THE BECKMANN AND SCHMIDT REARRANGEMENTS AS AN APPROACH TO THE SYNTHESIS OF DIAZABIPHENYLENES

A THESIS

SUBMITTED FOR THE DEGREE

OF

MASTER OF PHILOSOPHY

IN THE

UNIVERSITY OF LONDON

BY

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JUNE 1974

SCHOOL OF CHEMISTRY

THAMES POLYTECHNIC

LONDON

TO MOTHER AND FATHER

A B S T R A C T

The Schmidt reaction of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione, a photodimer of cyclopent-2-en-1-one was found to give a mixture of two dilactams. The structure of the major dilactam was established as cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione on the basis of its spectroscopic properties and those of its N,N'-dimethyl and N,N'-dibenzyl derivatives.

Single ring expansion of the diketone gave mainly cis,trans,cis-3-azatricyclo[6,3,0,$0^{2,7}$]undecane-4,9-dione, and a number of its transformation products are described.

The Beckmann rearrangement of the mixture of dioximes derived from the diketone, also gave a mixture of two dilactams; the major component was established as cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-3,9-dione on the basis of its spectroscopic data and those of its N,N'-dimethyl and N,N'-dibenzyl derivatives. The minor component was found to be identical with that of the other dilactam obtained from the Schmidt reaction and was tentatively assigned as cis,trans,cis-3,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-4,9-dione.

Attempted reduction of the dilactams to the corresponding diamines was not successful but reduction of N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione gave the corresponding diamine.

Attempted dehydrogenation of the above diamine did not give any diazabiphenylene.

A C K N O W L E D G E M E N T S

I would like to thank especially Dr. V. Rogers for his kind supervision and help which made this work possible and also Dr. A.R. Tatchell for reading the script and his interest.

My thanks are also due to Thomas Morson and Son Limited, Enfield, Middlesex, for giving day release and financial support. A grant from the Chemical Society Research Fund is also gratefully acknowledged.

Thanks are also accorded to Dr. T.C. Downie and Dr. G.H. Jeffery for providing laboratory facilities and chemicals.

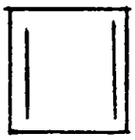
CONTENTS

Section		Page
I	INTRODUCTION	6
	Cyclobutadiene	7
	Biphenylene	11
	Heterocyclic analogues of biphenylene	16
II	DISCUSSION	23
	Synthesis of cis,trans,cis-tricyclo-[5,3,0,$0^{2,6}$]deca-3,8-dione	24
	The Schmidt reaction of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione	29
	Beckmann rearrangement of the dioximes of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$] deca-3,8-dione	44
III	EXPERIMENTAL	59
IV	SPECTRA	87
V	REFERENCES	114

INTRODUCTION

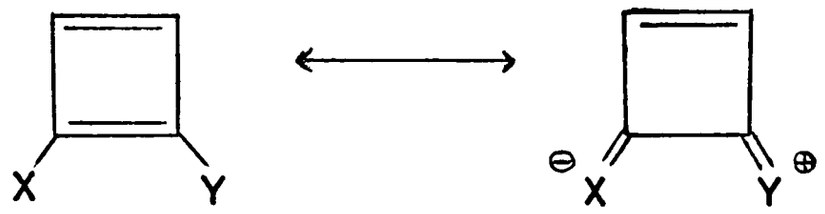
Cyclobutadiene

Cyclobutadiene(I) is the simplest member of the cyclic polyenes having alternate double and single bonds and a general composition $(C_2H_2)n$. At the beginning of this century it was believed that cyclobutadiene would be a stable aromatic system and its chemistry would be analogous to benzene. Various attempts[1,2,3,4] to isolate cyclobutadiene were unsuccessful and it was only recently that cyclobutadiene was formed and shown to be a reactive, unstable species.[5,6]

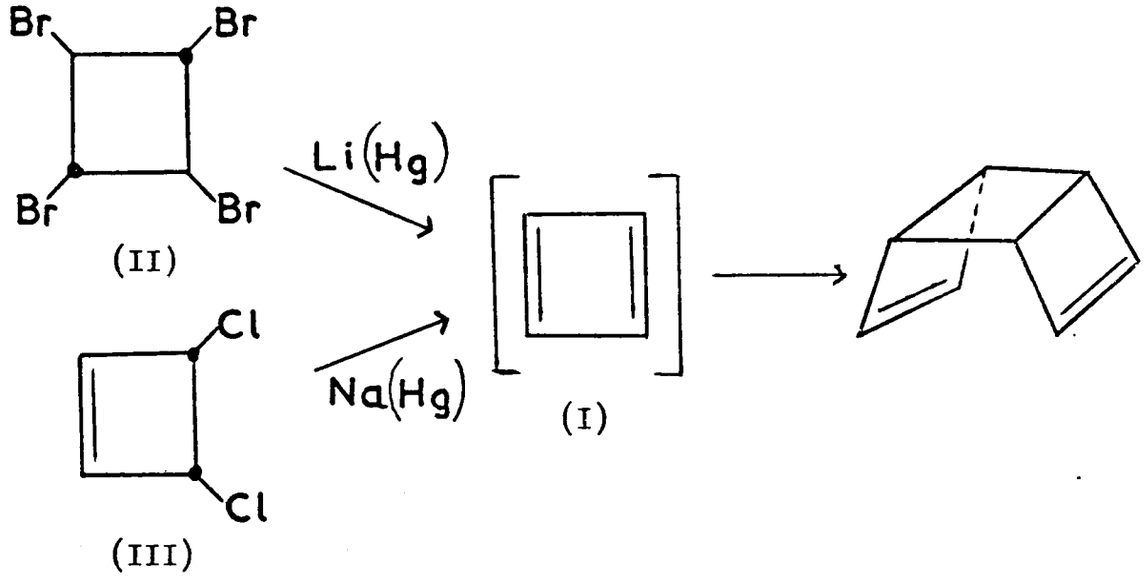


(I)

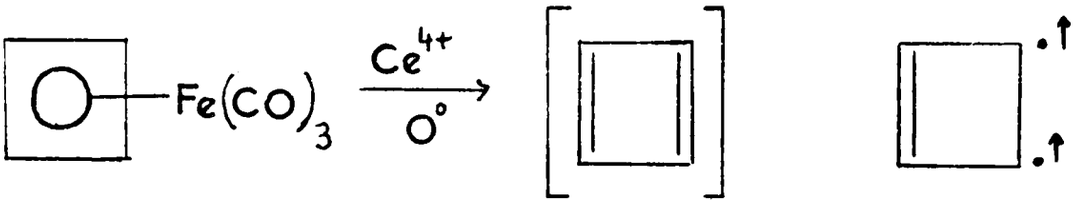
The reason for the instability of cyclobutadiene was not understood until the modern molecular orbital theory was developed. According to this theory, one of the requirements for aromaticity and thus stability, is that the molecule should have a $(4n + 2)\pi$ electron system, where n is an integer. This is the well-known Hückel rule which is applicable strictly to monocyclic systems. Since cyclobutadiene has a $4n\pi$ electron system, the molecule would be expected to be highly unstable, having zero delocalisation energy. Nevertheless many attempts have been made to synthesise cyclobutadiene and cyclobutadienoid systems in which the instability of the four-membered system would be diminished through some special structural or electronic feature. Thus Roberts suggested[7] that the cyclobutadiene system could be appreciably stabilised by a pair of neighbouring conjugative substituents, one of which would be electron-attracting and the other an electron-donating group.



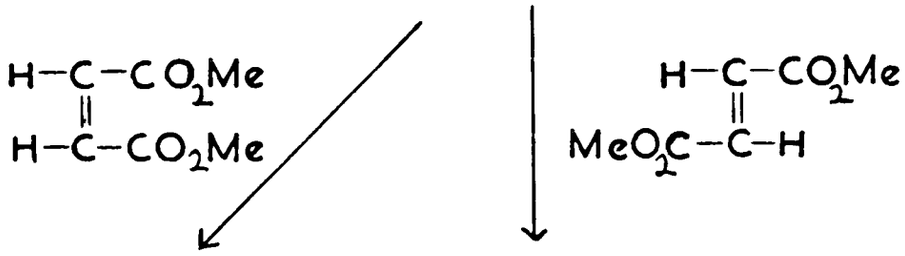
There are several reactions known in which cyclobutadiene is probably generated as a transient intermediate. For example, the completely trans system, trans-1,2,3,4-tetrabromocyclobutane(II), on treatment with lithium amalgam in ether gave the syn dimer of cyclobutadiene.[8] Similarly, cis-3,4-dichlorocyclobutene(III) when treated with sodium amalgam in ether also gave the same dimer.[9]

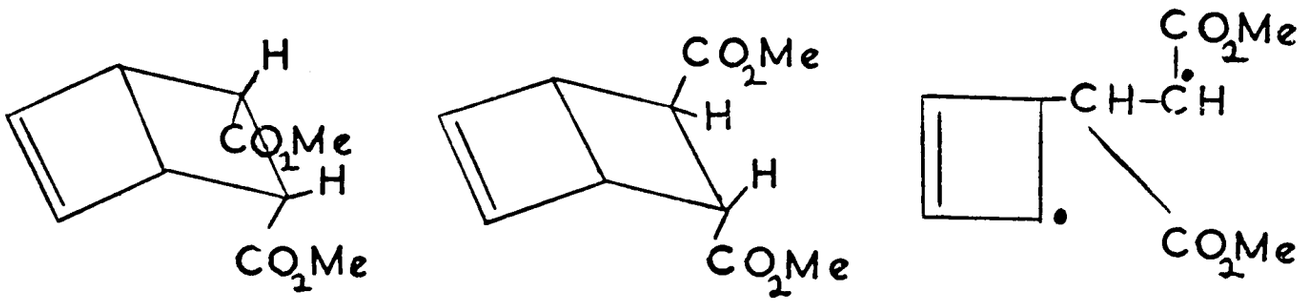


In 1965, Watts, Fitzpatrick and Pettit[5,6] described unambiguously the formation of free cyclobutadiene for the first time. They generated cyclobutadiene by the oxidation of cyclobutadieneiron tricarbonyl(IV) at 0^{o} with ceric ion. The cyclobutadiene reacted stereospecifically both as a diene and as a dienophile. Reaction with dimethyl maleate gave only endo-cis-5,6-dicarbomethoxybicyclohexene(V), while with dimethyl fumarate, only trans-5,6-dicarbomethoxybicyclohexene(VI) was formed. This was taken as indicating that cyclobutadiene has a singlet ground state rather than the triplet state (VII) at 0^{o}.



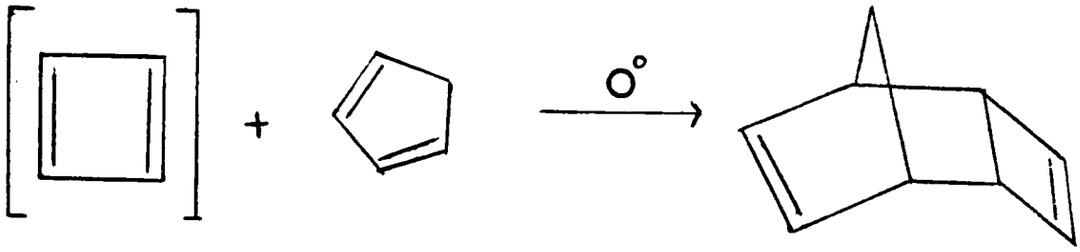
(IV) (I) (VII)



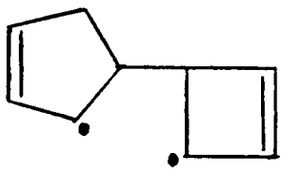


(V) (VI) (VIII)

The products V and VI are just those one would expect if cyclobutadiene were to react as a singlet diene in the normal Diels-Alder reaction. On the other hand one would not expect stereospecific addition to occur if cyclobutadiene were to be a triplet.[10] In such an event the addition to both the dimethyl maleate and dimethyl fumarate should be a two-step process involving the common triplet species VIII; assuming electron spin inversion and ring closure to be slow with respect to rotation about single bonds, then the same two adducts V and VI as well as the exo-cis isomer should be produced, which is not the case. Cyclobutadiene also reacts as a dienophile and in a stereospecific manner. The reaction with cyclopentadiene at 0° gives a single C_9H_{10} adduct IX. This is an additional evidence for the singlet ground state at 0°. If cyclobutadiene were a triplet then one could expect four C_9H_{10} hydrocarbons via the bisallyl radical species X.

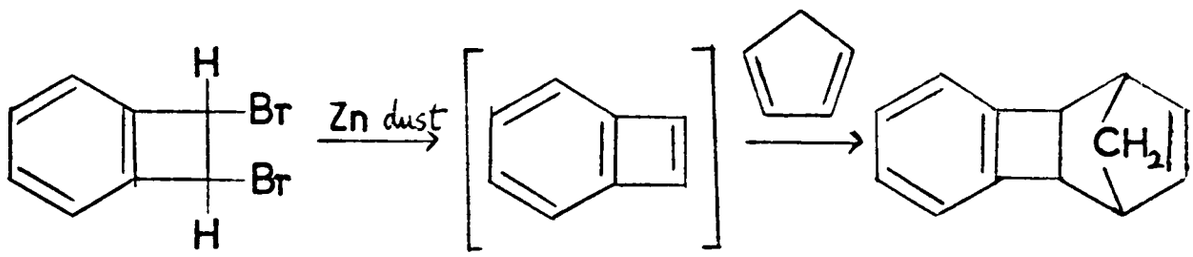


(I) (IX)



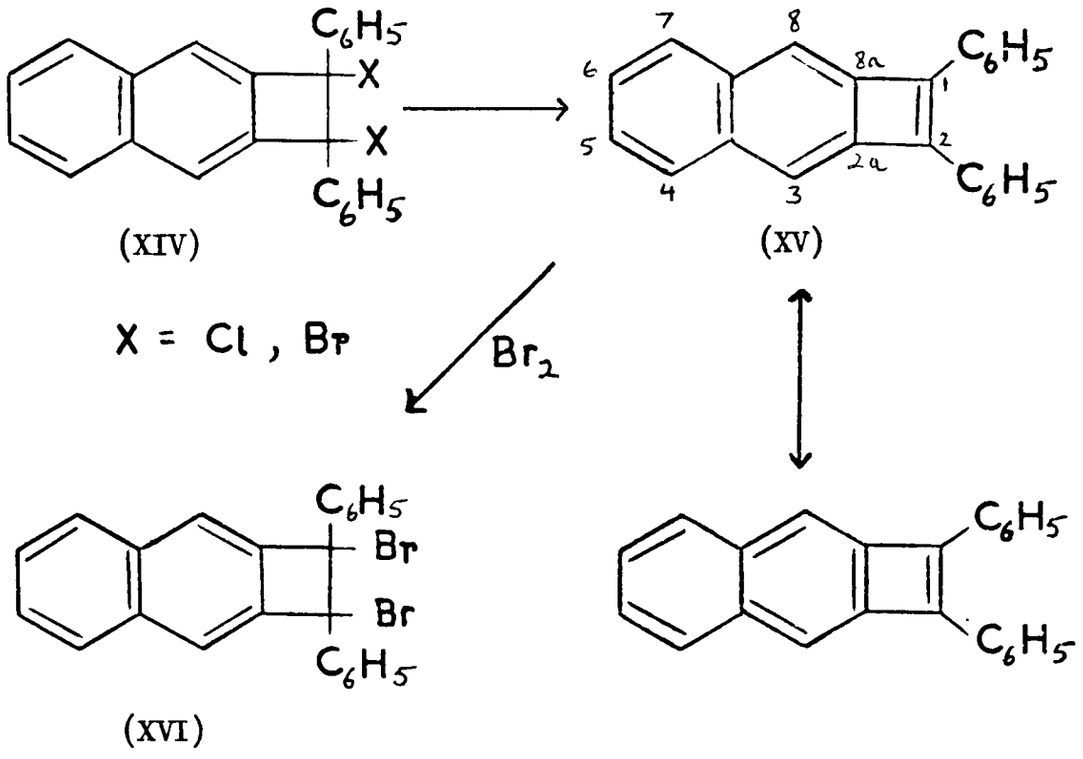
(X)

Prior to the above work many attempts were made to synthesise compounds containing a stabilised cyclobutadienoid system.[11] All attempts to isolate the monobenzo compound benzocyclobutadiene(XI) failed although Nenitzescu et al.[12] proved it exists as an intermediate in the zinc dust debromination of the dibromide XII, by forming its adduct XIII with cyclopentadiene.



(XII) (XI) (XIII)

In 1963, it was found that the reaction of 1,2-dichloro-1,2-diphenylnaphtho[b]cyclobutene(XIV, X=Cl) with zinc dust in boiling benzene gave 1,2-diphenylnaphtho[b]cyclobutadiene(XV), a bright red crystalline solid in 60% yield.[13] The dibromo anologue gave the same compound in 49% yield.

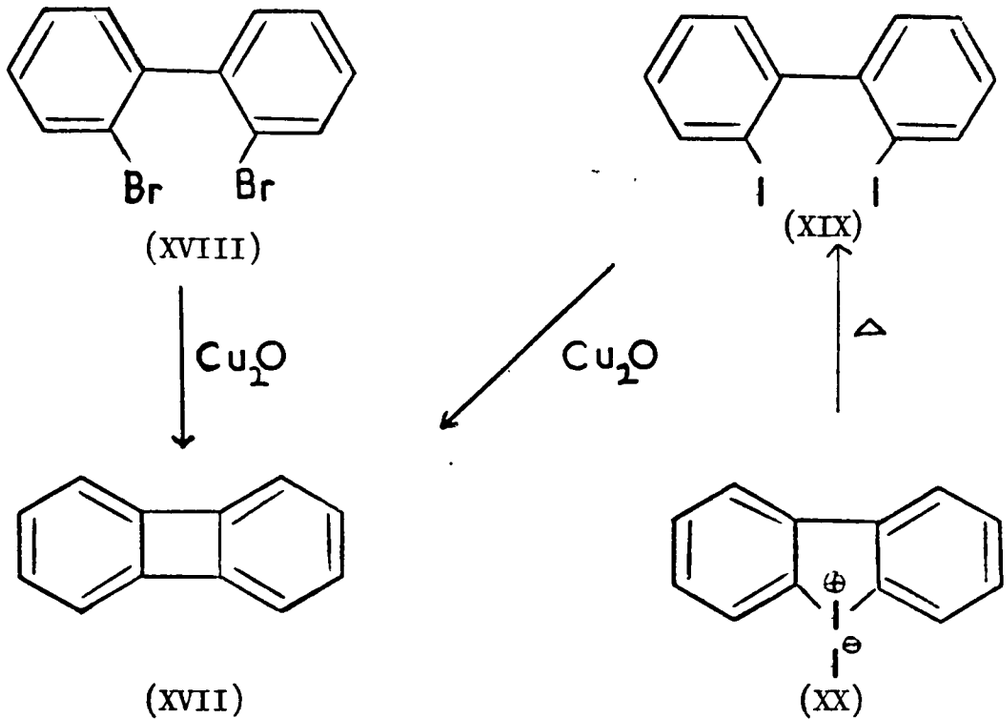


With regard to stability, this compound appears to occupy a borderline position between the unstable cyclobutadiene and the stable biphenylene described below. Thus bromine adds to the 1,2-bond in the four-membered ring to give the dibromo compound XVI; hydrogen adds to the same double bond on catalytic reduction. Four canonical structures may be written for the mesomeric naphthocyclobutadiene, two of which are shown above, and it does appear from its chemistry that the 1,2-bond has a high degree of double bond character and thus the compound is best represented by structure XV. In support of this, the n.m.r. spectrum of the compound showed two olefin-like protons at δ 6.50 p.p.m. indicating a considerable degree of π-bond fixation in the 2a,3- and the 8,8a-bonds.[14] It is interesting to note that the parent compound, naphtho[b]cyclobutadiene has not been isolated so far; thus it appears likely that the two phenyl groups contribute to the stability of compound XV.

Biphenylene

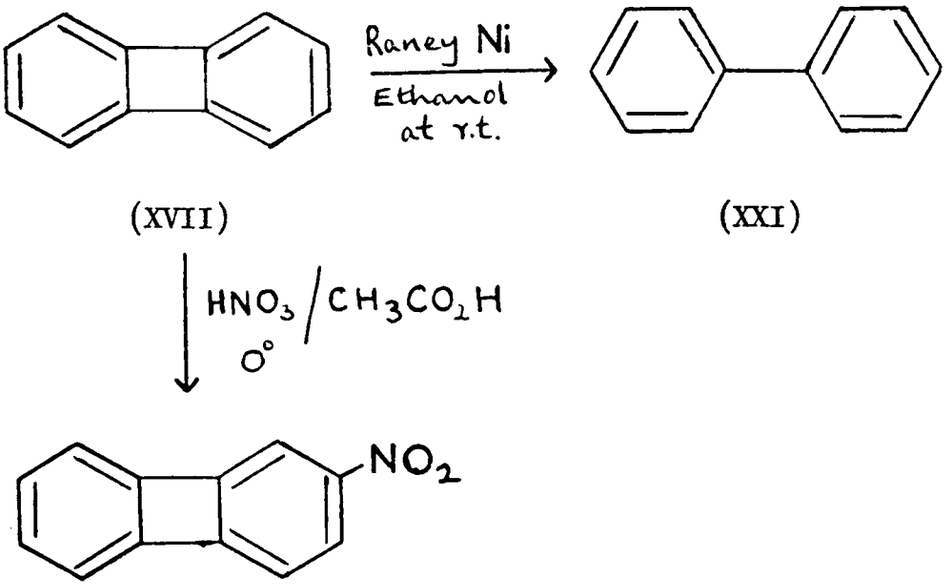
In contrast to the above compound(XV), biphenylene(XVII), a formal dibenzo derivative of cyclobutadiene, is an extremely stable compound and has been known for a considerable period of time.[11] Biphenylene

was first synthesised by Lothrop[15] in 1941, who obtained it by heating 2,2'-dihalobiphenyls with cuprous oxide at 350°. Although the yields were poor using the dibromo compound (XVIII), better yields were obtained with 2,2'-diiodobiphenyl(XIX) and with biphenylene iodonium iodide[16](XX) which is known to give the di-iodo compound on heating.



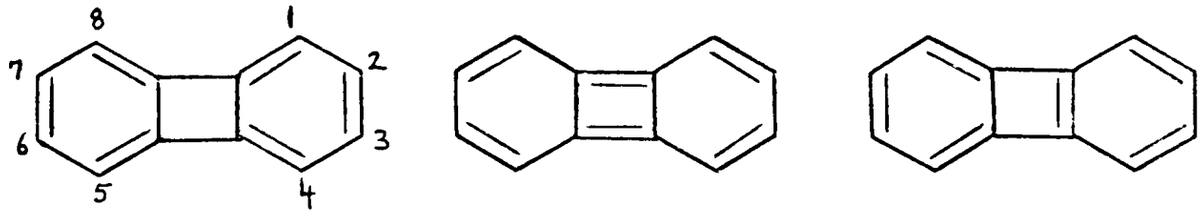
More recently it has been found that the reaction of several 2,2'-diiodobiphenyls with copper gave the corresponding biphenylenes in yields superior to those obtained with cuprous oxide.[17]

Biphenylene is extraordinarily stable as evidenced by its formation at 350°. Its chemistry has been studied and it has been shown to behave as a typical aromatic compound undergoing substitution rather than addition reactions; thus electrophilic substitution readily occurs and nitration,[18] chlorination, bromination and iodination gives the 2-substituted derivative. Like benzene it is unreactive towards free radicals, acetylation by lead tetra-acetate occurred in 1.5% yield only.[19] Despite the apparent considerable strain in the molecule the only reaction in which the four-membered ring itself is opened is catalytic reduction,[20,21] when biphenyl(XXI) is formed.



(XVII) (XXI)

Biphenylene has 5 canonical forms (XVII), (XXII), (XXIII), (XXIV), (XXV), and if the resonance theory is applied on the assumption that each form contributes equally to the resonance hybrid, the 1,2-bond of biphenylene should have 3/5 double bond character and the 2,3-bond only 2/5.



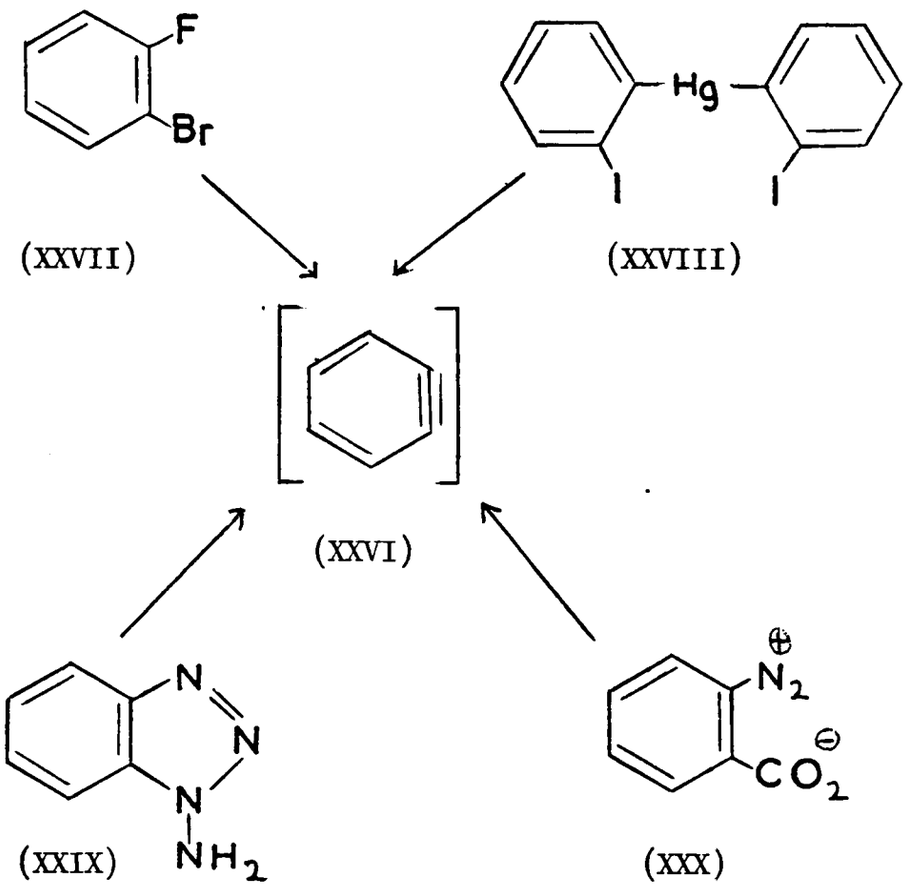
(XVII) (XXII) (XXIII)

(XXIV) (XXV)

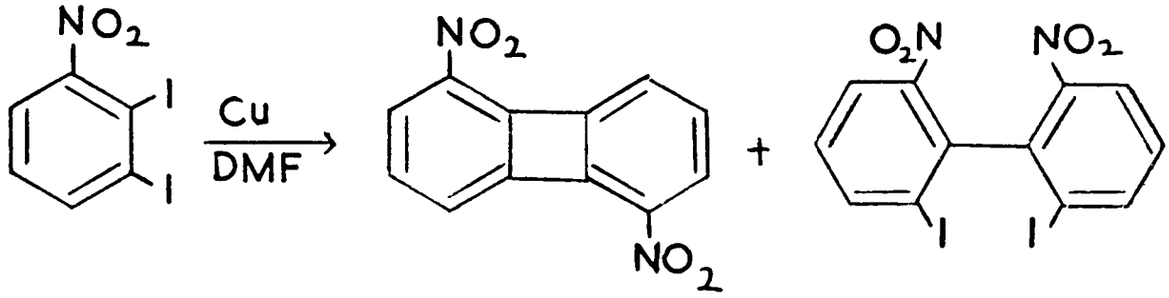
On this basis electrophilic substitution of a biphenylene with an ortho-para directing group at position 2 would be expected to occur at position 1. However, molecular orbital calculations by Longuet-Higgins[22] were at variance with this and predicted that further substitution would occur at position 3. This was confirmed experimentally[21] when it was

found that bromination of 2-acetamidobiphenylene gave the 2-acetamido-3-bromobiphenylene. This has been taken as indicating that the preferred bond structure of biphenylene is XVII, and suggests little contribution of the cyclobutadienoid structures XXII and XXIV to the resonance hybrid.

Biphenylene has been obtained by the dimerisation of benzyne(XXVI) generated from a variety of precursors. Treatment of o-fluorobromobenzene (XXVII) with lithium amalgam in ether gave the compound in 24% yield;[23,24] 54% yield was obtained by the gas phase flash pyrolysis[25] of bis-(o-iodophenyl)mercury(XXVIII), 83% yield by the oxidation of 1-amino-benzotriazole(XXIX) with lead tetra-acetate,[26] and 21-30% yield by the rapid decomposition of benzene diazonium carboxylate(XXX) in boiling ethylene chloride.[27] This last reaction is useful as a practical synthesis of biphenylene as the diazonium carboxylate is readily obtained by the aprotic diazotisation of readily available anthranilic acid.



Several substituted biphenylenes have been prepared by treatment of the appropriately substituted o-dihalobenzenes with dehalogenating agents. The reaction between 2,3-di-iodonitrobenzene(XXXI) and copper-bronze in dimethylformamide gave dinitrobiphenylene(XXXII) in 43% yield, other products being di-iodonitrobiphenyl(XXXIII) and a tetranitrophenylene-(XXXIV).[28] It has been suggested that this reaction proceeds via formation and dimerisation of the substituted benzyne.



(XXXI) (XXXII) (XXXIII)

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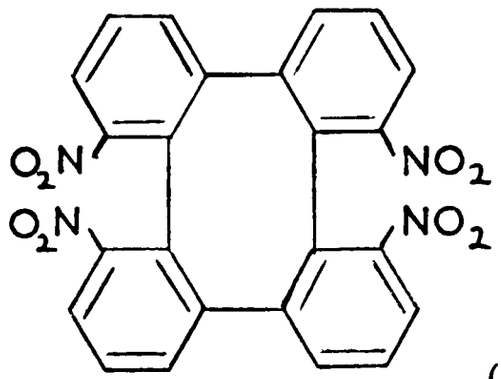
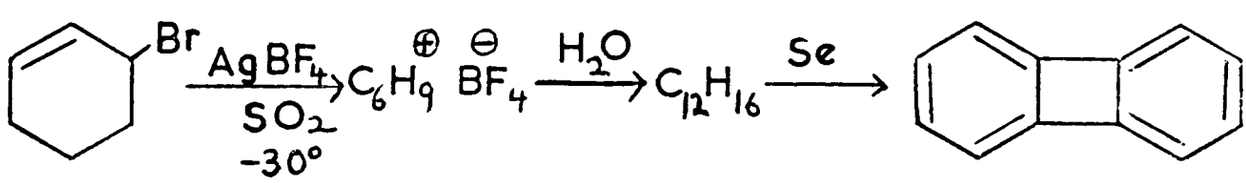


(XXXIV)

It is of interest to note that only one synthesis of biphenylene by a dehydrogenation procedure appears to have been reported; Olah and Tolgyesi[29] found that addition of water to the carbonium ion salt XXXV obtained by reaction of cyclohexenyl bromide 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.

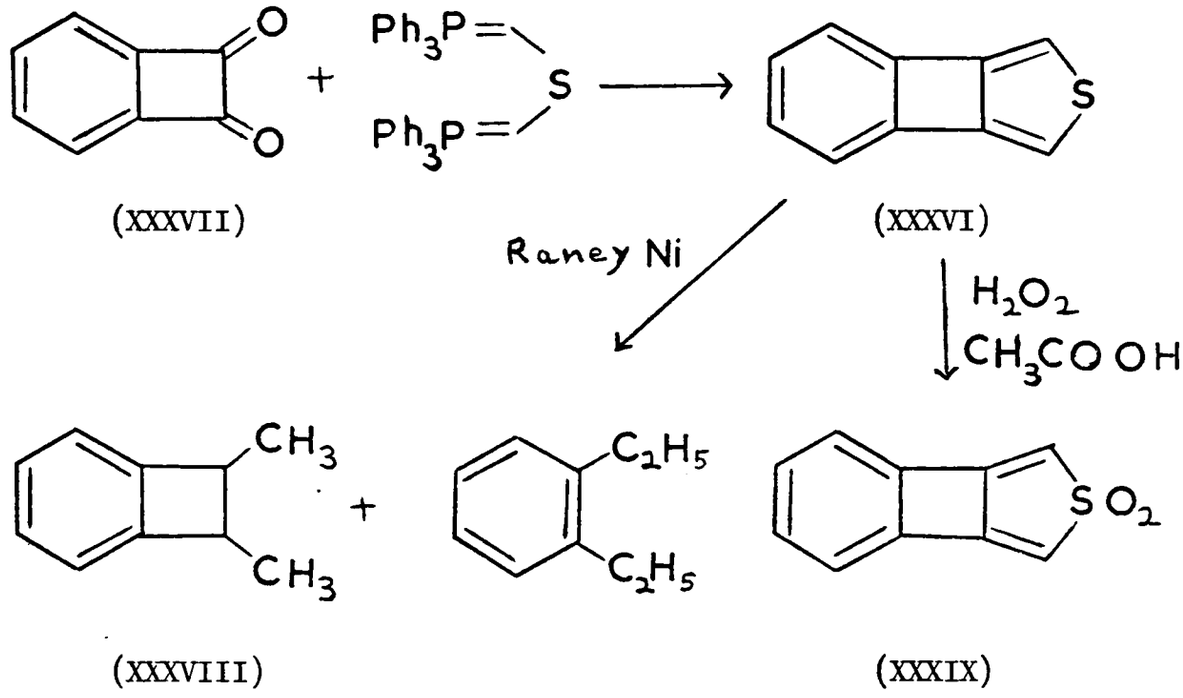


(XXXV)

Heterocyclic analogues of biphenylene

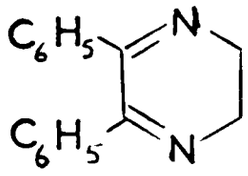
Although a great deal of work has been done on biphenylenes, very little had been published on the heterocyclic analogues of biphenylene at the commencement of this work. The study of such compounds would be of particular interest in connection with the influence of the hetero atoms on bond structure and the stability of the four-membered ring. Very recently, a number of investigations on the synthesis and attempted synthesis of such compounds have been reported.

In 1970, Garratt and Vollhardt[30] obtained benzo[3,4]cyclobuta[1,2-c]-thiophen(XXXVI) by the Wittig reaction of 1,2-benzocyclobutadienoquinone[31] (XXXVII) with sulphur triphenylphosphorane in dry ether under nitrogen.

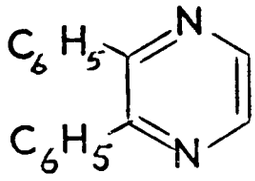


The compound was obtained as a crystalline solid in 14% yield, m.p. 98-98.5°. Desulphurisation with Raney nickel gave 1,2-dimethyl-benzocyclobutene(XXXVIII) and o-diethyl benzene. Oxidation of (XXXVI) gave benzo[3,4]cyclobuta[1,2-c]thiophen 2,2-dioxide(XXXIX), m.p. 213-215°.

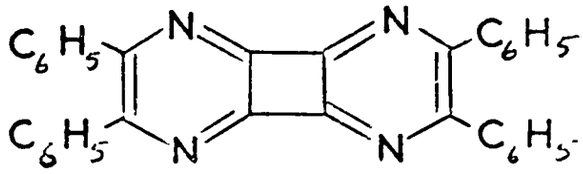
A tetra-azabiphenylene was postulated as early as 1893 by Mason and Dryfoos.[32] They reported that the reaction of 2,3-dihydro-5,6-diphenylpyrazine(XL) with alcoholic potassium hydroxide gave mainly 2,3-diphenylpyrazine(XLI) along with a compound called "tetraphenyldipiazine". They assigned the structure XLII to this compound on the basis of its elemental analysis and molecular weight determination. However, no attempt was made to confirm the structure.



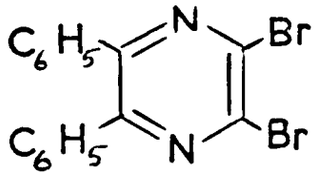
(XL)



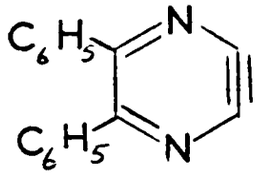
(XLI)



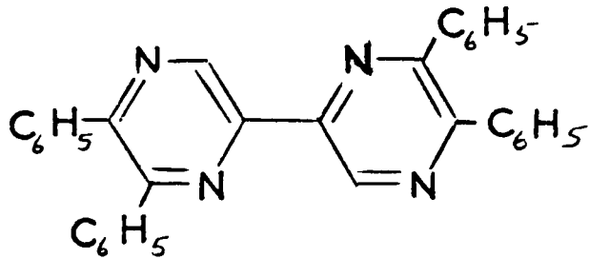
(XLII)



(XLV)



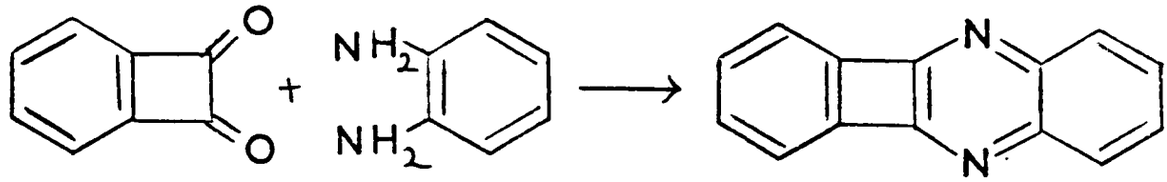
(XLIV)



(XLIII)

Recently, England and McDougall reinvestigated this reaction and showed that "tetraphenyldipiazine" was in fact 5,5',6,6'-tetraphenyl-2,2'-bipyrazinyl(XLIII).[33] They also attempted to prepare a 3,3'-dihalogeno derivative of this compound as a possible precursor of the tetra-azabiphenylene XLII but without any success. An alternative route, namely the possible generation and dimerisation of pyrazyne(XLIV) by treatment of dibromodiphenylpyrazine(XLV) with copper in dimethylformamide (cf. ref.28) gave much intractable material and a small amount of compound XLIII, formation of which need not have involved the pyrazyne as an intermediate.

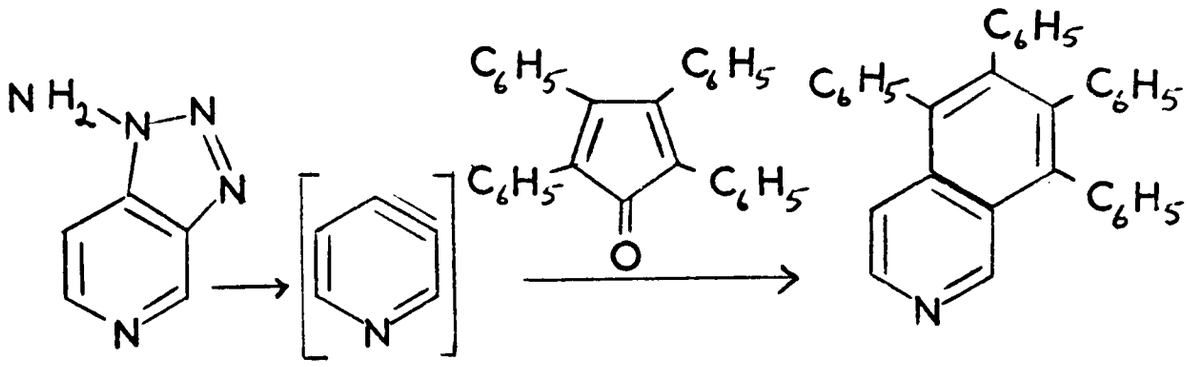
The first successful synthesis of a diaza analogue of biphenylene was reported in 1963 by Cava and associates,[31] who found that treatment of 1,2-benzocyclobutadienoquinone(XXXVII) with an equimolar amount of o-phenylenediamine gave 5,10-diazabenzo[b]biphenylene(XLVI) as long white needles, m.p. 238-239°.



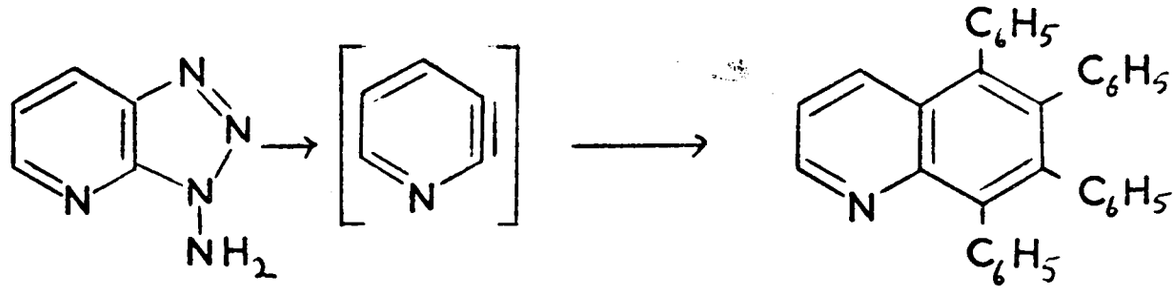
(XXXVII) (XLVI)

One logical approach to the synthesis of diazabiphenylenes with the nitrogens in different rings would be by the generation and dimerisation of pyridynes.

Fleet and Fleming[34] synthesised 1-aminotriazolo[4,5-c]pyridine(XLVII) and 3-aminotriazolo[4,5-b]pyridine(XLVIII), as potential precursors of diazabiphenylenes. The corresponding aminotriazoloquinolines were also synthesised. 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.



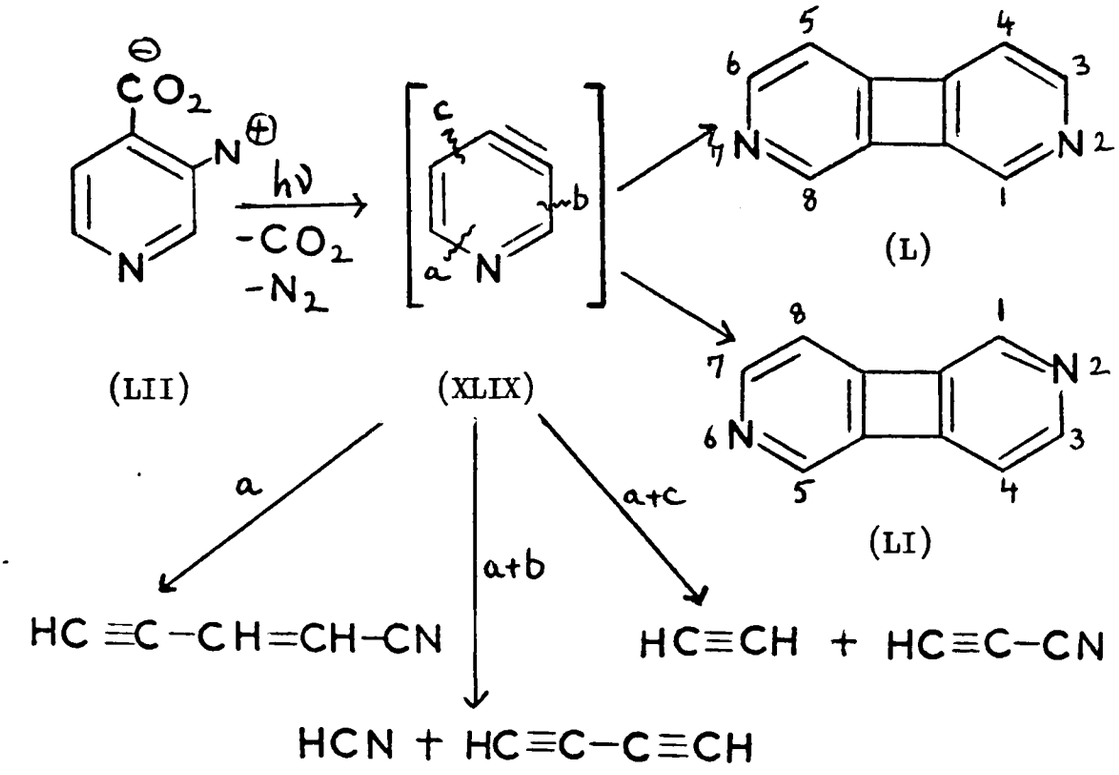
(XLVII)



(XLVIII)

The authors stated that they were investigating the products obtained from the lead tetra-acetate oxidation of the aminotriazoles in the absence of tetraphenylcyclopentadienone, but as yet no details of these studies have been published. Recently, Kramer and Berry reported[35] a study of gaseous 3,4-pyridyne[36](XLIX) and its unimolecular decomposition and dimerisation to 2,7-(or 2,6-) diazabiphenylene (L, LI). The method consisted of photolysing solid pyridine-3-diazonium-4-carboxylate[37](LII) and monitoring the reaction products by time-of-flight mass spectroscopy.

From the results of mass spectroscopy, the authors concluded that 3,4-pyridyne(XLIX) underwent unimolecular decomposition as shown below as well as dimerisation to diazabiphenylene(L or LI).



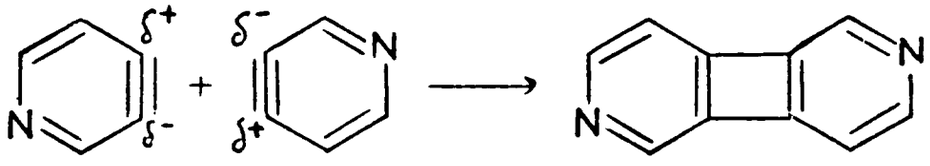
Dimerisation occurred in poor yield (~5%). In contrast to this, benzyne under similar conditions dimerises to biphenylene in good yield (~35%)[38] and shows no unimolecular decay.[39] The authors have explained this difference in the chemistry on the basis of the energy contents of the two species (XLIX and benzyne). The resonance energy of pyridine is ~15 kcal/mol less than benzene, a C-N bond is ~10 kcal/mol weaker than a C-C bond and a C≡N bond is ~13 kcal/mol stronger than a C≡C bond. This net difference of ~38 kcal/mol it was suggested, opens many bond breaking possibilities in XLIX.

The unimolecular reaction hypothesis was put to the test by the authors by studying the reaction products as a function of pressure of inert gas (nitrogen). It was expected that with increasing nitrogen pressure, XLIX would be stabilised, unimolecular reactions would be quenched, and the yield of L or LI would increase. This was found to be the case, L or LI was produced in 5% yield with no added gas, 12% with one-third atmosphere

of nitrogen and 11% with two-thirds atmosphere; the ratios of the products remained approximately constant except that it was noted that the relative amount of hyrogen cyanide increased and it was thought that this was due to unimolecular decay of the diazabiphenylene.

The diazabiphenylene was isolated as a white solid, m.p. 169-169.5° and high resolution mass spectrometry confirmed its molecular weight. The strongest band in the infrared 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 n.m.r. spectrum consisted of three sets of protons in the ratio of 1:1:1.

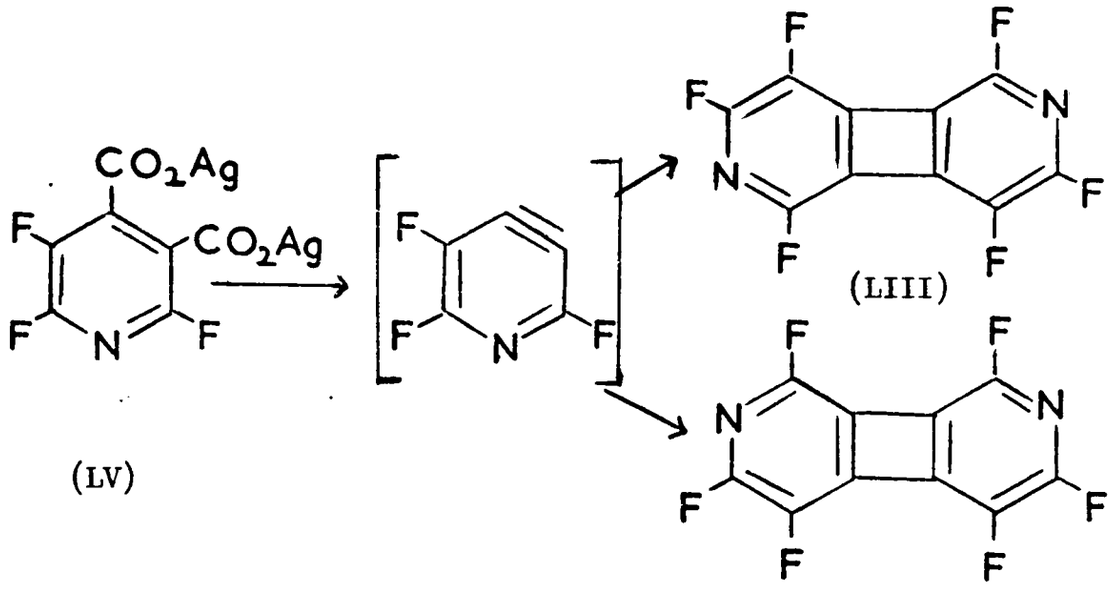
The authors further state that if the triple bond in 3,4-pyridyne(XLIX) is polarised significantly then the 2,6-isomer LI would be expected.[40]



(LI)

The compound was separated by gas chromatography on two different columns and on this basis and its narrow melting range the authors felt that a strong case could be made that the compound was pure. A weaker case could be made that it is the 2,6-isomer if the dehydro bond is polarised significantly by the electron-attracting nitrogen atom. However, the authors did not rule out the possibility of the 2,7-isomer L also being formed.

Very recently, Bartsch, Golloch and Sartori[41] have reported the synthesis of a mixture of the two perfluorodiazabiphenylenes(LIII) and (LIV) by the pyrolysis of the di-silver salt of 2,5,6-trifluoropyridine-3,4-dicarboxylic acid(LV).

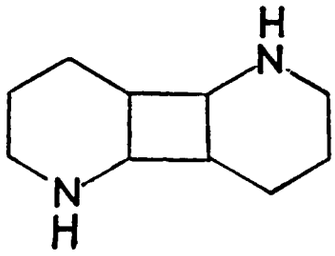


(LV)

(LIII)

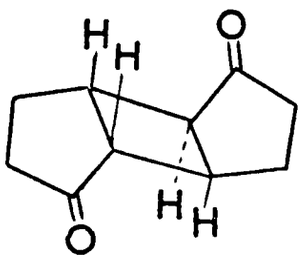
(LIV)

An alternative approach to the synthesis of diazabiphenylenes would be by the dehydrogenation of systems such as LVI.

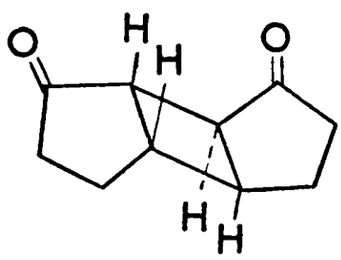


(LVI)

An attractive route to such systems would be insertion of a nitrogen atom in each of the cyclopentenone rings of the known cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione(LVII) and cis,trans,cis-tricyclo-[5,3,0,$0^{2,6}$]deca-3,10-dione(LVIII).[42] The following work describes investigations of the Beckmann and Schmidt reactions on diketone LVII as an approach to the synthesis of diazabiphenylenes.



(LVII)

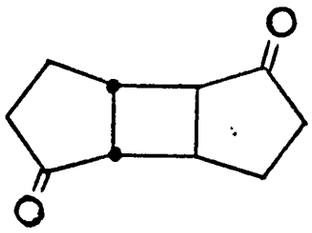


(LVIII)

DISCUSSION

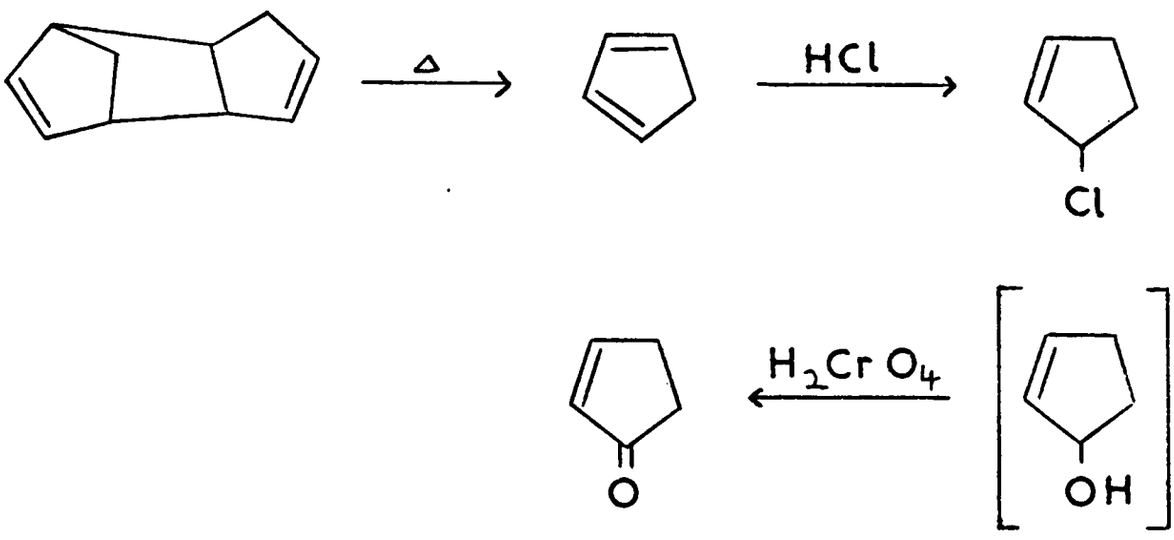
Synthesis of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione

The synthesis of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione(I) required for these investigations involved the synthesis of cyclopent-2-en-1-one as the immediate precursor.



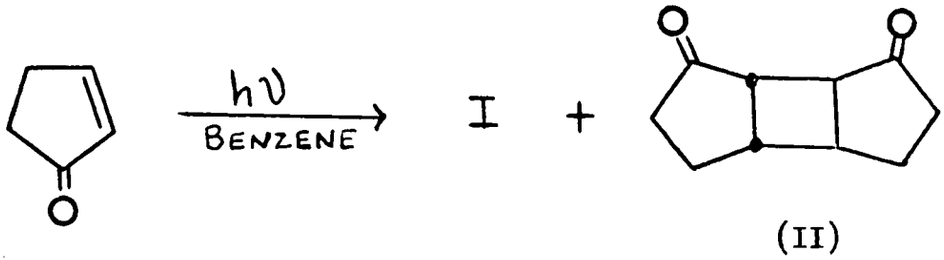
(I)

Cyclopent-2-en-1-one was prepared from cyclopentadiene, according to the method of Flock and Alder.[43] Addition of hydrogen chloride to cyclopentadiene, obtained by thermolysis of dicyclopentadiene,[44] gave 3-chlorocyclopentene which was converted to the hydroxy compound and then oxidised to cyclopent-2-en-1-one in a one step process on addition to aqueous chromic acid.



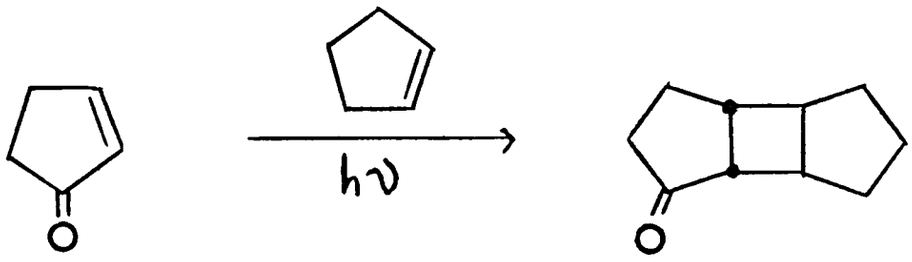
Eaton reported that photolysis of cyclopent-2-en-1-one itself or in solution in a variety of solvents with light of wavelength $\rangle$300nm, gave an approximately equal mixture of diketone I and cis,trans,cis-tricyclo-[5,3,0,$0^{2,6}$]deca-3,10-dione(II) in high yield.[42]

The mechanism has been represented as the attack of a photo-excited molecule on a non-excited substrate,[45] the initial excited species being formed by promotion of an electron from one of the oxygen non-bonding orbitals to an antibonding π orbital.



(II)

Since the original publication by Eaton, further work on this and similar reactions has been published by several authors.[46,47,48] Thus it was found that irradiation of a 10% solution of cyclopent-2-en-1-one in cyclopentene, gave cis,trans,cis-tricyclo $[5,3,0,0^{2,6}]$ decan-3-one(III).



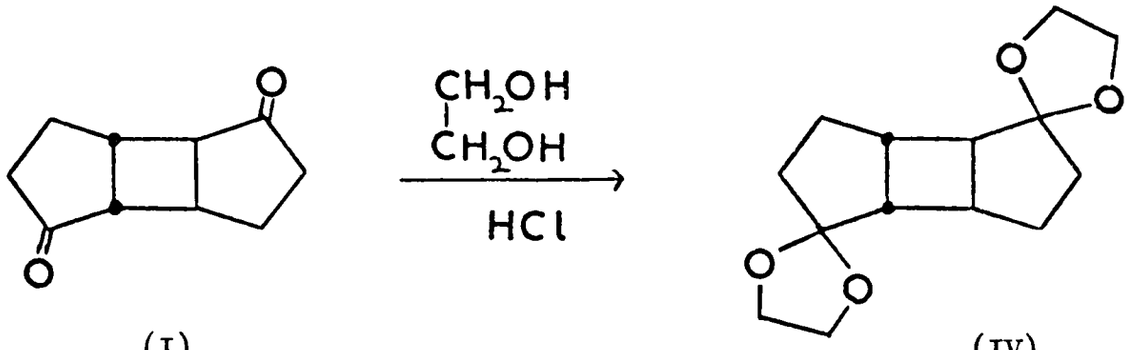
(III)

The above mixed addition was regarded as supporting the hypothesis that the mechanism of these cycloadditions involves attack of a photo-excited cyclopent-2-en-1-one 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-en-1-one was initially effected in benzene solution and the course of the reaction was monitored by g.l.c. on Carbowax 20M at 170°. Irradiation was continued until most of the ketone had reacted. The solid which had separated was collected, and a further quantity of the same material was obtained by evaporation of the filtrate and crystallisation of the residue from carbon tetrachloride. Recrystallisation gave diketone I, m.p. 125-126.5° in 29.5% yield.

Concentration and vacuum distillation of the mother liquors as described by Eaton[42] gave a waxy solid which was found by g.l.c. to be a mixture of diketones I and II in the approximate ratio of 1:3; repeated recrystallisation of this mixture failed to give either of the diketones in a pure form.

It had been reported by Eaton that diketone I readily forms diketal IV on treatment of its solution in ethylene glycol with dry hydrogen chloride but there was no mention that diketone II formed a corresponding diketal. It was hoped that diketones I and II could be separated by converting them to their corresponding diketals followed by recrystallisation; should the diketone II not be converted to the diketal readily, the separation of the resultant mixture would be expected to be easier.

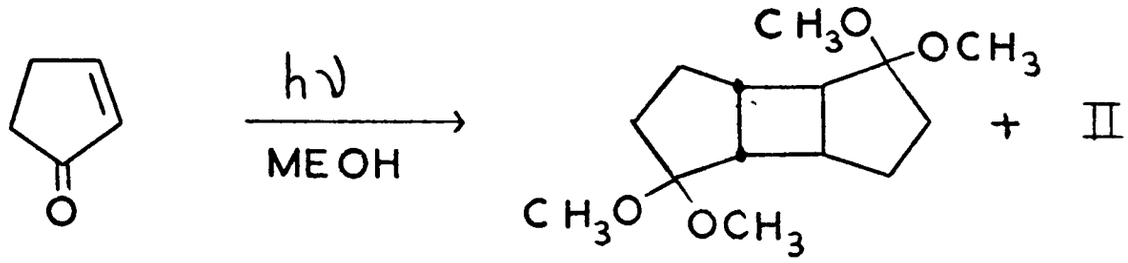


(I) (IV)

Treatment of the mixture in ethylene glycol solution with dry hydrogen chloride followed by work-up gave some pure diketal IV; the residue was shown by g.l.c. (Carbowax 20M, 170°) to consist mainly of unchanged diketone II. Thus this procedure appeared to be useful for separating the two diketones. However, further investigations of this method were not undertaken as it was subsequently found that photodimerisation in methanol led to a higher yield of diketone I.

Photolysis of a one molar solution of cyclopent-2-en-1-one in acid-free methanol with light of wavelength greater than 300nm in an inert atmosphere gave diketone II in 9% yield and an unexpected product,

cis,trans,cis-3,3,8,8-tetramethoxytricyclo[5,3,0,$0^{2,6}$]decane(V), m.p. 173-174° in 49.5% yield. During the photolysis, virtually pure diketal V separated from the solution as a white crystalline solid. On the other hand diketone II had to be recrystallised several times before a pure sample of it could be obtained; there was no evidence of the formation of its corresponding diketal.



(V)

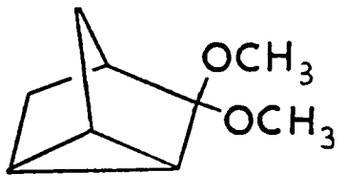
The structure of diketal V was established on the basis of its elemental analysis and spectroscopic data. The infrared spectrum (I.R.3) showed strong bands between 1030-1100 cm^{-1} characteristic of an ether type grouping, and the absence of any carbonyl band. Elemental analysis and mass spectroscopy indicated the molecular formula $C_{14}H_{24}O_4$ and the n.m.r. spectrum (N.M.R.1) confirmed the proposed structure, showing sharp singlets at δ3.13 (6H,s,2x OCH_3) and δ3.17 p.p.m. (6H,s,2x OCH_3) and a complex multiplet further upfield (12H, ring protons).

The structure of diketal V was further confirmed by its conversion to diketone I in 70% yield on heating at reflux in aqueous methanol containing hydrochloric acid. The diketone was obtained in much higher yield (95%) on heating the diketal in the two phase system of methylene chloride-hydrochloric acid, a method described by Janot and associates in their work on steroids.[49]

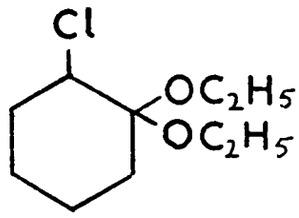
Heating a solution of diketone I in a mixture of dry methanol and benzene containing a small amount of toluene-p-sulphonic acid and allowing the condensate to percolate through a molecular sieve to remove

water followed by work-up gave the diketal in 14% yield, identical to that obtained from the photolysis reaction. T.l.c. examination of the crude product showed, in addition to unchanged starting material, a third component which was not isolated; it may possibly have been the mono-ketal.

In the photodimerisation reaction it was thought rather surprising that this diketal had not been observed previously. In a mechanistic investigation of the reaction, Eaton had photolysed cyclopent-2-en-1-one in methanol[46] and determined the ratio of the two diketones by g.l.c. Reactions were however run to only 10% completion and as the diketal would be expected to be formed from the dimer it would probably not have been formed or possibly not detected at that stage. In this context it is interesting to note that photoketalisation has been observed previously; thus irradiation of nortricyclanone in methanol,[50] and of 2-chlorocyclohexanone in ethanol,[51] gave the ketals VI and VII respectively.

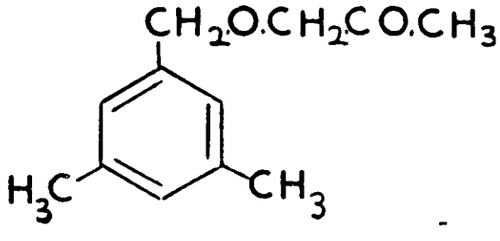


(VI)

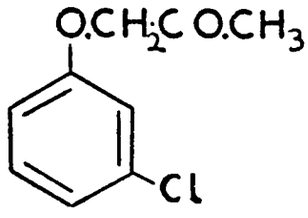


(VII)

In addition Dirania and Hill have reported[52] that ultraviolet irradiation of a number of ∝-aryloxyacetones, e.g. VIII and IX in methanol, ethanol or benzyl alcohol yield the corresponding dimethyl, diethyl or dibenzyl ketals respectively.



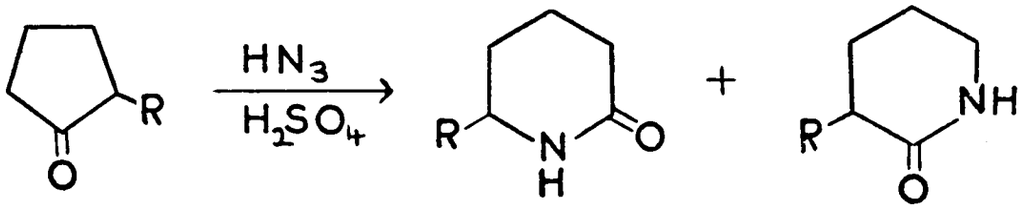
(VIII)



(IX)

The Schmidt Reaction of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione

Together with the Beckmann rearrangement of ketoximes the Schmidt reaction has been used extensively for the conversion of ketones to amides. When the ketones are cyclic, lactams are formed; thus α-substituted cyclopentanones give a mixture of lactams.[53]

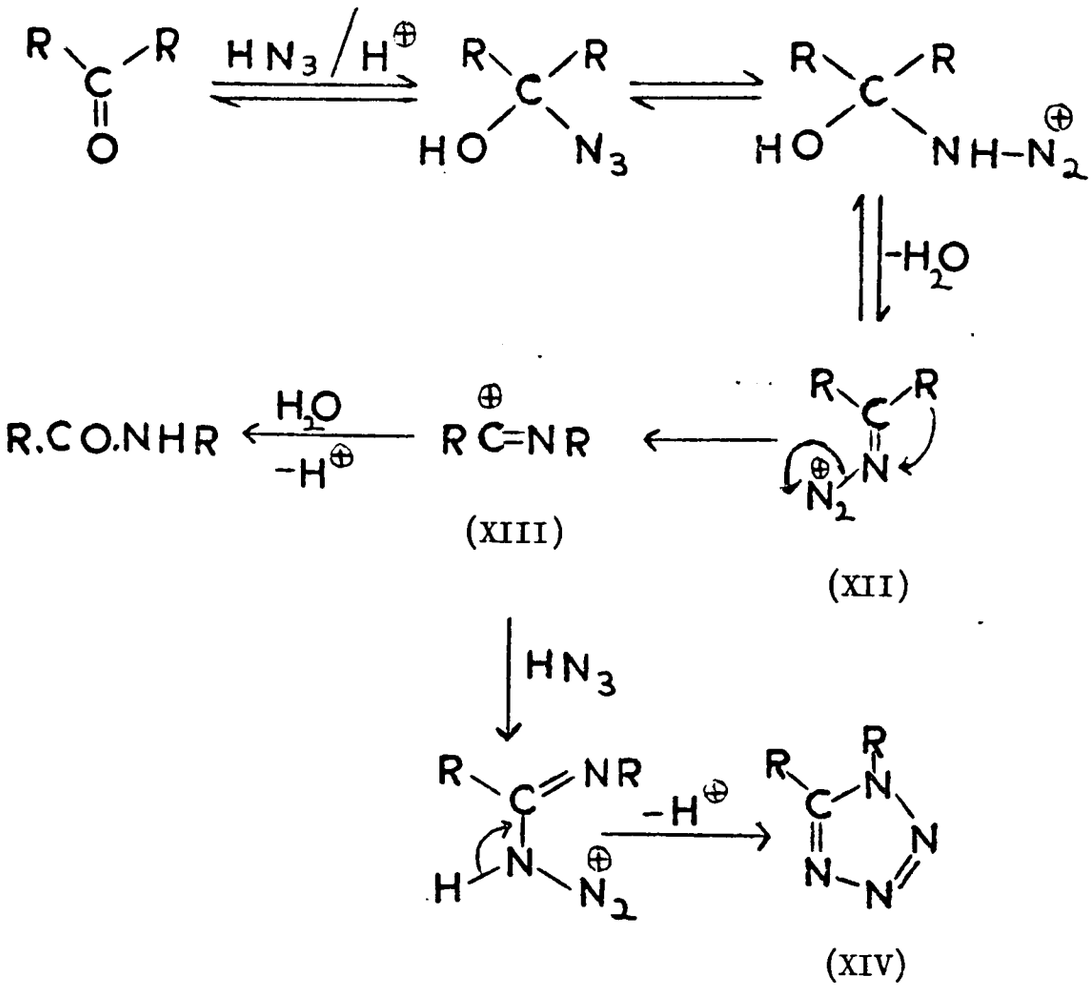


(X) (XI)

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 or sulphuric 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.[54]

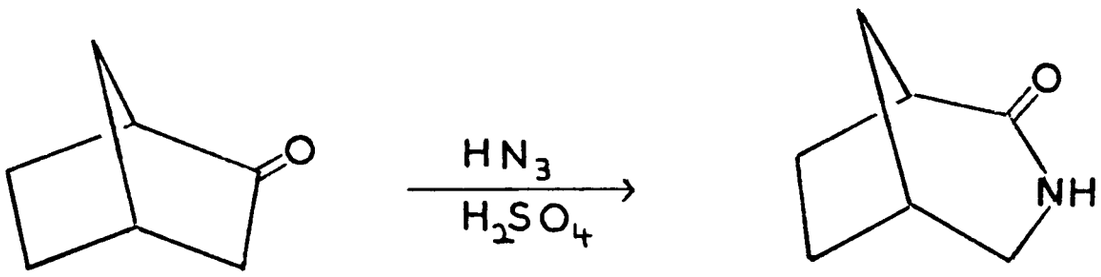
The currently accepted mechanism for this reaction involves attack of hydrazoic acid on the protonated ketone followed by elimination of water to give intermediate XII which rearranges as shown. Use of excess hydrazoic acid in the reaction often results in formation of tetrazoles, such as XIV, and this has been interpreted as supporting the intermediacy of species such as XIII.



(XIII) (XII)

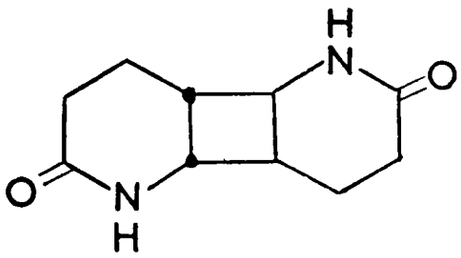
(XIV)

In the case of unsymmetrical ketones, two diazoketimine ions, the 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 X rather than XI.[53] Similarly the work of Fusco and Rossi[55] and Conley[56] appear to strengthen the case for the above rule. However, an exception has been reported by Elderfield and Losin;[57] they found that treatment of norcamphor(XV) with hydrazoic acid in sulphuric acid gave only lactam XVI (30% yield of crude material) in addition to the fragmentation product cyclopentene-3-acetonitrile.

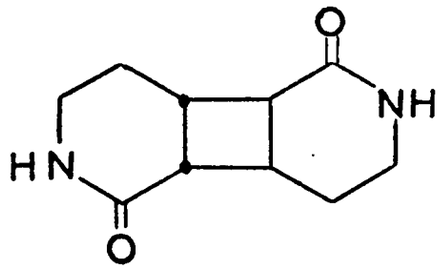


(XV) (XVI)

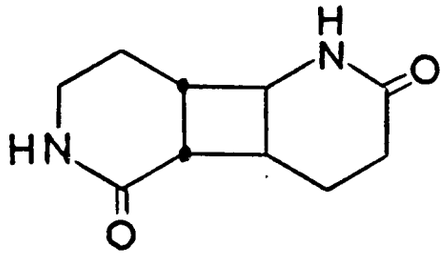
On the basis of the mechanism discussed above, the Schmidt reaction on diketone I would be expected to give mainly dilactam XVII together with dilactams XVIII and XIX.



(XVII)



(XVIII)



(XIX)

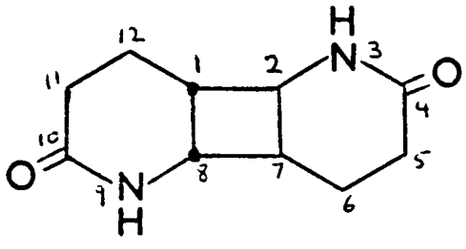
Treatment of diketone I with 2.2 molar equivalents of sodium azide in concentrated hydrochloric acid, followed by continuous chloroform extraction of the slightly basified (pH 8.5) aqueous reaction mixture gave a mixture of isomeric dilactams, m.p. 245-310° (with decomposition) in 90% yield. T.l.c. examination of the mixture with ethanol-water (9:1) as the developing solvent indicated two components with R_F 0.35 and 0.31 in an approximate ratio of 1:1. However, the t.l.c. resolution was not reproducible and hence the estimation was only tentative. Several other solvent systems were tested in order to obtain a better t.l.c. resolution but were found to be ineffective. A portion of the mixture (3g) was

eventually separated by fractional crystallisation from water to give two isomeric dilactams, m.p. $>338^{o}$ with decomposition (1.1g) and m.p. $265-268^{o}$ with decomposition (0.4g). The remaining fractions were mixtures of both the dilactams in varying proportions. No further attempts were made to separate these mixtures as it was found to be tedious and time-consuming. The mixture of dilactams could also be separated by fractional crystallisation from methanol, but water was found to be more suitable. The compounds were only slightly soluble in most of the other common organic solvents.

The higher melting compound was established to be cis,trans,cis-3,9-diazatricyclo$[6,4,0,0^{2,7}]$dodecane-4,10-dione(XVII) on the basis of spectroscopic and chemical evidence as described below.

Structure of dilactam m.p. $>338^{o}$ (decomp.)

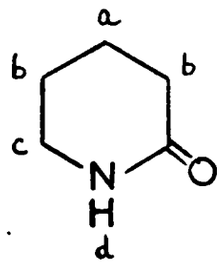
Elemental analysis indicated the molecular formula $C_{10}H_{14}N_2O_2$. The infrared spectrum (I.R.5) showed medium bands at 3180, 3060 cm^{-1} (bonded NH), a strong band at 1665 cm^{-1} (amide carbonyl) and a weak band at 1605 cm^{-1}. The n.m.r. spectrum (N.M.R.2) in trifluoroacetic acid was consistent with structure XVII.



(XVII)

A broad signal for four protons at δ2-2.5 was assigned to the methylene protons on C-6 and C-12; the multiplet at δ 2.7-3.0 representing four protons was assigned to the methylene protons adjacent to the two carbonyl groups and the signal for two protons at δ4-4.4 was assigned to the protons adjacent to the amide nitrogen on the basis that protons adjacent to amide nitrogen resonate at a lower field than protons adjacent

to amide carbonyl.[58,59] A reasonable correlation was observed when compared with the n.m.r. spectra of 2-piperidone.[60]

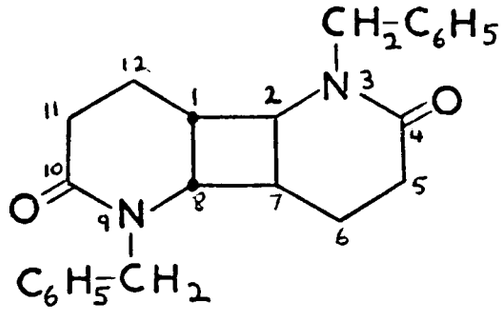


Proton	δ
a	1.77
b	2.20
c	3.23
d	8.09

The remaining multiplet for two protons at δ3-3.3 was assigned to the cyclobutyl protons on C-1 and C-7, and the sharp singlet for two protons at δ9.08 p.p.m. to the amide protons; the sharpness of the peak being due to rapid exchange of the protons with trifluoroacetic acid.

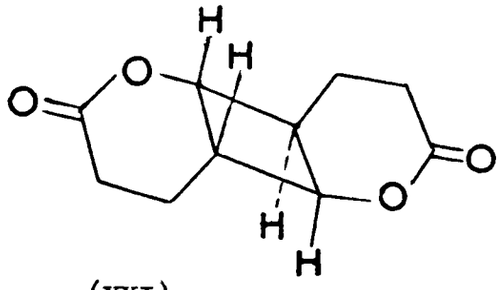
Confirmatory evidence was obtained by converting the dilactam to its N,N'-dimethyl and N,N'-dibenzyl derivatives and establishing their structures.

Treatment of the dilactam with sodium hydride and benzyl chloride in dimethylformamide followed by work-up gave a white solid, m.p. 225-234° in 96% yield; t.l.c. (ethanol) indicated that it consisted mainly of one component. Recrystallisation from methanol gave colourless prisms, m.p. 232-234°. Elemental analysis, i.r. and n.m.r. were consistent with the compound being N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$] dodecane-4,10-dione(XX).



(XX)

The infrared spectrum (I.R.6) showed a strong band at 1625 cm^{-1} for amide carbonyl and a band at 705 cm^{-1} for monosubstituted benzene. The n.m.r. spectrum (N.M.R.3) showed a four proton multiplet at δ 1.3-2.0 p.p.m. which was assigned to the protons at C-6 and C-12, and a six proton multiplet at δ 2-2.7 p.p.m. for protons at C-5, C-11, C-1 and C-7. A double doublet for two protons at δ 3.65 was attributed to the cyclobutyl protons at C-2 and C-8; the values of the coupling constants, 4.5 Hz and 10 Hz were consistent with those expected for vicinal <u>cis</u> and <u>trans</u> cyclobutyl proton coupling respectively. A similar pattern for the cyclobutyl protons adjacent to the lactone oxygens in compound XXI was noted by Eaton, coupling constants of 4.1 and 8.3 Hz were observed.[42]



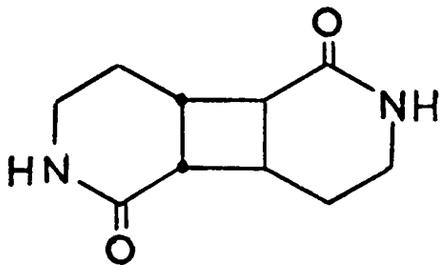
(XXI)

J_{cis} 1,2 = 4.1 Hz

J_{trans} 1,3 = 8.3 Hz

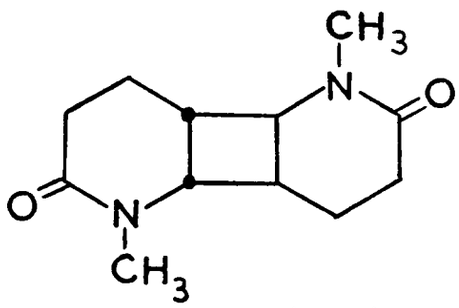
The remaining signals were particularly revealing; it was initially expected that the benzylic protons would appear as a singlet and that the aromatic protons would also appear as a singlet, this latter reflecting the symmetry of the molecule. The ten aromatic protons were indeed observed as a singlet at δ 7.24 p.p.m. with very fine splitting, but the benzylic protons appeared as a typical AB quartet at δ 4.45 p.p.m. with J 15 Hz, typical of geminal coupling. Inspection of a molecular model of structure XX indicated restriction of free rotation of each of the benzyl groups by the other lactam ring so that the benzylic protons were non-equivalent. This feature could only be accommodated by structure XX, and not by the <u>N</u>,<u>N</u>'-dibenzyl compound derived from the alternative symmetrical

dilactam XVIII which would also be expected to give a single peak for the aromatic protons but free rotation of the benzyl groups would result in equivalence of the benzylic protons. This in fact was observed and is discussed later (p. 49).



(XVIII)

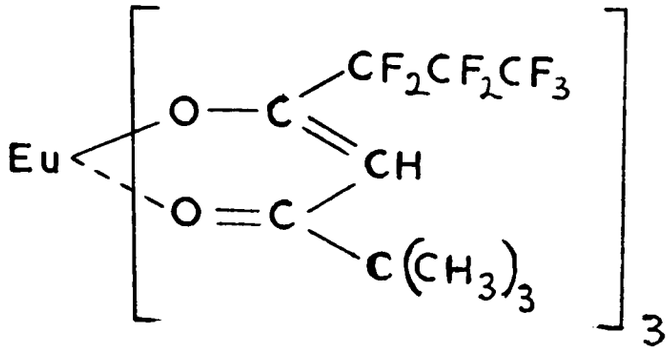
Treatment of the dilactam with sodium hydride and methyl iodide in dimethylformamide gave N,N'-dimethyl-cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-4,10-dione(XXII) in high yield. G.l.c. indicated one peak only, and the pure material was obtained as colourless prisms, mp. 148–149° from ethyl acetate.



(XXII)

The infrared spectrum (I.R.7) showed amide carbonyl absorption at 1620 cm^{-1}, and the n.m.r. spectrum (N.M.R.4) showed a singlet at δ2.9 p.p.m. for the two methyl groups consistent with the symmetry of the compound. The four protons at C-6 and C-12 appeared as a multiplet centred at δ2.0, the four protons at C-5 and C-11 as a multiplet at δ2.45 and two cyclobutyl protons at C-1 and C-7 as a multiplet at δ2.7 p.p.m. The cyclobutyl protons adjacent to the nitrogens appeared as a double doublet (Jcis 5 Hz, Jtrans 9 Hz) centred at δ3.7 p.p.m.

The effect of addition of the chemical shift reagent 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octane-dionato complex of europium $[Eu(fod)_3]$ on the n.m.r. spectrum was investigated.



It is known that such reagents complex with functional groups which include electron pairs and large downfield shifts are observed for protons in the vicinity of the functional group, the nearer protons being shifted more than those further from the complex.

Since the carbonyl oxygen in amides has higher electron density than nitrogen it was expected that $Eu(fod)_3$ would preferentially complex with the carbonyl groups of the N,N'-dimethyl compound. Consequently, on the basis that if the compound has structure XXII one would expect that on portionwise addition of $Eu(fod)_3$ to XXII the four protons at C-5 and C-11 would move more rapidly downfield than the two cyclobutyl protons at C-2 and C-8, these latter of course being initially at lower field. This was fully supported by results, (Fig.1,p. 37). Linear plots with varying slopes were obtained when δ values were plotted against the quantity of added complex; the largest slope was shown for the four protons at C-5 and C-11 followed by the N-methyl protons.

Structure of dilactam m.p. 265-268° (decomp.)

The minor component from the Schmidt reaction was found to be identical [m.p., mixed m.p. and i.r. (I.R.14)] with one of the two isomeric dilactams obtained from the Beckmann rearrangement of the dioxime(s) derived from cis,trans,cis-tricyclo$[5,3,0,0^{2,6}]$deca-3,8-dione(I). The

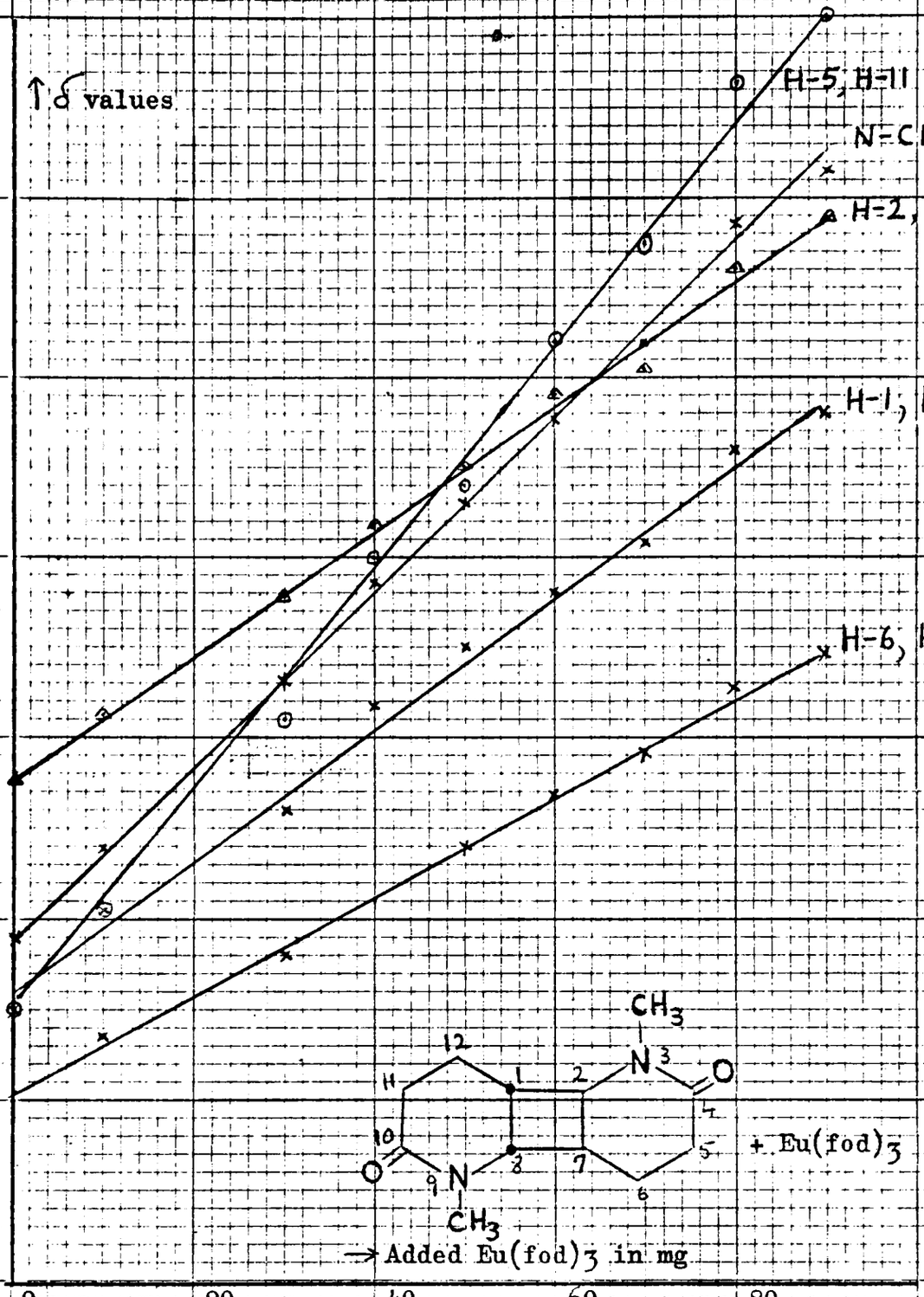
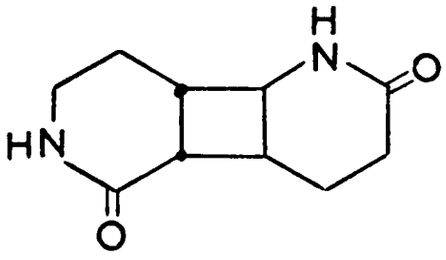

↑δ values
8
7
6
5
4
3
2
1
H-5, H-11
N-CH3
H-2, H-8
H-1, H-7
H-6, H-12
CH3
N
O
O
N
CH3
+ Eu(fod)3
→ Added Eu(fod)3 in mg
0
20
40
60
80
100

Fig. 1

compound was tentatively assigned the structure cis,trans,cis-3,10-diazatricyclo $[6,4,0,0^{2,7}]$dodecane-4,9-dione(XIX) on the basis of chemical and spectroscopic evidence as described later (p. 50).

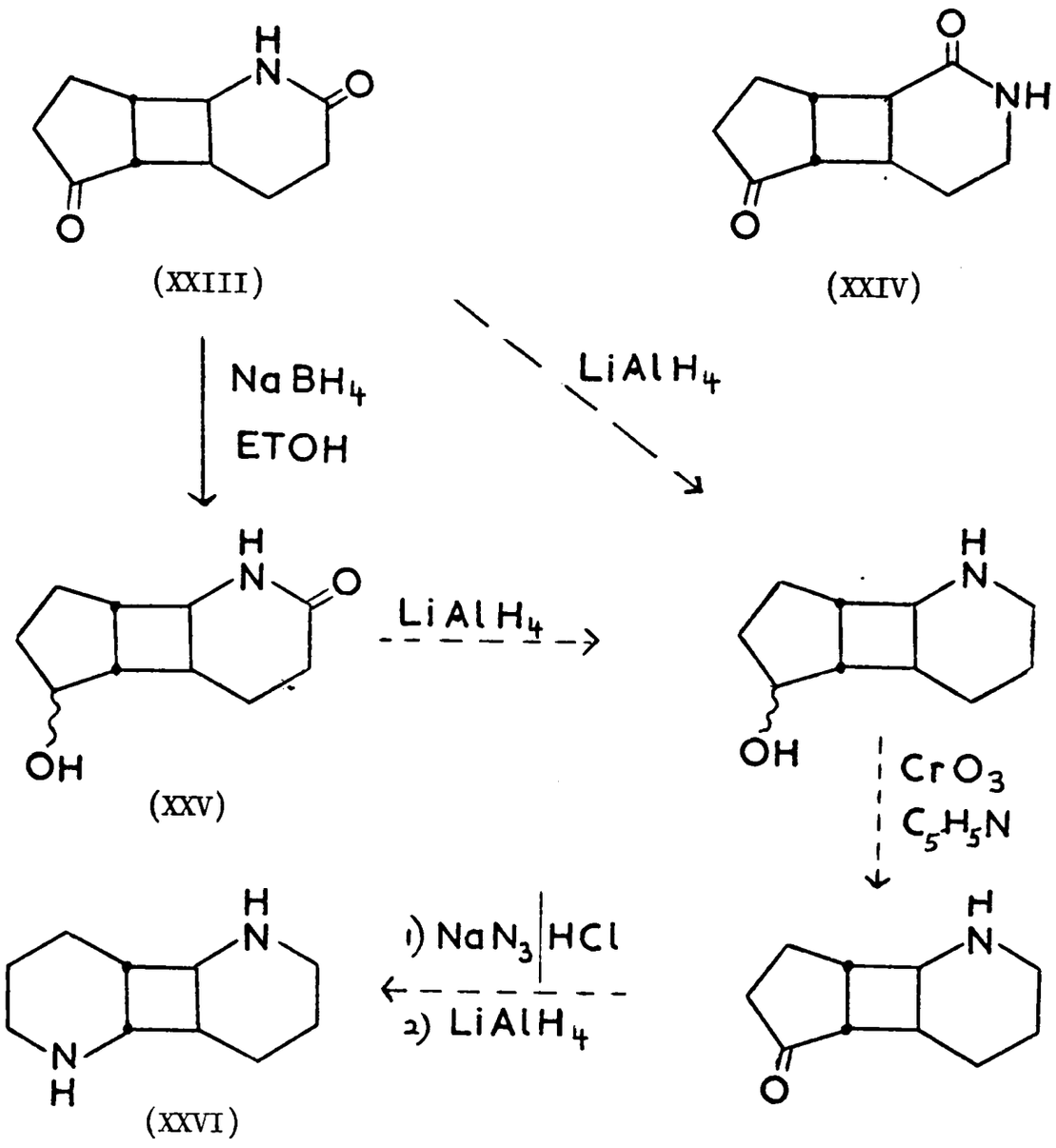


(XIX)

Single ring expansion of cis,trans,cis-tricyclo $[5,3,0,0^{2,6}]$deca-3,8-dione

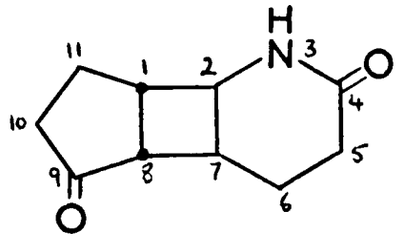
The difficulty in separating the mixture of dilactams obtained from the double ring expansion of diketone I, together with difficulties found in attempting to reduce the compounds, described later, p. 55, prompted an investigation to expand only one of the rings of the diketone. This could give rise to two isomers XXIII and XXIV but the keto-lactam XXIII would be expected to be the major product. Its solubility in common organic solvents would be expected to be greater than the dilactams allowing separation from any dilactams which would also be formed. Additionally the n.m.r. data from its solution in a solvent such as deuterochloroform would be more informative on these systems than the data obtained from the dilactams which was obtained in trifluoroacetic acid solution where line broadening occurred.

There was also the possibility that a keto-lactam such as XXIII, could be further elaborated to cis,trans,cis-3,9-diazatricyclo $[6,4,0,0^{2,7}]$-dodecane(XXVI) as shown, a possible precursor via dehydrogenation to diazabiphenylene.



Treatment of a solution of diketone I in concentrated hydrochloric acid with a 1:1 molar equivalent of sodium azide, followed by chloroform extraction of the neutralised aqueous reaction mixture gave a gummy yellow solid. Dry column chromatography gave a small quantity of starting material, a mixture of dilactams identical to those obtained from the first Schmidt reaction and a white solid m.p. 118-143° as the major fraction. T.l.c. indicated this solid consisted of two components in an approximate ratio of 9:1. Several attempts to separate these components by wet and also dry column chromatography proved unsuccessful. However, repeated recrystallisation from acetone gave a small quantity of the major product, m.p. 144.5-148 as colourless prisms. The molecular formula

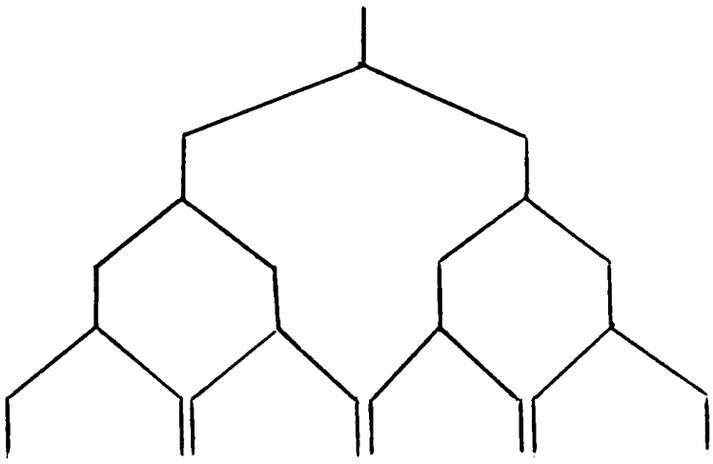
$C_{10}H_{13}NO_2$ and spectroscopic data were consistent with the compound being formulated as cis,trans,cis-3-azatricyclo $[6,3,0,0^{2,7}]$ undecane-4,9-dione(XXIII).



(XXIII)

The infrared spectrum (I.R.8) showed medium intensity bands at 3470, 3420 and 3270 cm^{-1} for amide N-H stretching, strong bands at 1728 cm^{-1} and 1660 cm^{-1} for ketone and amide carbonyl respectively and a medium band at 1605 cm^{-1} probably due to the N-H bending mode. In addition to a series of overlapping complex signals between δ1.7-3.1 p.p.m. for eleven protons, the n.m.r. spectrum (N.M.R.5) showed the amide proton as a broad signal centred at δ7.66, and a one proton approximate 1:2:2:2:1 quintet centred at δ3.8 p.p.m. which was assigned to the proton at C-2. This signal collapsed to a slightly distorted double doublet on shaking the sample with 5% NaOD in D_2O together with the disappearance of the amide hydrogen signal.

The alternative keto-lactam XXIV would have shown the lowfield signal for two protons rather than one. The splitting pattern obtained can be readily explained on the basis of structure XXIII; coupling of the cyclobutyl proton at C-2 firstly with adjacent trans and cis cyclobutyl protons would produce double doublets which would be further split by coupling with the amide proton and thus overlapping of peaks results in an apparent quintet as shown below. Substitution of amide hydrogen with deuterium would give the observed results.

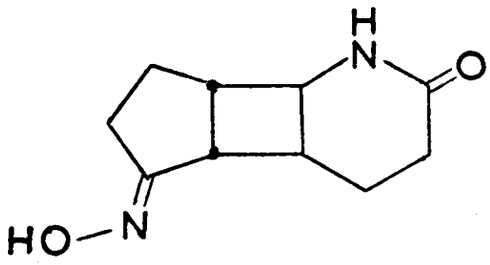


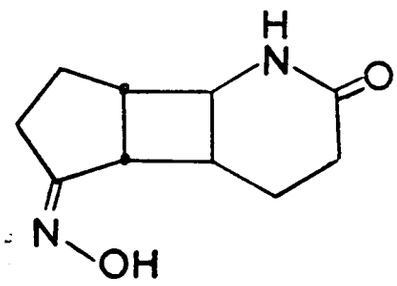
J_{trans} 8 Hz

J_{cis} 4 Hz

J_{NH-H} 4 Hz

Treatment of the keto-lactam in ethanol with aqueous hydroxylamine hydrochloride and sodium acetate followed by the usual work-up gave the oxime(s), m.p. 241-242° in high yield. Although the compound melted sharply over one degree the n.m.r. spectrum (N.M.R.6) showed two closely spaced singlets integrating for a total of one proton centred at δ10.17 p.p.m. (N-O<u>H</u>) which indicated that the compound was probably a mixture of two possible isomeric oximes.

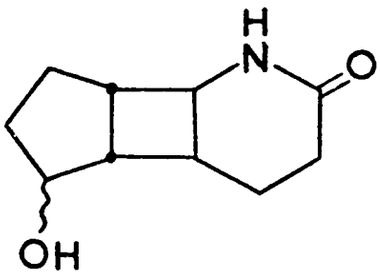




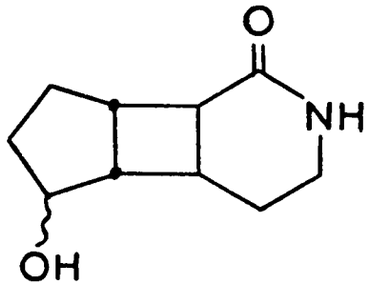
Treatment of keto-lactam XXIII in ethanol with sodium borohydride gave a colourless gum in high yield, t.l.c. of which indicated that it was essentially a single product. Recrystallisation from ethyl acetate gave 9-hydroxy-<u>cis</u>,<u>trans</u>,<u>cis</u>-3-azatricyclo $[6,3,0,0^{2,7}]$ undecan-4-one(XXV) as colourless prisms, m.p. 155.5-157°. Its infrared spectrum (I.R.10) showed bonded O-H and N-H absorptions at 3300 and 3190 $cm.^{-1}$ respectively and

amide carbonyl at 1640 cm.$^{-1}$, the n.m.r. spectrum (N.M.R.7) in deuterated dimethyl sulphoxide (DMSO) was in agreement with the above structure and in particular showed the hydroxy proton as a doublet centred at δ4.5 p.p.m. as expected for a secondary alcohol in DMSO.[61]

Although the single ring expansion of diketone I gave a reasonable yield of keto-lactam XXIII as the major product it was difficult to obtain it in a pure state. It was therefore suspected that the minor component was the alternative keto-lactam XXIV. It was hoped that reducing the mixture with sodium borohydride would give the respective hydroxy-lactams XXV and XXVII.



(XXV)



(XXVII)

Treatment of the mixture of keto-lactams, m.p. 118-143° with sodium borohydride as above gave a sticky white solid, m.p. 143.5-153° in high yield; t.l.c. of which indicated two components in an approximate ratio of 9:1. Chromatographic separation by graded elution gave the major component as a white solid, m.p. 153-156° and the minor component, also as a white solid, m.p. 173-183°. Recrystallisation of the former from chloroform gave colourless prisms, m.p. 155.5-157°, identified as hydroxy-lactam XXV by mixed m.p. and t.l.c. The minor component gave colourless prisms, m.p. 184-185° from ethyl acetate. Its molecular formula $C_{10}H_{15}NO_2$ and spectroscopic data suggested that it was 9-hydroxy-cis,trans,-cis-4-azatricyclo $[6,3,0,0^{2,7}]$ undecan-3-one(XXVII). The n.m.r. spectrum (N.M.R.8) in DMSO showed a characteristic doublet for the hydroxyl proton

and was very similar to that of the hydroxy-lactam XXV excepting the signal at 3-3.5 p.p.m. assigned to the two protons adjacent to nitrogen at C-5 were much more complex than those of the C-2 proton in structure XXV, as would be expected from coupling with two hydrogens at C-6. Unfortunately the spectrum was not definitive as the signals overlapped with those of water present in the solvent DMSO. Further investigations were not possible due to the insufficiency of material.

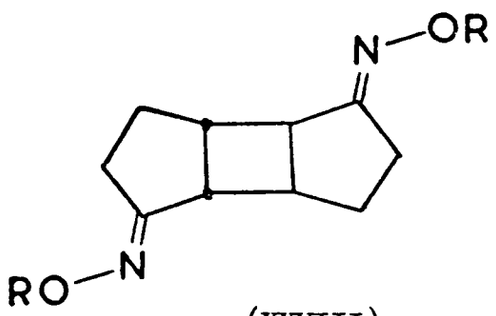
Attempted ketalisation of the mixture of keto-lactams with ethylene glycol was unsuccessful; the reaction gave only starting material.

Reduction of the mixture with lithium aluminium hydride followed by acetylation gave a complex mixture of products which appeared to consist mainly of one component with small amounts of other products. Column chromatography gave a small quantity of the major component as a gum. The n.m.r. spectrum was poorly resolved but did indicate that the compound was an acetyl derivative. Attempts to purify the material further by crystallisation were not successful.

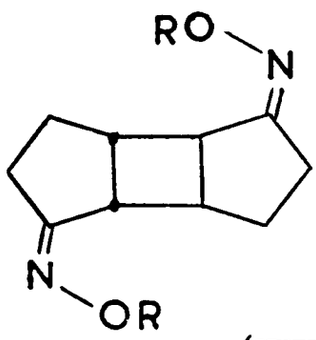
Reaction of the keto-lactam XXIII with 1.1 mol of sodium azide gave a mixture of di-lactams which appeared to be identical (t.l.c.) to the mixture of di-lactams obtained from the Schmidt reaction on diketone I.

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

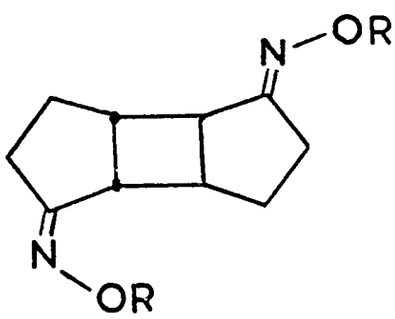
An alternative method of inserting nitrogen in both the five-membered rings of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione(I) would be the formation of its dioxime followed by Beckmann rearrangement. Thus treatment of diketone I in ethanol with hydroxylamine hydrochloride and either sodium hydroxide or sodium acetate gave a sharply melting product, m.p. 224.5-225.5° in high yield. However t.l.c. indicated two components in an approximate ratio of 1:1. Also the n.m.r. spectrum (N.M.R.9) in particular showed the oxime hydrogens as two closely spaced singlets at δ10.13 and δ10.28 p.p.m. in the ratio of 1:1.7, this together with the elemental analysis of the product, suggested that the product was a mixture of two or more of the possible isomeric dioximes XXVIII, XXIX, XXX (R = H).



(XXVIII)

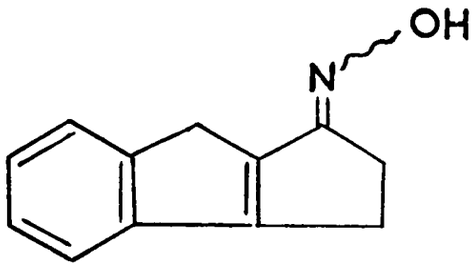


(XXIX)



(XXX)

In this respect it is interesting to note that Pinder has reported[62] that the oxime 1,2,3,8-tetrahydro-1-hydroxyiminocyclopent[a]indene, shown below, a sharply melting product and homogenous on t.l.c., appeared to be an equimolar mixture of syn and anti isomers, as indicated by its n.m.r. spectrum which showed a doublet at δ10.47 p.p.m. for the oxime hydrogen.

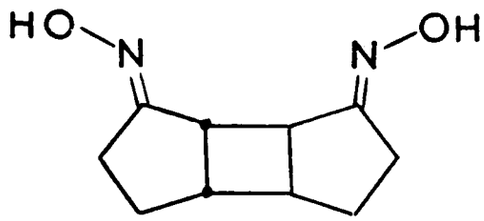


No attempt was made to separate the mixture of dioximes obtained from diketone I as t.l.c. showed a single spot in a number of solvent systems except in ethyl acetate where two spots were observed with only slight difference in R_F values (0.49, 0.58).

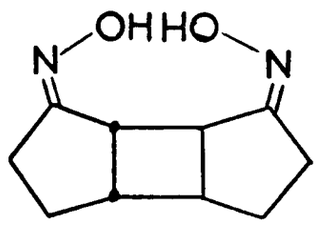
In order to obtain some information on this apparent mixture, the reaction of diketone I with methoxylamine hydrochloride was investigated. A similar mixture of isomeric products may be expected, excepting that the ratio of products would differ because of the greater bulk of the methyl group compared to a hydrogen. It was also expected that the O-methyl compounds would be of much lower melting point and therefore amenable to investigation by g.l.c. Thus treatment of diketone I with methoxylamine hydrochloride and sodium acetate in ethanol gave a white solid, m.p. 40-60° in high yield, g.l.c. of which showed three components in the ratio of 1:2:1. Microanalysis of the mixture indicated molecular formula $C_{12}H_{18}N_2O_2$ consistent with the mixture being only of the O-methyl isomers, possibly XXVIII, XXIX and XXX (R=CH_3), and the n.m.r. spectra (N.M.R.10, 10A) showed the methoxy protons as two singlets at δ3.78 and δ3.82 p.p.m. in the ratio

of 1:1.8.

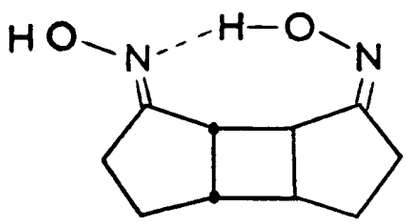
Oximation of the head-to-head diketone II, was also investigated in order to determine whether a similar apparent mixture of isomers is formed. The dioxime(s), which was obtained in high yield, melted over one degree, 216.5-217.5°; t.l.c. indicated a single compound only and the n.m.r. spectrum (N.M.R.11) showed the oxime hydrogens as two singlets at δ10.21 and δ10.38 p.p.m. in the ratio of 1:1. This data together with the low probability of the formation of isomer XXXII due to steric hindrance suggested that compound was XXXIII rather than XXXI which would be expected to show a singlet for the two equivalent oxime hydrogens.



(XXXI)



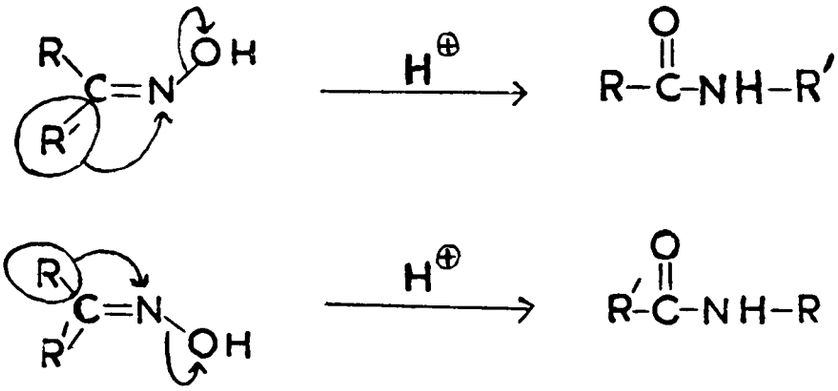
(XXXII)



(XXXIII)

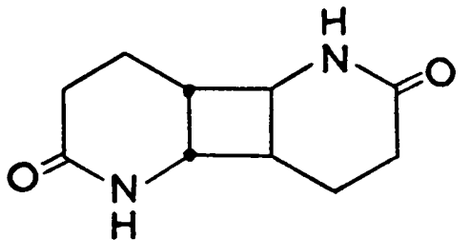
It is possible that hydrogen bonding would tend to stabilise structure XXXIII relative to the other possible isomers.

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

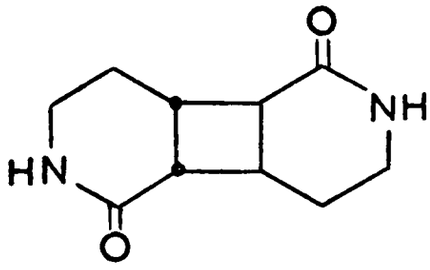


However there are some instances where this anti-migration rule does not appear to hold and in these cases it is believed that <u>syn</u> ⇌ <u>anti</u> interconversion of the oximes occurs prior to the actual Beckmann rearrangement.[63]

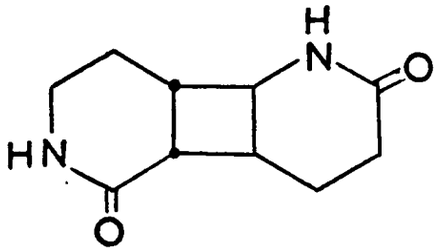
On this basis three possible dilactams XVII, XVIII and XIX may be expected from the Beckmann rearrangement of the isomeric dioximes obtained from diketone I.



(XVII)



(XVIII)



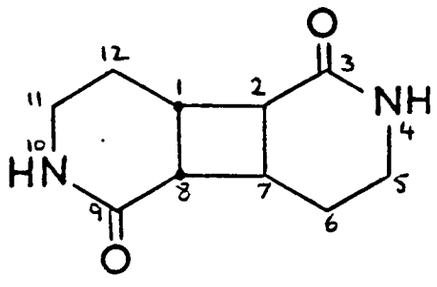
(XIX)

Treatment of the mixture of dioximes in polyphosphoric acid at 125°, followed by continuous chloroform extraction of the neutralised aqueous reaction mixture gave a white solid, m.p. 260-300° (decomp.) in high yield. T.l.c. indicated two components in an approximate ratio of 9:1. Fractional crystallisation from water gave the major component as white needles, m.p. >300° (decomp.) and the minor component as white lustrous plates, m.p. 265-268° (decomp.). The latter had identical m.p., mixed m.p. and i.r.

with that of the minor component obtained in the Schmidt reaction. The separation of the components and their poor solubility in most of the organic solvents posed similar problems as found in the Schmidt reaction. The structures of both these isomers were assigned on the basis of chemical and spectroscopic data.

Structure of dilactam m.p. >300 (decomp.)

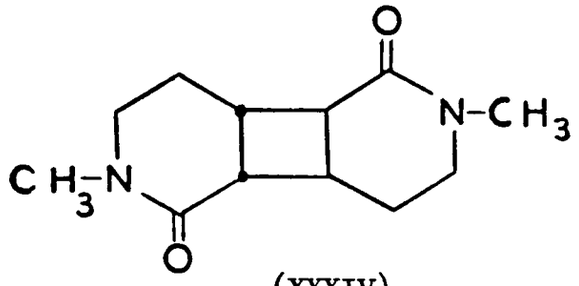
Elemental analysis indicated molecular formula $C_{10}H_{14}N_2O_2$ and the infrared spectrum (I.R.13) showed characteristic bands for N-H and amide carbonyl groups. Apart from the singlet for amide hydrogen at δ 9.03 p.p.m. the n.m.r. spectrum (N.M.R.12) showed essentially three broad signals, each integrating approximately for four protons and two small signals which were suspected of being due to trace impurities. The spectrum was regarded as being consistent with the formulation of the compound being cis,trans,cis-4,10-diazatricyclo $[6,4,0,0^{2,7}]$ dodecane-3,9-dione(XVIII). The downfield signal at δ 3.78 p.p.m. was assigned to the four hydrogens at C-5 and C-11 adjacent to nitrogen, the signal at δ 3.33 p.p.m. to the four cyclobutyl protons and the signal at δ 2.2 p.p.m. to the remaining methylene protons.



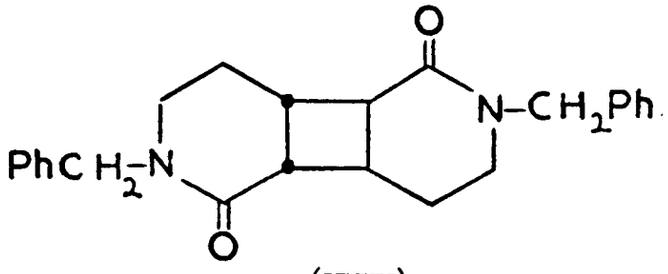
(XVIII)

More definitive evidence was obtained by converting the dilactam to its N,N'-dimethyl compound by treatment with sodium hydride and methyl iodide in dimethylformamide. Work-up gave a pale yellow gum which was found to be a single component, both by t.l.c. and g.l.c. The gum crystallised from ethyl acetate as colourless prisms m.p. 140-142° with phase change at 123.5-125°. Molecular weight as determined by mass spectroscopy, and the

n.m.r. spectrum (N.M.R.14,14A) were consistent with the compound being the expected N,N'-dimethyl-cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane-3,9-dione(XXXIV).



(XXXIV)



(XXXV)

The two N-methyl groups appeared as a singlet at δ3.0 p.p.m. indicative of the symmetry of the molecule. A four proton lowfield multiplet at δ 3.2-3.7 p.p.m. assigned to the hydrogens at C-5 and C-11, a four proton singlet at δ2.8 p.p.m. to the cyclobutyl protons and a four proton multiplet at δ1.8-2.2 p.p.m. was attributed to the hydrogens at C-6 and C-12.

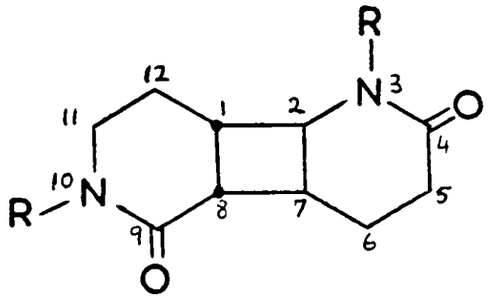
Benzylation of the dilactam with sodium hydride and benzyl chloride gave a mixture of two products (1:2) as indicated by t.l.c. Chromatographic separation with graded elution gave the major component as colourless prisms, m.p. 137-138°. Elemental analysis and mass spectroscopy indicated molecular formula $C_{24}H_{26}N_2O_2$. The n.m.r. spectrum (N.M.R.15) was entirely in agreement with the formulated compound, N,N'-dibenzyl-cis,trans,cis-4,10-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-3,9-dione(XXXV).

The benzylic protons appeared as a singlet at δ4.62 p.p.m. which indicated the symmetry of molecule and unhindered rotation of the benzyl groups. A singlet at δ7.28 p.p.m. was assigned to the aromatic protons. The remaining signals were very similar to those obtained for the N,N'-dimethyl compound XXXIV.

The minor component, which appeared to have slight traces of the above compound, could not be obtained pure and was not investigated further.

Structure of dilactam m.p. 265-268°

Elemental analysis indicated molecular formula $C_{10}H_{14}N_2O_2$ and the infrared spectrum (I.R.14A) showed characteristic bands for N-H and amide carbonyl groups. The n.m.r. spectrum (N.M.R.13) in trifluoroacetic acid showed five broad complex signals in addition to the amide proton signal at δ9.08. The two lowfield signals for one and two protons respectively centred at δ4.22 and δ3.8 p.p.m. allowed assignment of the compound as the remaining possible dilactam cis,trans,cis-3,10-diazatricyclo$[6,4,0,0^{2,7}]$-dodecane-4,9-dione(XIX,R=H) as these indicate the number of hydrogens adjacent to nitrogen and this is readily accommodated by the unsymmetrical structure shown. A three proton multiplet at δ3-3.5 was assigned to the hydrogens at C-5 and C-8, a two proton multiplet at δ2.7-3.0 p.p.m. to the hydrogens at C-1 and C-7, and a four proton multiplet at δ2-2.5 p.p.m. to those at C-6 and C-12.



(XIX) R = H

(XXXVI) R = CH_3

It was hoped that the above structure could be confirmed by the n.m.r. investigation of its N,N'-dimethyl and N,N'-dibenzyl derivatives as in the case of the other two dilactams. The N-methylated compound would be expected to show two singlets as the N-methyl groups would be in different environments and the N-benzylated compound to show one group of benzyl protons as a singlet and the other as a double doublet, probably overlapping with the singlet.

Methylation of the dilactam in the usual way gave a mixture of at least two products (ca. 5:1). Extensive column chromatography on alumina

gave two fractions which appeared to be almost pure on g.l.c. The major fraction was a colourless gum which could not be obtained crystalline. Elemental analysis of the compound was unsatisfactory but its n.m.r. spectrum (N.M.R.16) did show the expected two singlets for the N-methyl protons at δ2.86 and δ3.02 p.p.m. In addition two low field multiplets for three protons in the region δ3.3-3.8 p.p.m. were as expected for the three protons adjacent to nitrogen (C-2 and C-11) in structure XXXVI.

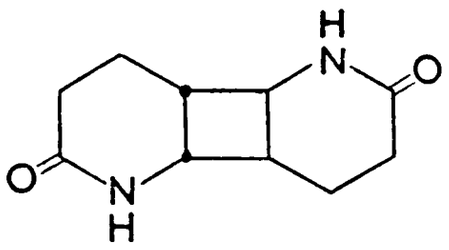
Only a small amount of the minor component was obtained as a white solid m.p. 138.5-142.5° and was not further investigated.

Benzylation of the dilactam also gave a mixture of at least two products (ca. 4:1). Column chromatography gave the two products, each of which was slightly contaminated with the other. The major component was a colourless gum which on crystallisation from ether-ethyl acetate gave a white solid m.p. 88-90° mainly with some portion remaining unmelted up to 115°. Repeated recrystallisation from the above solvent system as well as from other solvents failed to give a pure product. However the n.m.r. spectrum (N.M.R.17) of the material was recorded but did not show the expected features mentioned above. The minor component was a white fibrous solid and was also difficult to purify and hence was not further investigated.

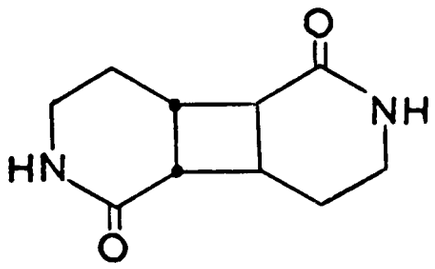
The chemical shift position of the informative signals in the n.m.r. spectra of the N,N'-dimethyl and N,N'-dibenzyl derivatives of the three isomeric dilactams are shown below (Table 2) and shows the interrelationships.

Table 2

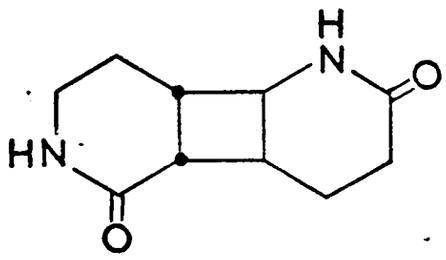
N,N'-Dimethyl Compounds	Protons adjacent to N p.p.m.	Protons adjacent to C=O p.p.m.	N-CH_3
ex. Schmidt, m.p. > 338°	3.7	2.45	2.9 s
ex. Beckmann, m.p. > 300°	3.2 - 3.7	2.8 s	3.0 s
ex. Beckmann, m.p. 265-268°	3.3 - 3.8	Not assignable	2.86 s, 3.02 s
N,N'-Dibenzyl compounds			CH_2-C_6H_5
ex. Schmidt, m.p. > 338°	3.65	2.2 - 2.65	4.55
ex. Beckmann, m.p. > 300°	3.1 - 3.6	2.88 s	4.62 s



(XVII), m.p. > 338°



(XVIII), m.p. > 300°



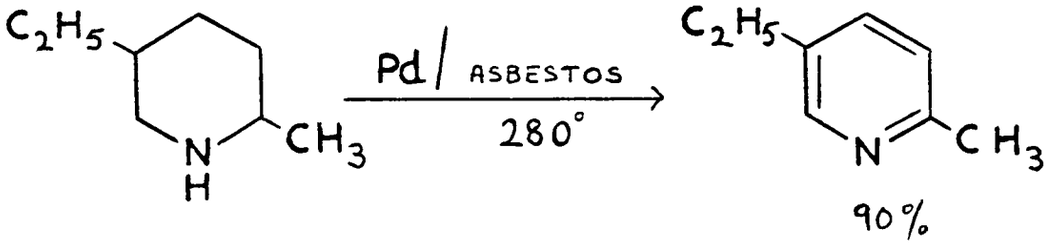
(XIX), m.p. 265-268°

Attempted formation of a Diazabiphenylene

The dilactams and their N,N'-dimethyl and N,N'-dibenzyl derivatives appeared to be promising precursors of diazabiphenylenes. It was expected that reduction of the dilactams would result in the formation of fully hydrogenated analogues of diazabiphenylenes which could then possibly be dehydrogenated to the corresponding diazabiphenylenes.

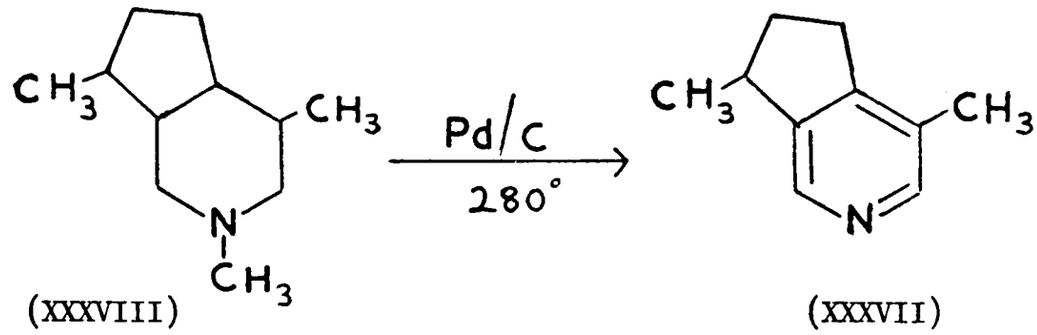
Dehydrogenation of piperidines to pyridines has been carried out quite extensively.[64] As early as 1927, pyridine was obtained[65] by passing the vapour of piperidine over manganous oxide at 600°. Catalysts such as concentrated sulphuric acid, nitrobenzene and silver acetate have also been used.[66] More recently palladium, platinum, selenium, sulphur and nickel have been found to be very effective in the dehydrogenation of piperidines.[64]

Adkins and Lunstead obtained 4-methylpyridine in 64% yield by heating 4-methylpiperidine with nickel or its chromite at 350° for 5h.[67] Baliah and Ekambaram reported[68] that when substituted piperidines and piperidinols were heated with sulphur at 200° for 30 min. pyridines were obtained in high yield. Finkelstein and Elderfield[69] found that a pyridine was formed in high yield when a disubstituted piperidine was heated with palladium on asbestos at 280°.



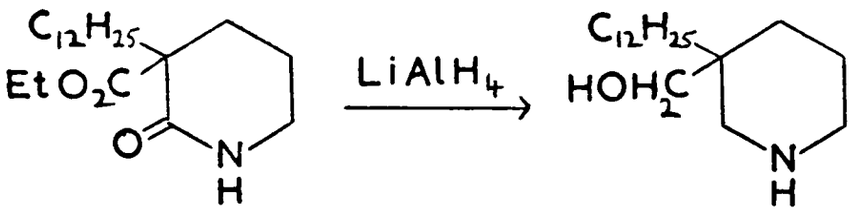
Palladium on carbon appears to have been the most commonly used of these catalysts and in particular has been used extensively for the dehydrogenation investigation of complex nitrogenous compounds such as alkaloids. Thus Djerassi, Kutney and Shamma[70] have obtained a good yield

of XXXVII from skytanthine (XXXVIII) on heating with palladium on carbon at 280°.

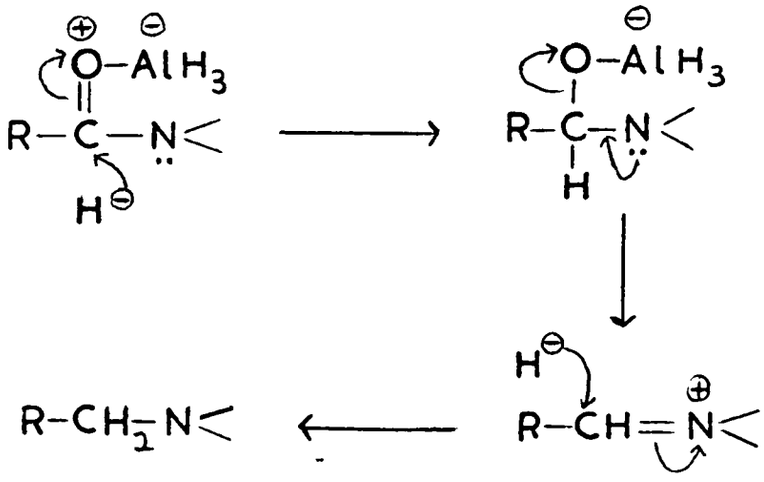


(XXXVIII) (XXXVII)

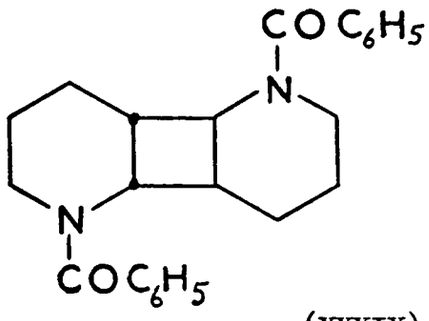
The reduction of amides and lactams with lithium aluminium hydride, aluminium hydride, lithium trimethoxyaluminium hydride and diborane is well known[71] and the reduction of piperidones to the corresponding piperidines has been successfully carried out with lithium aluminium hydride.[72] Thus Ames and Bowman[73] reduced 3,3-disubstituted piperidone with lithium aluminium hydride to the corresponding piperidine.



The reaction is thought to proceed by attack of hydride ion on the carbonyl carbon as shown.



Several attempts to reduce the mixture of dilactams from the Schmidt reaction with lithium aluminium hydride in ether as well as dioxan gave complex mixture of products in very low yields and it was thought that the low yields were possibly due to poor solubility of the dilactams. The use of a soxhlet type extractor so that the dilactams were slowly leached into the reaction mixture also proved unsatisfactory. However reduction in tetrahydrofuran followed by benzoylation of the crude reaction product gave a gum, t.l.c. of which showed essentially two products. Dry column chromatography gave the major product as a colourless gum. Recrystallisation from ethyl acetate gave only a small quantity of the compound which was identified N,N'-dibenzoyl-cis,trans,cis-3,9-diazatricyclo [6,4,0,$0^{2,7}$] dodecane, fawn prisms, m.p. 135-139°(XXXIX).



(XXXIX)

The structure was assigned to the compound on the basis of its molecular weight (M^+374.2031) and n.m.r. spectrum (N.M.R.18). The ten aromatic protons appeared as a singlet at δ 7.37 p.p.m. thus indicating the symmetry of the molecule. The rest of the spectrum showed four broad signals; the low field signals of two protons at δ 4.2 and four protons at δ 3.35 p.p.m. were assigned to protons adjacent to nitrogen, (C-2, C-8) and (C-4, C-10) respectively, a two proton signal at δ 2.8 was attributed to the protons at C-1 and C-7 and an eight proton signal at δ 1.65 p.p.m. to the remaining methylene protons. Also the spectrum was, in general, similar to that of N-benzoylpiperidine (N.M.R.19),

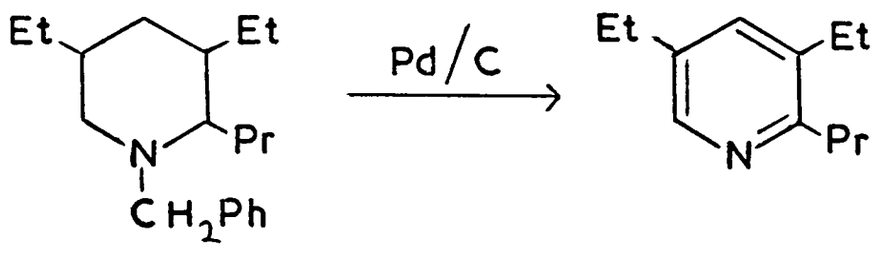
prepared according to the method described by Vogel.[74]

The minor component was obtained in very low quantity and was contaminated with some of the above compound and was therefore not investigated.

Attempted reduction of the mixture of dilactams using sodium and absolute ethanol which has previously been employed in the reduction of lactams,[75] gave only a small amount of recovered material of which the major portion appeared to be the starting material.

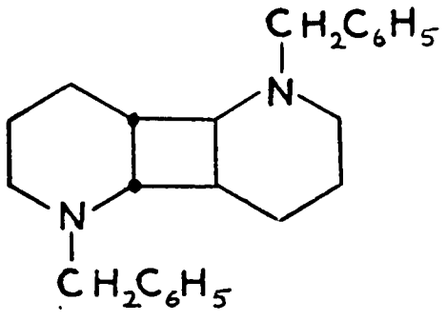
The difficulty in the reduction of the dilactams prompted an investigation into the reduction of the N,N'-dibenzyl derivative XX of the higher melting dilactam from the Schmidt reaction (p. 32). This dilactam was the most readily obtainable and it was expected that there would be no solubility problem associated with the reduction.

With regard to the dehydrogenation stage it was expected that the N-benzyl groups as such would not affect the possibility of the diazabiphenylene being formed as it is well known that N-alkyl or N-benzyl groups are readily lost from substituted piperidines on dehydrogenation. Thus the benzylated piperidine shown below is readily dehydrogenated with palladium on carbon to give the derived pyridine in 62% yield.[76]



Reduction of N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-4,10-dione(XX) with lithium aluminium hydride in tetrahydrofuran gave a colourless gum in high yield; t.l.c. and g.l.c. indicated that it was essentially a single component. The compound could not be obtained crystalline and it was observed that the material gradually darkened. Hence it was characterised as its dipicrate, obtained as a yellow crystalline solid, m.p. 215-216°. Elemental analysis supported its formulation as dipicrate of N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane(XL) and the n.m.r. spectrum (N.M.R.20) showed the benzyl and picric acid aromatic protons in the expected ratio of 10:4.

An attempt to obtain the dihydrochloride of the amine gave a solid which could not be obtained pure; it was observed that it discoloured during recrystallisation, the material so obtained had anamolous melting characteristics.



(XL)

Heating of the free amine with 10% palladium on carbon at 240-250° and extraction with ethanol gave a brown gum which had an odour somewhat similar of pyridine based heterocyclics. Examination of the gum by g.l.c. indicated that it consisted of at least four components, none of which corresponded to pyridine or toluene. In addition to aliphatic as well as other protons, the n.m.r. spectrum (N.M.R.21) showed broad signals at δ 8.5 and δ 7.1-7.6 p.p.m.; these positions

corresponding to those expected for protons associated with a pyridine type system. The α, β and γ protons of pyridine itself appear at δ 8.5, 7.06 and 7.46 p.p.m. respectively.[77] The mass spectrum of the gum however did not show any appreciable molecular ion at m/e 154 corresponding to that of a diazabiphenylene but a peak observed at m/e 156 could possibly be derived from a bipyridyl. The most intense peak in the higher region of the mass spectrum was at m/e 169. Treatment of the gum with picric acid gave a brown solid which could not be obtained pure and was not investigated further.

The work described above lays the basis for future investigations into the synthesis of diazabiphenylenes. In addition to varying the conditions of the dehydrogenation described, investigation of N,N'-dibenzyl-cis,trans,cis-4,10-diazatricyclo $[6,4,0,0^{2,7}]$dodecane-3,9-dione, obtained from the Beckmann rearrangement, along similar lines would be appropriate.

Although lithium aluminium hydride was not entirely successful in the reduction of the dilactams themselves, it is probable that diborane,[71d,78] or triethyloxonium fluoroborate[79] followed by sodium borohydride would give the expected tricyclic diamines which could then possibly be dehydrogenated.

With respect to this approach to diazabiphenylenes it would be worthwhile to investigate similar sequence of reactions with the head-to-head photodimer II and also the recently described symmetrical diketone, cis,trans,cis-tricyclo $[5,3,0,0^{2,6}]$deca-4,9-dione.[80]

EXPERIMENTAL

General Techniques

Infrared (i.r.) spectra were determined as mulls in nujol unless otherwise stated, using a Perkin Elmer 257, 177 or Unicam S.P.200 spectrophotometer, the intensities of the band being indicated by vs (very strong), s (strong), m (medium) and w (weak).

Nuclear magnetic resonance (n.m.r.) spectra were obtained for the appropriate compounds in solvents as indicated, at 60, 100 and 220 MHz on varian A60, HA-100D and HR-220 spectrometers respectively; tetramethylsilane was used as an internal standard. Mass spectra were determined on A.E.I. MS 902 spectrometer. 100 MHz and 220 MHz and mass spectra were run by the Physico-Chemical-Measurement Unit at Harwell and Aldermaston.

Thin layer chromatography (t.l.c.) was run on silica gel G or HF_{254} (0.25-0.30 mm thickness) and components were detected by ultraviolet light or with iodine vapour. Melting points were normally determined on a Kofler melting point apparatus (Reichert), otherwise as mentioned in sealed tubes in a Gallenkamp electric melting point apparatus.

Wet column chromatography was carried out on neutral alumina type 0 "CAMAG" M.F.C., about 100-250 mesh, Brockman Activity = 1. For dry column chromatography, the above alumina was deactivated (Activity 2-3) by adding 4ml of water per 100g and mixing it thoroughly on a mechanical shaker for at least two hours and then packed into a nylon tube of appropriate dimensions.

Benzene for chromatography was purified by drying over calcium chloride and then distilled.

Dimethylformamide was dried by distilling azeotropically with benzene followed by distillation and stored over molecular sieve type 4A.

Tetrahydrofuran and dioxan were passed through "Woelm" basic alumina, Activity 1, and then distilled over lithium aluminium hydride before use.

Light petroleum refers to the fraction b.p. 40-60°.

Synthesis of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione

Cyclopentadiene[44]

Liquid paraffin (200ml) was heated to 200-240° in a round bottom flask fitted with a dropping funnel, thermometer and a fractionating column. Dicyclopentadiene (300ml) was added slowly via the dropping funnel and the cyclopentadiene b.p. 40-42° which formed was collected. Cyclopentadiene dimerizes rapidly at room temperature and hence was used immediately or stored in dry-ice.

3-Chlorocyclopent-1-ene[43]

Cyclopentadiene (230g) was placed into a measuring cylinder and cooled to -15° to -20° in a dry-ice bath. A rapid stream of dry hydrogen chloride gas was passed into the material until a volume increase of 42ml was obtained (approximately 4h). The crude material was distilled in vacuo to give 3-chlorocyclopent-1-ene (221.7g) b.p. 25-30° at 20 mmHg (lit.,[43] ~30° at 20 mmHg). 3-Chlorocyclopentene is unstable at room temperature and soon polymerises to a black tar, it was therefore either used at once or stored in dry-ice.

Cyclopent-2-en-1-one[43]

3-Chlorocyclopent-1-ene (221.7g, 2.16mol) was added slowly over 0.75h to a rapidly stirred solution of sodium dichromate ($Na_2Cr_2O_7.2H_2O$, 272g, 0.91mol) in water (1.1L) keeping the reaction mixture at 0-10° by cooling in ice-salt bath. The mixture was further stirred at 0° for 0.5h and then 50% sulphuric acid (455ml) was added dropwise maintaining the reaction mixture at 0-10°. The black-brown mixture was saturated with sodium chloride and extracted with ether (6x200ml). The combined extracts were washed with saturated sodium chloride solution (3x150ml) followed by 10% sodium bicarbonate (2x100ml) and finally washed with saturated sodium chloride solution (2x100ml). The ether solution was

dried ($MgSO_4$), concentrated and distilled in vacuo to give cyclopent-2-en-1-one (63.7g, 36%) b.p. 42-44° at 13 mmHg (lit.,[43] 42° at 11 mmHg) as a colourless liquid. G.l.c. on Carbowax 20M at 80° showed one peak, R_t 4.1 min. T.l.c. (ethyl acetate) showed only one spot, R_F 0.65, νmax. (I.R.1) 1708 vs (C=O) cm^{-1}.

Photolysis[42] of Cyclopent-2-en-1-one in benzene

Cyclopent-2-en-1-one (51.4g 0.63mol) in dry benzene (800 ml) was placed in a water-cooled Pyrex chamber of a 1L Hanovia photochemical reactor and exposed under a slow stream of oxygen-free nitrogen, through two thicknesses of Pyrex glass, to the output of a 100 watt, mercury arc lamp. A steady stream of oxygen-free nitrogen was also maintained in the lamp chamber to eliminate ozone. The irradiation was continued at room temperature for a total of 61h by which time g.l.c. (Carbowax 20M, 170°) indicated that most of cyclopentenone had reacted. The crystalline white solid which separated was filtered, washed with cold benzene (20 ml) and dried (8.0g), m.p. 116-129°. The mother liquors were concentrated to remove benzene and the residue was crystallised from carbon tetrachloride to give a further quantity of the same material (9.4g). Recrystallisation of the combined solids (17.4g) from carbon tetrachloride gave cis,trans,cis-tricyclo$[5,3,0,0^{2,6}]$deca-3,8-dione (15.2g, 29.5%) as white plates m.p. 125-126.5° (lit.,[42] 125-126.5°), νmax. (I.R.2) 1730 vs (C=O) cm^{-1}.

The mother liquors from the recrystallisation were concentrated under reduced pressure and distilled quickly at 125° at 1 mmHg. The distillate on cooling gave a waxy solid (7.0g). G.l.c. on Carbowax 20M at 170° showed two peaks in the ratio of 3:1, R_t 41 min. and 30 min. respectively. By comparison with pure compounds the minor component proved to be the foregoing 3,8-dione and the other was cis,trans,cis-tricyclo$[5,3,0,0^{2,6}]$deca-3,10-dione. Several recrystallisations from hexane failed to give the 3,10-isomer in a pure form, however a sample of the pure material was isolated from photolysis of the cyclopent-2-en-1-one in methanol as

described below.

Attempted separation of a mixture of cis,trans,cis-tricyclo [5,3,0,$0^{2,6}$]-deca-3,10-dione and cis,trans,cis-tricyclo [5,3,0,$0^{2,6}$]deca-3,8-dione (3:1) by ketalisation[42]

The mixture of diketones (2.8g, 0.017mol) was dissolved in ethylene glycol(25ml) at 100°. Anhydrous hydrogen chloride was passed through the solution for a few seconds. On cooling to 55° the solution gelled. After cooling to 10°, the product was collected, washed thoroughly with 5% sodium bicarbonate and taken up in methylene chloride. The solution was separated from adhering water and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a white solid (3.23g), m.p. 56-58° mainly, completely liquid at 108°. G.l.c. on carbowax 20M at 170° indicated two components in an approximate ratio of 1:5.8, R_t 50 min. and 39 min. respectively. Recrystallisation from hexane gave bis-ethylene ketal of cis,trans,cis-tricyclo [5,3,0,$0^{2,6}$]deca-3,8-dione(0.4g) as white glistening platelets, m.p. 141-142.5° (lit.,[42] 143-143.5°); not depressed on admixture with an authentic sample prepared as described by Eaton.

Examination of the mother liquors by g.l.c. indicated two components in an approximate ratio of 34:1; the minor component corresponded to the above bis-ethylene ketal and the major component corresponded to cis,trans,cis-tricyclo [5,3,0,$0^{2,6}$]deca-3,10-dione. The mixture was not further investigated.

Photolysis of Cyclopent-2-en-1-one in methanol

Cyclopent-2-en-1-one (49.9g, 0.61mol) was dissolved in methanol (800ml, distilled over potassium hydroxide) and exposed to ultraviolet radiation, as in the above experiment, for 14h. The white solid which separated overnight was filtered, washed with cold methanol (20ml) and

dried to give white platelets (11.9g), m.p. 172-173.5°. Further irradiation for 15h, gave an additional quantity of the same material (9.6g). Recrystallisation of the combined solids (21.5g) from methanol gave cis,trans,cis-3,3,8,8-tetramethoxytricyclo[5,3,0,$0^{2,6}$]decane (19.3g, 49.5%), m.p. 173-174° (Found: C,65.86; H,9.38. M^+ 256. $C_{14}H_{24}O_4$ requires C,65.59; H,9.44%. M^+ 256), ν max. (I.R.3) 1100 s, 1060 s, 1030 s (C-O-C) cm.$^{-1}$ δ (N.M.R.1, $CDCl_3$) 3.13 (6H, s, 2xOCH_3), 3.17 (6H, s, 2xOCH_3) p.p.m.

The concentration of the mother liquors to remove methanol followed by distillation in vacuo, gave unreacted cyclopentenone(8.6g), b.p. 40-50° at 20 mmHg. The residue on cooling gave a yellow gum (9.8g) which, after several recrystallisations from carbon tetrachloride-hexane and a final recrystallisation from hexane, gave cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]-deca-3,10-dione(2.24g, 9%), m.p. 66-67° (lit.,[42] 66-67°). ν max. (I.R.4) 1730 vs (C=O) cm.$^{-1}$.

Reaction of cis,trans,cis-3,3,8,8-tetramethoxytricyclo[5,3,0,$0^{2,6}$]decane with acid

(a) Cis,trans,cis-3,3,8,8-tetramethoxytricyclo[5,3,0,$0^{2,6}$]decane (0.48g, 1.87 mmol) was dissolved in methanol (22ml); water (2ml) and concentrated hydrochloric acid (1ml) were added and heated under reflux for 5.5h. The mixture was evaporated under reduced pressure to near dryness. Water (10ml) was added to the residue and the mixture extracted with methylene chloride (3x20ml). The combined extracts were washed with water (10ml), dried ($MgSO_4$) and concentrated under reduced pressure to give a white solid (0.29g). Recrystallisation from carbon tetrachloride gave cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione(0.21g, 70%) m.p. 125-126.5°; not depressed on admixture with an authentic sample.

(b) Cis,trans,cis-3,3,8,8-tetramethoxytricyclo[5,3,0,$0^{2,6}$]decane (15g, 0.058mol) was dissolved in methylene chloride(225ml) and 2N

hydrochloric acid (30ml). The mixture was stirred and heated under reflux for 1h, cooled and allowed to settle. The organic layer was separated and the acid layer was further extracted with methylene chloride (2x40ml). The extracts were combined and washed with 10% sodium bicarbonate solution (50ml), water (50ml), dried ($MgSO_4$) and evaporated to dryness. Recrystallisation of the resulting solid (9.7g) from carbon tetrachloride gave cis,trans,cis-tricyclo$\left[5,3,0,0^{2,6}\right]$deca-3,8-dione (9.13g, 95%), m.p. 125-126.5°; not depressed on admixture with an authentic sample.

Cis,trans,cis-3,3,8,8-tetramethoxytricyclo$\left[5,3,0,0^{2,6}\right]$decane

Cis,trans,cis-tricyclo$\left[5,3,0,0^{2,6}\right]$deca-3,8-dione (0.2g, 1.22 mmol) was dissolved in a mixture of dry methanol(50ml) and dry benzene(50ml); toluene-p-sulphonic acid (0.010g) was added and the mixture was heated under reflux for 34h. A soxhlet containing molecular sieve type 4A was interposed between the reflux condenser and the reaction flask to remove water formed during the reaction. The mixture was distilled slowly to dryness and the residue was dissolved in benzene(50ml), washed with 10% sodium bicarbonate(10ml), dried ($MgSO_4$) and evaporated to dryness to give a solid residue (0.29g). T.l.c. (ethyl acetate) showed three spots R_F 5.2, 6.0, 7.5 (2:1:1) corresponding to starting material, expected product and an unknown product respectively. The last mentioned product was possibly the mono-ketal. Recrystallisation of the residue from methanol gave a first crop cis,trans,cis-3,3,8,8-tetramethoxytricyclo-$\left[5,3,0,0^{2,6}\right]$decane (0.044g, 14%) m.p. 173-174°; not depressed on admixture with the material obtained from photolysis of the above diketone in methanol.

T.l.c. examination of the mother liquors showed the presence of the titled compound, an unknown product, and the starting material.

Schmidt reaction of cis,trans,cis-tricyclo-[5,3,0,$0^{2,6}$]deca-3,8-dione

Reaction with 2.2 molar equivalents of sodium azide

Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione(10g, 0.061mol) was dissolved in hydrochloric acid (100ml), cooled to 5° and sodium azide (8.72g, 0.134 mol) was added in portions over approximately 15 min. The maximum temperature attained during the addition was 50°. The mixture was allowed to stand at room temperature for 24h with occasional stirring, then poured onto ice-water (500g), basified to pH 8.5 with anhydrous sodium carbonate and extracted exhaustively with chloroform for six days. The extract was concentrated under reduced pressure to give a creamish-white solid (10.6g, 90%) m.p. 245-310° (decomp.). T.l.c. [ethanol-water(9:1)] showed two spots R_F 0.35 and 0.31. Fractional crystallisation of a portion of the crude mixture (3g) from water gave the major constituent cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione (1.1g) as creamish-white plates, which decomposes (chars) from 338° (sealed tube). (Found: C,61.97; H,7.37; N,14.45. $C_{10}H_{14}N_2O_2$ requires C,61.83; H,7.27; N,14.42%), ν max. (I.R.5) 3180m, 3060m (bonded NH) 1665 vs (amide C=O) 1605w, 1183m, 1119m, 825m,br, 749m $cm.^{-1}$ δ (N.M.R.2,TFA) 2-2.5 (4H,m, 2xH-6, 2xH-12), 2.7-3.0 (4H,m, 2xH-5, 2xH-11), 3-3.3 (2H,m, H-1, H-7), 4-4.4 (2H,m, H-2, H-8), 9.08 (2H,s, 2xNH) p.p.m.

The mother liquors gave the minor constituent cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione(0.4g) as white lustrous plates, m.p. 265-268°. Identical m.p., mixed m.p. and i.r. (I.R.14) with the lower melting dilactam m.p. 265-268° obtained from the Beckmann rearrangement as described later (p. 77).

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

Cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione (0.25g, 1.29mmol) was added in portions over 5 min. to a stirred mixture of sodium hydride (0.136g, 2.85mmol, 50% dispersion in oil, washed with light petroleum) in dry dimethylformamide (5 ml) under nitrogen. The stirred mixture was heated at 70° for 1h, then cooled to room temperature, benzyl chloride (1 ml) added and stirred at 70° for 4h. The mixture was cooled, water (20 ml) added and stirred vigorously at room temperature. The solid which separated was collected, washed with cold water (5 ml) and dried to give an off-white solid (0.465g, 96%), m.p. 225-234°. T.l.c. (ethanol) showed mainly one component. Recrystallisation from methanol gave N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione as colourless prisms, m.p. 232-234°. (Found: C,77.43; H,7.20: N,7.21. $C_{24}H_{26}N_2O_2$ requires C,76.97; H,7.00; N,7.48%), νmax. (I.R.6) 3060w, 3020w, (aromatic C-H) 1625 (amide C=O), 705 (monosubstituted benzene), δ (N.M.R.3, 3A, $CDCl_3$) 1.3-2.0 (4H, m, 2xH-6, 2xH-12), 2.2-2.65 (6H, m, 2xH-5, 2xH-11, H-1, H-7), 3.65 (2H, dd, J_{cis} 4.5 Hz, J_{trans} 10 Hz, H-2, H-8), 4.55 (4H, AB quartet, J 15 Hz, 2xC_6H_5.$\underline{CH_2}$), 7.24 (10H, s, aromatic protons) p.p.m.

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

Cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione (0.25g, 1.29mmol) was added in portions over 5 min. to a stirred mixture of sodium hydride (0.136g, 2.85mmol, 50% dispersion in oil, washed with light petroleum) in dry dimethylformamide (5 ml) under nitrogen. The stirred mixture was heated at 70° for 1h, then cooled to room temperature, methyl iodide (2 ml) added and the mixture stirred for 1h at this temperature and then at 70° for 3h. Dimethylformamide was removed in vacuo, the residue was treated with cold water (5 ml) and the resulting solution was extracted with chloroform (4x25 ml). The combined extracts were washed with saturated sodium chloride solution (20 ml), dried ($MgSO_4$) and evaporated under reduced

pressure to give a pale yellow solid (0.221g, 77%), m.p. 140-148°, softening at 134°. G.l.c. (S.E.52/chromosorb W,230°) showed one peak, R_t 3.8 min. Recrystallisation from ethyl acetate gave N,N'-dimethyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,10-dione as colourless prisms, m.p. 148-149°. T.l.c. [chloroform-methanol(9:1)] showed one spot R_F 0.44. (Found: C,64,76; H,8.28; N,12.55. $C_{12}H_{18}N_2O_2$ requires C,64.84; H,8.16; N,12.60%), $\nu_{max.}$ (I.R.7) 1620(amide C=0)$cm.^{-1}$, δ(N.M.R.4, 4A, $CDCl_3$) 2.0 (4H, m, 2xH-6, 2xH-12), 2.45 (4H, m, 2xH-11,2xH-5) 2.7 (2H, m, H-1, H-7), 2.9 (6H, s, 2xNMe), 3.7 (2H, dd, J_{cis} 5Hz, J_{trans} 9Hz, H-2, H-8) p.p.m.

The effect of added $Eu(fod)_3$ on the above spectrum is described in the discussion. Changes in position of chemical shift with added complex were as follows:

$Eu(fod)_3$ mg	Chemical Shift (δ)				
	H-6,H-12	H-1,H-7	H-5,H-11	$N-CH_3$	H-2,H-8
nil	2.0	2.5	2.5	2.9	3.75
10	2.35	3.05	3.05	3.38	4.11
30	2.8	3.6	4.1	4.3	4.78
40	3.1	4.17	5.0	4.85	5.17
50	3.4	4.5	5.4	5.30	5.5
60	3.68	4.8	6.2	5.77	5.9
70	3.9	5.08	6.75	6.18	6.03
80	4.28	5.6	7.61	6.84	6.6
90	4.45	5.8	8.0	7.13	6.87

Reaction with 1.1 molar equivalents of sodium azide

Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione(4g, 0.023 mol) was dissolved in concentrated hydrochloric acid(20ml). The solution was cooled to 10° and sodium azide(1.74g, 0.026 mol) was added in portions over 10 min., maintaining the temperature at 10°. The mixture was kept at room temperature for 24h with occasional stirring and then poured onto ice-water (85g); the solution was made slighly basic (pH~8) with anhydrous sodium carbonate and extracted with chloroform(6x100ml). Evaporation of the dried ($MgSO_4$) extracts gave a gummy yellow solid (3.5g) which was dissolved in chloroform(20ml) and chromatographed on dry alumina (neutral, Activity 2-3, 18"x2") with ethyl acetate as the developing solvent. The column was cut into six equal portions, each portion was eluted with ethanol and monitored by t.l.c. (ethanol) and the appropriate extracts combined to give three fractions (i) unchanged starting material (0.2g), identified by mixed m.p. and t.l.c., (ii) a mixture of isomeric dilactams (0.4g), identified by t.l.c. and i.r. as being the same as the mixture from the above experiment, (iii) a white solid (2.69g), m.p. 118-143°, t.l.c. [methylene chloride-methanol(9:1)] showed two spots R_F 0.41 and 0.35 in the ratio of 9:1 respectively. Several recrystallisations from acetone gave a small quantity of the major constituent cis,trans,cis-3-azatricyclo[6,3,0,$0^{2,7}$]undecane-4,9-dione (0.58g) as prisms, m.p. 144.5-148°. T.l.c. showed one spot. (Found: C,66.85; H,7.20; N,7.85. $C_{10}H_{13}NO_2$ requires C,67.05; H,7.31; N,7.82%), νmax. (I.R.8, KBr) 3470,3420,3270(NH), 1728 (C=O), 1655 (amide C=O), δ(N.M.R.5, $CDCl_3$) 1.7-3.1 (11H,m), 3.8 (1H, quintet, H-2), 7.7 (1H, s,br,NH) p.p.m. After shaking with 5% NaOD in D_2O (N.M.R.5A) the NH proton signal disappears and the five peaks at δ3.8 p.p.m. collapse to a double doublet (J_{trans} 8Hz, J_{cis} 4Hz).

Attempts to obtain a pure sample of the minor constituent by fractional crystallisation, dry and wet column chromatography and preparative t.l.c. were not successful.

Reaction of cis,trans,cis-3-azatricyclo $[6,3,0,0^{2,7}]$undecane-4,9-dione with sodium azide

Chloroform (ca. 1ml) was added dropwise to a suspension of the above keto-lactam(0.2g, 1.1 mmol) in hydrochloric acid(2ml) until a clear two phase system was obtained. The mixture was cooled to 0-10° and sodium azide (0.08g, 1.2mmol) was added to the stirred solution. The reaction mixture was kept at room temperature for 24h with occasional stirring, poured into ice-water (20ml), neutralised with anhydrous sodium carbonate and extracted exhaustively with chloroform for five days. Evaporation of the dried ($MgSO_4$) extract gave an off-white solid (0.103g), m.p. 248-330° (decomp.). T.l.c. [ethanol-water(9:1)] indicated a mixture of two components similar to the mixture of isomeric dilactams obtained from the Schmidt reaction of cis,trans,cis-tricyclo $[5,3,0,0^{2,6}]$deca-3,8-dione. No attempt was made to separate or identify these components.

9-Hydroxyimino-cis,trans,cis-3-azatricyclo $[6,3,0,0^{2,7}]$undecan-4-one

A solution of cis,trans,cis-3-azatricyclo $[6,3,0,0^{2,7}]$undecane-4,9-dione(0.1g, 0.56 mmol) in ethanol (3ml) was added to a solution of hydroxylamine hydrochloride (0.116g, 1.67 mmol), and hydrated sodium acetate (0.2g) in water (0.5ml). The solution was heated under reflux for 15 min. and then concentrated under reduced pressure to almost dryness. Water (1ml) was added to the residue and the mixture cooled in an ice-bath, the solid(0.077g, 71%) m.p. 241-242° (decomp.), collected by filtration, washed with cold water (2ml) and dried. T.l.c. (ethanol) showed one spot R_F 0.55. Recrystallisation from absolute alcohol gave 9-hydroxyimino-cis,trans,cis-3-azatricyclo $[6,3,0,0^{2,7}]$undecan-4-one as

syn and anti isomers, colourless needles, m.p. 241-242° (decomp.) (Found: C,61.78; H,7.23; N,14.33. $C_{10}H_{14}N_2O_2$ requires C,61.83; H,7.27; N,14.42%), $\nu_{max.}$ (I.R.9, KBr) 3250br (NH, N-OH), 1650s (amide C=O), 935 $cm.^{-1}$, δ [N.M.R.6, $(CD_3)_2SO$] 1.5-2.0 (4H, m, 2xH-6, 2xH-11) 2.0-3.2 (7H, m, 2xH-5, 2xH-10, H-1, H-7, H-8), 3.5 (1H, m, H-2), 7.6 (1H, d,br,NH), 10.17 (1H, d,N-OH) p.p.m.

Sodium borohydride reduction of cis,trans,cis-3-azatricyclo [6,3,0,$0^{2,7}$]-undecane-4,9-dione

Cis,trans,cis-3-azatricyclo [6,3,0,$0^{2,7}$] undecane-4,9-dione (0.050g, 0.28 mmol) was dissolved in absolute alcohol (1ml), sodium borohydride (0.011g, 0.29 mmol) was added and the solution stirred at room temperature for 3.5h. Water (5ml) was added dropwise to the reaction mixture and the ethanol removed under reduced pressure. The residue was dissolved in water (5ml) and the solution saturated with sodium chloride and extracted exhaustively with methylene chloride. Evaporation of the dried ($MgSO_4$) extract gave a gummy residue (0.042g, 84%). T.l.c. [chloroform-methanol (9:1)] showed mainly one spot R_F 0.38. Recrystallisation from ethyl acetate gave 9-hydroxy-cis,trans,cis-3-azatricyclo [6,3,0,$0^{2,7}$] undecan-4-one as colourless prisms, m.p. 155.5-157° (Found: C,66.57; H,8.05; N,7.62. $C_{10}H_{15}NO_2$ requires C,66.27; H,8.34; N,7.73%), $\nu_{max.}$ (I.R.10) 3300 (bonded OH), 3190 (bonded NH), 1640 (amide C=O), 1090 (OH bending) $cm.^{-1}$, δ [N.M.R.7, $(CD_3)_2SO$] 1.3-2.0 (6H, m, 2xH-6, 2xH-10, 2xH-11), 2.0-2.35 (3H, m, H-1, H-8, H-7), 2.35-2.85 (2H, m, 2xH-5), 3.0-3.4 (1H, m, H-2), 3.7-4.3 (1H, m, H-9), 4.5 (1H, d,OH), 7.5 (1H, s,br,NH) p.p.m.

Sodium borohydride reduction of the mixture of keto-lactams obtained from the Schmidt reaction (p. 69)

The mixture of isomeric keto-lactams (1.5g, 9.0mmol), m.p. 118-143°, was treated with sodium borohydride (0.33g, 9.0mmol) as in the preceeding

experiment to give a sticky white solid (1.4g), m.p. 143.5-153°. T.l.c. [chloroform-methanol(9:1)] showed two spots in an approximate ratio of 9:1. A portion of the above product (0.74g) was dissolved in chloroform (20ml) and chromatographed on alumina(60g) and subjected to graded elution with ethyl acetate, ethyl acetate-ethanol and finally with ethanol to yield 15 fractions of 80ml each. Each of the fractions (80ml) were examined by t.l.c. and the appropriate fractions were combined to give two main fractions.

The major fraction, eluted with ethyl acetate-ethanol(95:5) gave a white solid (0.3g), m.p. 153-156° which on recrystallisation from chloroform gave 9-hydroxy-cis,trans,cis-3-azatricyclo $[6,3,0,0^{2,7}]$undecan-4-one as prisms, m.p. 155.5-157°, identical (mixed m.p., t.l.c. and i.r.) with a sample obtained from the above experiment.

The minor fraction, eluted with ethyl acetate-ethanol(9:1) gave a white solid (0.075g) m.p. 173-183°. Recrystallisation from ethyl acetate gave prisms, m.p. 184-185°, tentatively assigned as 9-hydroxy-cis,trans,-cis-4-azatricyclo $[6,3,0,0^{2,7}]$undecan-3-one. (Found: C,66.08; H,8.02; N,7.74. $C_{10}H_{15}NO_2$ requires C,66.27; H,8.34; N,7.73%), δ [N.M.R.8,$(CD_3)_2SO$] 1.2-2.0 (6H, m, 2xH-6, 2xH-10, 2xH-11), 2.0-2.9 (4H, m, H-1, H-2, H-7, H-8), 3.0-3.5 (2H, m, 2xH-5), 4.02 (1H, m, H-9), 4.58 (1H, d, OH), 7.5 (1H, s, br, NH) p.p.m.

Attempted ketalisation of the mixture of keto-lactams obtained from the Schmidt reaction (p. 69)

The mixture of isomeric keto-lactams (0.3g, 1.6mmol) was dissolved in ethylene glycol(3ml) by warming to 50°. Dry hydrogen chloride gas was passed through the solution for a few seconds, then heated to 90° and maintained at this temperature for 10 min. After cooling and neutralising with 10% aqueous sodium bicarbonate (ca. 10ml), the mixture was extracted with methylene chloride (5x25ml). Evaporation of the

combined washed (30ml water) and dried ($MgSO_4$) extracts gave a sticky white solid (0.29g). T.l.c. with ethanol and also methylene chloride-methanol(9:1) as developing solvents indicated that the product was mainly the unreacted mixture of trans keto-amides, and it was not investigated further.

Lithium aluminium hydride reduction of the mixture of keto-lactams

A solution of the mixture of keto-lactams (0.3g, 1.6mmol) in dry dioxan(9ml) was added over 15 min. to a stirred suspension of lithium aluminium hydride(0.254g, 6.66mmol) in dioxan(9ml). The stirred mixture was heated under reflux for 2h, cooled and the excess lithium aluminium hydride was decomposed by adding water (1ml) dropwise. The inorganic solids were filtered off, washed with a little dioxan and then ether (25ml). The filtrate and washings were combined, dried (K_2CO_3) and evaporated to yield an oily residue which was treated with 2.5N hydrochloric acid and suspended impurities were filtered off. The solution was made basic (pH 8-9) with 10% sodium bicarbonate, extracted with methylene chloride(5x10ml), washed with water (10ml) and dried (K_2CO_3). Removal of solvent under reduced pressure gave a small amount (0.024g) of pale yellow crystalline solid. T.l.c. [methylene chloride-methanol (9:1)] indicated mainly two components (9:1), both near the origin and two trace impurities.

Exhaustive extraction of the aqueous phase with methylene chloride gave a further amount of a gummy product (0.157g), identical t.l.c. as above. The combined product (0.181g) was taken in acetic anhydride (2ml) and heated on a steam bath for 15 min. The mixture was then poured into ice-water (10ml), heated to boiling, neutralised with sodium bicarbonate and extracted with methylene chloride(5x20ml). Evaporation of the washed (saturated sodium chloride) and dried ($MgSO_4$) extract gave a yellow gum (0.12g). T.l.c. [methylene chloride-methanol

(9:1) indicated mainly one component with a number of trace impurities. The gum was chromatographed on alumina(10g) and subjected to graded elution with methylene chloride, methylene chloride-ethyl acetate, ethyl acetate and finally ethyl acetate-methanol. Ten fractions of 80 ml each were taken, examined by t.l.c. and combined accordingly to give the main component (68 mg) as a gum. The n.m.r. spectrum was poorly resolved but a strong singlet at δ 2.22 p.p.m. indicated that the compound was an acetyl derivative. Attempts to crystallise the material were not successful and it was not further investigated.

Beckmann rearrangement of the dioximes of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione

Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione dioxime

(a) Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione (10g, 0.061mol) was dissolved in ethanol (100 ml) by warming. A mixture of hydroxylamine hydrochloride (25.43g, 0.366mol), water (100 ml) and 10% sodium hydroxide (100 ml) was added, stirred and heated under reflux for 15 min. The mixture was cooled slowly to 0-5°, the crystals which separated were collected, washed with cold water (50 ml) and dried to give a white solid (10.1g, 85%), m.p. 223.5-225.5° (decomp.). T.l.c. (ethyl acetate) showed two spots R_F 0.49, 0.58 in an approximate ratio of 1:1. The mother liquors were diluted with two volumes of water and allowed to stand for several days to give a further quantity of the same material (0.48g, 4.0%). Recrystallisation of the combined solids from ethanol gave cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione dioxime as a mixture of stereoisomers, m.p. 224.5-225.5° (decomp.) (Found: C,61.91; H,7.04; N,14.61. $C_{10}H_{14}N_2O_2$ requires C,61.83; H,7.27; N,14.42%). T.l.c. (ethyl acetate) showed two spots (1:1). νmax.(I.R.11) 3270, 3170 (N-OH bonded), 1680 w (C=N), 925 cm^{-1}, νmax. (I.R.11A, KBr) 3260vs, br (N-OH bonded), 1670 w (C=N), 1630 w, 1445, 1429, 1218, 922, 932, 942, 735 cm^{-1}, δ[N,M.R.9, $(CD_3)_2SO$] 1.6-2.1 (4H, m, 2 x H-5, 2 x H-10), 2.1-2.85 (6H, m, 2 x H-4, 2 x H-9, H-1, H-6), 2.85-3.25 (2H, m, H-2, H-7), 10.13 and 10.28 (2H total, 2xs, 1:1.7, 2 x N-OH) p.p.m.

(b) Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione (0.5g, 3.05mmol) was added to a mixture of hydrated sodium acetate (2g) and hydroxylamine hydrochloride (1.25g, 18mmol), water (5 ml) and ethanol (7.5 ml). The mixture was heated under reflux for 1 h; cooled and diluted with water (45 ml). After cooling to 0-5°, the product was collected, washed with cold water (10 ml) and dried to give a white solid (0.49g, 82%), m.p.

220-223° (decomp.). T.l.c. (ethyl acetate) showed two spots (1:1) as in the above experiment. Recrystallisation from ethanol gave cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione dioxime as a mixture of stereoisomers, m.p. 224.5-225.5°; not depressed on admixture with the material obtained in (a).

Reaction of cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione with methoxylamine hydrochloride

Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione (1g, 6.1mmol) was added to a solution of methoxylamine hydrochloride (1.12g, 13.4mmol), sodium acetate trihydrate (1.824g, 13.4mmol), water (4 ml) and ethanol (10 ml). The resulting solution was heated under reflux for 20 h, diluted with water (20 ml) and extracted with ether (4 x 50 ml). The extracts were combined and washed with 5% sodium bicarbonate solution (2 x 10 ml), water (2 x 10 ml) and dried ($MgSO_4$). Evaporation gave 3,8-di(methoxyimino)cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]decane (1.32g, 96.5%) as a mixture of stereoisomers, m.p. 40-60° mainly, completely melted at 82°. G.l.c. on Carbowax 20M at 160° showed three peaks in an approximate ratio of 1:2:1 (R_t 10, 12.1 and 15.1 min. respectively); injection of the product at 140° and 180° gave the same relative ratio as above with varying retention times. (Found: C,64.98; H,7.90; N,12.60. $C_{12}H_{18}N_2O_2$ requires C,64.84; H,8.16; N,12.60%), δ (N.M.R.10, $CDCl_3$) 1.7-2.4 (4H, m, 2 x H-5, 2 x H-10), 2.5-3.33 (8H, m, remaining ring protons), 3.78 and 3.82 (6H, 2 x s, 2 x OCH_3) p.p.m. Integration of the two methoxy singlets showed a ratio of 1:1.8 (N.M.R.10A).

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

Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,10-dione (1.55g, 9.15mmol) was added to a solution of hydroxylamine hydrochloride (3.75g, 54mmol), water (15 ml) and 10% sodium hydroxide (10 ml). Ethanol (22 ml) was added

and the mixture heated under reflux for 15 min. The resulting solution was cooled slowly to 0-5° and the crystals which separated were collected, washed with cold water (20 ml) and dried to give a white crystalline product (1.64g, 89%), m.p. 212-213.5°; t.l.c. (ethyl acetate) showed one spot. Recrystallisation from ethanol gave cis,trans,cis-tricyclo-[5,3,0,$0^{2,6}$]deca-3,10-dione dioxime as colourless prisms, m.p. 216.5-217.5° (Found: C,62.07; H,7.33; N,14.23. $C_{10}H_{14}N_2O_2$ requires C,61.83; H,7.27; N,14.42%), ν max. (I.R.12) 3260, 3110 (N-OH bonded), 1675 w (C=N), 965 cm^{-1}, δ [N.M.R.11, $(CD_3)_2SO$] 1.5-2.0 (4H, m, 2 x H-5, 2 x H-8), 2.5-2.9 (6H, m, 2 x H-4, 2 x H-9, H-7, H-6), 2.9-3.3 (2H, m, H-1, H-2), 10.21 (1H, s, N-OH), 10.38 (1H, s, N-OH) p.p.m.

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

The dioxime(s) (5g, 0.0258mol) was powdered and added to polyphosphoric acid (125g) at 50° and the stirred mixture was heated for 15 min. at 120°, then cooled and poured onto ice-water (400g). Neutralisation with anhydrous sodium carbonate followed by continuous chloroform extraction for several days and evaporation of the dried ($MgSO_4$) extract gave a white solid (4.68g, 93.4%), m.p. 260-300° (decomp.). T.l.c. [ethanol-water(9:1)] showed two spots R_F 0.29 and 0.32. Fractional crystallisation from water gave the major constituent, cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-3,9-dione (1.9g), as colourless needles, m.p.> 300° (decomp., sealed tube) (Found: C,61.98; H,7.35; N,14.17. $C_{10}H_{14}N_2O_2$ requires C,61.83; H,7.27; N,14.42%), ν max. (I.R.13, KBr) 3290, 3170, 3030 (bonded NH), 1640 (amide C=O) cm^{-1}, δ (N.M.R.12, TFA) 2.2 (4H, br, 2 x H-6, 2 x H-12), 3.33 (4H, br, H-1, H-2, H-8, H-7), 3.78 (4H, br, 2 x H-5, 2 x H-11), 9.03 (2H, br, s, 2 x NH) p.p.m.

The mother liquors gave the minor constituent cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione (0.7g) as white lustrous

plates, m.p. 265-268° (decomp.) (Found: C,61.67; H,7.28; N,14.33. $C_{10}H_{14}N_2O_2$ requires C,61.83; H,7.27; N,14.42%), ν max. (I.R.14A) 3280, 3180, 3035 (bonded NH), 1660vs (amide C=O) cm^{-1}, δ (N.M.R.13, TFA) 2-2.5 (4H, m, 2 x H-6, 2 x H-12), 2.7-3.0 (2H, m, H-1, H-7), 3-3.5 (3H, m, 2 x H-5, H-8), 3.5-4.0 (2H, br peak, split, 2 x H-11), 4.22 (1H, m, H-2), 9.08 (2H, s, 2 x NH) p.p.m.

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

A mixture of cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-3,9-dione (0.6g, 3.1mmol), sodium hydride (0.33g, 6.8mmol, 50% dispersion in oil), dimethylformamide (12.5 ml) was stirred at 70° for 1 h, cooled and methyl iodide(3 ml) added and stirred for further 4 h. Removal of solvent, addition of water and extraction with chloroform gave a pale yellow gum (0.47g). T.l.c. [chloroform-methanol(9:1)] showed mainly one spot R_F 0.44. G.l.c. on S.E.52 (support Chromosorb W) at 230° showed essentially one component R_t 5.2 min. Recrystallisation from ethyl acetate gave N,N'-dimethyl-cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-3,9-dione, as colourless prisms m.p. 140-142° with phase change at 123.5-125° (Found: C,63.98; H,8.29; N,12.44; M^+ 222.1359. $C_{12}H_{18}N_2O_2$ requires C,64.84; H,8.16; N,12.60%; M^+ 222.1368. (N.M.R.14, 14A, $CDCl_3$) 1.8-2.2 (4H, m, 2 x H-6, 2 x H-12), 2.8 (4H, apparent singlet, H-1, H-2, H-7, H-8), 3.0 (6H, s, 2 x N-CH_3), 3.2-3.7 (4H, m, 2 x H-5, 2 x H-11) p.p.m.

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

A mixture of cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-3,9-dione (0.25g, 1.29mmol), dimethylformamide (5 ml) and sodium hydride (0.136g, 2.85mmol, 50% dispersion in oil) was stirred at 70° for 1 h, cooled benzyl chloride (1 ml) added and stirred for a further 4 h. The solvent was removed in vacuo and the residue was treated with water (10 ml) and extracted with chloroform (5 x 25 ml). Evaporation of the washed and dried

($MgSO_4$) extract gave a pale yellow gum (0.42g). T.l.c. [chloroform-methanol(9:1)] showed two constituents, R_F 0.67 and 0.71, in the ratio of approximately 1:2 respectively. The gum was dissolved in benzene and chromatographed on alumina (30g) and subjected to graded elution with benzene, benzene-chloroform and finally with chloroform to yield 21 fractions. Each of the fractions (80 ml) were examined by t.l.c. and the appropriate fractions were combined to give two main fractions.

Fraction (i), eluted with benzene-chloroform (3:1) gave the major product as a pale yellow gum (0.25g). Recrystallisation from ethyl acetate gave N,N'-dibenzyl-cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$] dodecane-3,9-dione, m.p. 137-138° as colourless prisms. (Found: C,76.34; H,6.99; N,7.47; M^+ 374.2002. $C_{24}H_{26}N_2O_2$ requires C,76.97; H,7.00; N,7.48%; M^+ 374.1994), νmax. (I.R.15) 3065 w, 3030 w (aromatic CH) 1640vs (amide C=O), 730 m, 700 m (monosubstituted benzene) cm^{-1}. δ(N.M.R.15, $CDCl_3$) 1.92 (4H, apparent singlet, 2 x H-6, 2 x H-12), 2.88 (4H, apparent singlet, H-1, H-2, H-7, H-8), 3.1-3.6 (4H, m, 2 x H-5, 2 x H-11), 4.62 (4H, s, 2 x CH_2-C_6H_5), 7.28 (10H, s, 2 x C_6H_5) p.p.m.

Fraction (ii), eluted with benzene-chloroform (1:1) gave the minor product as a colourless gum (0.1g) which was difficult to purify and was not further investigated.

Methylation of dilactam m.p. 265-268°

A mixture of the dilactam (0.25g, 1.29mmol), dimethylformamide (5 ml), sodium hydride (0.136g, 2.85mmol, 50% dispersion in oil) and methyl iodide (2 ml) was treated as in the previous methylation experiment. Removal of dimethylformamide, addition of water to the residue and extraction with chloroform gave a gum (0.27g). G.l.c. (S.E.52 on Chromosorb W) at 230° showed two components in an approximate ratio of 1:5, R_t 6.0 and 7.5 min. respectively. The gum was chromatographed on alumina (20g) and subjected to graded elution with benzene, benzene-chloroform and finally with

chloroform to yield 28 fractions. Each of the fractions (80 ml) were examined by g.l.c. and the appropriate fractions were combined to give two main fractions.

Fraction (i), eluted with benzene-chloroform (3:1) gave the major product as a colourless gum (0.137g), R_t 7.5 min. Attempts to crystallise the gum from various solvents were unsuccessful and hence it was analysed as such with poor results and was tentatively assigned as N,N'-dimethyl-cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione on the basis of its n.m.r. spectrum. (Found: C,62.07; H,8.59; N,10.98. $C_{12}H_{18}N_2O_2$ requires C,64.84; H,8.17; N,12.60%). δ(N.M.R.16, $CDCl_3$) 2.86 (3H, s, N-CH_3), 3.02 (3H, s, N-CH_3), 3.3-3.8 (3H, m, H-2, 2 x H-11) p.p.m.; expansion (N.M.R.16A) of the 3.3-3.8 region showed two multiplets in the ratio of 1:2 i.e. 3.32-3.6 (2H, m, 2 x H-11) and 3.6-3.8 (1H, m, H-2) p.p.m.

Fraction (ii), eluted with benzene-chloroform (9:1) gave the minor component as a white solid (0.030g), m.p. 138.5-142.5°, R_t 6.0 min., which was not further investigated.

Benzylation of dilactam m.p. 265-268°

The dilactam (0.3g, 1.55mmol) was added in portions over 5 min. to a stirred mixture of sodium hydride (0.163g, 3.39mmol, 50% dispersion in oil, washed with light petroleum) in dry dimethylformamide (6 ml) under nitrogen. The stirred mixture was heated at 70° for 1 h, then cooled to room temperature, benzyl chloride (1 ml) added and the stirring continued at 70° for 4 h. After cooling and addition of water (15 ml), an oil separated out which was extracted with chloroform (5 x 25 ml). The combined extracts were washed with saturated sodium chloride solution (20 ml), dried ($MgSO_4$) and concentrated under reduced pressure to give a pale yellow gum (0.65g). T.l.c. [chloroform-methanol(9:1)] showed mainly two components in the approximate ratio of 4:1, R_F 0.67 and 0.33

respectively. The gum was chromatographed on alumina (30g) and subjected to graded elution with benzene, benzene-chloroform and finally chloroform to yield 25 fractions. Each of the fractions (80 ml) were examined by t.l.c. and the appropriate fractions were combined to give two main fractions, each of which, however was slightly contaminated with traces of the other.

Fraction (i), eluted with benzene-chloroform (3:1) gave mainly the major product as a colourless gum (0.343g). Recrystallisation from ether-ethyl acetate gave a solid, m.p. 88-90^{o} mainly but some material did not melt until 115^{o} and attempts to purify the compound were to no avail. The n.m.r. spectrum was recorded (N.M.R.17, $CDCl_3$).

Fraction (ii), eluted with benzene-chloroform (1:3) gave largely the minor component as a white sticky fibrous solid (0.117g). Attempts to purify this compound were also unsuccessful.

Attempted formation of a Diazabiphenylene

Lithium aluminium hydride reduction of the mixture of dilactams from the Schmidt reaction

(a) The mixture of dilactams (0.5g, 2.58mmol) was placed in the thimble of a soxhlet apparatus fitted to a flask containing a suspension of lithium aluminium hydride (0.4g, 10.55mmol) in dry dioxan (95 ml) which was then stirred under reflux for 4 days. After cooling, wet ether (95 ml) and ethyl acetate (10 ml) were added to the mixture to decompose excess lithium aluminium hydride, the inorganic material was separated by filtration and washed with ether (2 x 25 ml). The filtrate and washings were combined and dried (K_2CO_3) and evaporated to give a small quantity of gum (0.034g); t.l.c. using ethanol-2.5N ammonia (4:1) as development solvent indicated a complex mixture of products and was not investigated further.

A small amount (0.025g) of the starting material remained in the soxhlet thimble at the end of the experiment.

When ether was used as solvent in a similar experiment, only a very small amount of the mixture of dilactams (19%) was leached from the soxhlet thimble after 9 days at reflux; 81% of starting material remained in the thimble.

(b) The mixture of dilactams (1g, 5.15mmol) was finely ground and added slowly in portions during 0.5 h to a stirred suspension of lithium aluminium hydride (0.9g, 23.7mmol) in dry tetrahydrofuran (80 ml). The mixture was stirred under reflux for 48 h, cooled and water (80 ml) added cautiously followed by 20% sodium hydroxide until the pH reached a value of 12. Benzoyl chloride (4g) was added to the solution which was then stirred vigorously at room temperature for 3.5 h whilst maintaining the solution at pH 12. The solution was extracted with chloroform (5 x 50 ml) and the combined extracts were washed with water (30 ml), dried ($MgSO_4$) and concentrated under reduced pressure to give

a gum (0.830g). T.l.c. (ethyl acetate) showed mainly two components (R_F 0.48, 0.34). The gum was dissolved in chloroform (20 ml) and chromatographed on a column of dry alumina (18" x 1", Activity 2-3); ethyl acetate was used as developing solvent. The column was cut into six portions, each portion was extracted with methylene chloride followed by ethanol. The extracts were examined by t.l.c. and the appropriate portions were combined to give two main fractions.

Fraction (i) was obtained as a colourless gum (0.346g). Recrystallisation from ethyl acetate gave N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane as fawn prisms (0.035g), m.p. 135-139° (Found M^+ 374.2031, $C_{24}H_{26}N_2O_2$ requires M^+ 374.1994), (N.M.R.18, $CDCl_3$) 1.65 (8H, br, 2 x H-5, 2 x H-6, 2 x H-11, 2 x H-12), 2.8 (2H, br, H-1, H-7), 3.35 (4H, br, 2 x H-4, 2 x H-10), 4.2 (2H, br, H-2, H-8), 7.37 (10H, s, aromatic protons). The rather poor spectrum was due to insufficient material. T.l.c. examination of the mother liquors indicated mainly the above compound, attempts to obtain further quantity of the pure material were however not successful.

Fraction (ii) was also obtained as a colourless gum (0.055g). This material was not characterised as it was found to be slightly contaminated with the major product.

N-Benzoylpiperidine[74]

This was prepared by addition of freshly distilled benzoyl chloride to a solution of piperidine in aqueous sodium hydroxide. Colourless liquid b.p. 175-8° at 15 mm Hg. (lit.,[74] b.p. 184-186° at 15 mmHg), δ(N.M.R.19, $CDCl_3$) 1.62 (6H, br, 2 x H-3, 2 x H-4, 2 x H-5), 3.5 (4H, br, 2 x H-2, 2 x H-6), 7.35 (5H, s, C_6H_5-CO) p.p.m.

Attempted reduction of the mixture of dilactams, obtained from the Schmidt reaction, with sodium and ethanol

The mixture of dilactams (0.3g, 1.54mmol) was dissolved in absolute ethanol (30 ml) by heating under reflux and then sodium (1g) was added in portions over 1 h. The solution was heated under reflux for 2 h, cooled and acidified (pH 1-2) with dilute hydrochloric acid. After removal of most of the ethanol, the aqueous solution was made basic (pH 10) and extracted continuously with ether. Evaporation of the dried (K_2CO_3) extract gave a gum (0.060g), t.l.c. [methanol-water(4:1)] indicated a complex mixture of products which was not investigated further.

The aqueous phase was extracted continuously with methylene chloride. Evaporation of the solvent gave a small quantity (0.077g) of the starting material.

N,N'-Dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]dodecane (as its dipicrate)

A mixture of lithium aluminium hydride (0.41g, 10.7mmol), tetrahydrofuran (25 ml) and N,N'-dibenzyl-cis,trans,cis-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane-4,10-dione (0.5g, 1.33mmol) was stirred and heated under reflux for 4 h. The mixture was cooled and water (1 ml) was added cautiously to decompose the excess hydride, followed by ether (75 ml). The mixture was stirred vigorously and filtered through a bed of celite. The inorganic material was washed thoroughly with ether (3 x 25 ml). The filtrate and washes were combined, dried (K_2CO_3) and concentrated under reduced pressure to give a colourless gum (0.4g, 86%). T.l.c. (ethyl acetate) showed essentially one component, R_F 0.7, and g.l.c. on silicone oil at 134° showed mainly (>95%) one peak R_t 4 min. The material was characterised as the dipicrate, yellow solid (from aqueous ethanol), m.p. 215-216° (decomp.) (Found: C,53.44; H,4.45; N,13.74. $C_{36}H_{36}N_8O_{14}$ requires C,53.73; H,4.51; N,13.92%). The n.m.r. spectrum

[N.M.R.20 $(CD_3)_2$ SO] showed the expected two singlets at δ 7.44 and δ8.55 p.p.m. for the aromatic benzyl and the picric acid protons, in the expected ratio of 10:4.

The free amine could not be obtained crystalline and it darkened slowly on standing.

Attempted formation of N,N'-dibenzyl-cis,trans,cis-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane dihydrochloride

Ethanol (10 ml) saturated with dry hydrogen chloride was added to a solution of the free base (0.273g), from the above experiment, in ether (50 ml). A white precipitate separated and the solution was further saturated with dry hydrogen chloride. Decanting the liquors left an off-white sticky solid (0.092g) and evaporation of the liquors gave a further quantity (0.32g) of solid. During attempted recrystallisation from ethanol-ether the material appeared to decompose as the solution gradually changed from pale yellow to red-brown. However an amorphous greenish-yellow solid (0.31g) was obtained which softened from 149°, collapsing to a gum by ca. 160°, which, on increasing the temperature, gradually changed to a mass of prismatic needles. The material was almost completely solid by 190° and then melted slowly, with decomposition, from 200-220°. The material was not investigated further.

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

The amine (0.412g, 1.19mmol) was mixed intimately with 10% palladium on carbon (0.205g) and heated at 240-250° for 0.75 h. The mixture was cooled and extracted with ethanol (100 ml) and the extract filtered and concentrated under reduced pressure to give a yellow gum (0.098g). G.l.c. on Carbowax 20M at 150° showed four peaks (7%, 9.6%, 25% and 58.4%) with retention times 8, 11.2, 15.4 and 72.4 min. respectively;

none of these peaks corresponded to pyridine or toluene. The ultra-violet spectrum showed absorption at 222, 264 and 270.5 nm, and the n.m.r. spectrum (N.M.R.21, $CDCl_3$) showed the presence of aromatic protons centred at δ 8.5 p.p.m. and δ 7.1-7.6 p.p.m. (typical of α and γ pyridine protons) as well as aliphatic protons. The mass spectrum however did not show a molecular ion corresponding to that of a diazabiphenylene (m/e 154) but an ion was observed at m/e 156, possibly due to a bipyridyl; the most intense ion was observed at m/e 169.

Treatment of the gum in ethanol with ethanolic picric acid gave a gummy brown solid. Attempts to crystallise this material were not successful.

SPECTRA

INFRARED SPECTRA

I.R.1. Cyclopent-2-en-1-one

2. Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione

3. Cis,trans,cis-3,3,8,8-tetramethoxytricyclo[5,3,0,$0^{2,6}$]-decane

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

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

6. N,N'-Dibenzyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane-4,10-dione

7. N,N'-Dimethyl-cis,trans,cis-3,9-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane-4,10-dione

8. Cis,trans,cis-3-azatricyclo[6,3,0,$0^{2,7}$]undecane-4,9-dione

9. 9-Hydroxyimino-cis,trans,cis-3-azatricyclo[6,3,0,$0^{2,7}$]-undecan -4-one (mixture of syn and anti isomers)

10. 9-Hydroxy-cis,trans,cis-3-azatricyclo[6,3,0,$0^{2,7}$]undecan-4-one

11. Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,8-dione dioxime(s)

12. Cis,trans,cis-tricyclo[5,3,0,$0^{2,6}$]deca-3,10-dione dioxime

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

14. Cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione (ex. Schmidt)

14A. Cis,trans,cis-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione (ex. Beckmann)

15. N,N'-Dibenzyl-cis,trans,cis-4,10-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane-3,9-dione

NUCLEAR MAGNETIC RESONANCE SPECTRA

N.M.R.1. Cis, trans, cis-3,3,8,8-tetramethoxytricyclo $[5,3,0,0^{2,6}]$-decane

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

3. N,N'-Dibenzyl-cis, trans, cis-3,9-diazatricyclo $[6,4,0,0^{2,7}]$-dodecane-4,10-dione

4. N,N'-Dimethyl-cis, trans, cis-3,9-diazatricyclo $[6,4,0,0^{2,7}]$-dodecane-4,10-dione

5. Cis, trans, cis-3-azatricyclo $[6,3,0,0^{2,7}]$undecane-4,9-dione

6. 9-Hydroxyimino-cis, trans, cis-3-azatricyclo $[6,3,0,0^{2,7}]$-undecan-4-one

7. 9-Hydroxy-cis, trans, cis-3-azatricyclo $[6,3,0,0^{2,7}]$undecan-4-one

8. 9-Hydroxy-cis, trans, cis-4-azatricyclo $[6,3,0,0^{2,7}]$undecan-3-one (tentatively assigned)

9. Cis, trans, cis-tricyclo $[5,3,0,0^{2,6}]$deca-3,8-dione dioxime(s)

10. Mixture of isomeric 3,8-di(methoxyimino) cis, trans, cis-tricyclo $[5,3,0,0^{2,6}]$ decane

11. Cis, trans, cis-tricyclo $[5,3,0,0^{2,6}]$deca-3,10-dione dioxime

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

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

14. N,N'-Dimethyl-cis, trans, cis-4,10-diazatricyclo $[6,4,0,0^{2,7}]$-dodecane-3,9-dione

15. N,N'-Dibenzyl-cis, trans, cis-4,10-diazatricyclo $[6,4,0,0^{2,7}]$-dodecane-3,9-dione

N.M.R.16. Tentatively assigned as N,N'-dimethyl-*cis*,*trans*,*cis*-3,10-diazatricyclo[6,4,0,$0^{2,7}$]dodecane-4,9-dione

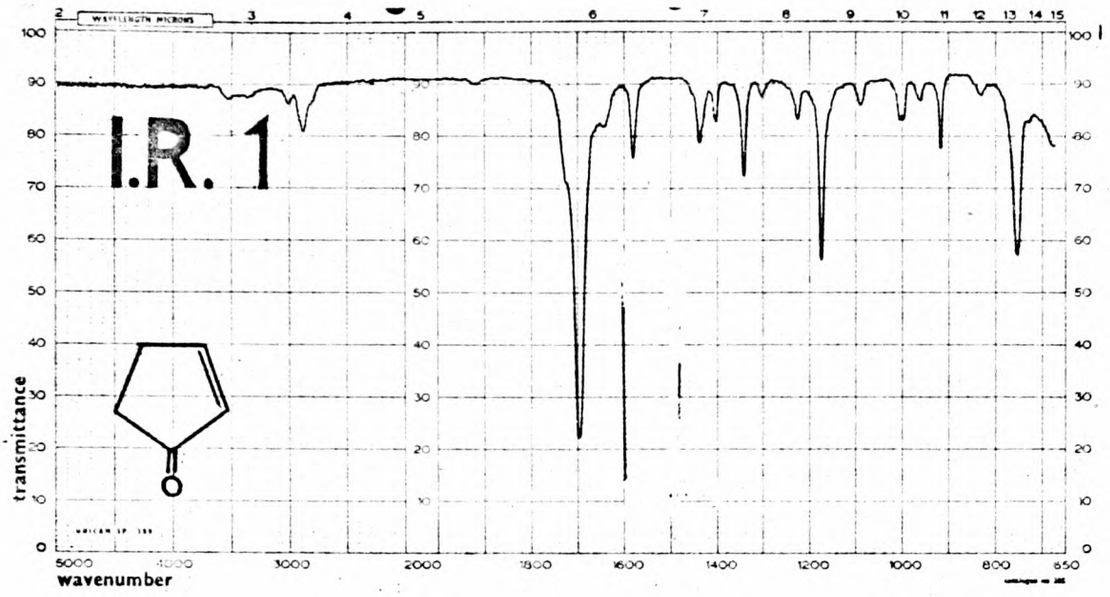
17. Unknown compound m.p. 88-90° mainly, completely melting by 115°

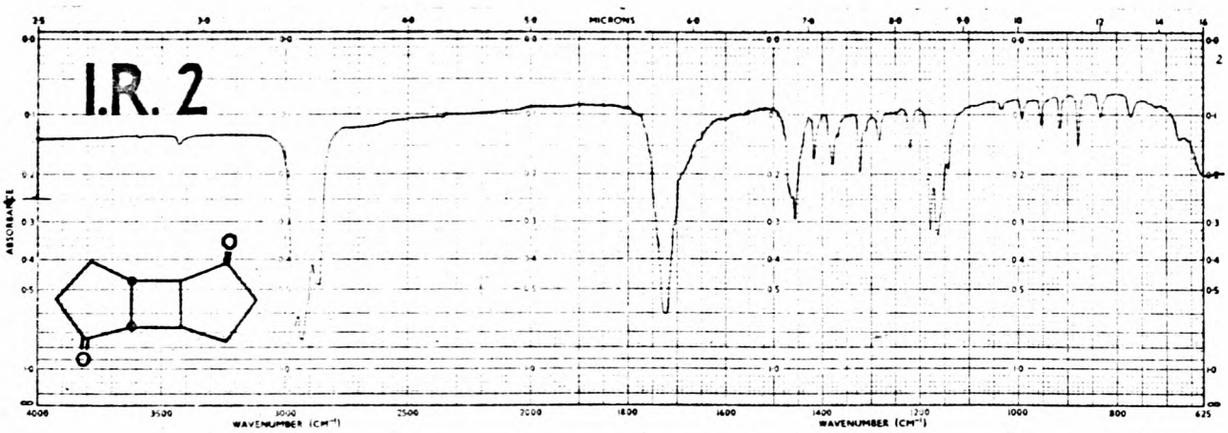
18. N,N'-Dibenzoyl-*cis*,*trans*,*cis*-3,9-diazatricyclo[6,4,0,$0^{2,7}$]-dodecane

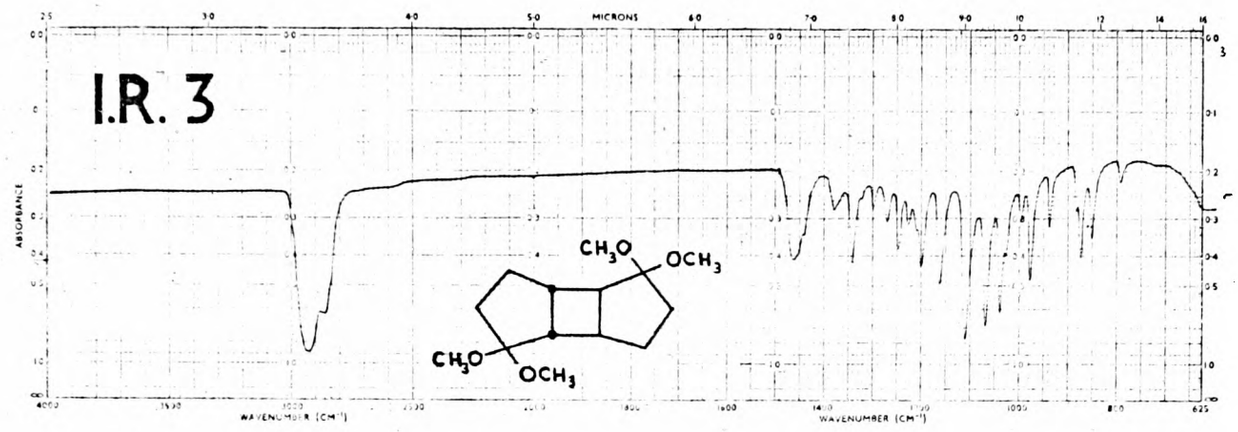
19. N-Benzoylpiperidine

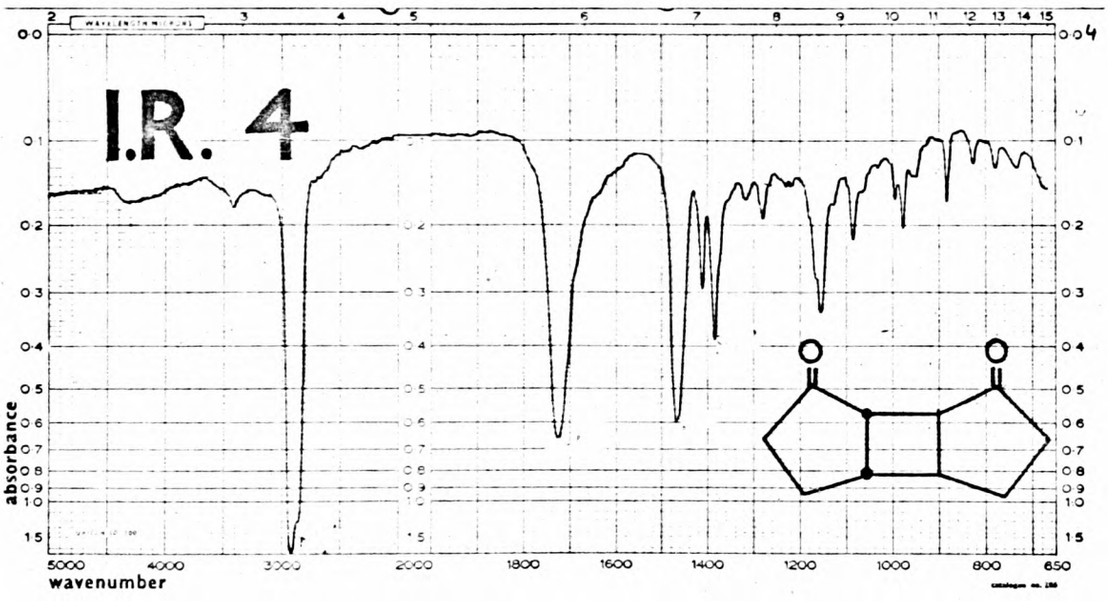
20. Dipicrate of N,N'-dibenzyl-*cis*,*trans*,*cis*-3,9-diazatricyclo-[6,4,0,$0^{2,7}$]dodecane

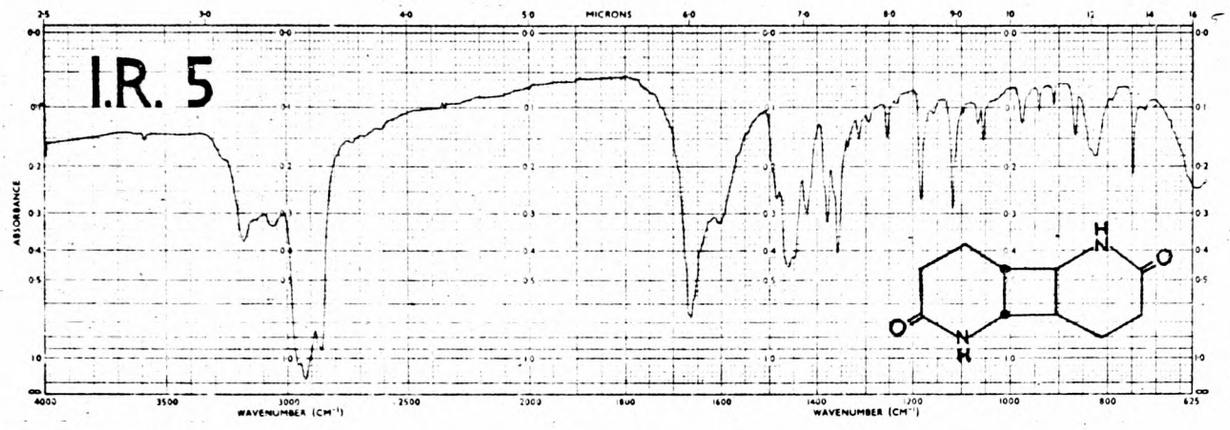
21. Unknown mixture of compounds from the dehydrogenation.

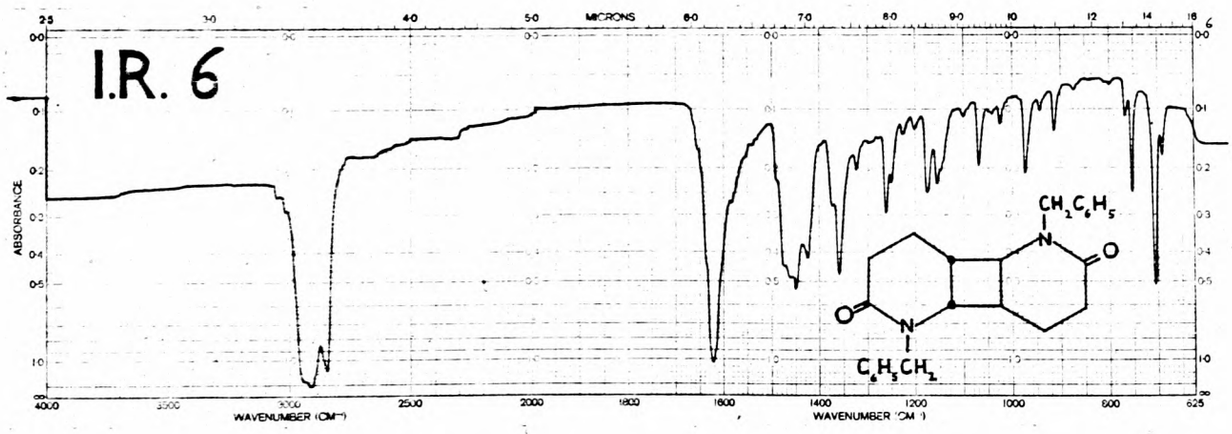

I.R. 1
transmittance
wavenumber

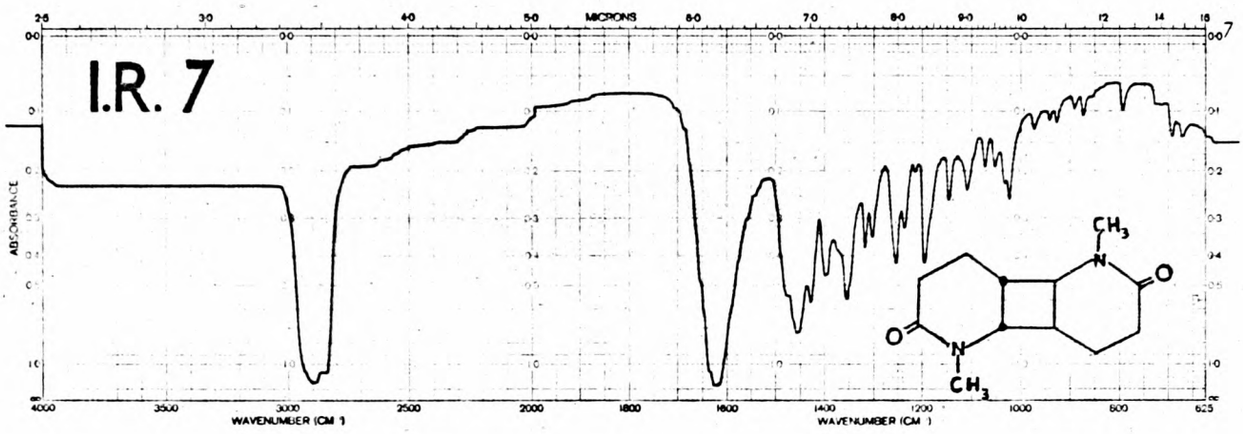

I.R. 2
MICRONS
WAVENUMBER (CM⁻¹)

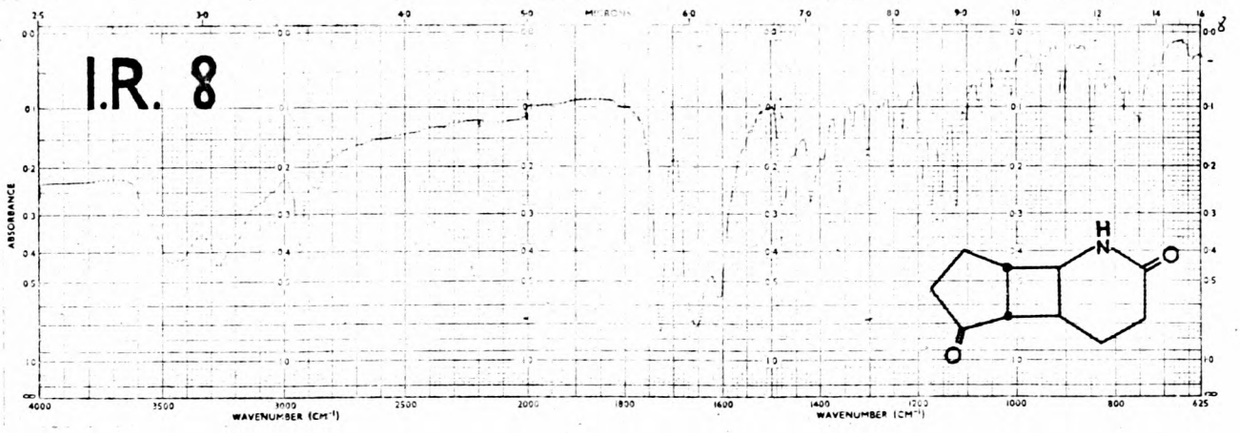

I.R. 3
MICRONS
ABSORBANCE
WAVENUMBER (CM⁻¹)
CH3O
OCH3
CH3O
OCH3

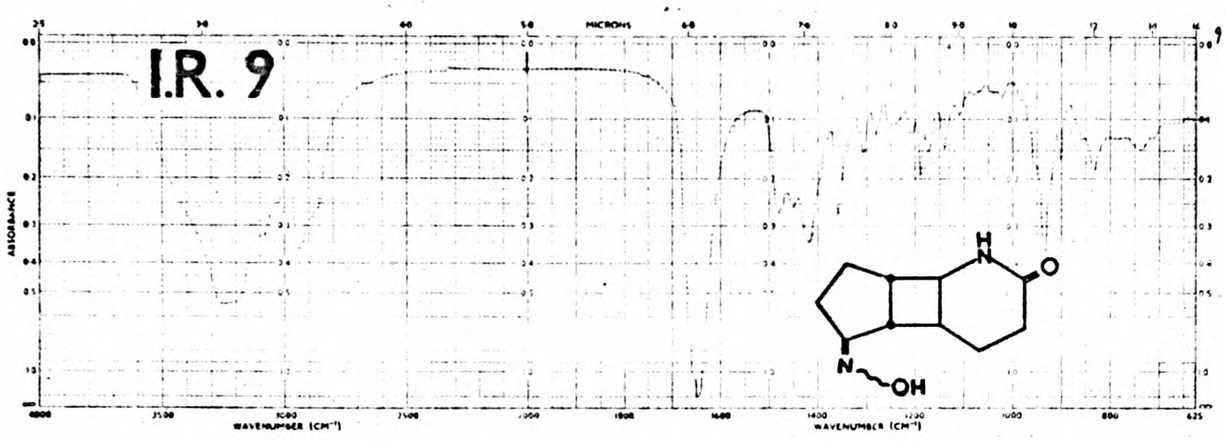

I.R. 4
absorbance
wavenumber
5000
4000
3000
2000
1800
1600
1400
1200
1000
800
650

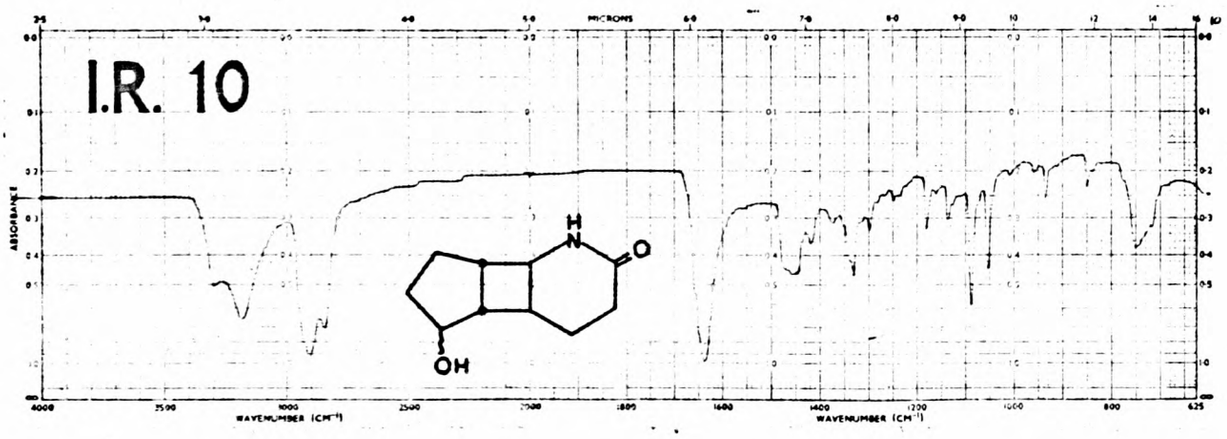

I.R. 5
MICRONS
ABSORBANCE
WAVENUMBER (CM⁻¹)
WAVENUMBER (CM⁻¹)
H
N
O
O
N
H

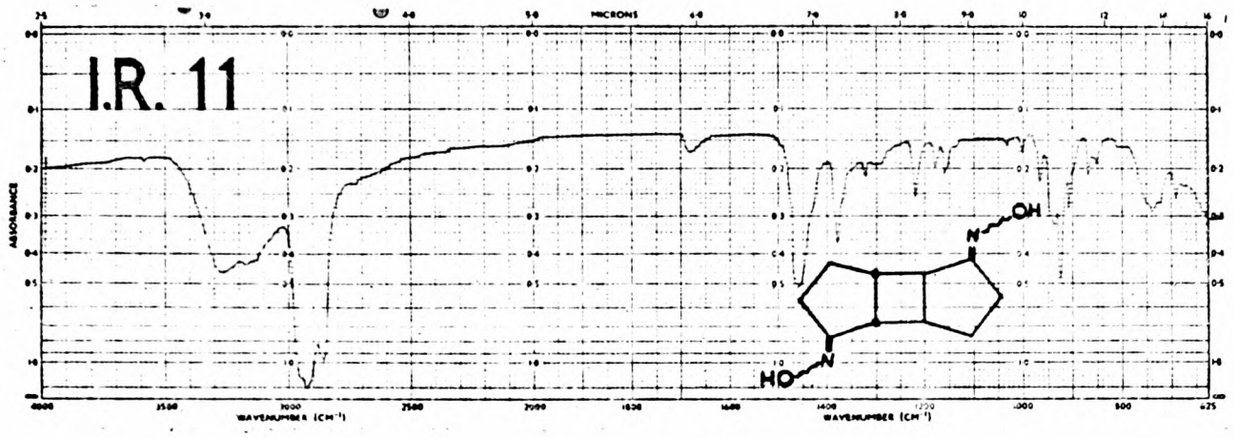

I.R. 6
MICRONS
ABSORBANCE
WAVENUMBER (CM⁻¹)
WAVENUMBER (CM⁻¹)
CH2C6H5
N
O
O
N
C6H5CH2

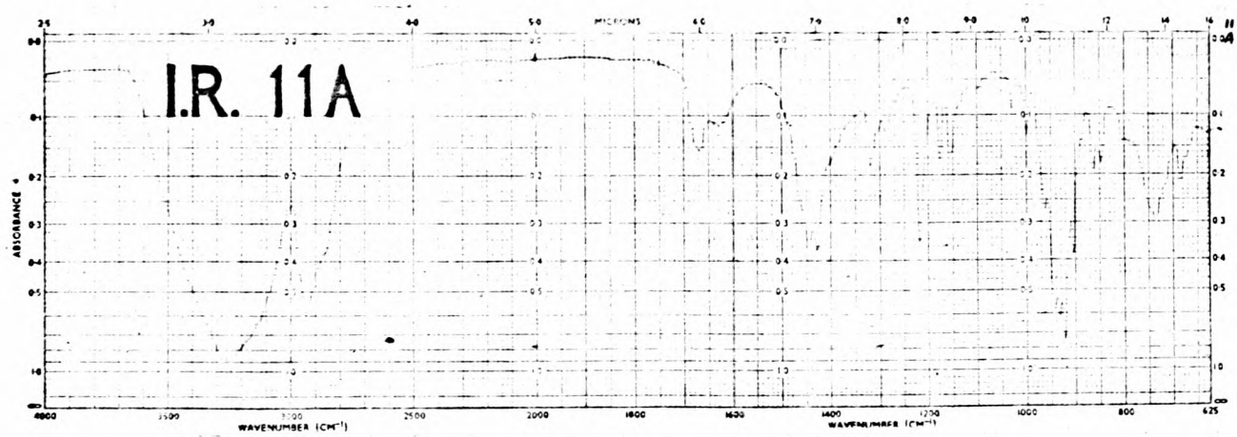

I.R. 7
MICRONS
ABSORBANCE
WAVENUMBER (CM⁻¹)
CH3
N
O
O
N
CH3

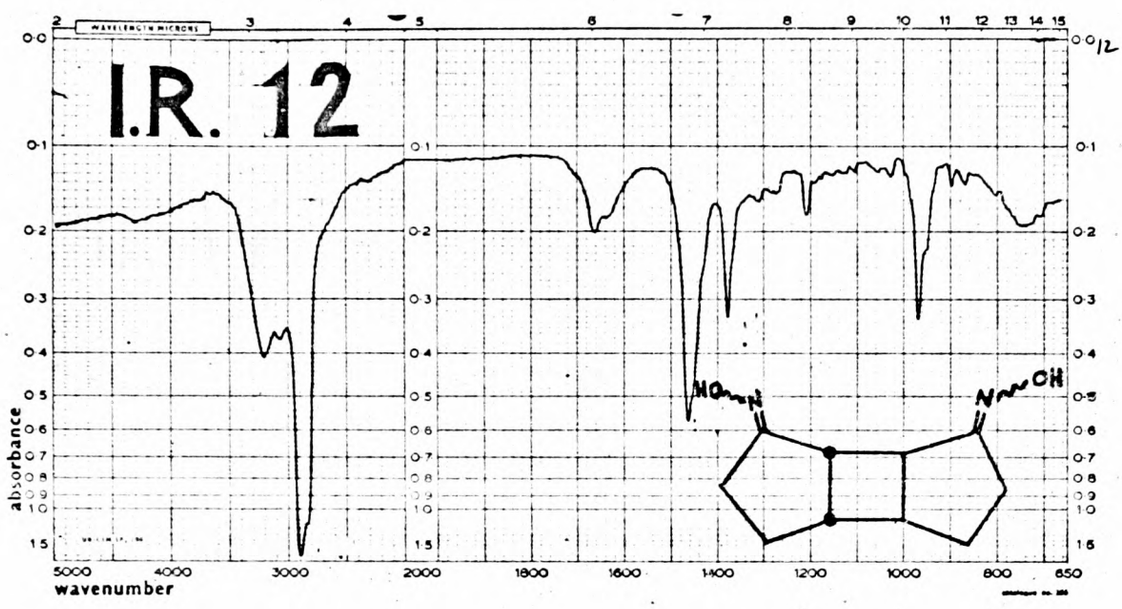

I.R. 8
MICRONS
ABSORBANCE
WAVENUMBER (CM⁻¹)
H
N
O
O

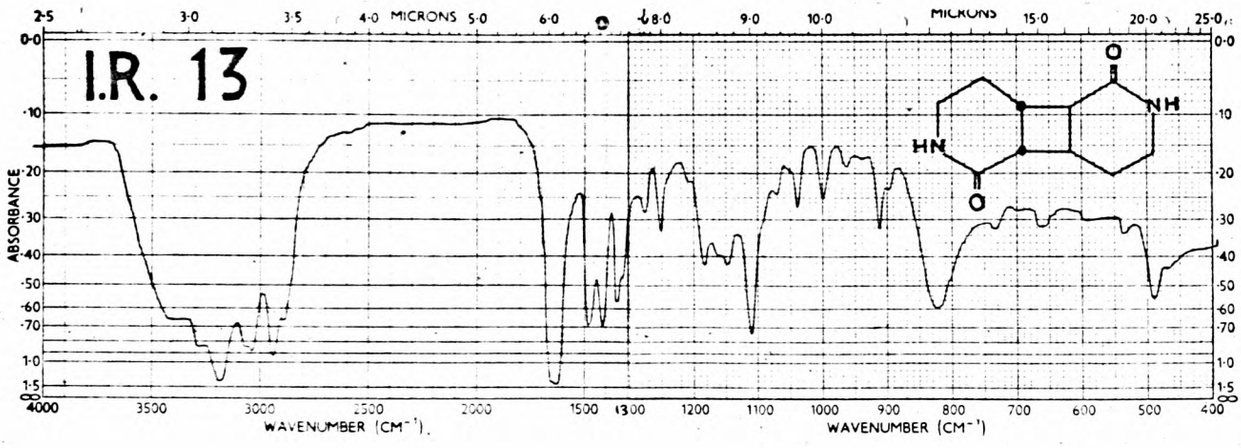

I.R. 9
MICRONS
ABSORBANCE
WAVENUMBER (CM⁻¹)
H
N
O
N
OH

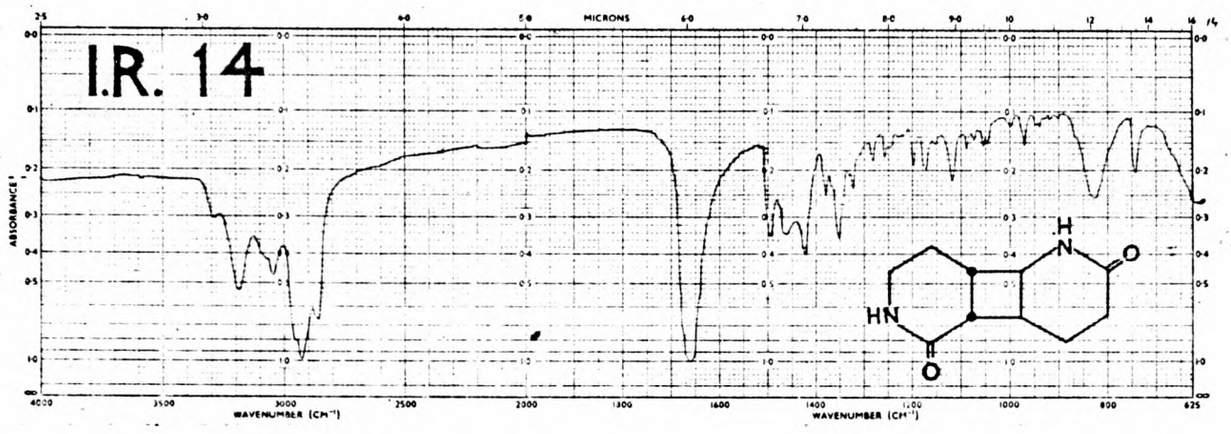

I.R. 10
MICRONS
ABSORBANCE
WAVENUMBER (CM⁻¹)
H
N
O
OH

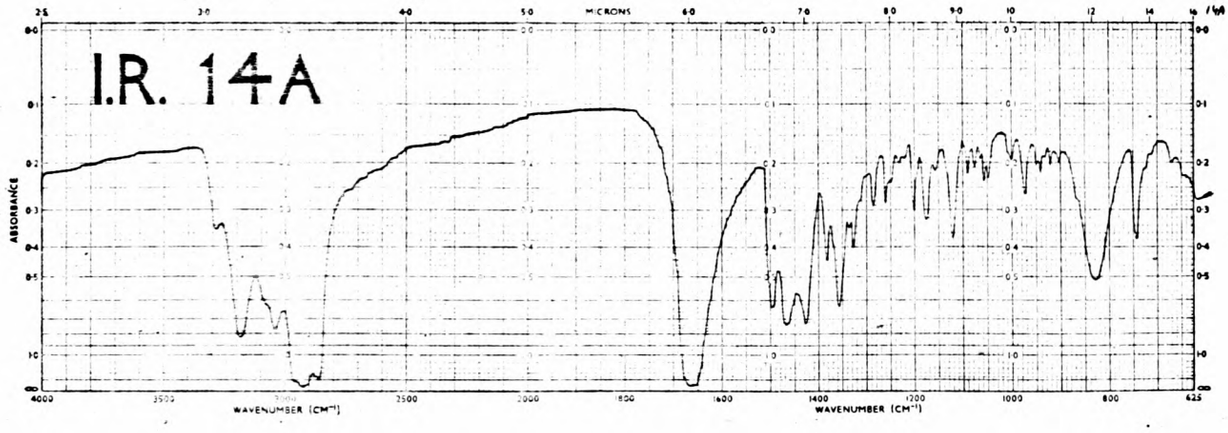

I.R. 11
ABSORBANCE
WAVENUMBER (CM⁻¹)
MICRONS
OH
N
HO
N

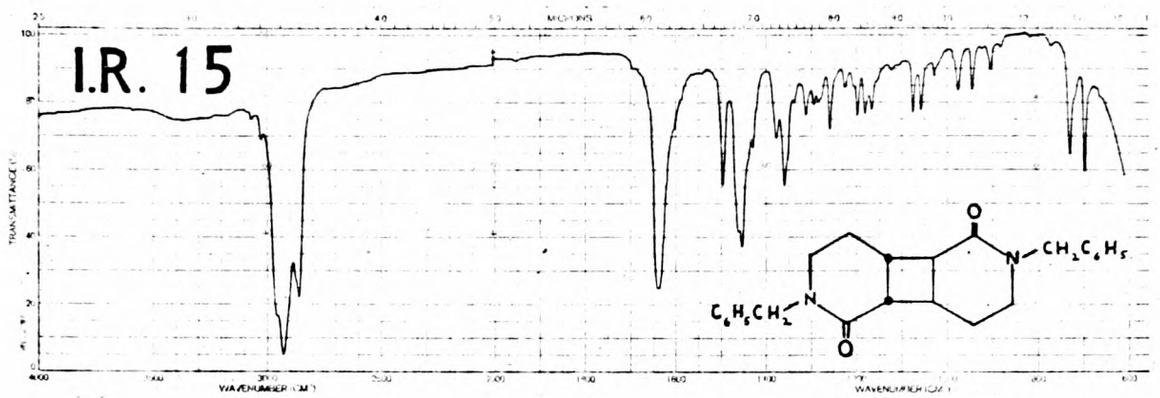

I.R. 11A
ABSORBANCE
WAVENUMBER (CM⁻¹)
MICRONS

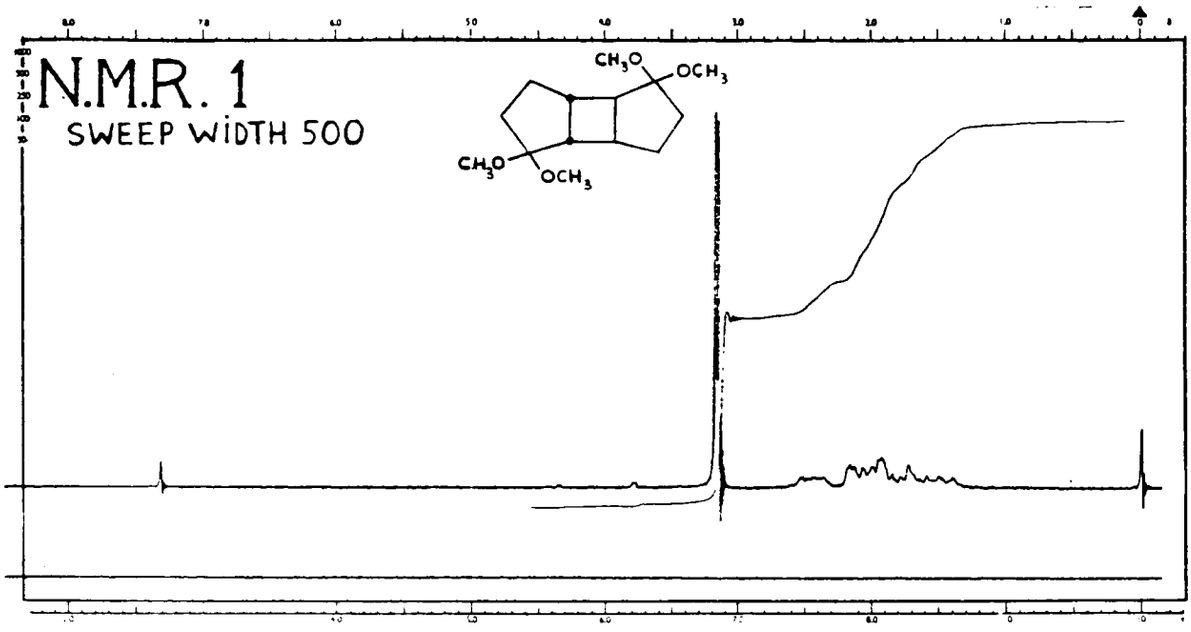

I.R. 12
absorbance
wavenumber
5000
4000
3000
2000
1800
1600
1400
1200
1000
800
650

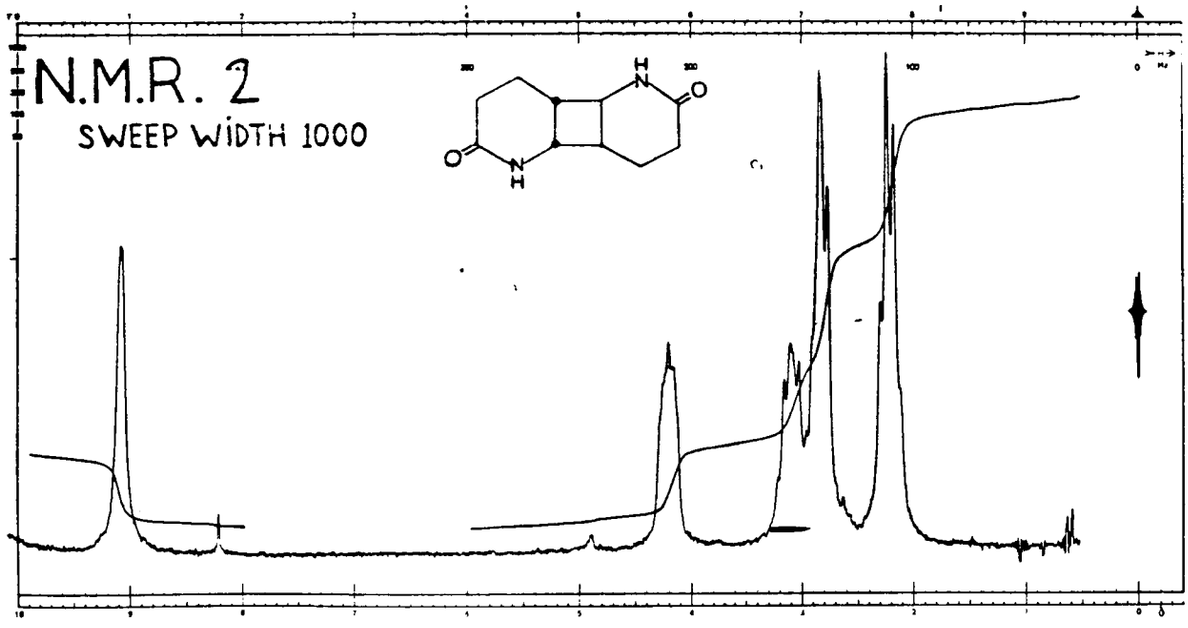

I.R. 13
ABSORBANCE
WAVENUMBER (CM⁻¹)
4000
3500
3000
2500
2000
1500
1300
1200
1100
1000
900
800
700
600
500
400
MICRONS
HN
NH
O
O

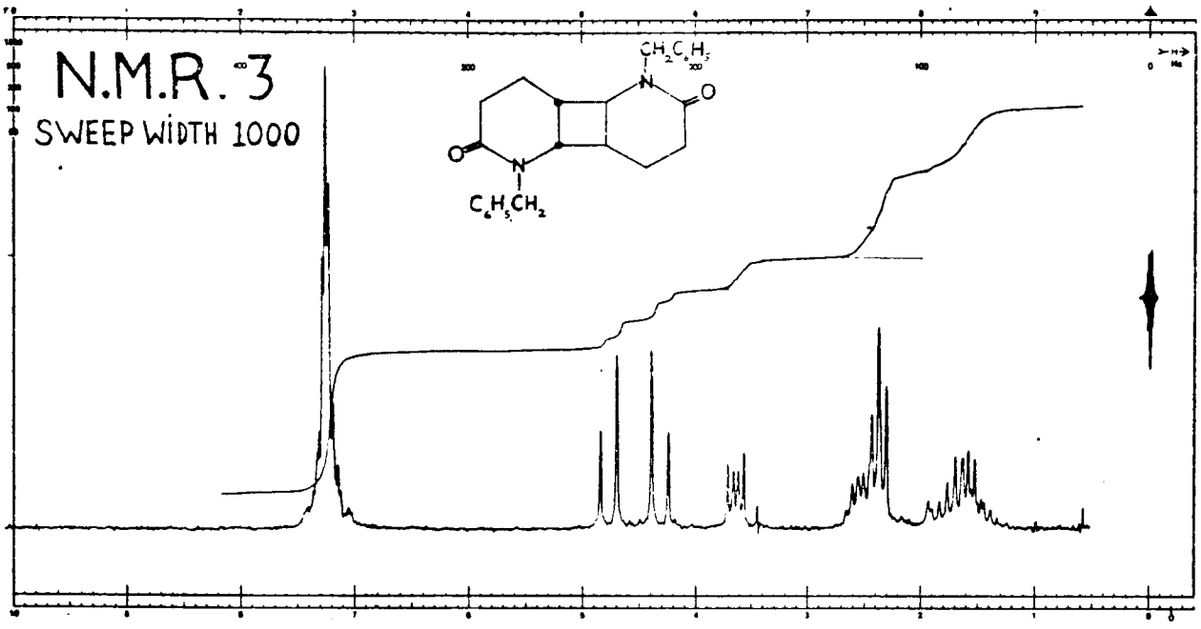

I.R. 14
MICRONS
ABSORBANCE
WAVENUMBER (CM⁻¹)
WAVENUMBER (CM⁻¹)
HN
O
H
N
O

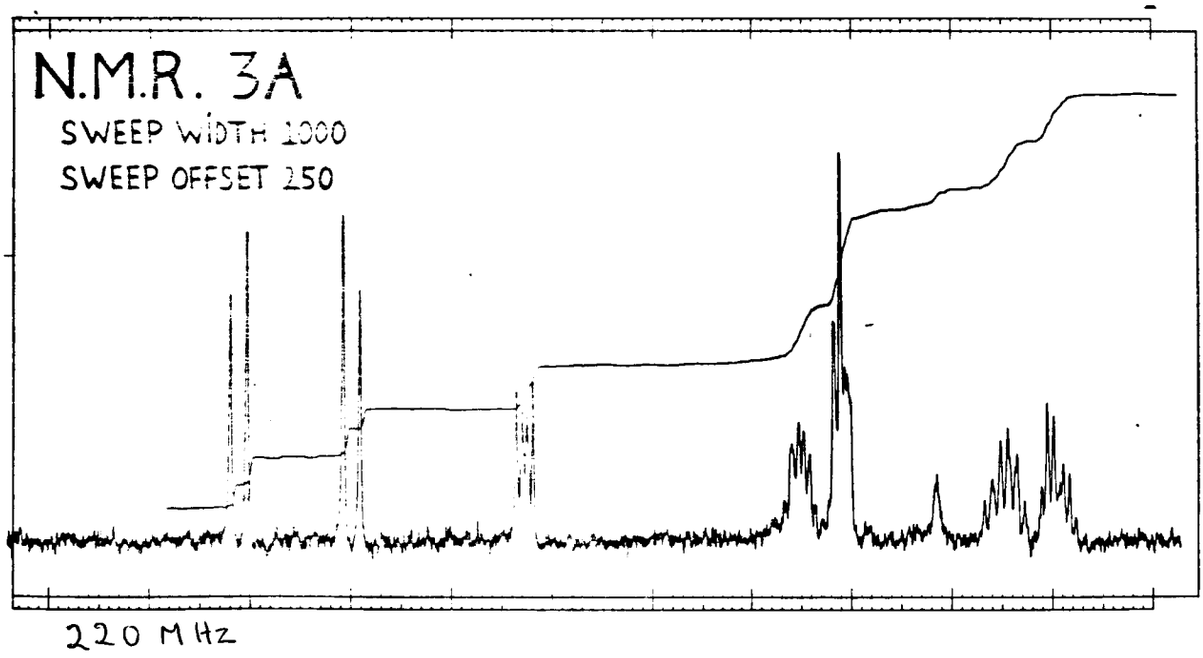

I.R. 14A
MICRONS
ABSORBANCE
WAVENUMBER (CM⁻¹)
WAVENUMBER (CM⁻¹)

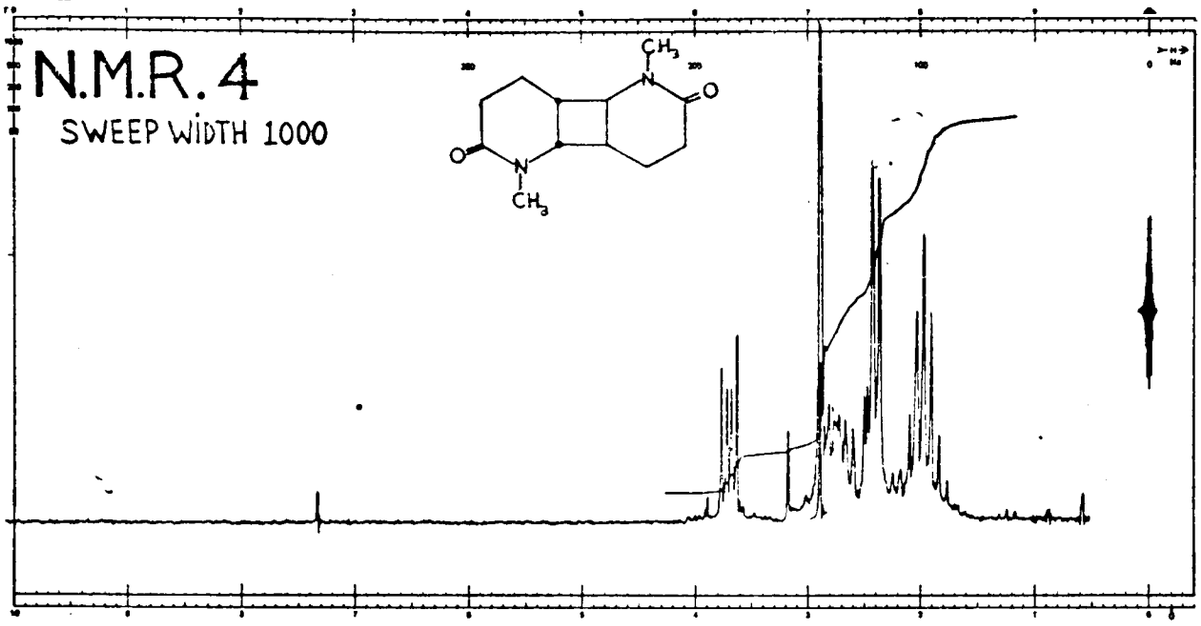

I.R. 15
O
N
CH2C6H5
C6H5CH2
N
O

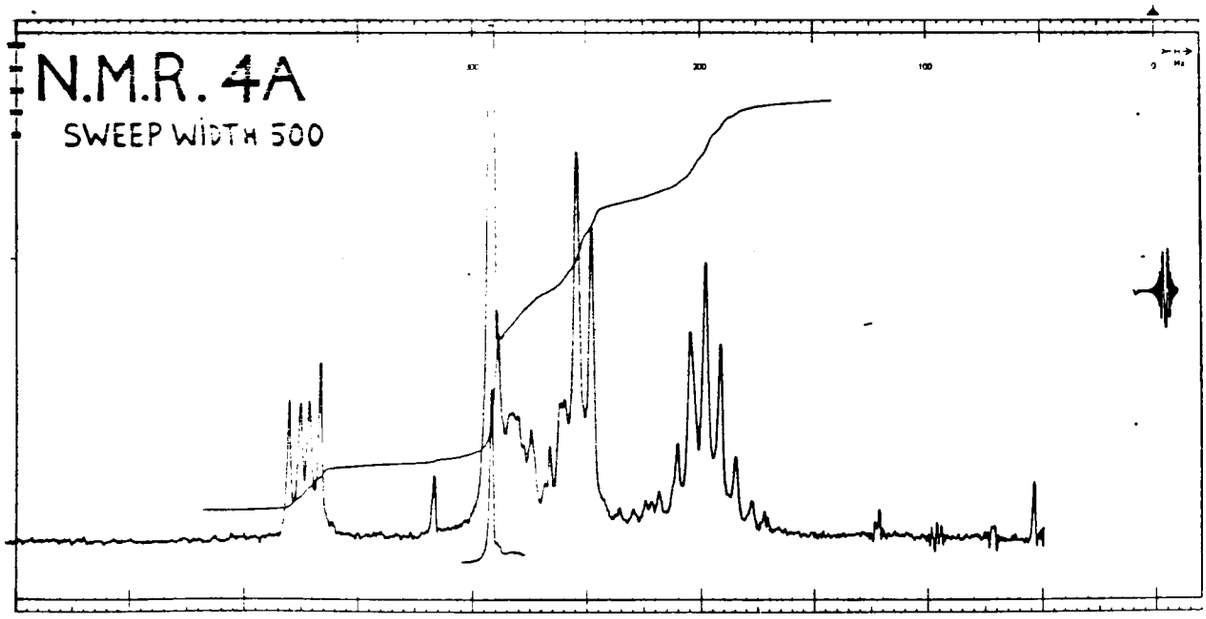

N.M.R. 1
SWEEP WIDTH 500
CH3O
OCH3
CH3O
OCH3

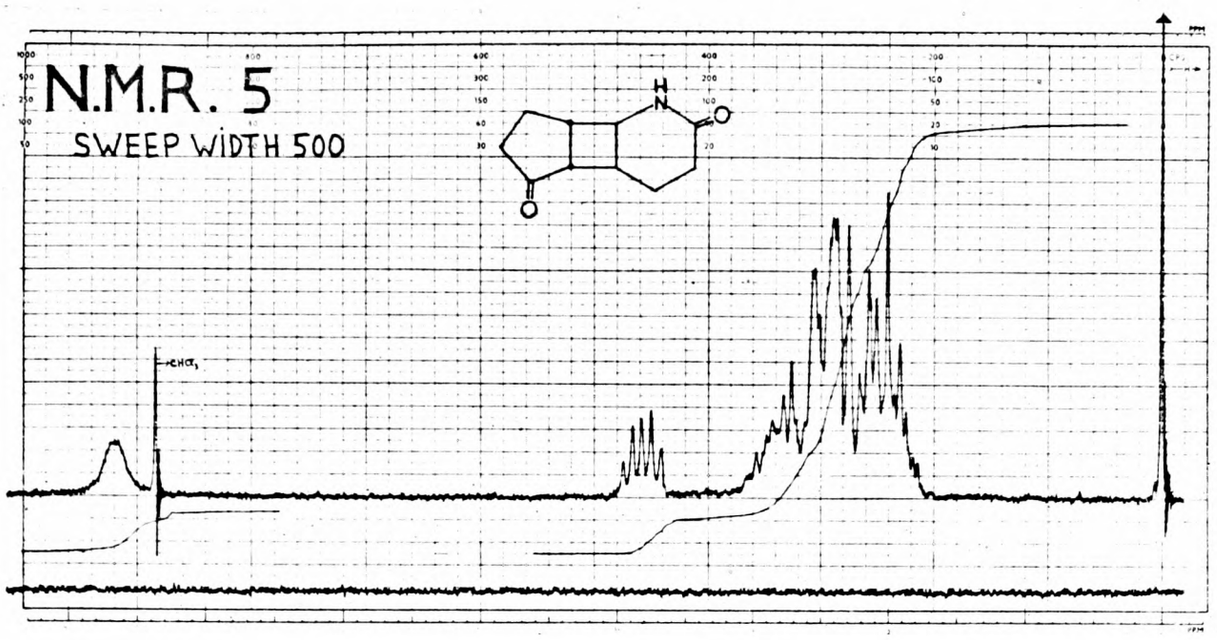

N.M.R. 2
SWEEP WIDTH 1000
H
N
O
O
N
H

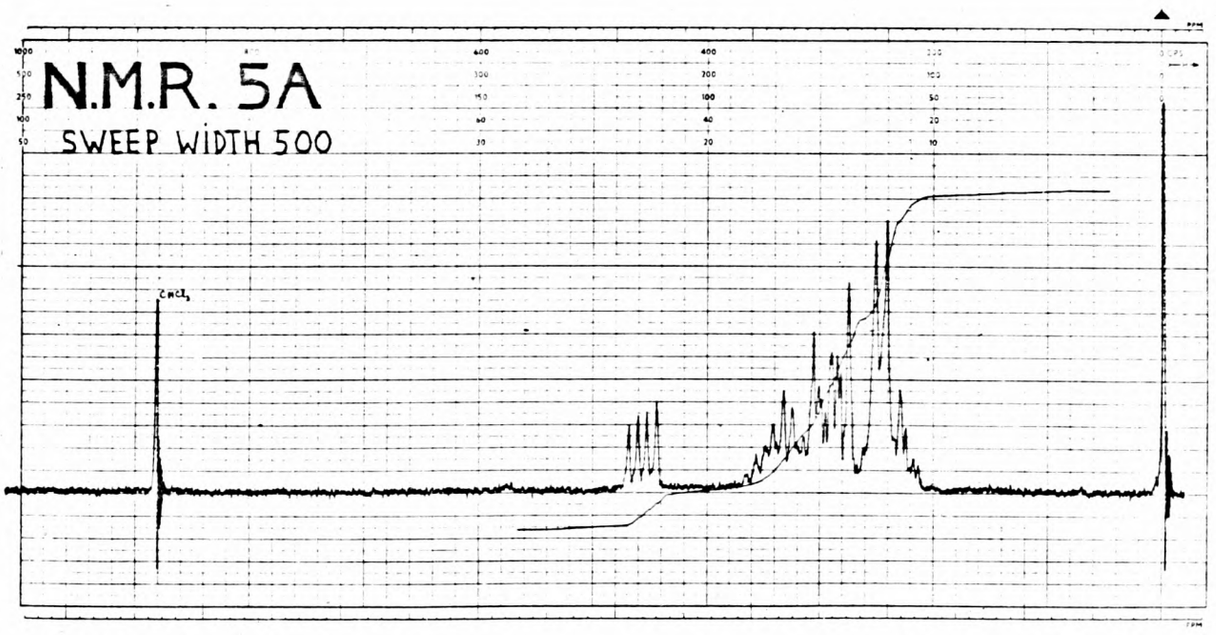

N.M.R. 3
SWEEP WIDTH 1000
$CH_2C_6H_5$
N
O
O
N
$C_6H_5CH_2$


N.M.R. 3A
SWEEP WIDTH 1000
SWEEP OFFSET 250
220 MHz


N.M.R. 4
SWEEP WIDTH 1000
CH3
N
O
O
N
CH3


N.M.R. 4A
SWEEP WIDTH 500


N.M.R. 5
SWEEP WIDTH 500
CHCl3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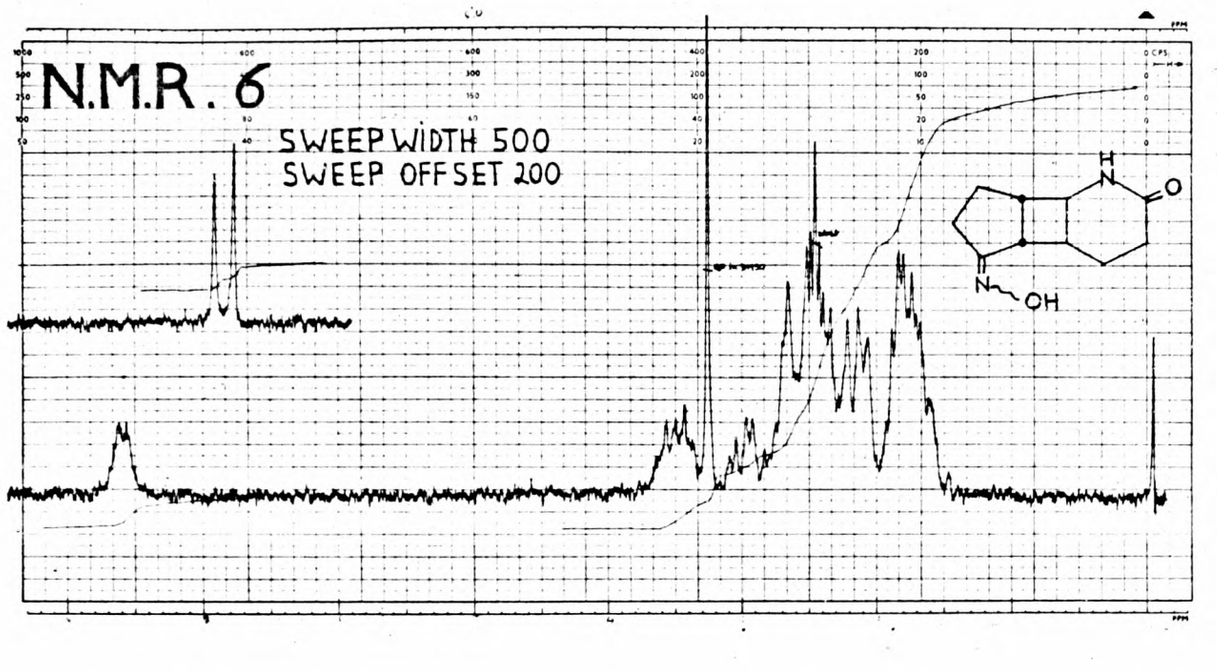
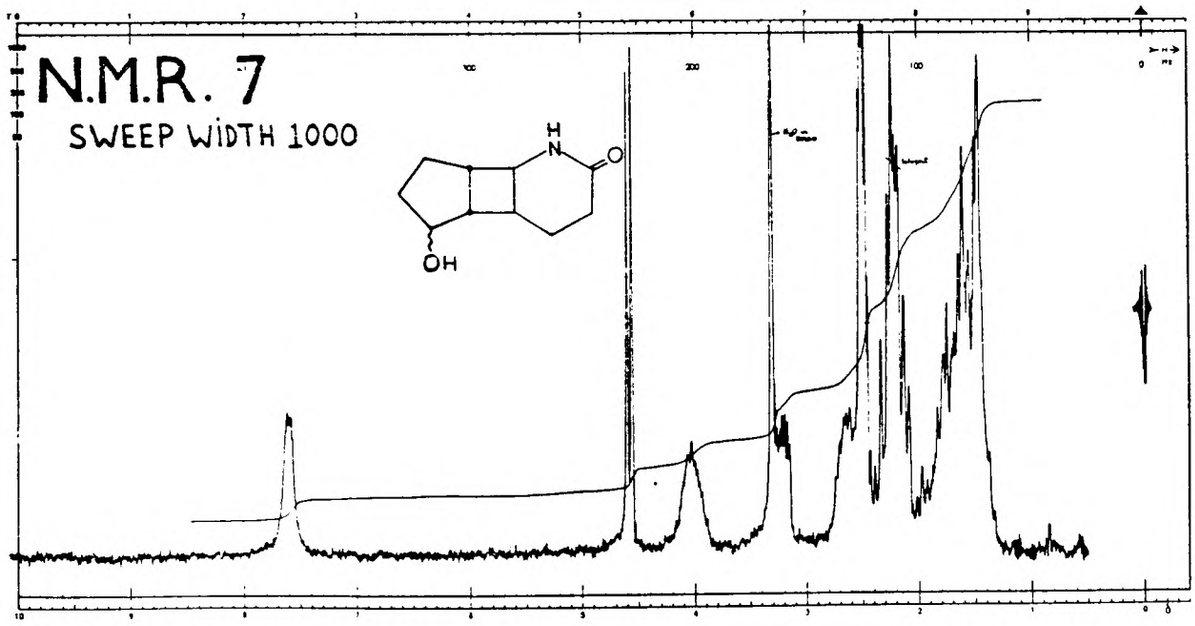
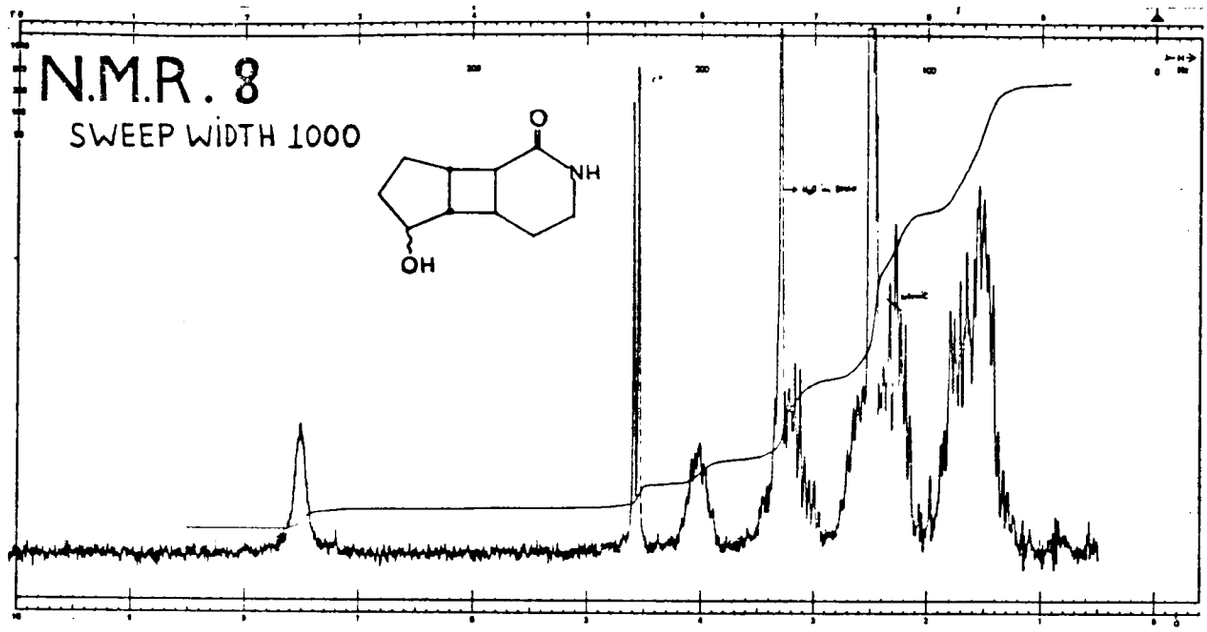
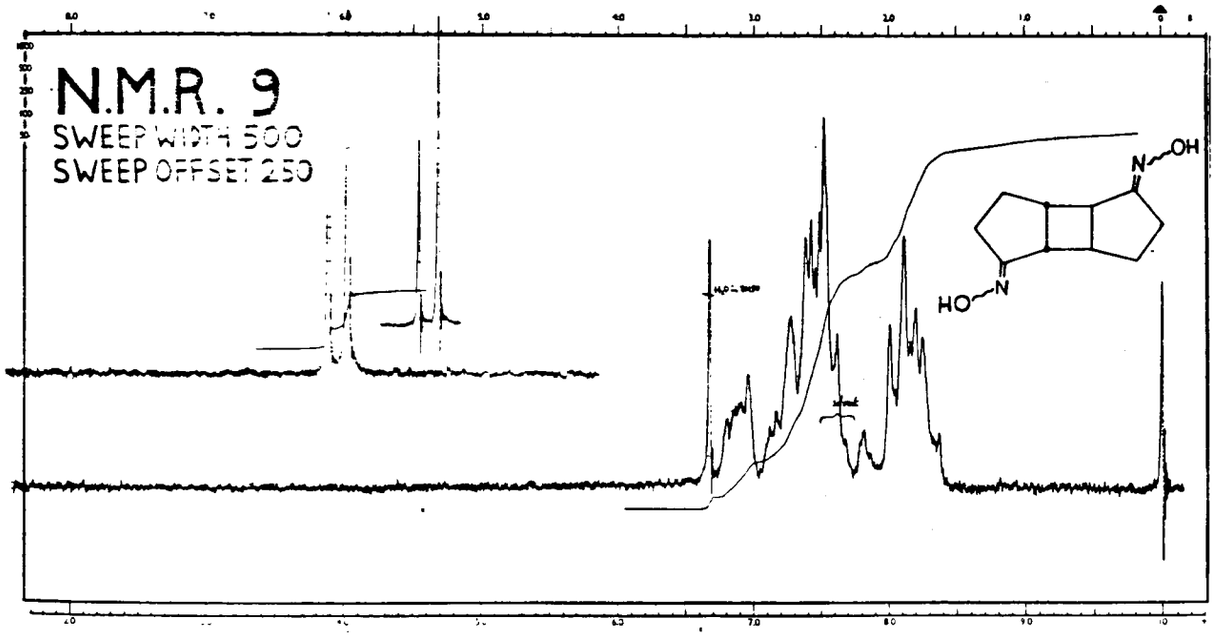
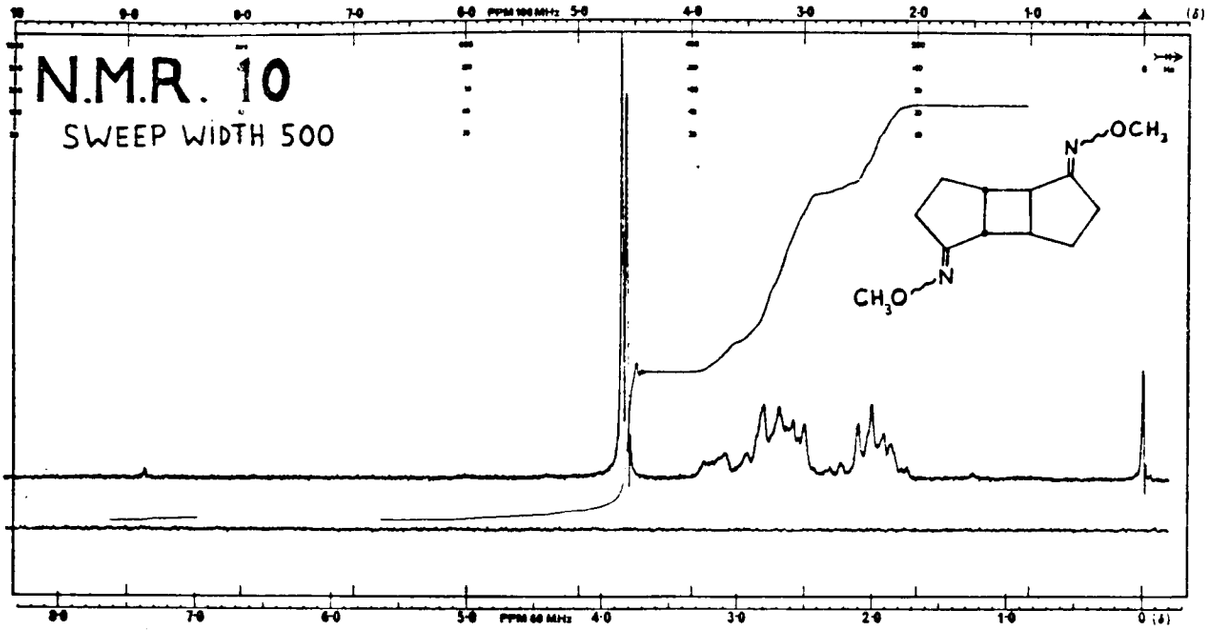
SWEEP WIDTH 500
CHCl3

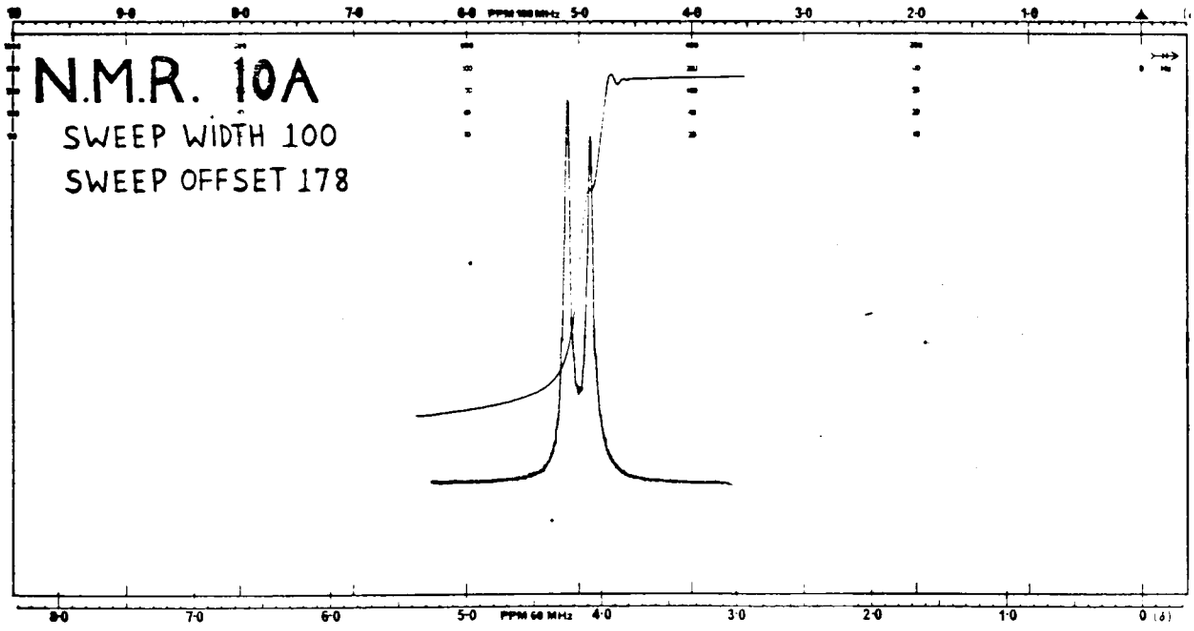

N.M.R. 6
SWEEP WIDTH 500
SWEEP OFFSET 200
H
N
O
N
OH

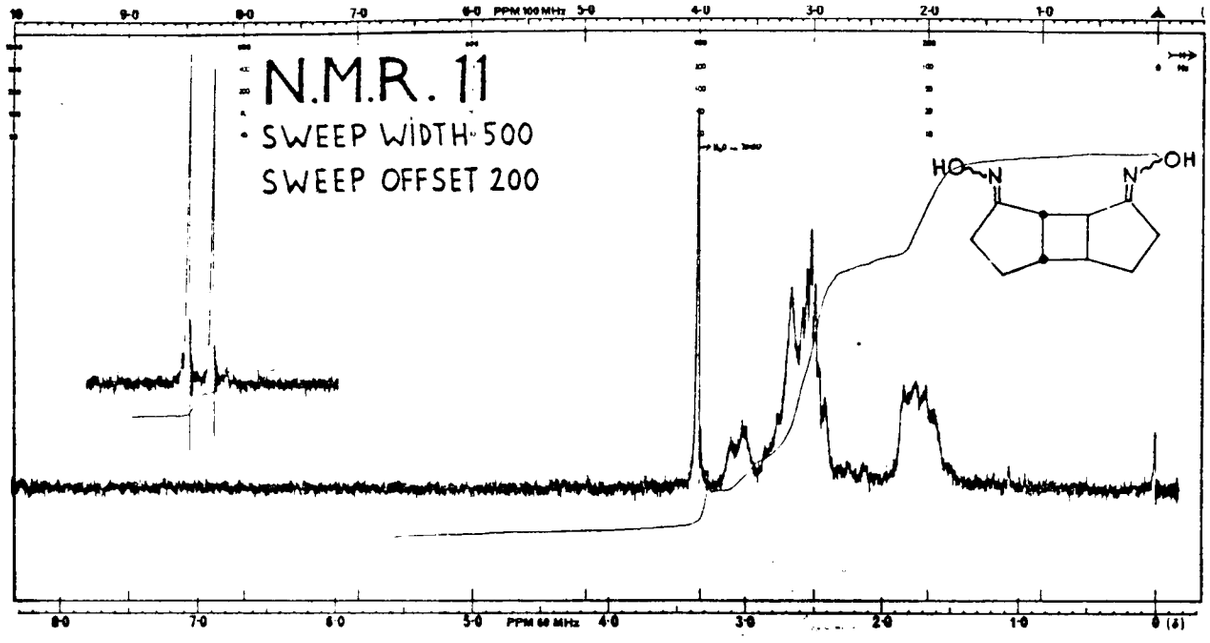

N.M.R. 7
SWEEP WIDTH 1000
H
N
O
OH

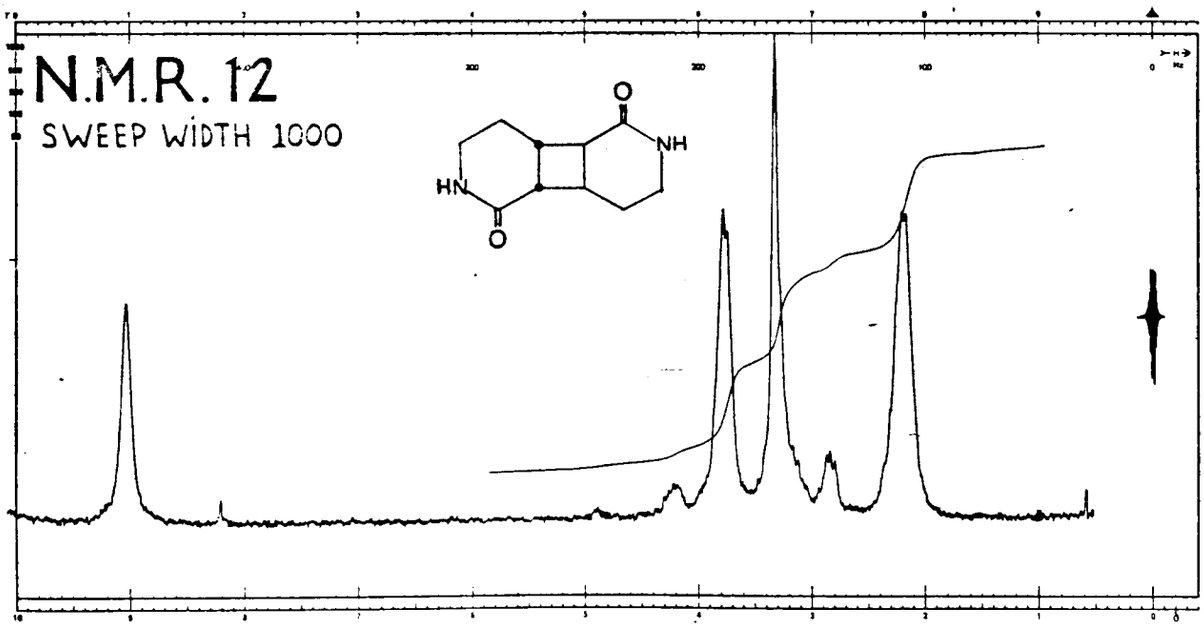

N.M.R. 8
SWEEP WIDTH 1000
O
NH
OH

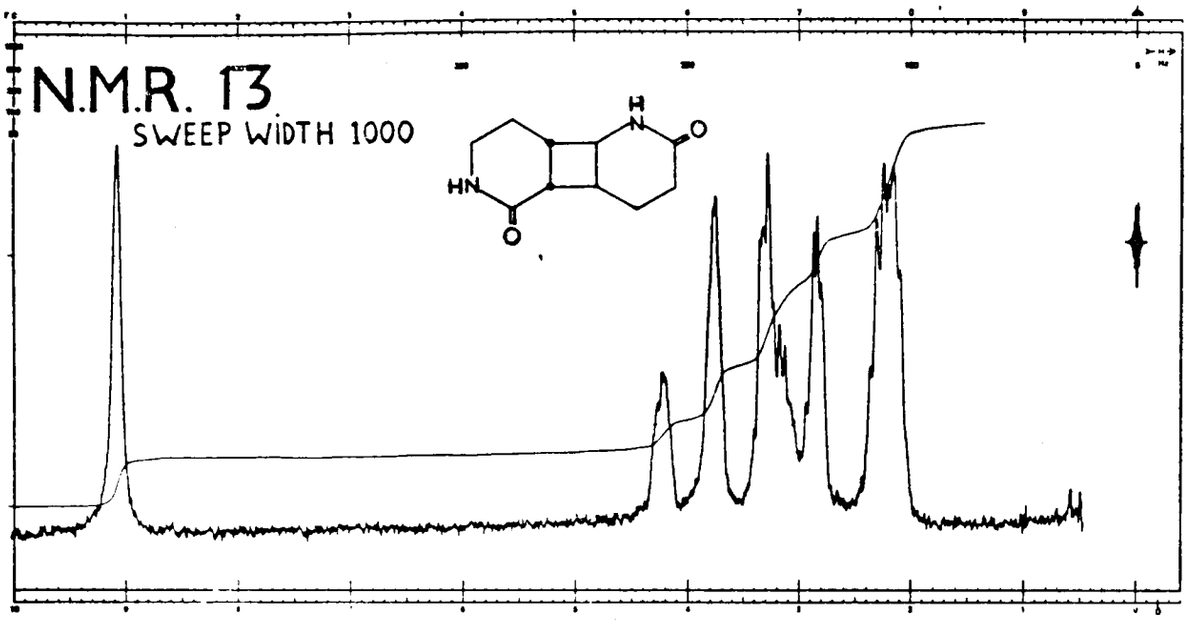

N.M.R. 9
SWEEP WIDTH 500
SWEEP OFFSET 250
N
OH
HO
N

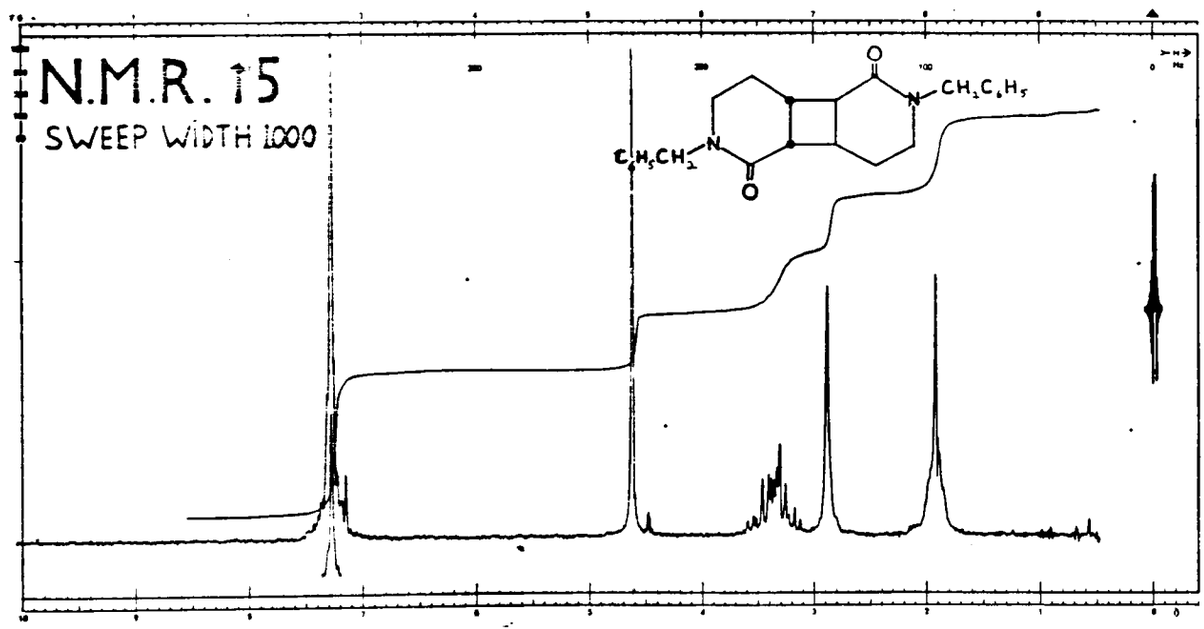

N.M.R. 10
SWEEP WIDTH 500
N
OCH3
CH3O
N

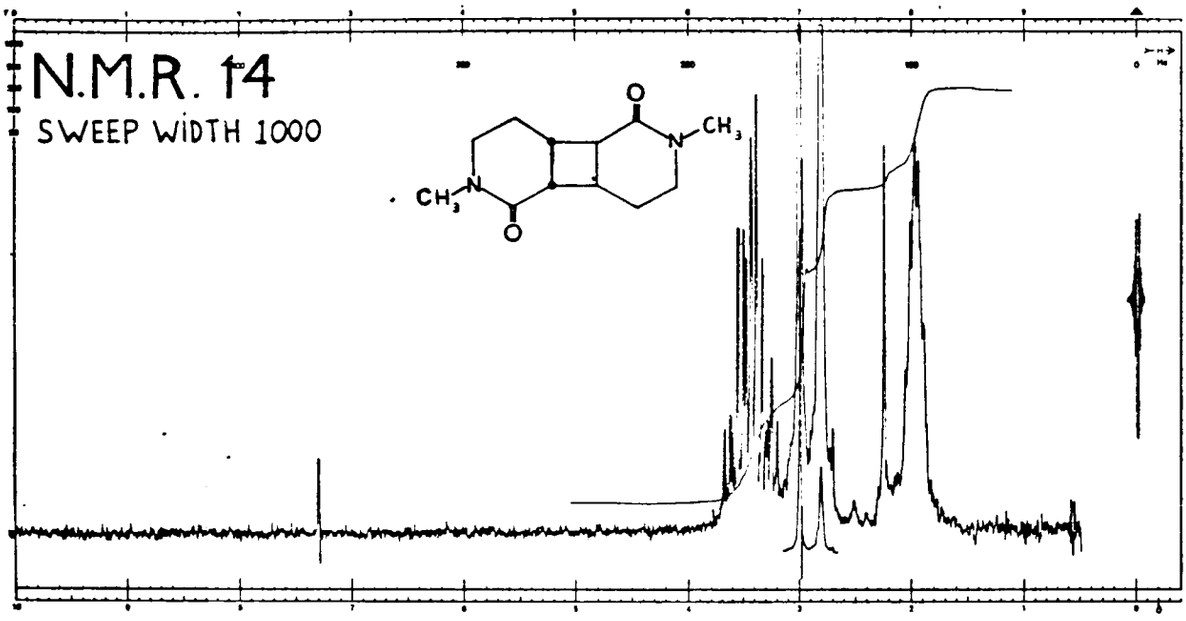

N.M.R. 10A
SWEEP WIDTH 100
SWEEP OFFSET 178

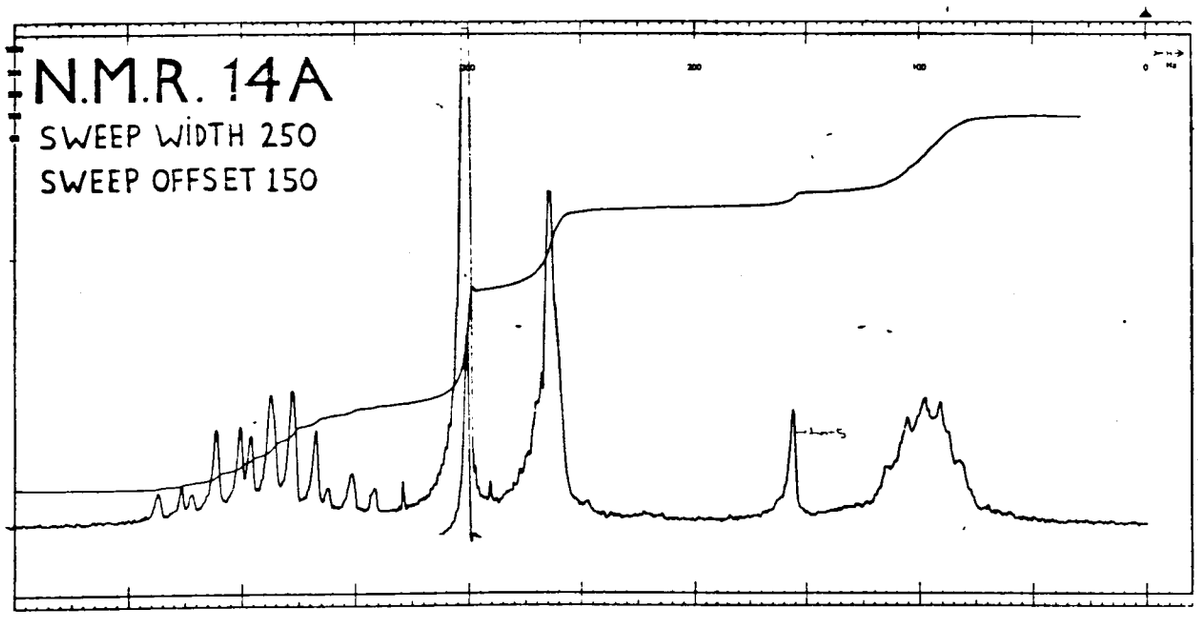

N.M.R. 11
SWEEP WIDTH 500
SWEEP OFFSET 200
HO
N
N
OH


N.M.R. 12
SWEEP WIDTH 1000
O
NH
HN
O


N.M.R. 13
SWEEP WIDTH 1000
H
N
O
HN
O


N.M.R. 15
SWEEP WIDTH 1000
O
N
CH2C6H5
C6H5CH2
N
O


N.M.R. 14
SWEEP WIDTH 1000
O
N
CH3
CH3
N
O


N.M.R. 14A
SWEEP WIDTH 250
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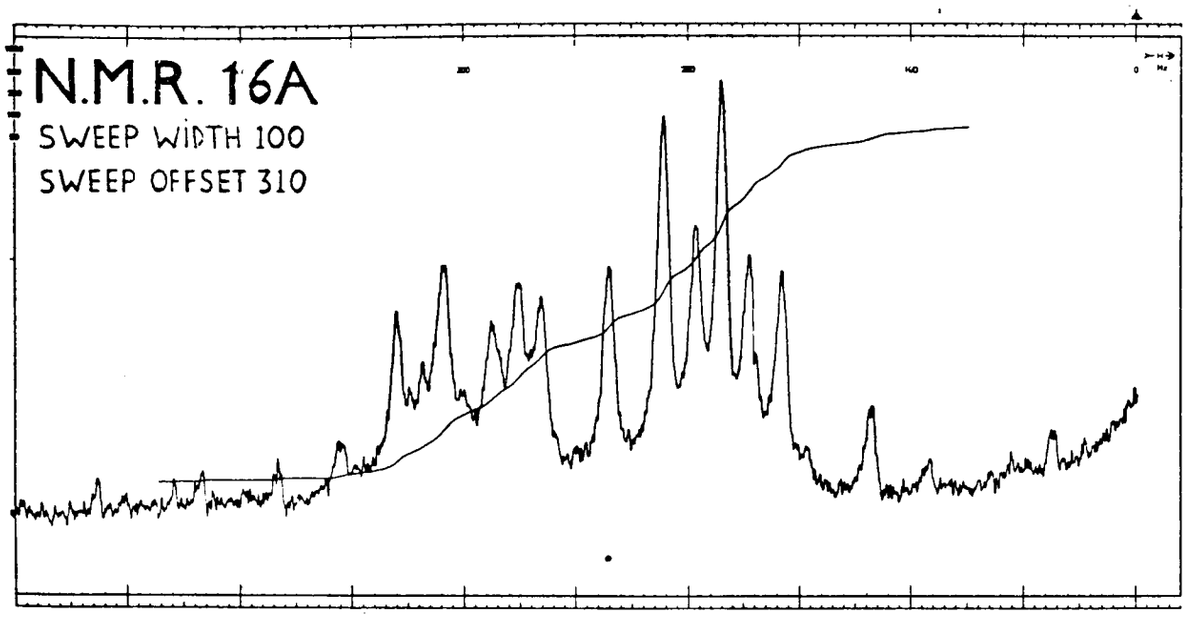
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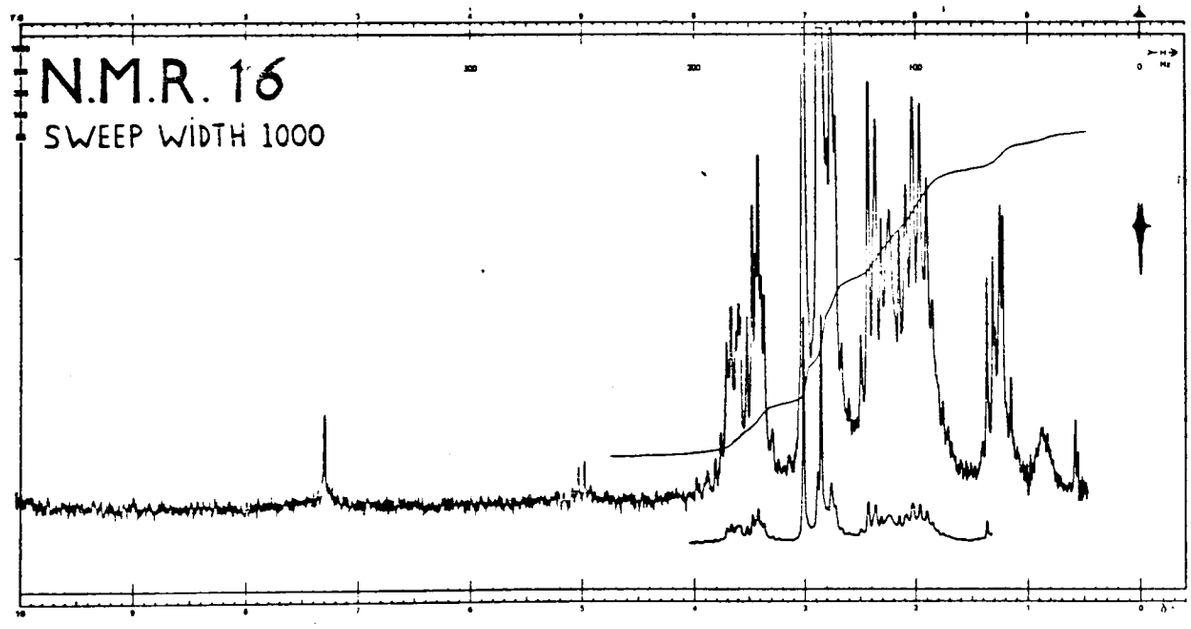
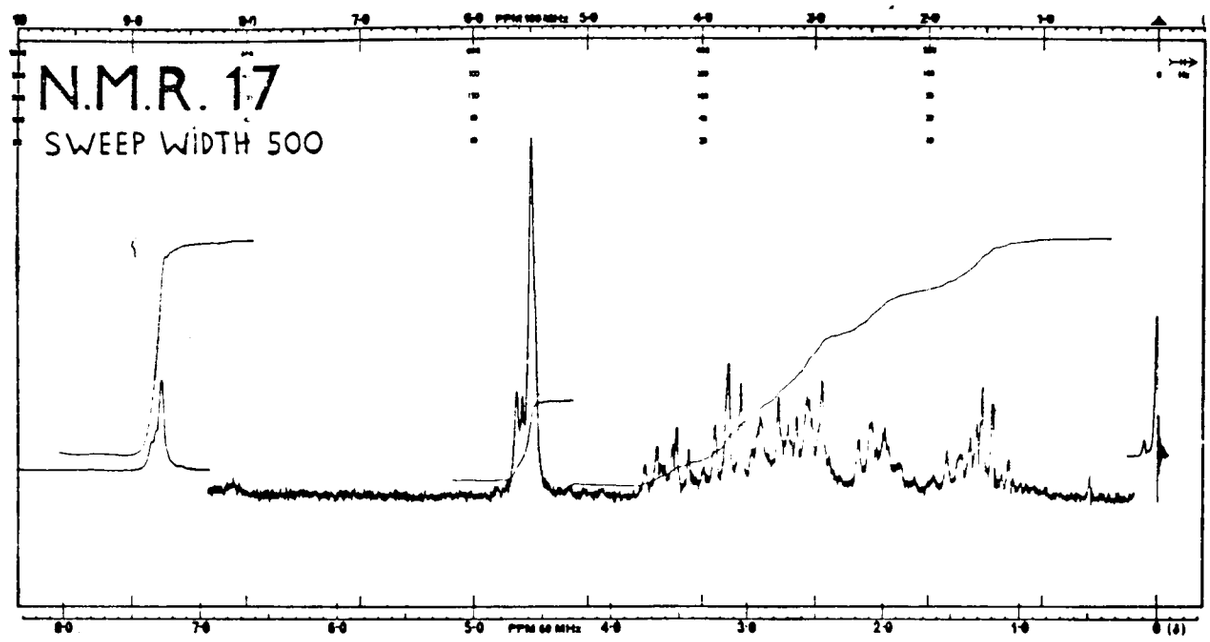
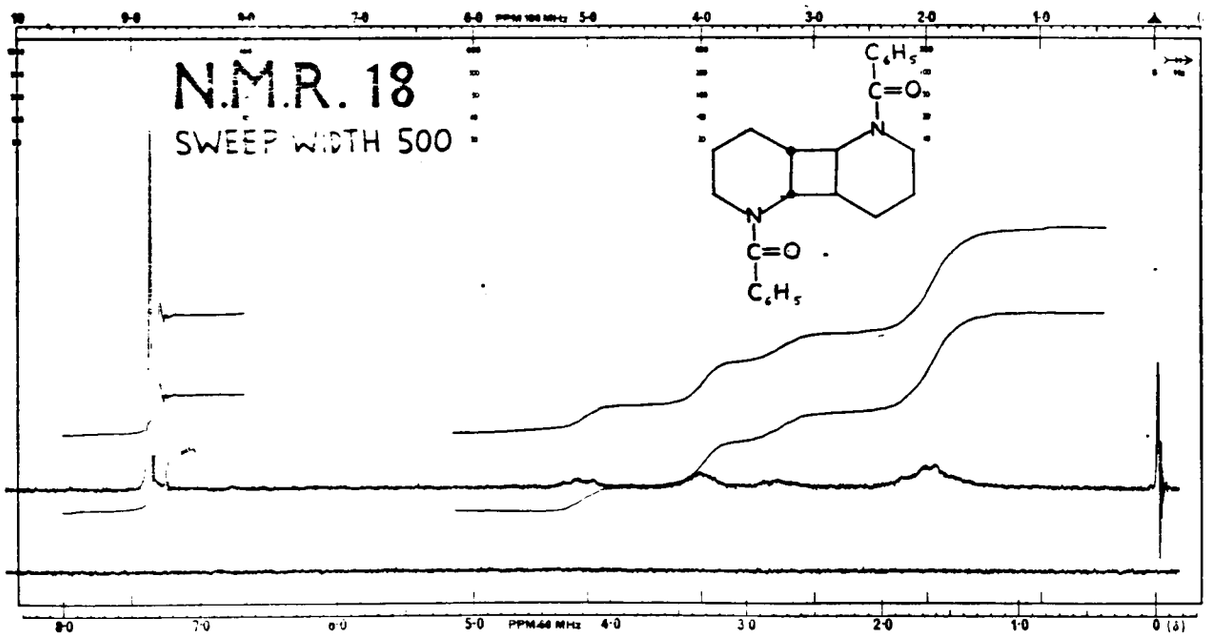
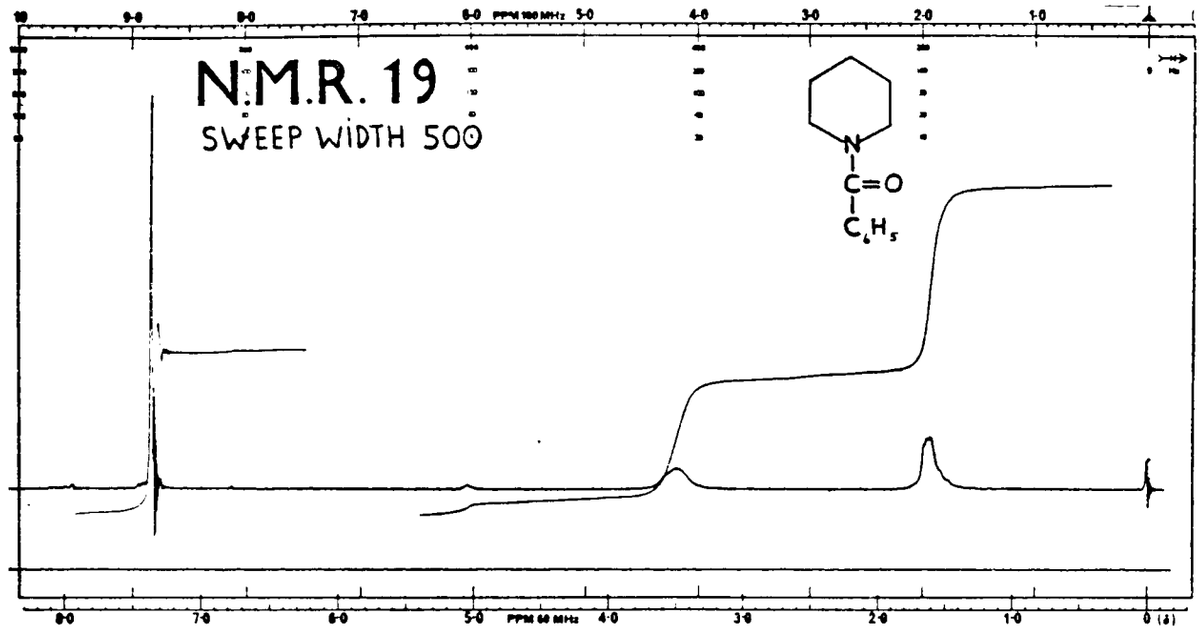
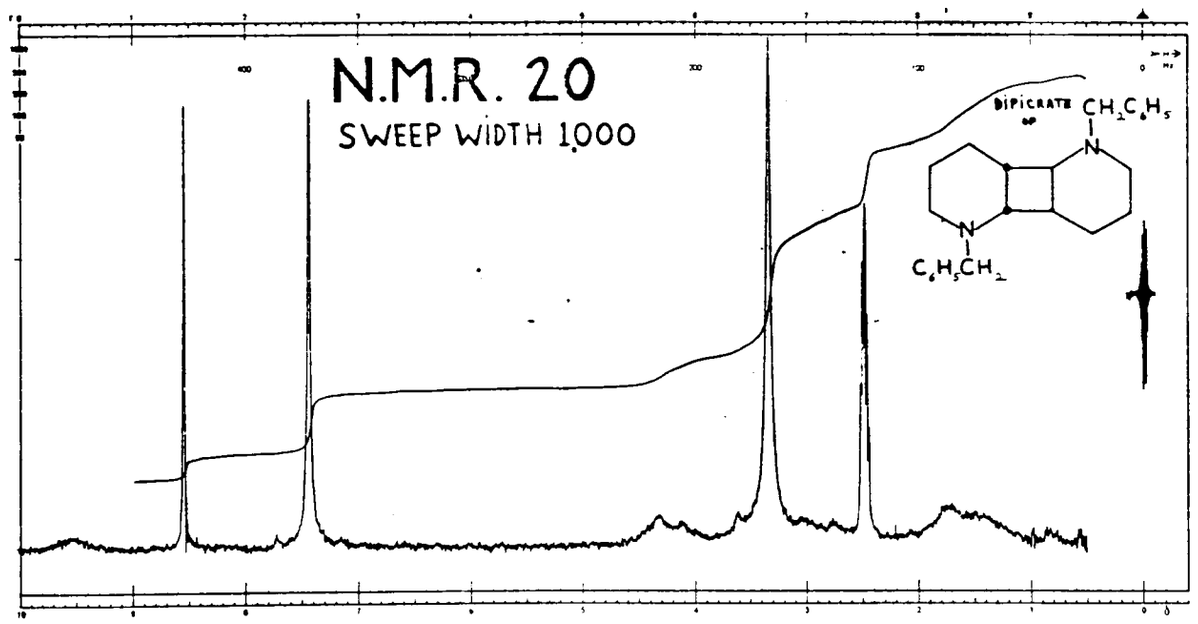
SWEEP OFFSET 310

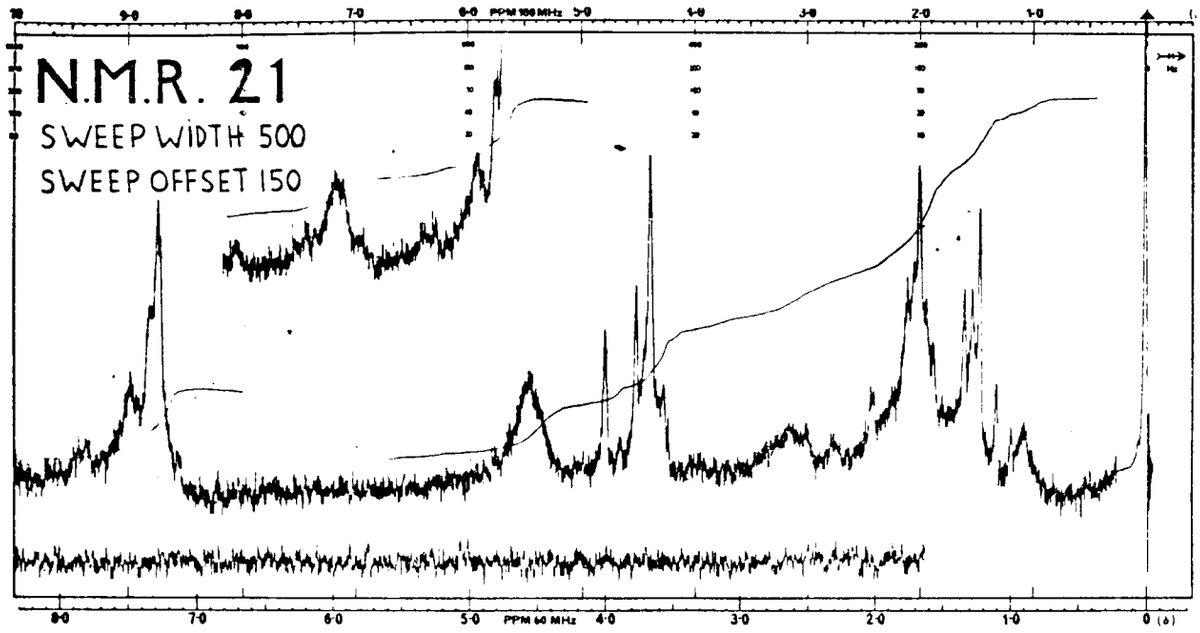

N.M.R. 16
SWEEP WIDTH 1000


N.M.R. 17
SWEEP WIDTH 500


N.M.R. 18
SWEEP WIDTH 500
C6H5
C=O
N
N
C=O
C6H5


N.M.R. 19
SWEEP WIDTH 500
N
C=O
C6H5


N.M.R. 20
SWEEP WIDTH 1000
DIPICRATE
CH2C6H5
N
N
C6H5CH2


N.M.R. 21
SWEEP WIDTH 500
SWEEP OFFSET 150
8·0
7·0
6·0
5·0
PPM 60 MHz
4·0
3·0
2·0
1·0
0 (δ)

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