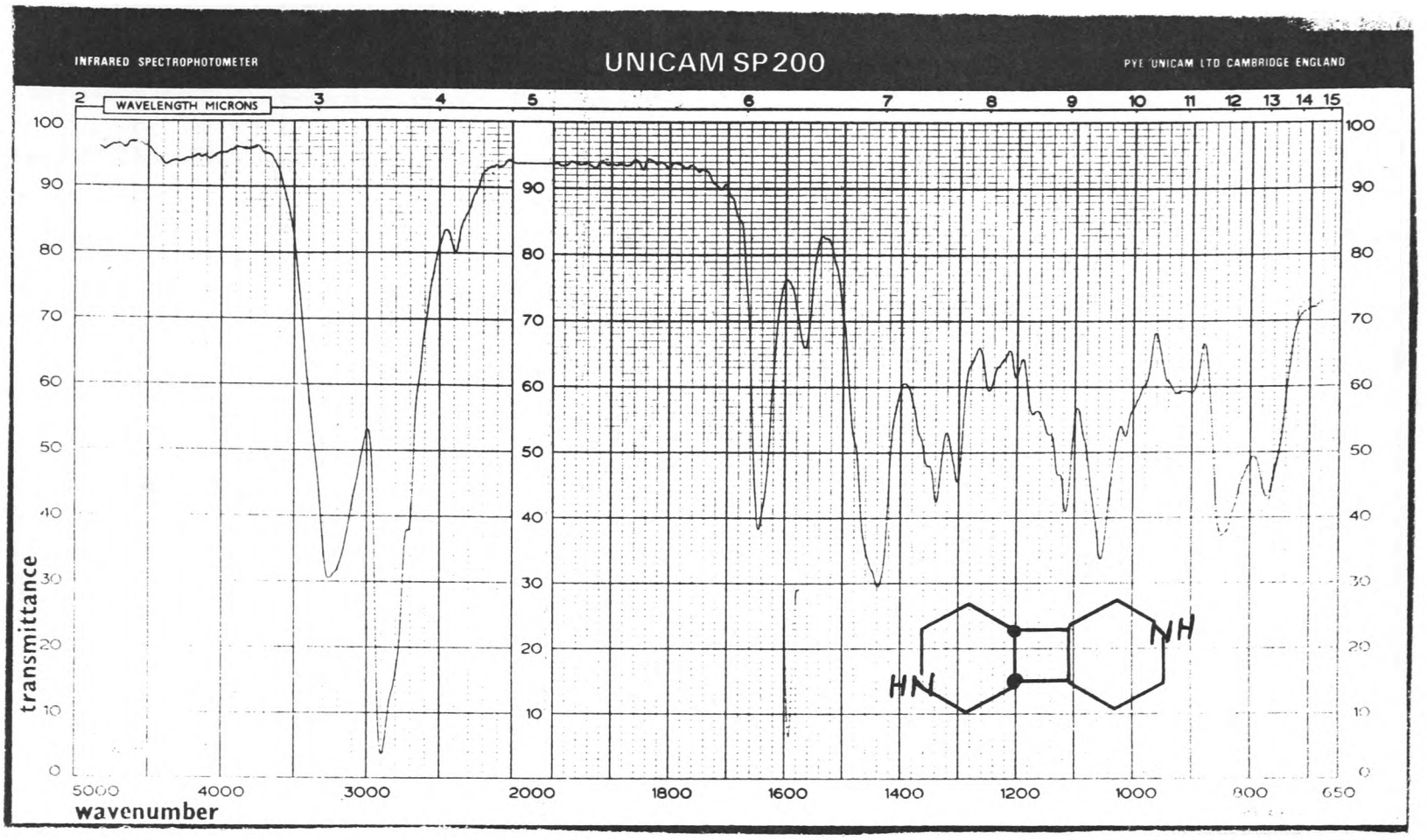
3000
2000
1800
1600
1400
1200
1000
800
600
400
200
WAVENUMBER (CM-1)

IR 3


INFRARED SPECTROPHOTOMETER
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PYE UNICAM LTD CAMBRIDGE ENGLAND
WAVELENGTH MICRONS
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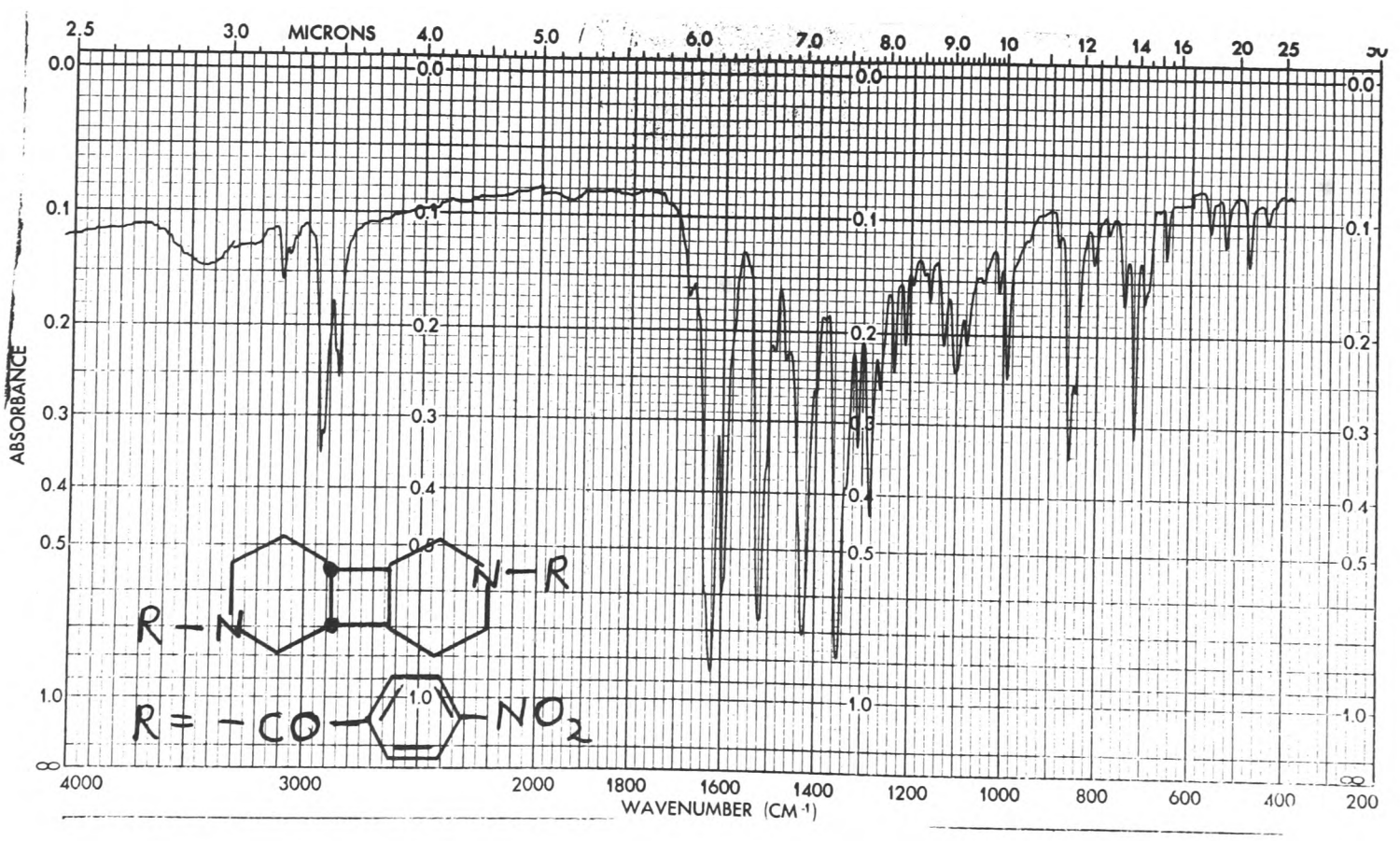
100 90 80 70 60 50 40 30 20 10 0
transmittance
5000 4000 3000 2000 1800 1600 1400 1200 1000 800 650
wavenumber
NH
HN

IR 4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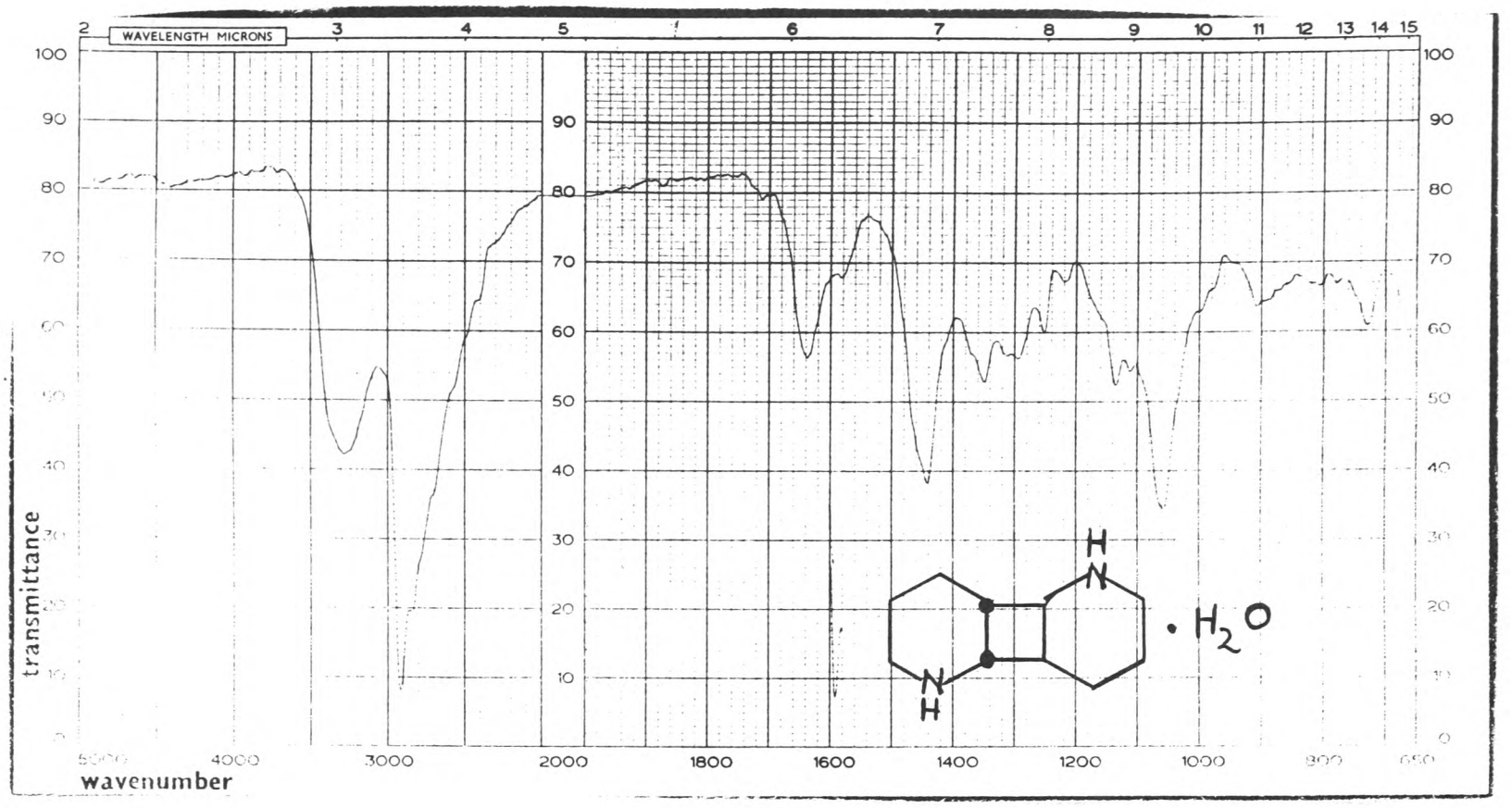
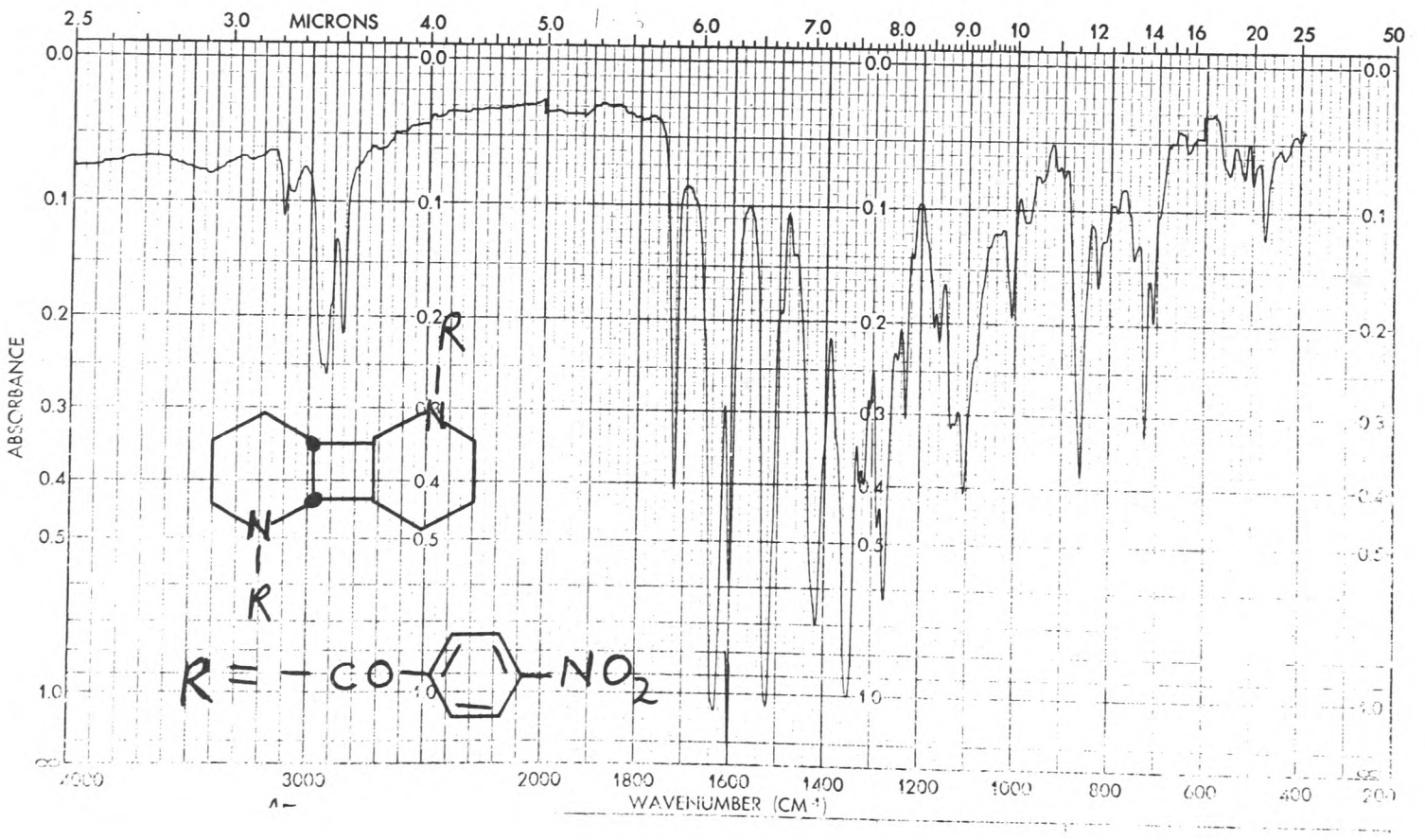
0.0 0.1 0.2 0.3 0.4 0.5 1.0 ∞
ABSORBANCE
4000 3000 2000 1800 1600 1400 1200 1000 800 600 400 200
WAVENUMBER (CM-1)
N-R
R-N
R = -CO- -NO2

IR 5


WAVELENGTH MICRONS
2
3
4
5
6
7
8
9
10
11
12
13
14
15
transmittance
wavenumber
4000
3000
2000
1800
1600
1400
1200
1000
H
N
N
H
· H2O

IR 6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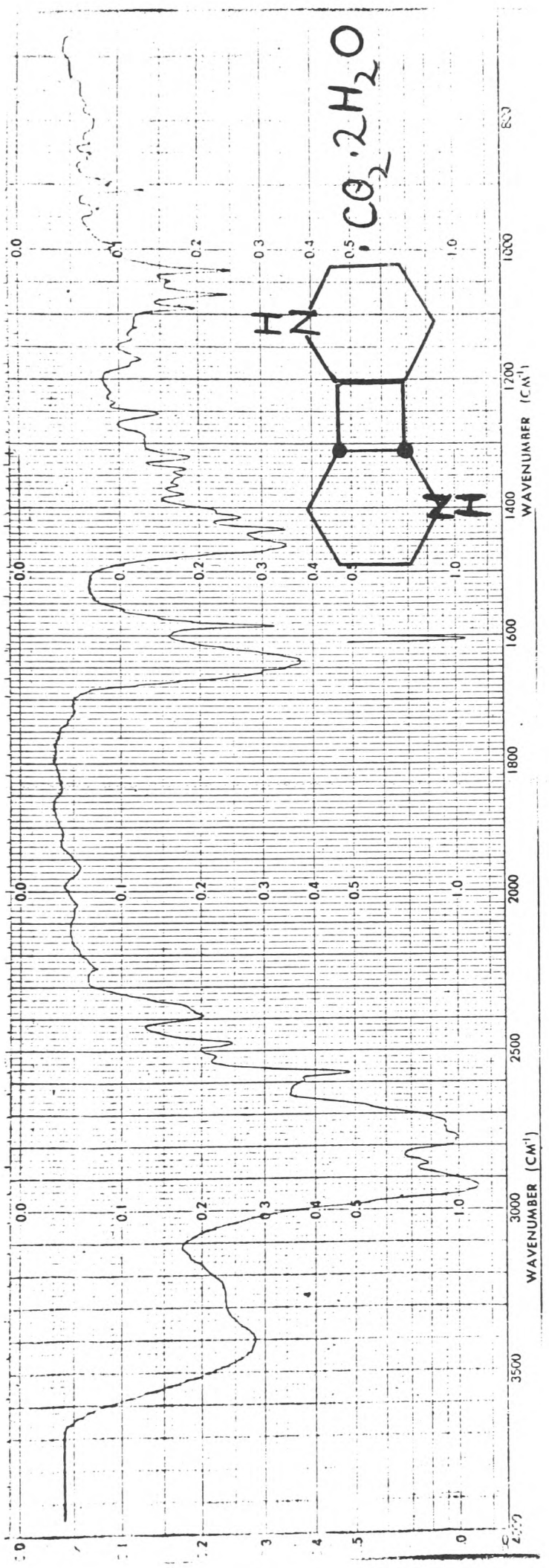
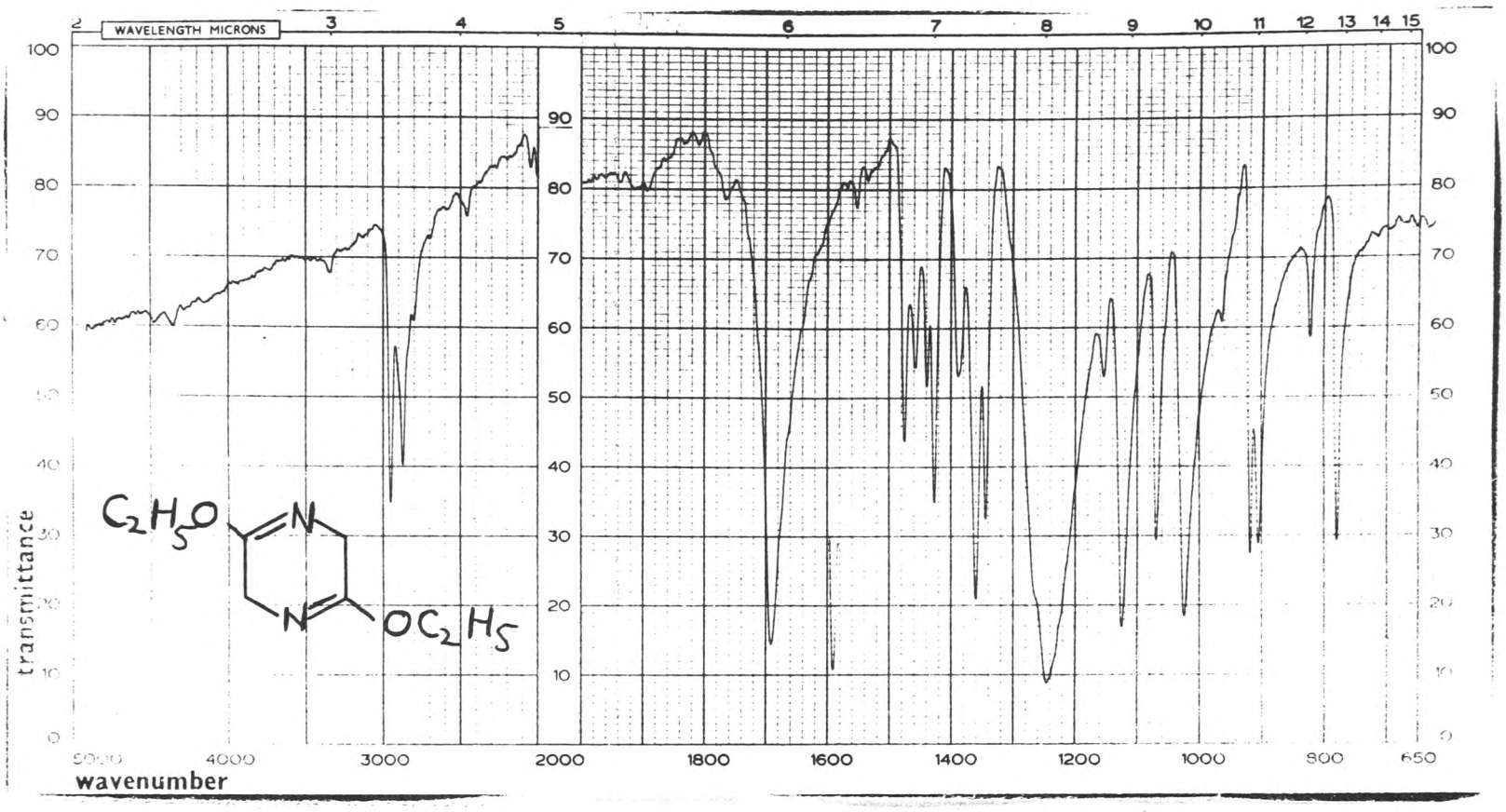
4.0
5.0
6.0
7.0
8.0
9.0
10
12
14
16
20
25
50
ABSORBANCE
WAVENUMBER (CM-1)
3000
2000
1800
1600
1400
1200
1000
800
600
400
R
N
N
R
R = — CO — NO2

IR 7



IR 8


WAVELENGTH MICRONS
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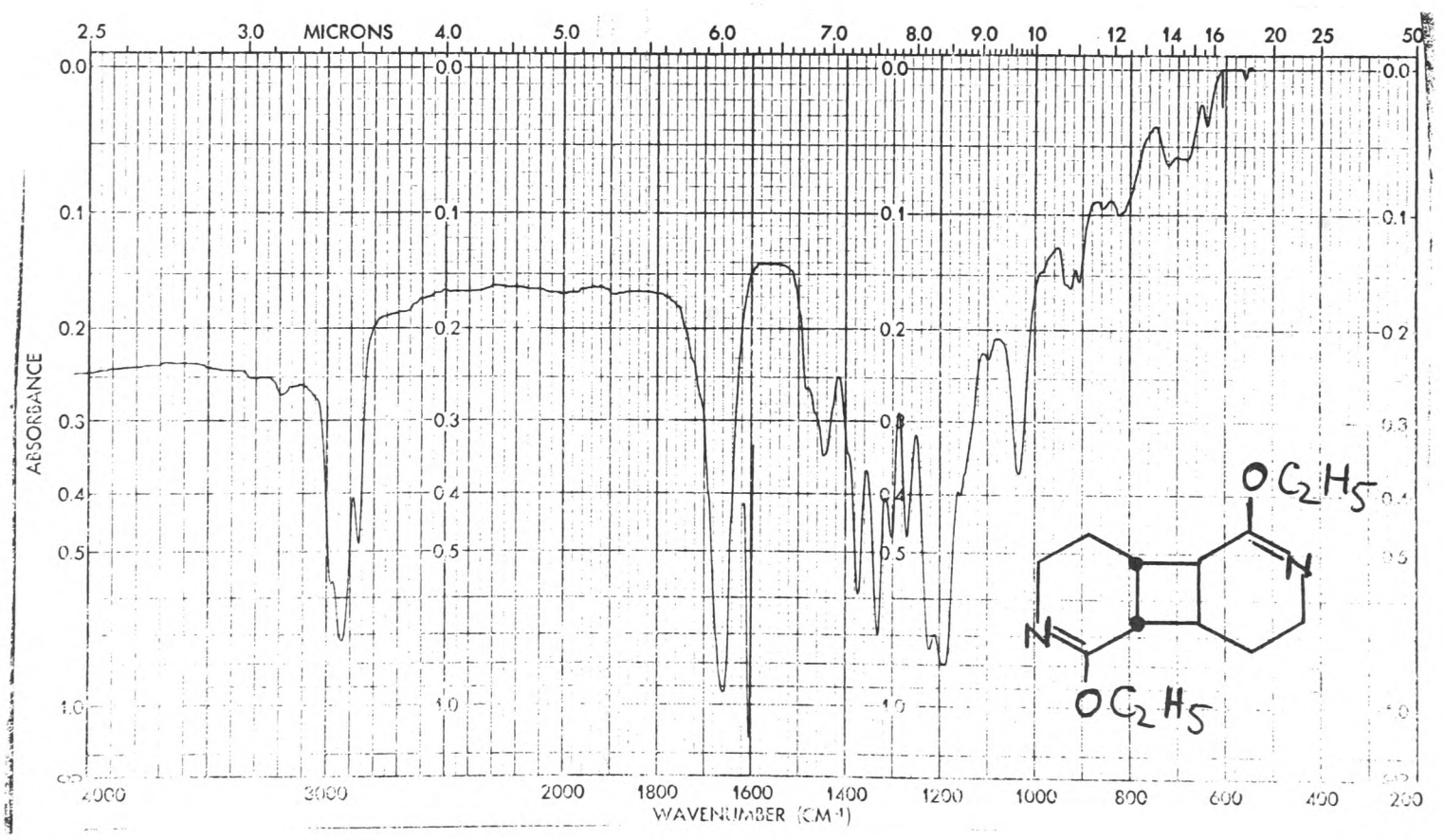
3
4
5
6
7
8
9
10
11
12
13
14
15
transmittance
100
90
80
70
60
50
40
30
20
10
0
5000
4000
3000
2000
1800
1600
1400
1200
1000
800
650
wavenumber
$C_2H_5O$
N
N
$OC_2H_5$

IR 9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MICRONS
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8.0
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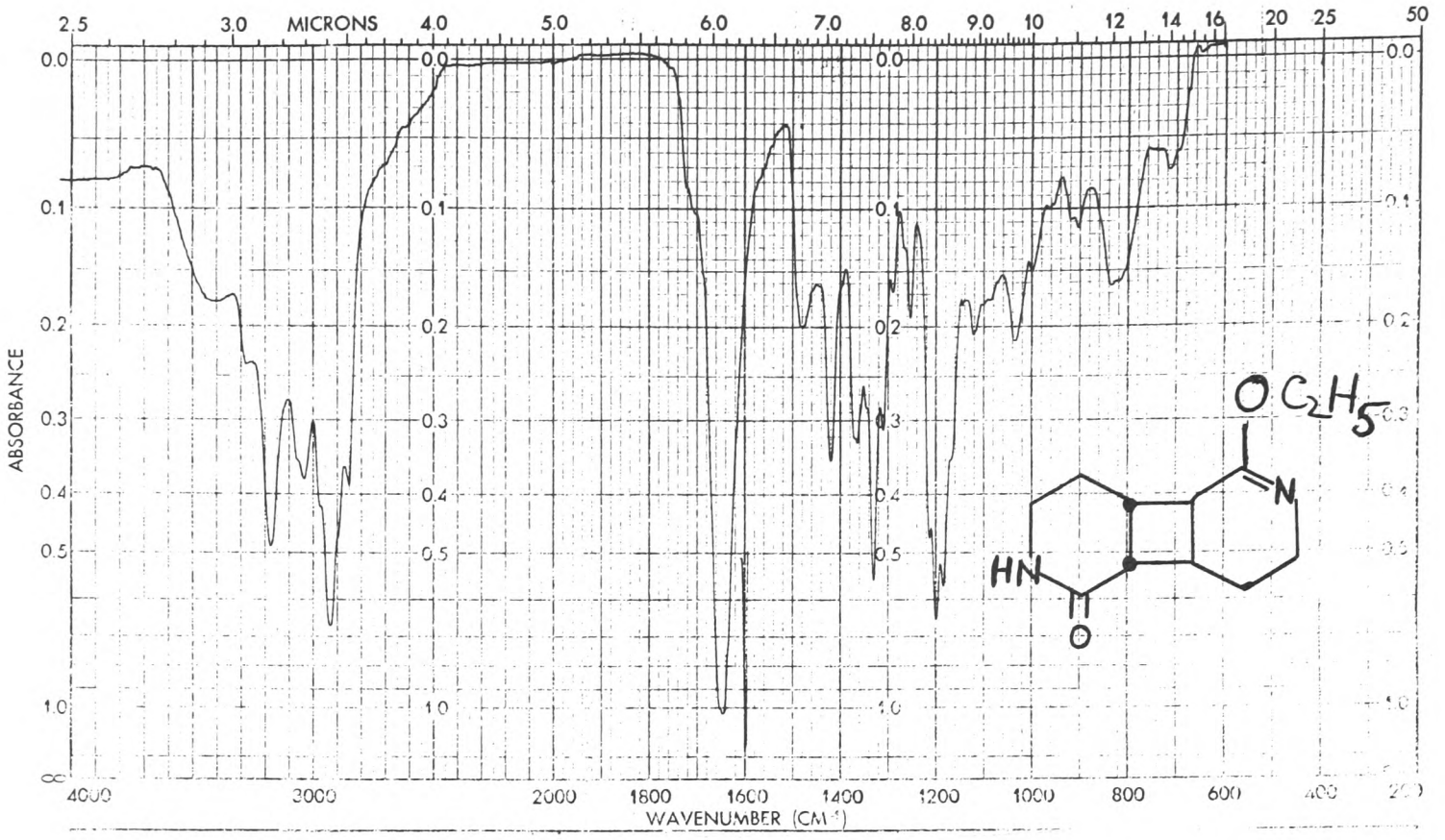
10
12
14
16
20
25
50
ABSORBANCE
0.0
0.1
0.2
0.3
0.4
0.5
1.0
4000
3000
2000
1800
1600
1400
1200
1000
800
600
400
200
WAVENUMBER (CM-1)
$OC_2H_5$
N
N
$OC_2H_5$

IR 10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MICRONS
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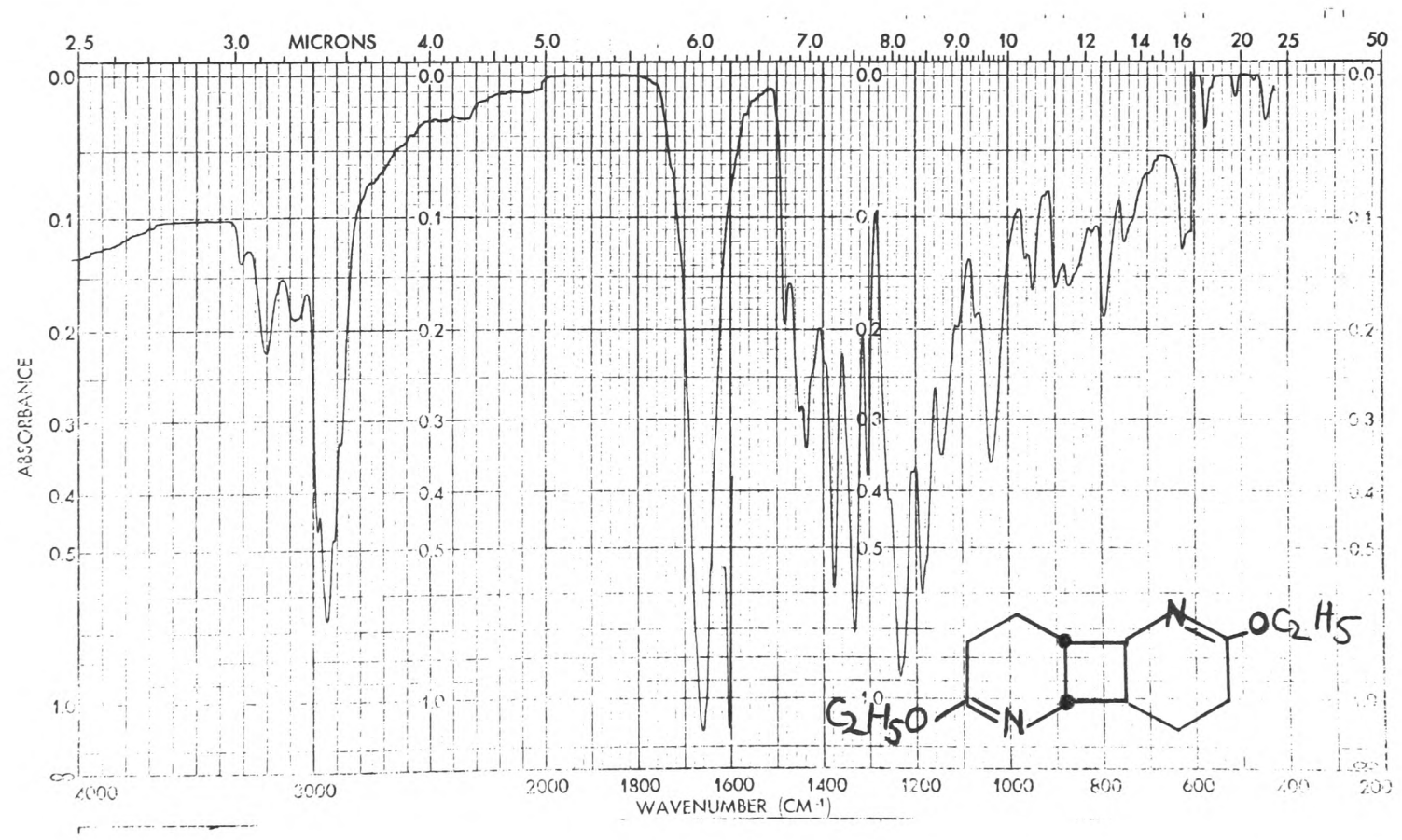
5.0
6.0
7.0
8.0
9.0
10
12
14
16
20
25
50
ABSORBANCE
0.0
0.1
0.2
0.3
0.4
0.5
1.0
∞
4000
3000
2000
1800
1600
1400
1200
1000
800
600
400
200
WAVENUMBER (CM⁻¹)
O
C2H5
N
HN
O

IR 11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MICRONS
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7.0
8.0
9.0
10
12
14
16
20
25
50
ABSORBANCE
0.0
0.1
0.2
0.3
0.4
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WAVENUMBER (CM⁻¹)
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OC2H5
C2H5O
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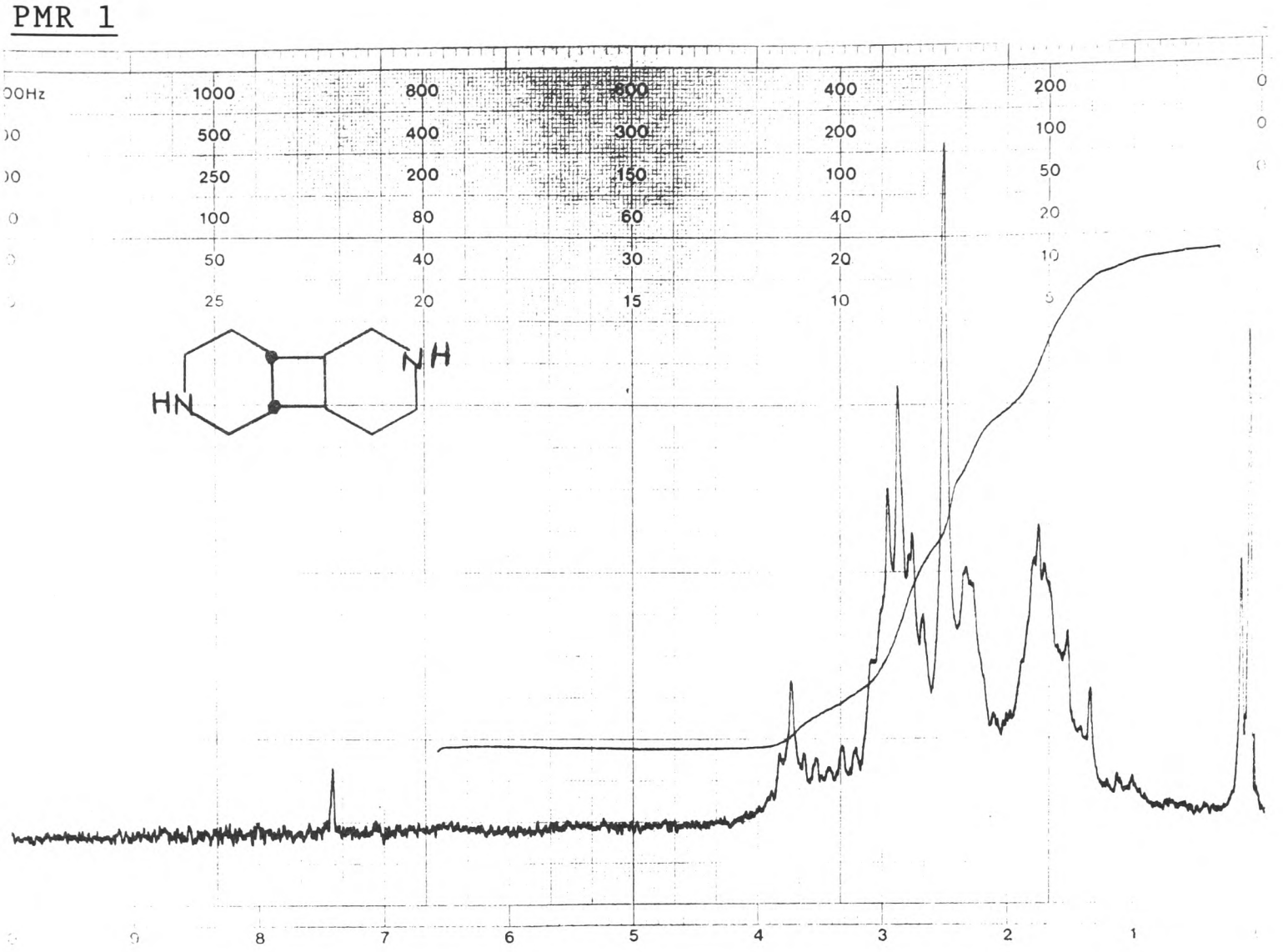
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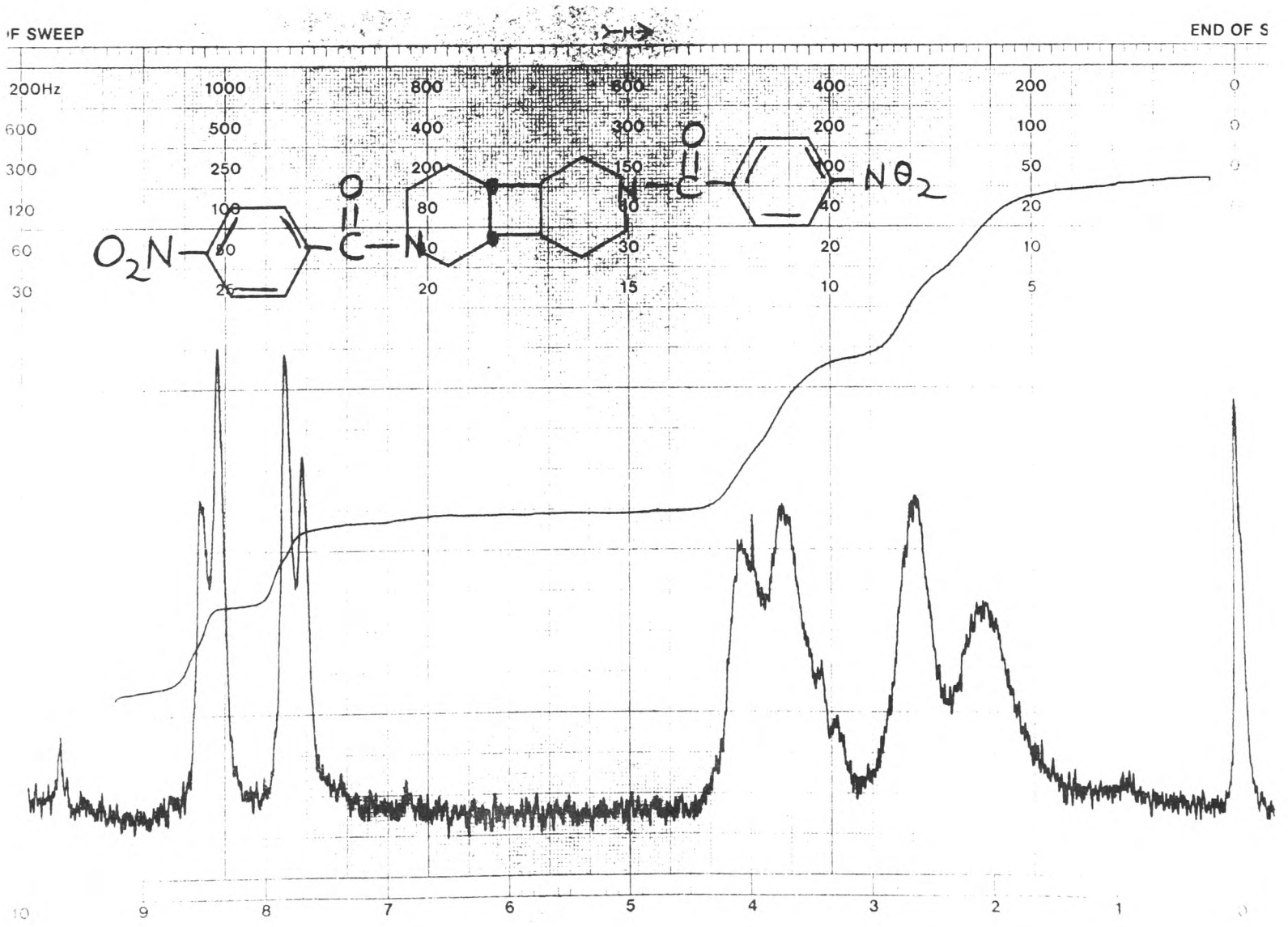
PMR 2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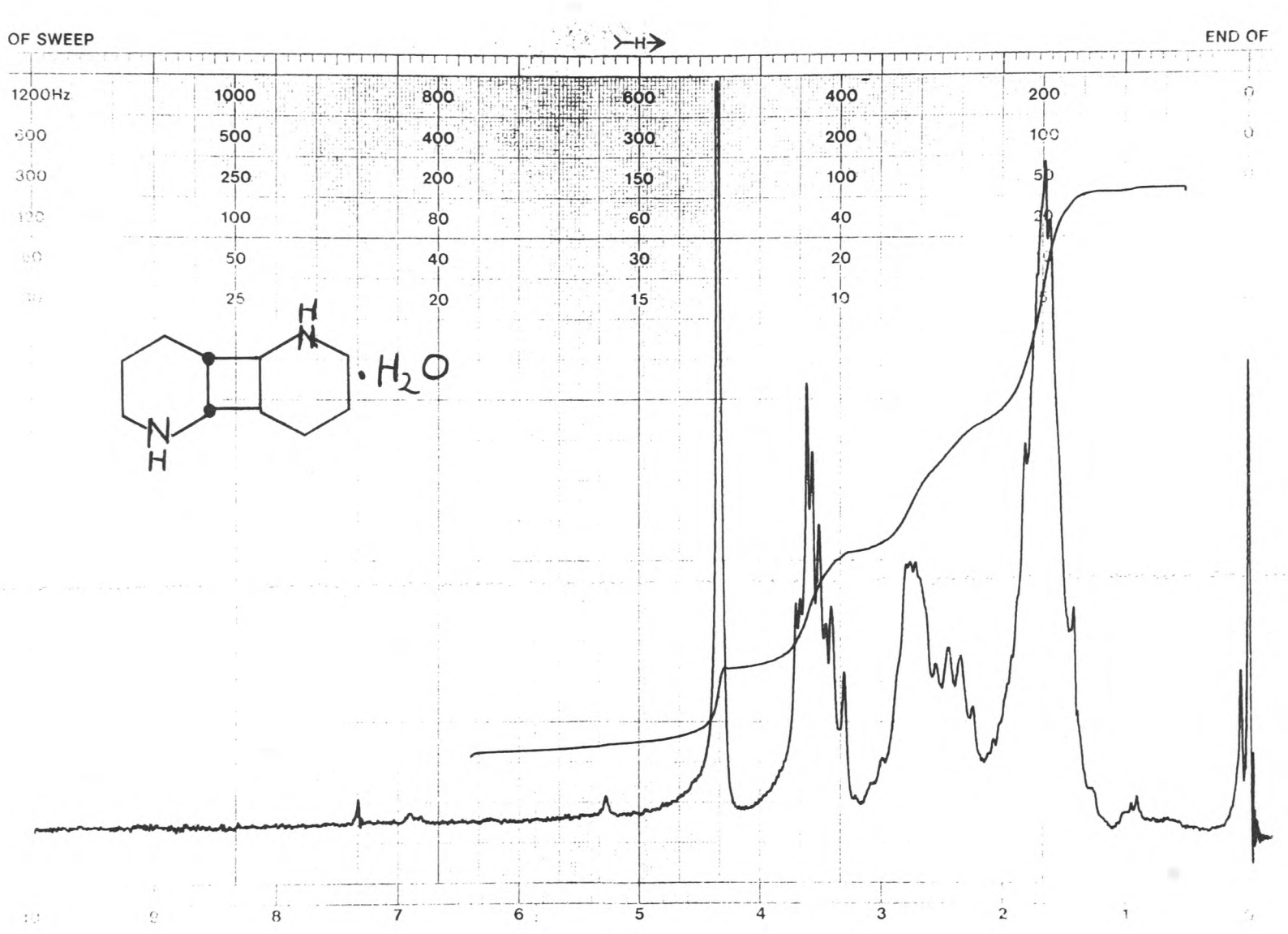
PMR 3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· H2O
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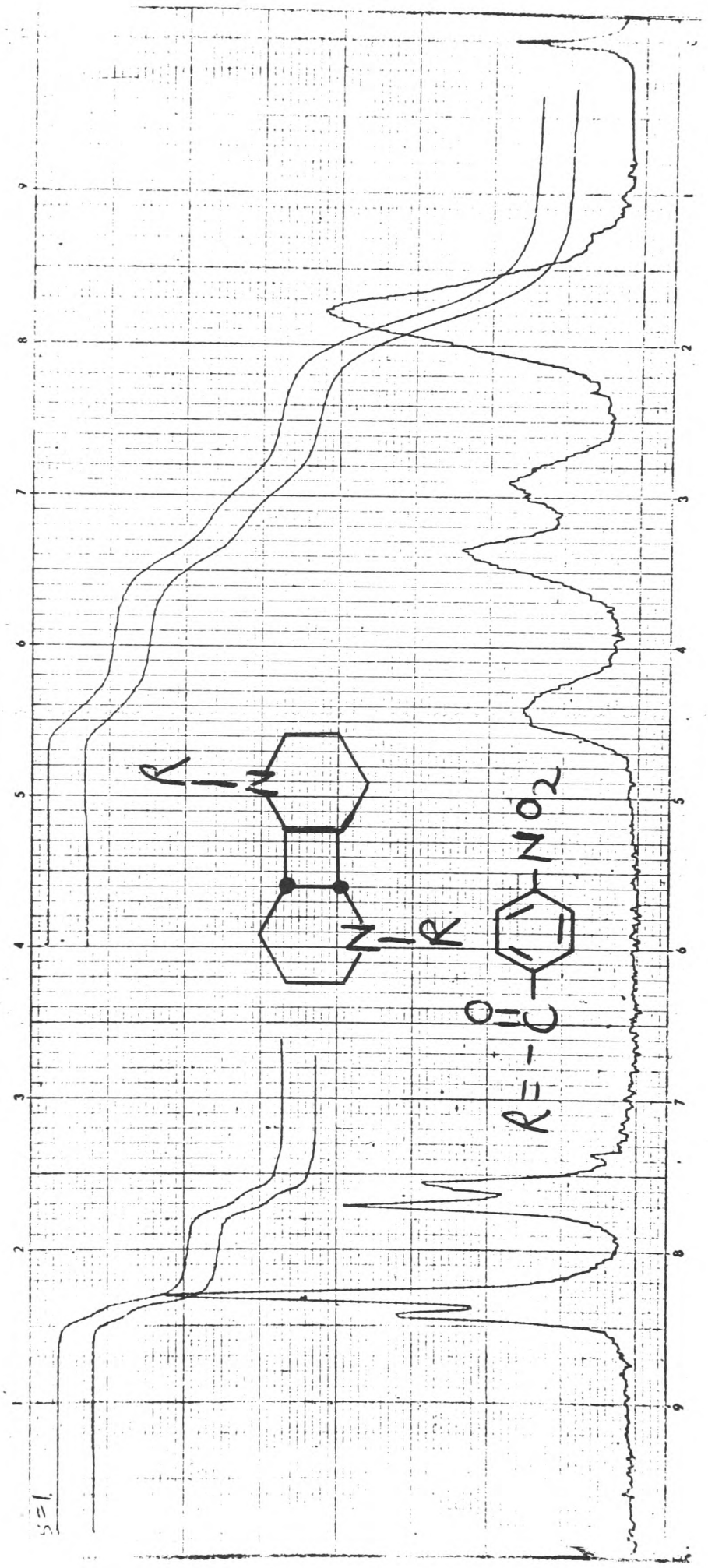
PMR 4



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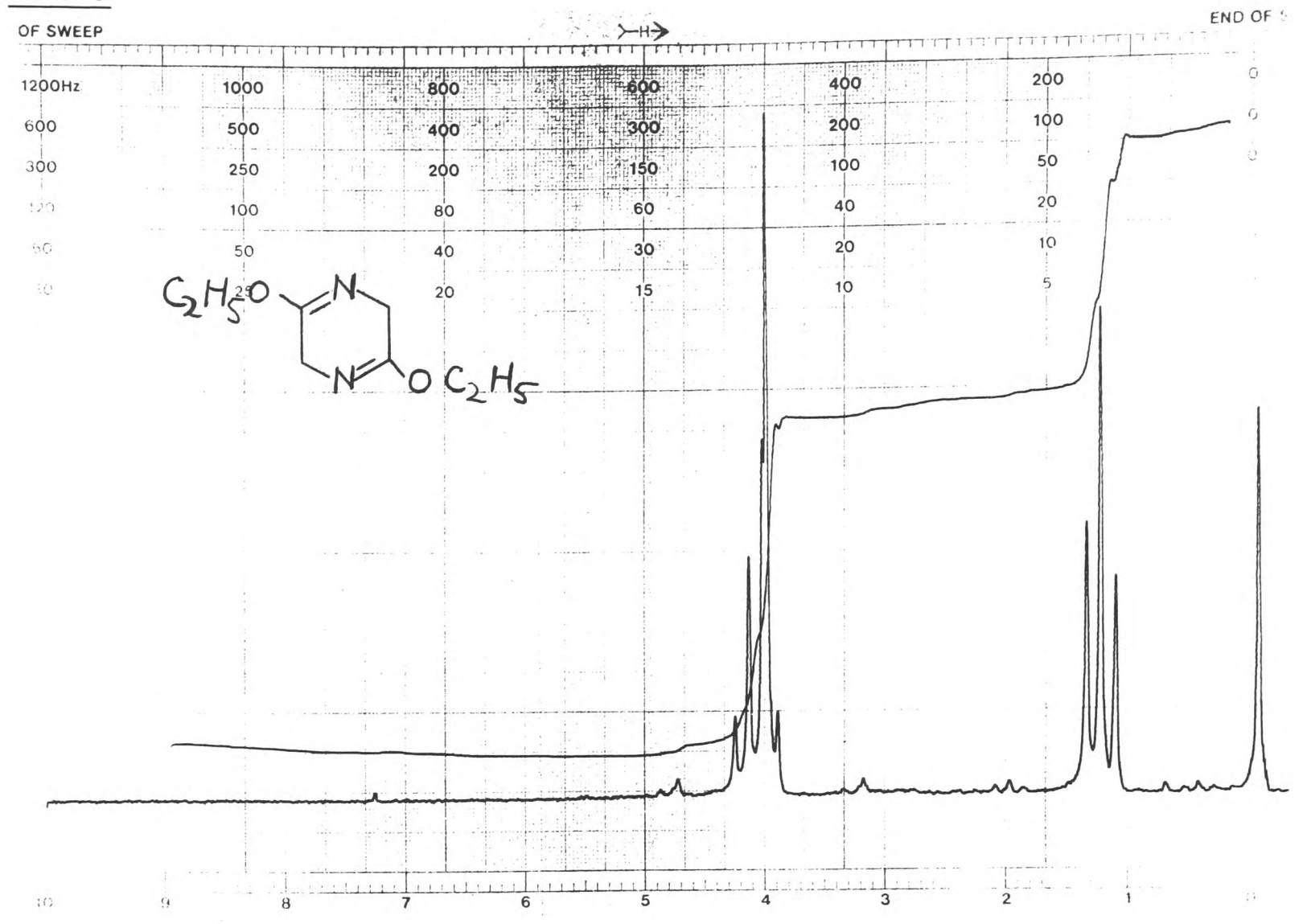
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20
10
5
$C_2H_5O$
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O $C_2H_5$
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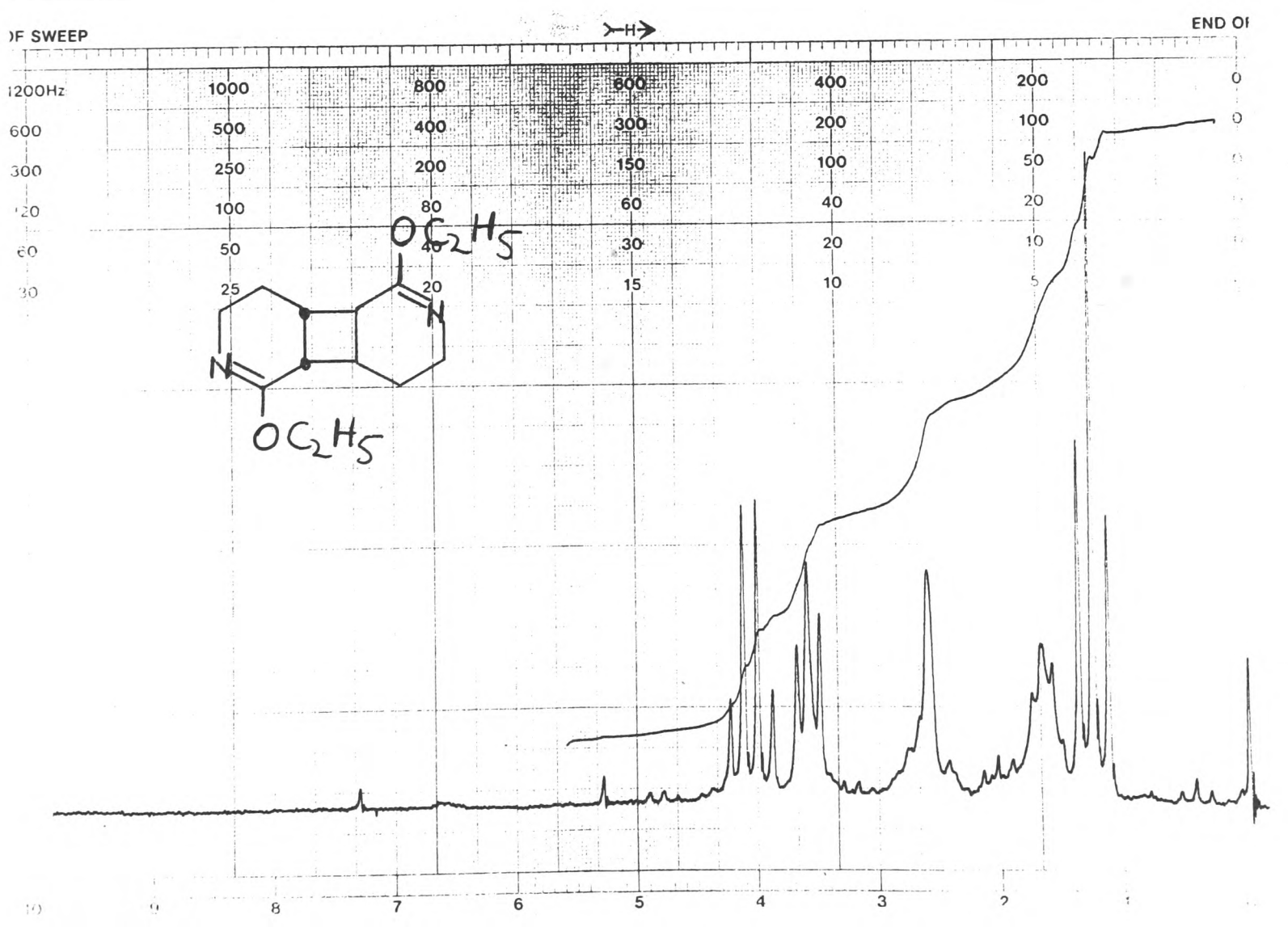
PMR 6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10
200
100
50
20
10
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N
$OC_2H_5$
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3
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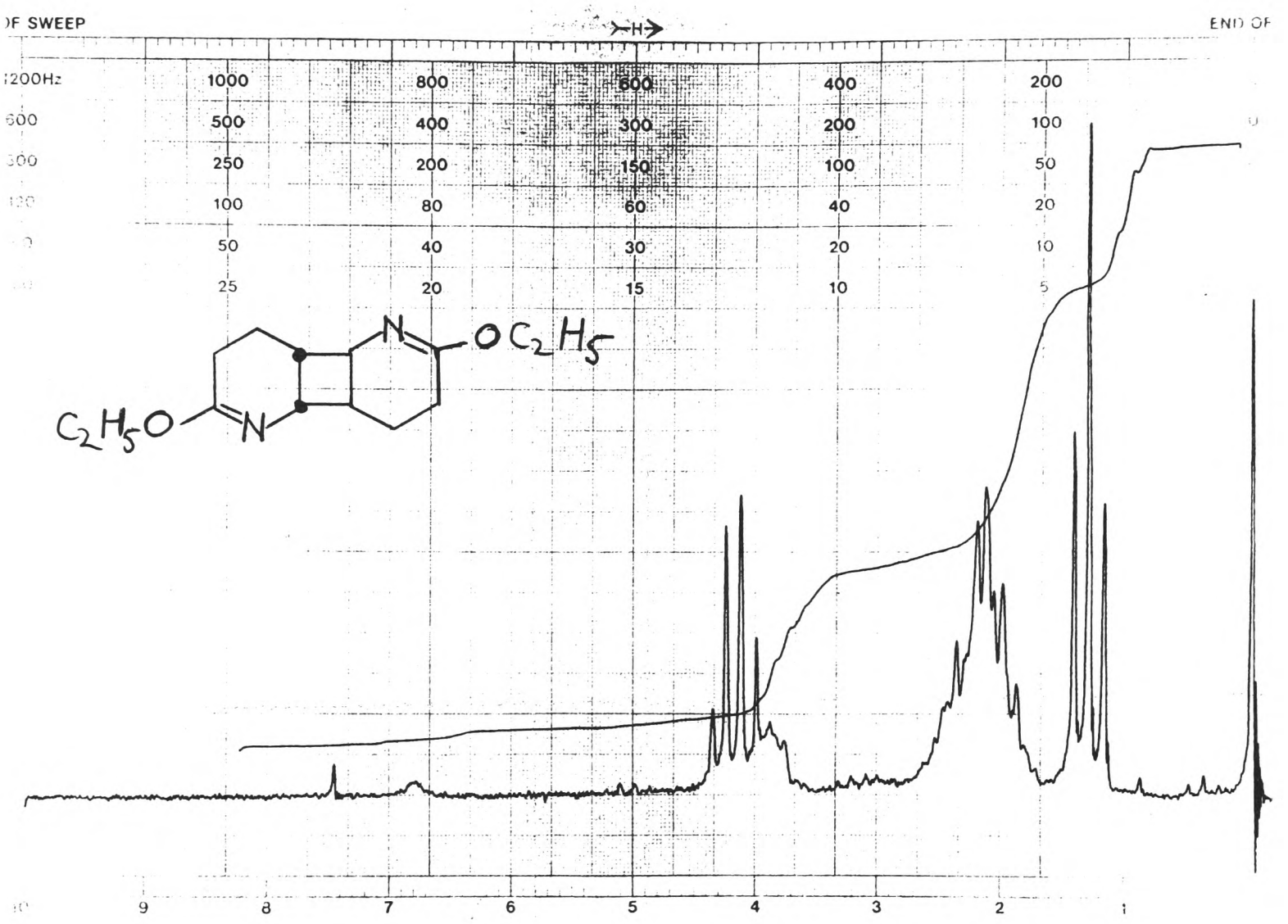
PMR 7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25
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O C2H5
C2H5O
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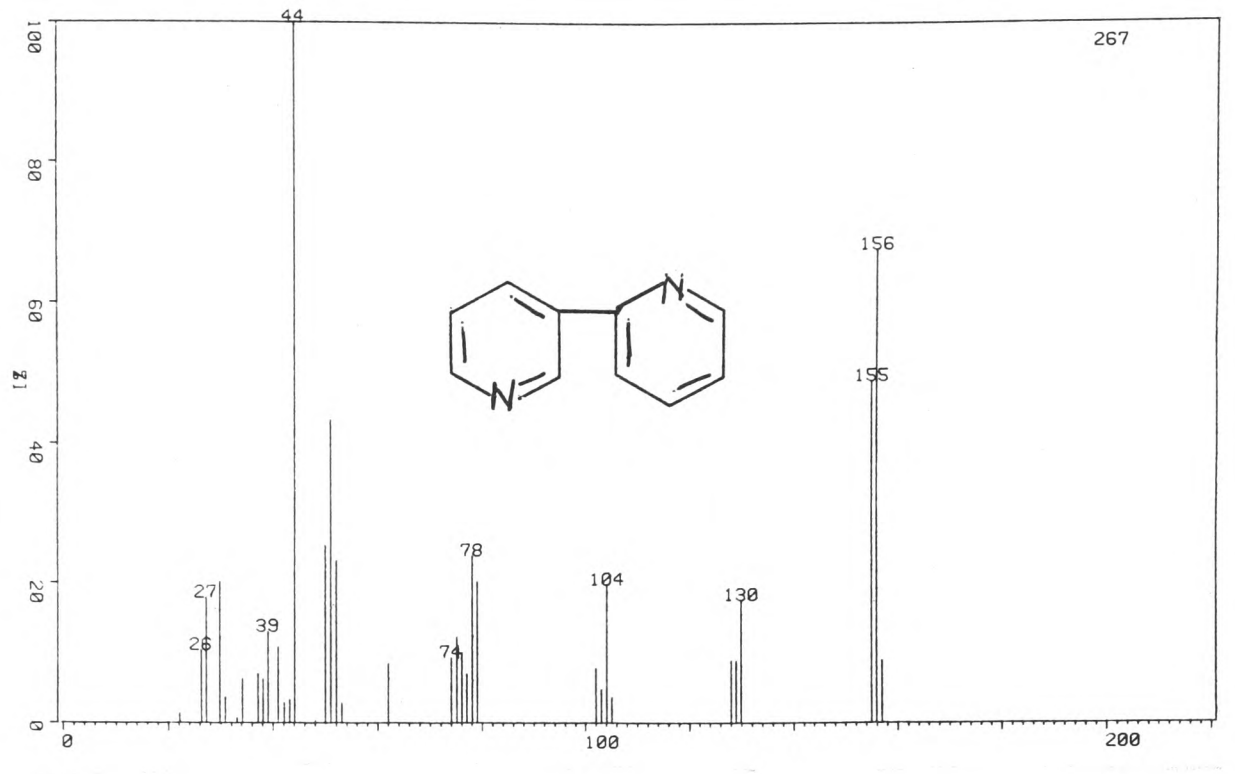
1

MS 1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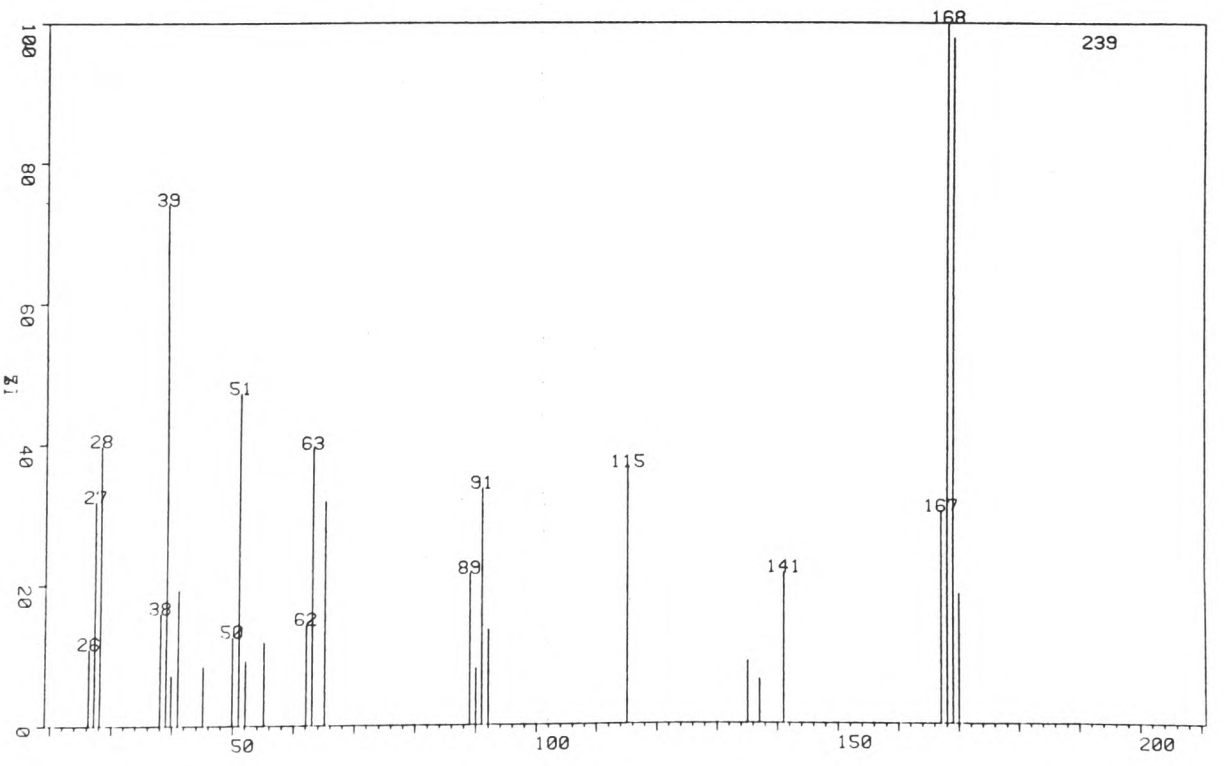
MS 2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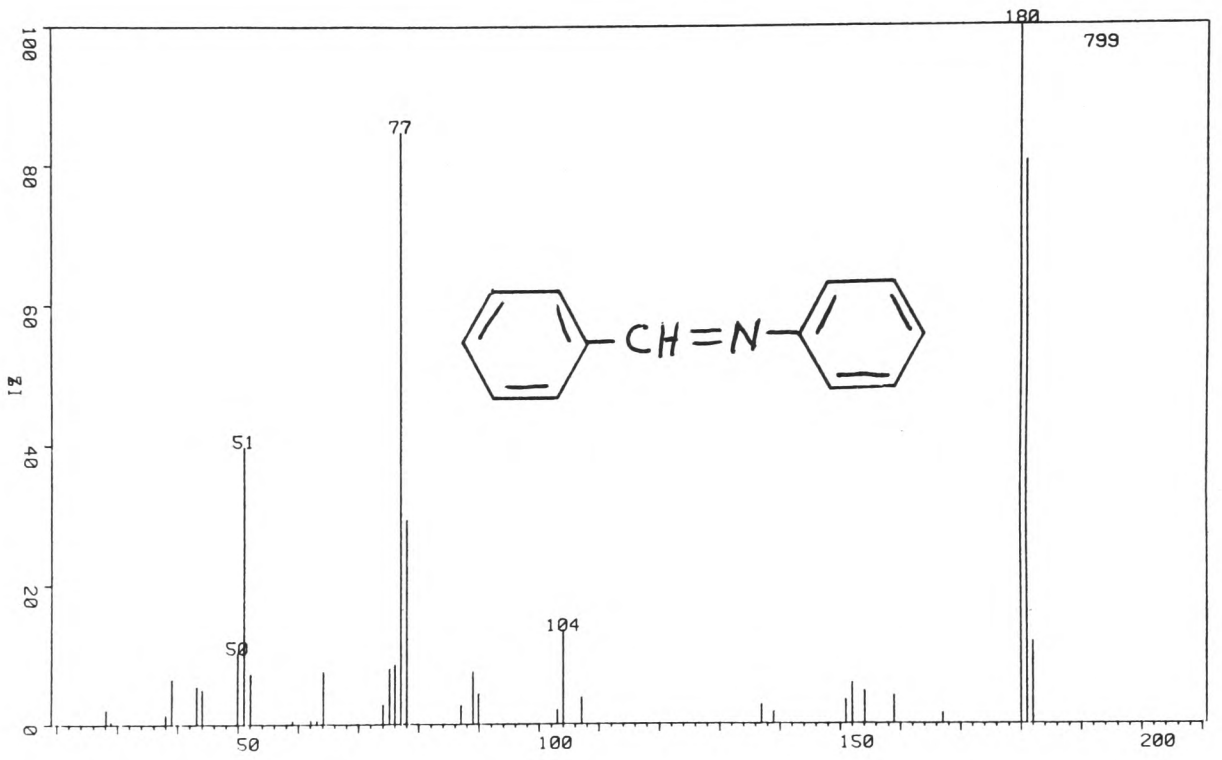
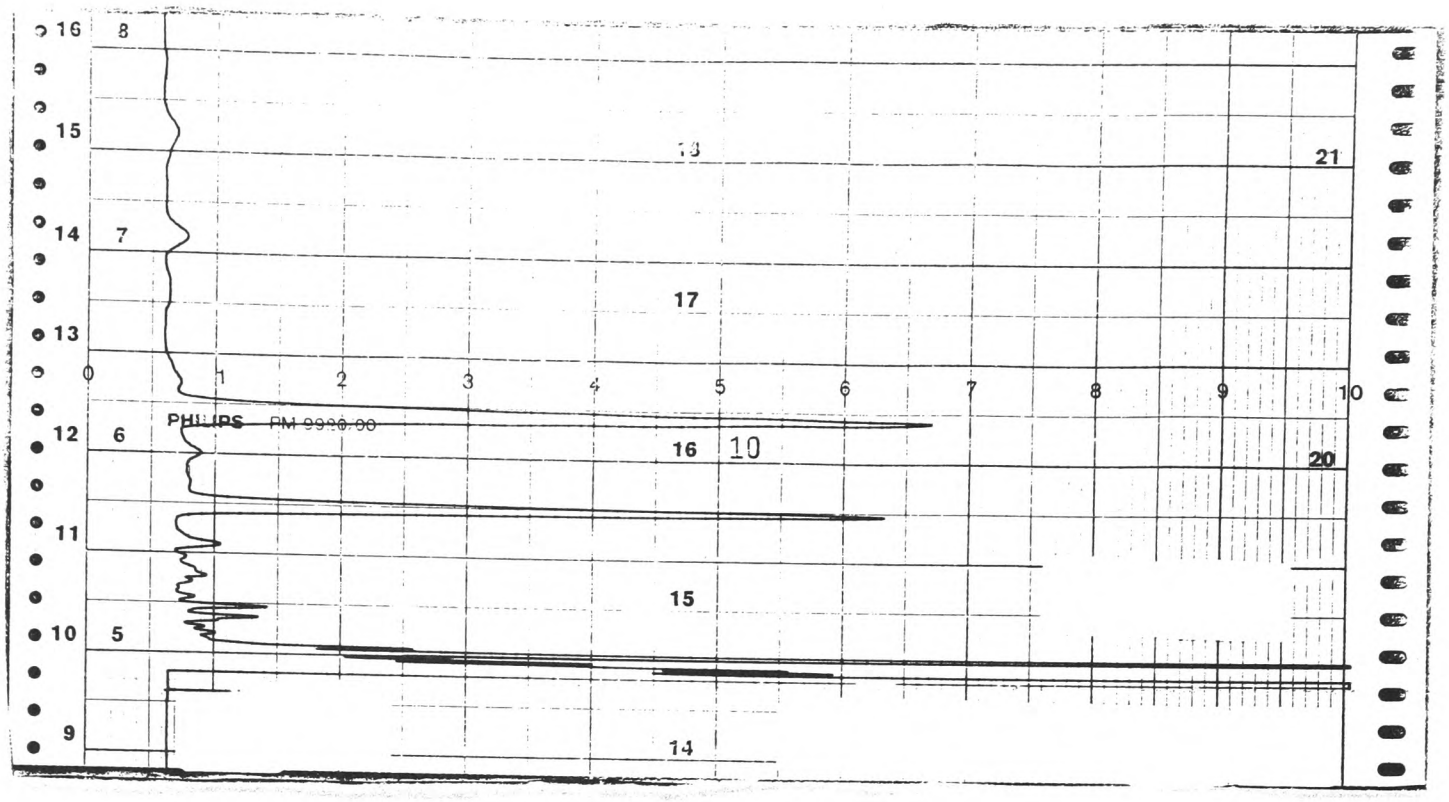
100

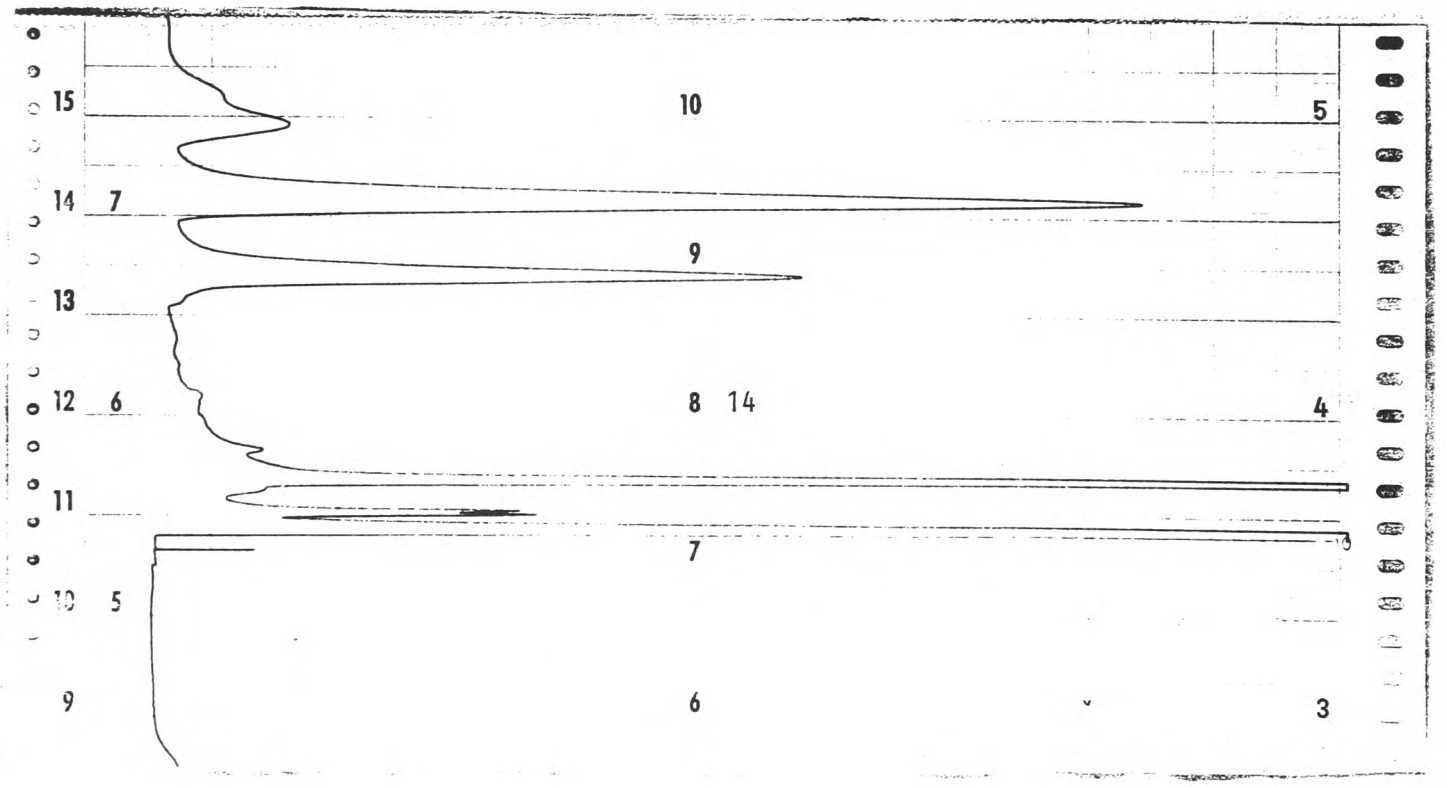
MS 3



GLC 1




GLC 2



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