STUDIES ON NEW AROMATIC SYSTEMS

BY

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TO MY PARENTS

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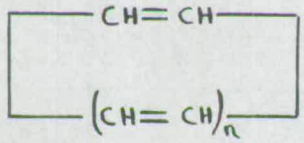
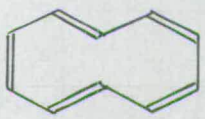
INTRODUCTION

THE ANNULENES

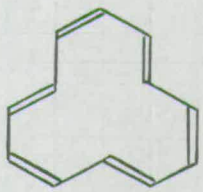
The name annulene was given by Sondheimer[1] to monocyclic hydrocarbons formally constituted of alternating single and double bonds (I), the ring size being indicated by a number in parenthesis. Thus cyclodecapentaene (II) and cyclododecahexaene (III) are known respectively as [10] annulene and [12] annulene.



I



II



III

A study of these compounds together with their dehydro derivatives (in which one or more of the double bonds has been replaced by a triple bond), could provide valuable information regarding present day theories of aromaticity.

Until comparatively recently, aromaticity was equated with benzene-like stability and chemical behaviour. This, however, is unsatisfactory since chemical reactivity is not a property of the molecule in the ground state.[2] A compound is now considered to be aromatic if there is a measurable degree of cyclic delocalisation of the π-electron system in the ground state of the molecule. This will result in a lower energy content than would be predicted from classical considerations, and in carbon-carbon bonds intermediate in length between those usual for single and double bonds. A further consequence of π-electron delocalisation will be the ability to sustain a diamagnetic ring current in an applied magnetic field.[3,4] In the case of annulenes possessing protons both inside and outside the ring, this current will shield the inner protons and deshield the outer protons.

This phenomenon can be investigated by the nuclear magnetic resonance (n.m.r.) spectrum, since in an aromatic annulene the inner protons should appear at unusually high field and the outer ones at unusually low field. At present this is the most convenient way of determining whether or not an annulene is aromatic.

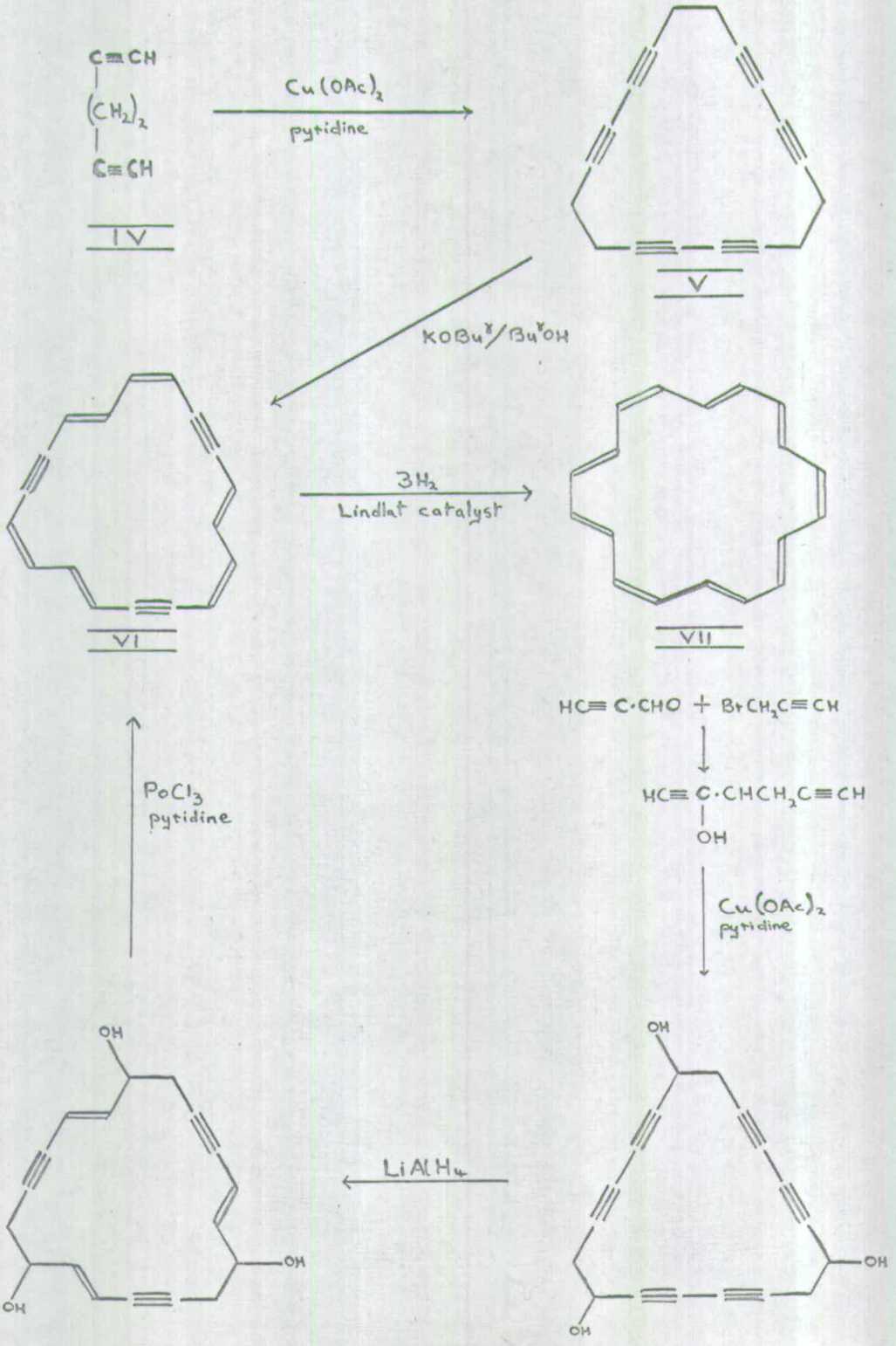
Huckel[5.], in arguments based on quantum mechanical considerations, predicted that an annulene will be aromatic if the carbon skeleton is not seriously distorted from a mean plane and if it contains a closed shell of $(4n + 2)\ \pi$-electrons. Also it has been postulated [6.] that the ring size should be below a certain limit.

Scale drawings of the annulenes [7.] have shown severe steric interference between the internal hydrogen atoms of all annulenes from $C_{10}H_{10}$ to $C_{28}H_{28}$. Such molecules would therefore probably be buckled. However, it has been pointed out[8.] that some compounds are known which are buckled or possess rings with angles distorted from preferred values and yet remain aromatic in character; e.g. di-p-xylylene and di-m-xylylene[9.]. Overcrowded ring systems, such as 3,4 - 5,6 - dibenzophenanthrene[10.], also contain distorted benzene rings. It has been suggested [8.11.] that [18] annulene should be almost, if not completely, planar and should, since it obeys Huckel's rule, show aromatic character.

Many attempts have been made to synthesise annulenes [12-18.], but recently the only known annulene, besides benzene, was cyclooctatetraene ([8] annulene)[19]:

The most successful approach to the synthesis of annulenes has been that of Sondheimer and his co-workers, who used an oxidative coupling of α,ω-diacetylenes as the ring closure step. Sondheimer originally [20.21.] oxidised the acetylenes in aqueous ethanol in the presence of cupric chloride

Figure 1.


C≡CH
(CH2)2
C≡CH
IV
Cu(OAc)2
pyridine
V
KOBu^t/Bu^tOH
VI
3H2
Lindlar catalyst
VII
HC≡C·CHO + BrCH2C≡CH
HC≡C·CHCH2C≡CH
OH
Cu(OAc)2
pyridine
POCl3
pyridine
LiAlH4
OH

and ammonium chloride (Glaser conditions[22.]); but independently he[23.] and Eglinton and Galbraith[24.] discovered an alternative method of cyclisation using copper acetate in pyridine. Sondheimer also discovered that the cyclic poly-ynes obtained in these oxidative coupling reactions, undergo prototropic rearrangement with base[25.], and that the resulting conjugated polyenynes (dehydroannulenes) can be partially hydrogenated to the corresponding annulenes.

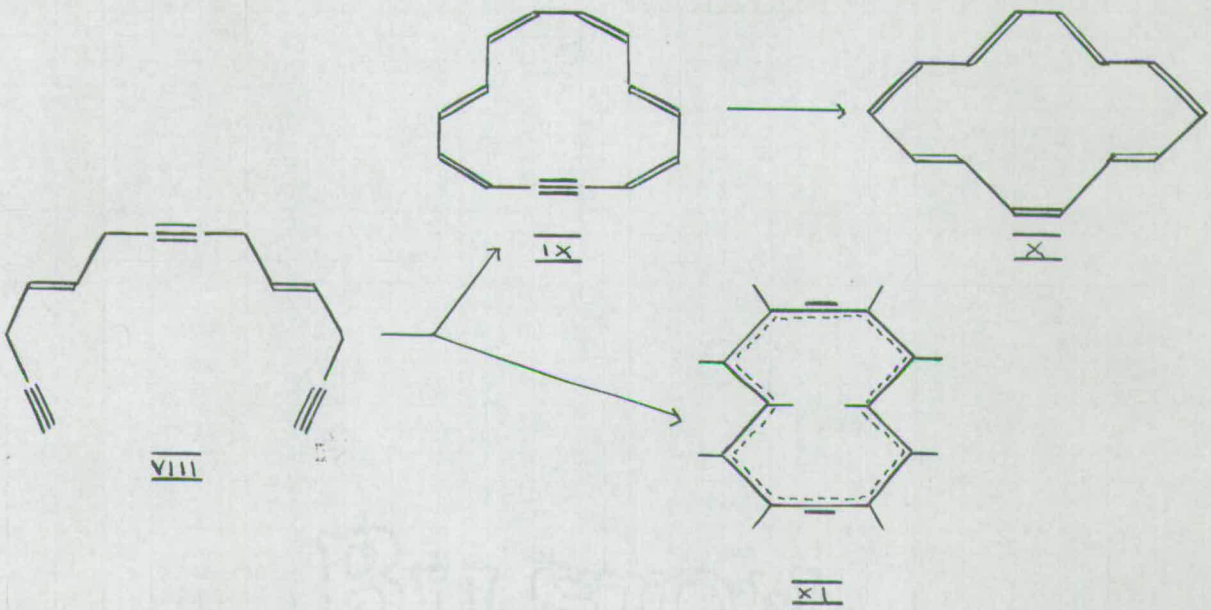
Figure 1. illustrates this series of reactions for the synthesis of [18] annulene (VII). The oxidative coupling of hexa-1,5-diyne (IV)[1.23.] gave the cyclic trimer (V), along with the cyclic tetramer, pentamer, hexamer and heptamer. The trimer (V) was also obtained from hexa-1,5-diyne-3-ol by a similar route[26.]. Treatment of the cyclic trimer with base gave the symmetrical tridehydro [18] annulene (VI), along with an unsymmetrical isomer and a tetradehydro [18] annulene.[1.27.] Partial hydrogenation of these dehydroannulenes gave [18] annulene (VII).[28.29.] [24] Annulene and [30] annulene[1.29.30.31.32.] were prepared by an identical method from the cyclic tetramer and cyclic pentamer respectively.

Similarly the oxidative coupling of deca-1,5,9-triyne[33.] gave a cyclic dimer and a cyclic trimer. These were converted to [20] annulene and [30] annulene respectively.

Sondheimer has also synthesised three systems containing fewer than eighteen carbon atoms.

The coupling of hexa-1,5-diyne under Glaser conditions and immediate treatment with base yielded two dehydro [12] annulenes.[34.] Partial hydrogenation of these dehydroannulenes led to complex mixtures which possibly contain [12] annulene.

Trans - trans - tetradeca - 4,10 - diene - 1,7,13 - diyne (VIII), on oxidation with copper acetate in pyridine and subsequent treatment with base, yielded two conjugated monocyclic compounds.[35] The major product, monodehydro [14] annulene (IX), on partial hydrogenation gave [14] annulene (X). The minor product was shown to be bis - 1,8 - dehydro [14] annulene[36], an unusual aromatic compound which is most conveniently represented by formula (XI).

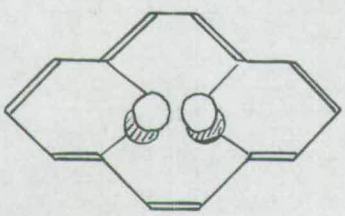


Finally [16] annulene and four isomeric dehydro [16] annulenes were obtained from trans - oct - 4 - ene - 1,7 - diyne by application of the general methods outlined above.[37]

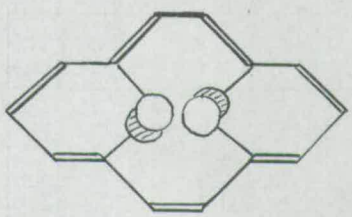
As mentioned previously the n.m.r. spectrum of an annulene may be used to investigate ring current effects, which in turn indicate whether or not there is complete cyclic delocalisation of the π -electrons in the molecule. At -60°, [14] annulene and [18] annulene, both of which comply with Huckel's rule, show n.m.r. spectra[38] typical of aromatic systems, the outer protons appearing at low field (τ 2.4 and 0.72 respectively), and the inner protons at high field (τ 11.00 and 12.99 respectively). At higher temperatures

the n.m.r. spectra[4.35.38.] of both these annulenes consist of singlets (τ 4.42 and 4.45 respectively), the chemical shifts of which represent average values owing to conformational changes, which cause a rapid interchange of protons between inner and outer sites. At room temperature the n.m.r. spectra of [16] annulene[39.] and [24] annulene[4], neither of which comply with Huckel's rule consist of sharp singlets (τ 3.27 and 3.16 respectively). At -110°, the n.m.r. spectrum of [16] annulene[40.] consists of inner proton bands at τ -0.43 and outer proton bands at τ 4.60. Similarly at -80°, the n.m.r. spectrum of [24] annulene[41.] consists of inner proton bands at τ -2.9 to -1.2 and outer proton bands at τ 5.27. It is remarkable that, in the low-temperature n.m.r. spectra of $4n\ \pi$-electron systems, the signals from the inner protons appear at a low field and those from the outer protons at a high field. This is a reversal of the situation found for $(4n + 2)\pi$-electron systems. A similar reversal has been observed in the dehydroannulene series[42.] and an explanation based on quantum-mechanical considerations has been advanced[43.].

It has been noticed that unless the solution of [14] annulene under investigation has been freshly prepared, the n.m.r. spectrum at room temperature shows two singlets at τ 4.42 and τ 3.93 due to the presence of two conformers A and B (XII)[35.]. These differ in the spatial arrangement of the endocyclic hydrogen atoms and from an equilibrium mixture in solution. The conformers have been separated by thin-layer chromatography on kieselguhr coated with silver nitrate. Two unequal neighbouring spots were formed.[44.]



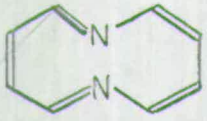
A



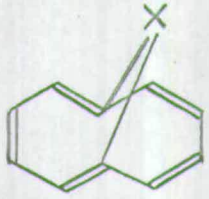
B

XII

Figure 2.

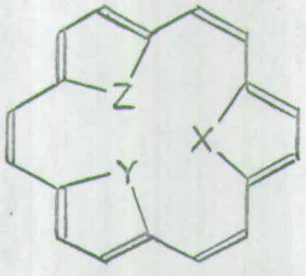


XIII



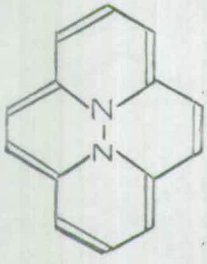
XIV

a: X = O.
b: X = CH_2.
c: X = NH.
d: X = NAc.

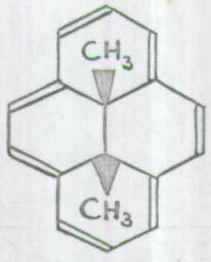


XV

a: X=Y=Z=O.
b: X=Y=O ; Z=S.
c: X=O ; Y=Z=S.
d: X=Y=Z=S.



XVI



XVII

X-ray examination of [14] annulene[45] indicates that the crystalline annulene consists entirely of the centrosymmetric conformer A. A similar investigation of [18] annulene[46] also shows a centrosymmetric molecule, confirming Baker's and Sondheimer's predictions and contradicting that of Coulson and Golebiewski[47].

Although n.m.r. spectra have shown [14] annulene and [18] annulene to be aromatic, the compounds show little classical aromatic behaviour[29,26]. However electrophilic substitution of [18] annulene has recently been achieved with the formation of nitro- and acetyl derivatives.[48]

All annulenes are relatively unstable, owing partly to steric interference between the inner hydrogen atoms, forcing the molecule out of planarity. The following structural modifications have been suggested to avoid steric interference.

(a) Replacement of inwardly pointing C H groups by tervalent atoms such as nitrogen, as in the hypothetical 1, 6 - diazacyclodecapentaene (XIII)[49].

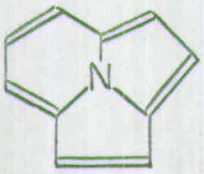
(b) Replacement of inwardly pointing hydrogen atoms by a bridge structure, as in the [10] annulene derivatives (XIV a - d).[50-55].

(c) Replacement of pairs of hydrogen atoms by divalent atoms such as oxygen and sulphur, as in the [18] annulene derivatives (XV a - d)[56-59]

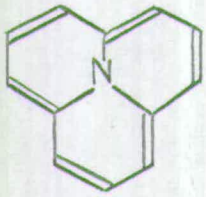
(d) Replacement of two pairs of hydrogen atoms by one pair of tervalent atoms as in 10b, 10c - diazapyrene[60]. (XVI); or by one pair of tetravalent carbon atoms as in trans - 15, 16 - dimethyl - 15, 16 - dihydropyrene (XVII)[61].

(e) Replacement of three internal hydrogen atoms by one tervalent atom such as nitrogen, as in the cyclazines.

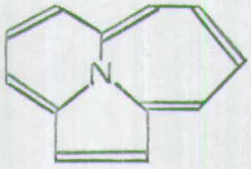
Figure 3.



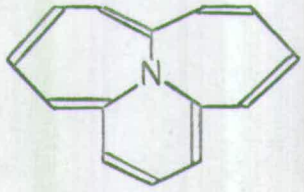
XVIII



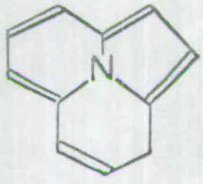
XIX



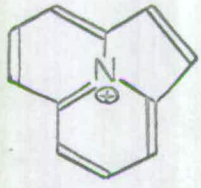
XX



XXI



XXII



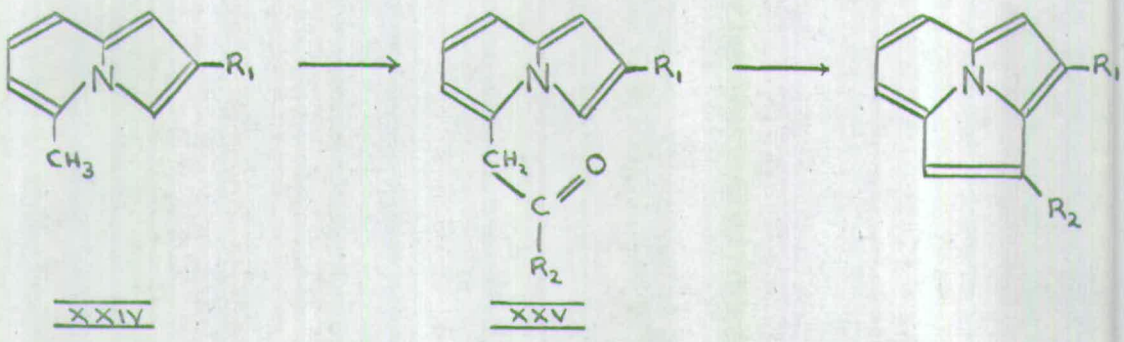
XXIII

THE CYCLAZINES

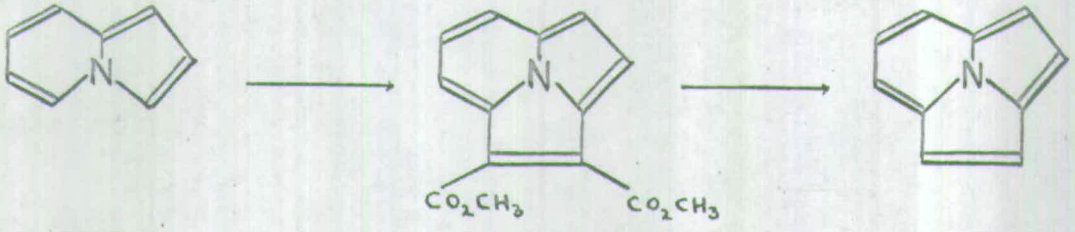
The name cyclazine was proposed by Boekelheide[62.] for the general case of a fully conjugated ring held planar by three covalent bonds to an internal nitrogen atom. The individual members are distinguished by placing, in brackets, numerals corresponding to the number of atoms on the peripheral cycle between points of bonding to the internal nitrogen atom. Thus in this scheme structure (XVIII) becomes cycl [3,2,2] azine; (XIX) becomes cycl [3,3,3] azine; (XX) becomes cycl [4,3,2] azine; and (XXI) becomes cycl [4,4,3] azine. This system also accommodates such structures as (XXII) 3H - cycl [3,3,2] azine and (XXIII) the dehydrocycl [3,3,2] azinium ion.

Boekelheide and his co-workers have synthesised cycl [3,2,2] azine and some of its derivatives by two distinct methods. The first method[62.] involved the treatment of 5-methylindolizine (XXIV) with n-butyllithium to give the 5-lithiomethylindolizine. Subsequent reaction with a N.N - dimethylamide followed by hydrolysis gave either an aldehyde or a ketone (XXV). Cyclodehydration then gave cycl [3,2,2] azine or its phenyl substituted derivatives. The second synthesis[63,64.] utilised the reactivity of dimethyl acetylenedicarboxylate as a dipolarophile. When indolizine (XXVI) was treated with dimethyl acetylenedicarboxylate in boiling toluene using 5% palladium on charcoal as a dehydrogenation catalyst, 1,2 - dimethoxycarbonylcycl [3,2,2] azine (XXVII) was obtained. Subsequent hydrolysis and decarboxylation gave cycl [3,2,2] azine. Similar reactions of indolizine with methyl propiolate or methyl phenylpropiolate gave the cyclazine and its 2-phenyl derivative respectively.

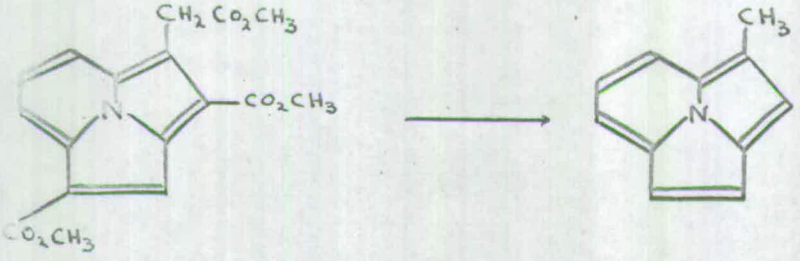
Figure 4.



XXIV XXV



XXVI XXVII XVIII

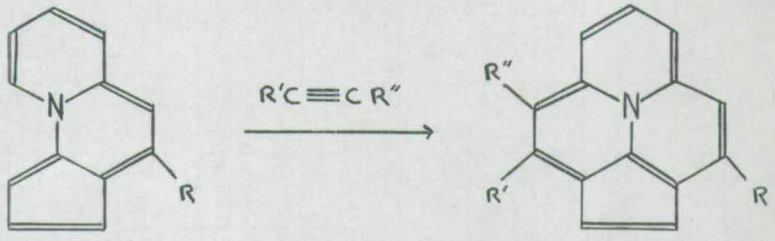


XXVIII XXIX

More recently Acheson and Robinson[65] investigated the reaction of pyridine and methyl propiolate in acetonitrile. The cyclazine (XXVIII) was the sole product isolable and hydrolysis followed by decarboxylation gave 1 - methylcycl [3,2,2] azine (XXIX).

Cycl [3,2,2] azine is an analogue of [10]annulene and is therefore the first example of a large conjugated carbocycle held planar by bonding to an internal atom. The molecule is stable to heat and light[66], non basic, and undergoes electrophilic substitution, though attempts to induce the molecule to undergo nucleophilic substitution have been unsuccessful. Hanson[67] has shown by X-ray studies that the molecule of 1,4-dibromocycl [3,2,2] azine is nearly planar; in particular the group consisting of the nitrogen atom and its three bonded carbon atoms shows no significant departure from planarity. N.m.r. spectroscopy [68] has shown that the protons of cycl [3,2,2] azine show chemical shifts in the region normally attributed to aromatic protons.

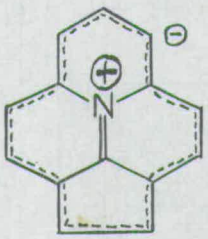
The calculations carried out for cycl [3,3,3] azine[62] predict a high resonance energy, perhaps larger than that of cycl [3,2,2,] azine, despite the fact that it does not conform to the Huckel rule. Many attempts have been made to synthesise cycl [3,3,3] azine but until recently decahydrocycl [3,3,3] azine[69] was the only known derivative of this compound.



XXXI XXX

Derivatives of cyclopenta [cd] cycl [3,3,3] azine (XXX)[70] have been prepared by the reaction of cyclopenta [c] quinolizines (XXXI) with electrophilic

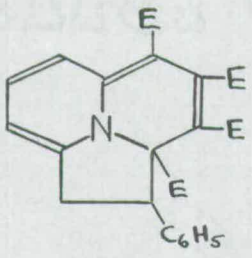
acetylenes in an oxidising solvent. N.m.r. studies show that the nuclear protons absorb at rather a high field for aromatic systems, and this may be evidence for a high electron-density perimeter. The fact that the 1 and 2 protons show relatively low τ-values further suggests that the ring current pathway includes carbon atoms 1 and 2. Boekelheide [71.] has suggested that these compounds are not truly cycl [3,3,3] azine in character but are more truly represented as (XXXII), but this is highly speculative.



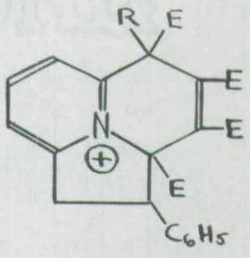
XXXII

A diethoxycarbonyl derivative of cycl [3,3,3] azine has recently been prepared by Mr. D. Farquhar in this department. The n.m.r. spectrum indicates that the compound is polyolefinic rather than aromatic.

Acheson, investigating the adducts from 2 - styrylpyridine and dimethyl acetylenedicarboxylate [72.] has identified the "second stable adduct" as the cycl [3,3,2] azine (XXXIII).



XXXIII

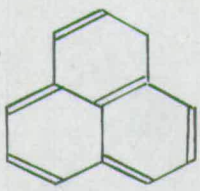


XXXIV

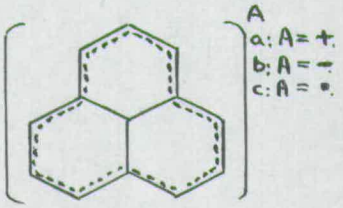
The cyclazine (XXXIII) with strong acids protonates mainly at position -1, yielding the cation (XXXIV, R = H), and with nitric acid gives the nitrate of the cation (XXXIV, R = OH). The "second stable adduct" appears to be the first compound recognised, containing the cycl [3,3,2] ring system.

2 H - BENZ [c d] AZULENE

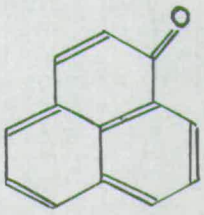
Phenalene (XXXV) is a hydrocarbon of some interest since calculations[74.] predict that the carbonium ion (XXXVIa), carbanion (XXXVIb), and free radical (XXXVIc) derived from phenalene should all possess the same value of the π-electron delocalisation energy.



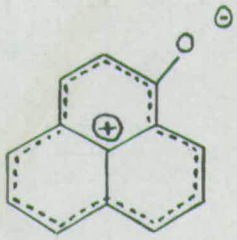
XXXV



XXXVI



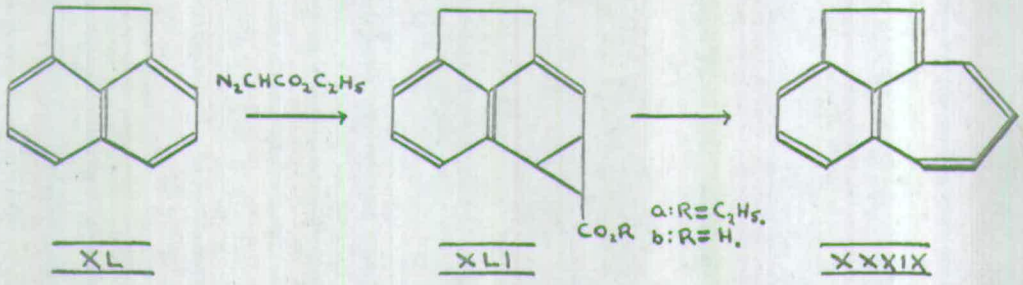
XXXVII



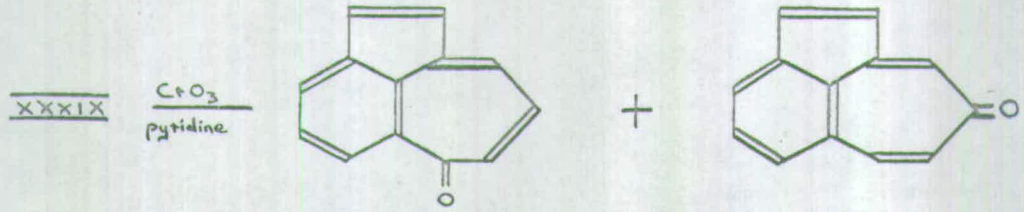
XXXVIII

The explanation for this behaviour is that phenalene, being an odd-alternant hydrocarbon, has a non-bonding orbital in which can be placed zero, one or two electrons (corresponding to carbonium ion, radical and anion), without causing a significant change in the delocalisation energy. The anion (XXXVIb) has not been isolated although its existence in solution has been well established.[75.] The radical, phenalenyl (XXXVIc), has been prepared[76.] but can only be kept in solution under nitrogen. The cation (XXXVIa), however, has been isolated in the form of its perchlorate salt.[73.] The latter reacts with water to give phenalene and phenalenone (XXXVII), probably due to the disproportionation of the alcohol formed on hydrolysis of the salt. The reaction of phenalenium perchlorate with zinc dust yields dibenz [c d,l m] perylene (peropyrene) and the same hydrocarbon is formed when phenalenyl is heated in benzene. Phenalenyl reacts with iodine in benzene, and the dark green product is currently being investigated in connection with its possible relationship to the phenalenium cation. The corresponding ketone, phenalenone (XXXVII), is a stable compound whose unusual basicity is attributed to the formation of a hydroxyphenalenium ion by protonation on the carbonyl oxygen atom.

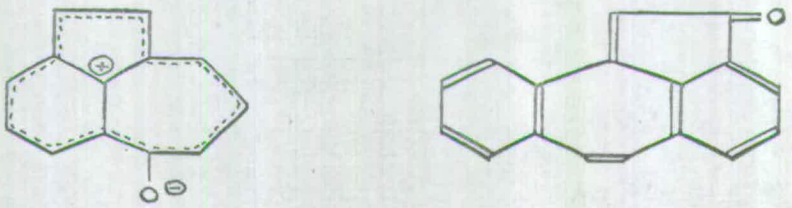
Figure 5.



XL XLI XXXIX



XXXIX XLII XLIII



XLIV XLV

The canonical structure (XXXVIII) is considered to make an important contribution to resonance in phenalenone.

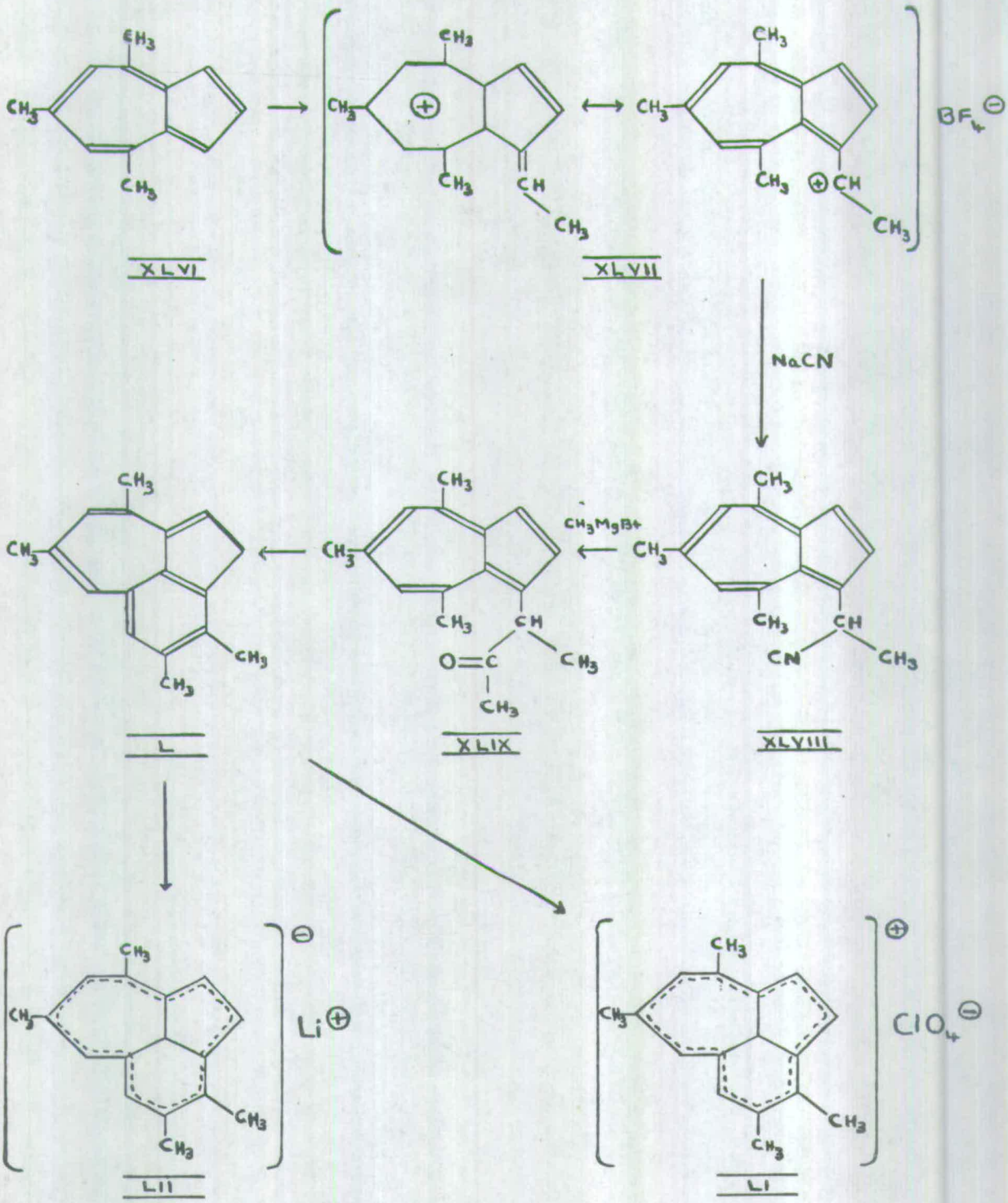
The ions or radical derived from phenalene, however, have a high degree of symmetry, and the question of the degree to which symmetry plays a role in stablising these species is a pertinent one. Interest has therefore been focussed on derivatives of the isomeric benz [cd] azulene (e.g. XXXIX) an odd-nonalternant hydrocarbon with a lower degree of symmetry. Calculations predict that the properties of this compound should be similar, qualitatively, to those of phenalene.

2 H - Benz [cd] azulene (XXXIX) was synthesised by Boekelheide[77] by the reaction of acenaphthene (XL) with ethyl diazoacetate. The adduct (XLIa) was isolated from other products and hydrolysed to the acid (XLI b), Treatment with bromine followed directly by aqueous sodium acetate led to the formation of (XXXIX). 2 H - Benz [cd] azulene could not be isolated in the pure state so studies were limited to its behaviour in solution. 2 H - Benz [cd] azulene is much more prone to polymerisation than phenalene but its conversion to carbonium ion, carbanion and radical occurred as predicted although no pure products could be isolated.

It was predicted that carbonyl derivatives of 2 H - benz [cd] azulene would show similar behaviour to phenalenone (XXXVII). Oxidation of 2 H - benz [cd] azulene gave two ketones, the red crystalline benz [cd] azulen-6-one (XLII) and the yellow benz [cd] azulen - 8 - one (XLIII). These benz [cd] azulenones are readily soluble in strong acid and are regenerated by the addition of base. Although no dipole measurements were taken, the prediction that dipolar structures such as (XLIV) make an important contribution to the resonance hybrid appears well justified.

2 H - Dibenz [cdh] azulen - 2 - one (XLV) has also been prepared[78] and can be converted via the alcohol to crystalline derivatives of the dibenz [cdh] azulenium cation.

Figure 6.

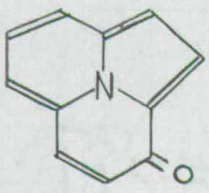

XLVI
XLVII
XLVIII
XLIX
L
LI
LII
NaCN
CH_3MgBr
$BF_4^\ominus$
$ClO_4^\ominus$
$Li^\oplus$

Derivatives of 2 H - benz[cd] azulene were also prepared by Hafner and Schaum[79]. 4,6,8 - Trimethylazulene (XLVI) condensed with acetaldehyde in the presence of fluoboric acid to give the fluoborate (XLVII), which with sodium cyanide gave the nitrile (XLVIII). This was converted to the ketone (XLIX) which reacted with sodium N-methylanilide to give 3,4,7,9 - tetramethyl - 2 H - benz [cd] azulene (L). Hydride ion abstraction with trityl perchlorate gave a stable carbonium salt (LI) which contains a 12 π - electron system, while proton abstraction with strong base formed the anionic system (LII), containing 14 π -electrons.

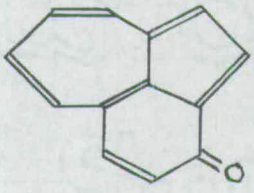
OBJECT OF RESEARCH

The object of this research was to synthesise, from indolizines, derivatives of cycl [3,3,2] azin - 3 - one (LIII). The latter is related to the parent compound (XXII) in the same way as tropolone is related to cycloheptatriene.

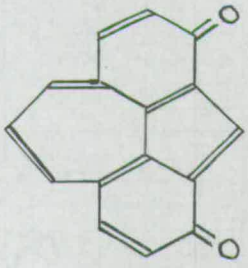
By making use of the well known chemical relationship between indolizines and azulenes[80]. it was thought that analogous reactions would lead to derivatives of benz [cd] azulen - 3 - one (LIV) and the quinone (LV) of cyclohepta [def] fluorene. Cyclohepta [def] fluorene is a hypothetical hydrocarbon for which a triplet ground state or low lying triplet excited state has been predicted.[81]. Attempts to synthesise the compound have been unsuccessful.[82].



LIII



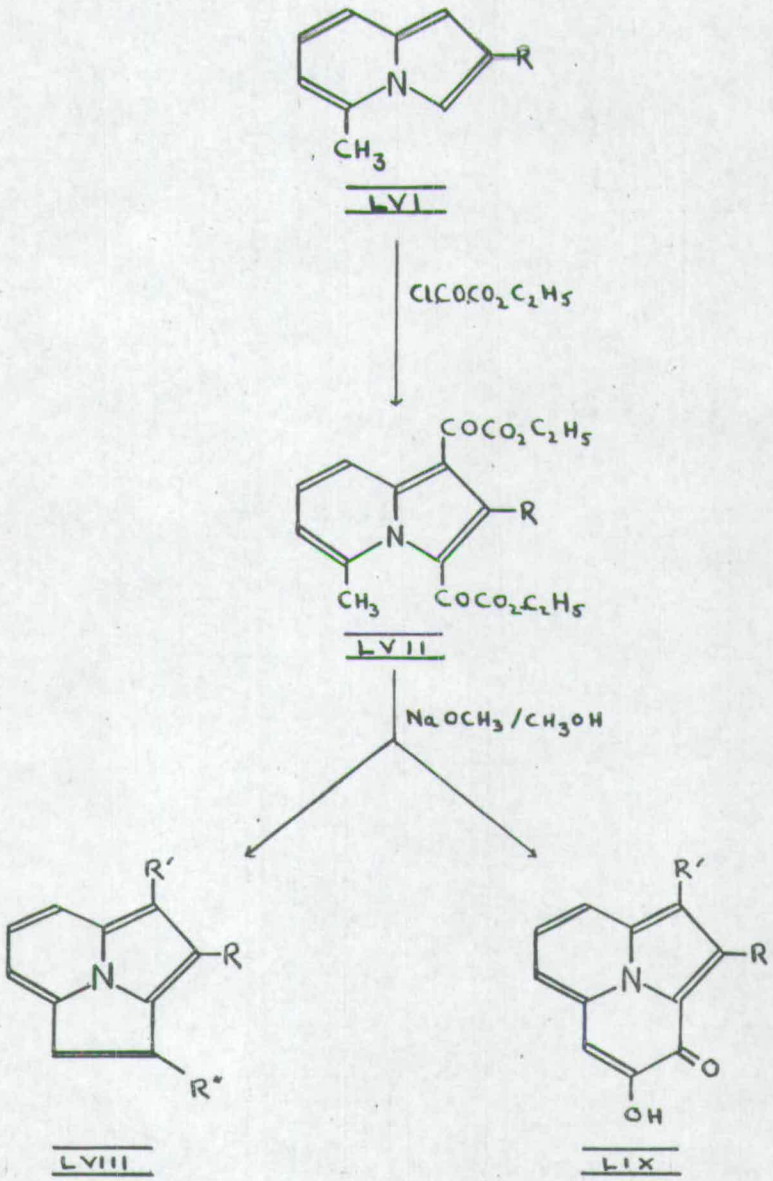
LIV



LV

DISCUSSION

Figure 7.


R
N
CH3
LVI
ClCOCO2C2H5
COCO2C2H5
R
N
CH3
COCO2C2H5
LVII
NaOCH3/CH3OH
R'
R
N
R"
LVIII
R'
R
N
O
OH
LIX

The synthesis of derivatives of 3H - cycl [3,3,2] azin - 3 - one:

Much experimental work has been done on the acylation of indolizines,[83] all of which indicates that substitution occurs initially in the 3-position of the nucleus, a second group entering into the 1-position should conditions be severe enough. Boekelheide, in his synthesis of cycl [3,2,2] azine,[62] found that a methyl group in the 5-position of indolizine is acidic and comparable in activity to that in ∝-picoline. It was the intention, therefore, in this investigation to acylate a suitable 5-methylindolizine with groups that would readily cyclise with the 5-methyl group, under basic conditions, to give a cycl [3,3,2] azin-3-one.

Leaver and Gibson[84] reacted 5-methyl-2 phenylindolizine (LVI, R = C_6H_5) with ethoxalyl chloride, to give the 1,3 - diethoxalyl derivative (LVII, R=C_6H_5). Heating this compound with sodium ethoxide in ethanol converted it partly to the ethanol- soluble cycl [3,2,2] azine (LVIII, R = C_6H_5, R′= $COCO_2C_2H_5$, R″= $CO_2C_2H_5$), and partly to the insoluble sodium salt of the hydroxycycl- [3,3,2] azinone (LIX, R = C_6H_5, R′= $COCO_2C_2H_5$). Standard procedures of hydrolysis, decarbonylation, and decarboxylation were then used to convert the former product into 2 - phenylcycl [3,2,2] azine (LVIII, R = C_6H_5, R′= R″= H), identical with an authentic sample, and the latter into 4-hydroxy-2-phenyl-3H-cycl [3,3,2] azin - 3 - one (LIX, R = C_6H_5, R′= H).

However, for the purpose of n.m.r. spectroscopy it was desirable to obtain the 2 - methyl derivative (LIX, R = CH_3, R′= H), and it seemed reasonable to expect that this compound could be obtained by an identical method.

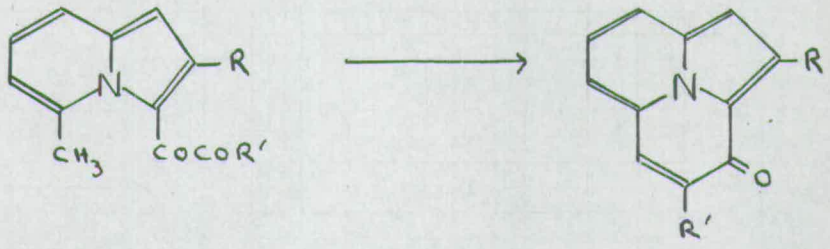
Treatment of 2,5 - dimethylindolizine (LVI, R = CH_3)[85] with ethoxalyl chloride gave 1,3-diethoxalyl - 2,5 - dimethylindolizine (LVII, R = CH_3). Cyclisation with sodium methoxide in dry methanol gave two products, namely, 1-methoxalyl - 3 - methoxycarbonyl - 2 - methylcycl [3,2,2] azine (LVIII, R = CH_3, R′= $COCO_2CH_3$, R″= CO_2CH_3), and 4 - hydroxy - 1 - methoxalyl-2-methyl -

3H-cycl-[3,3,2]azin - 3 - one (LIX, R = CH_3, R′= $COCO_2CH_3$). Clearly both products had undergone ester-exchange reactions with the solvent. Their ultraviolet spectra were similar to the spectra obtained by Leaver and Gibson for the corresponding 2-phenyl derivatives. The methoxalyl compound (LIX, R = CH_3, R′= $COCO_2CH_3$) was hydrolysed by alkali to the oxalyl compound (LIX, R = CH_3, R′= $COCO_2H$), which on treatment with alkaline hydrogen peroxide gave 4 - hydroxy - 2 - methyl - 3 - oxo - 3H - cycl[3,3,2]azin - 1 - carboxylic acid (LIX, R = CH_3, R′= COOH). In the preparation of 4 - hydroxy - 2 - phenyl - 3H - cycl[3,3,2]azin - 3 - one, it was pointed out that the carboxylic acid (LIX, R = C_6H_5, R′= COOH) was structurally related to tropolone -α- carboxylic acid which may be decarboxylated by heating at its melting point. Similarly when the carboxylic acid (LIX, R = C_6H_5, R′= COOH) was sublimed at 0.03 m.m., it lost carbon dioxide smoothly to give compound (LIX, R = C_6H_5, R′= H). However, the melting point of the acid (LIX, R = CH_3, R′= COO H) is greater than 360° and rapid decomposition occurred when the acid was heated at 0.03 m.m., so that a poor yield of the hydroxycyclazinone was obtained.

As expected this compound showed evidence of aromatic character. In the n.m.r. spectrum all the ring protons appeared as a multiplet (relative intensity 5) between τ 2.1 and 3.1 in the region normally attributed to aromatic protons. The hydroxylic proton gave a sharp peak (relative intensity 1) at τ 2.25 which disappeared when the solution was shaken with deuterium oxide, and the methyl protons gave a singlet (relative intensity 3) at τ 7.05. The infrared spectrum showed absorptions characteristic of a hydrogen-bonded hydroxyl group (3300 $cm.^{-1}$) and of a highly polarised carbonyl group (1590 $cm.^{-1}$).

To summarise 4 - hydroxy - 2 - methyl - 3H - cycl[3,3,2]azin - 3 - one has been synthesised but only in a very small yield. It possesses aromatic character and stability and shows some similarity to tropolone, possessing an acidic hydroxylic proton.

In a second approach to the synthesis of derivatives of 3H - cycl [3,3,2] azin - 3 - one, the possibility of preparing compounds, such as the 3-pyruvoylindolizine (LX, $R' = CH_3$) and the 3-phenylglyoxyloylindolizine (LX, $R' = C_6H_5$), was investigated.



LX LXI

It was hoped that, if these compounds could be prepared, subsequent cyclisation would give, respectively, the 4-methylcyclazinone (LXI, $R' = CH_3$), and the 4 - phenyl-cyclazinone (LXI, $R' = C_6H_5$).

It has been reported[86] that the reaction of pyruvic acid with thionyl chloride gives pyruvoyl chloride along with a large proportion of other products. This reaction was repeated but pyruvoyl chloride could not be isolated. A similar report [87] describes the preparation of phenylglyoxyloyl chloride by the reaction of benzoylformic acid[88] with oxalyl chloride. Repetition of this experiment gave mainly benzoyl chloride; the phenylglyoxyloyl chloride is probably formed but under the experimental conditions loses carbon monoxide.

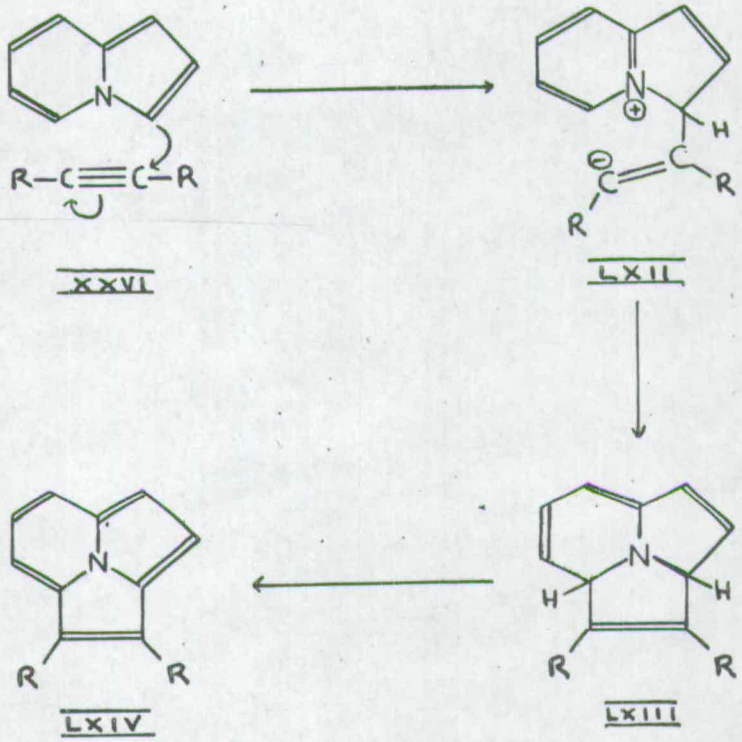
A convenient method of converting an amine hydrobromide (- NH_2,H Br) to the pyruvamide (- $NHCOCOCH_3$) has recently been described[89]. Treatment of the hydrobromide with a mixture of phosphoryl chloride and pyruvic acid in the presence of triethylamine proved to be a very efficient acylation procedure. It was thought that a similar reaction with a 5 - methylindolizine might lead to the 3 - pyruvoyl derivative. Addition of phosphoryl chloride to a cooled solution of 5 - methyl - 2 phenylindolizine and pyruvic acid, in the presence of triethylamine, gave 5 - methyl - 2 phenyl-3-pyruvoylindolizine (LX, $R = C_6H_5$, $R' = CH_3$). Attempts to prepare the 3-phenylglyoxyloyl derivative

by a similar method using benzoylformic acid, gave a tar from which no definite compound could be isolated. The treatment of 2,5-dimethylindolizine with pyruvic acid and phosphoryl chloride in the presence of triethylamine gave a mixture of the 1- and 3- monopyruvoyl isomers. The orientation of the pyruvoylindolizines was established by comparing their n.m.r. spectra with the n.m.r. spectra of the two monoethoxalyl derivatives of 5-methyl-2-phenylindolizine, the orientation of which was known from ultraviolet studies. The n.m.r. spectrum of 1-ethoxalyl-5-methyl-2-phenylindolizine showed a low-field doublet at τ 1.60 (J = 8 c.p.s.) attributed to the deshielding of the 8-proton by the 1-ethoxalyl group. Only the n.m.r. spectrum of the major product from the 2,5-dimethylindolizine reaction showed a low-field doublet (τ 1.90; J = 8 c.p.s.) and this was attributed to the deshielding of the 8 - proton by the 1 - pyruvoyl group. There seems no obvious explanation for the preferred substitution in the 1 - position in this case.

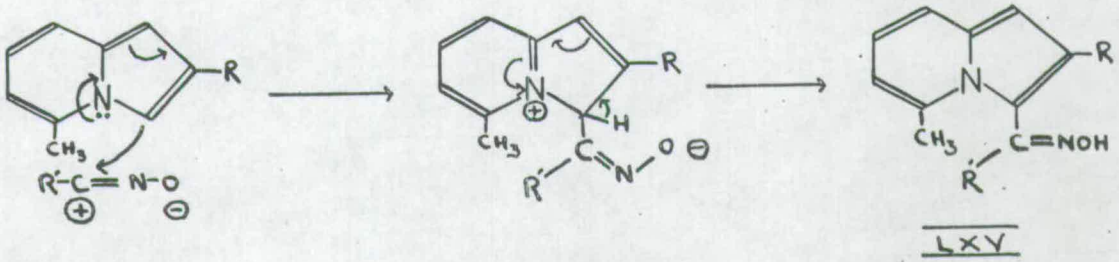
Treatment of 5-methyl-2-phenyl-3 pyruvoylindolizine (LX, R = C_6H_5, R' = CH_3) with sodium methoxide in dry methanol gave a small amount of 4-methyl-2-phenyl-3H-cycl [3,3,2] azin-3-one (LXI, R = C_6H_5, R' = CH_3); a large amount of starting material was recovered.

The cyclazinone (LXI, R = C_6H_5, R' = CH_3) was an orange crystalline compound and as expected showed evidence of aromatic character. Its n.m.r. spectrum showed a complex but well resolved multiplet in the region τ 1.8 - 2.8 (relative intensity 10) and a doublet (J = 1 c.p.s.) at 7.6 (relative intensity 3) due to the 4 - methyl group. The pattern of peaks in the aromatic region was very similar to that shown by the 4 - hydroxy compound (LIX, R = C_6H_5, R' = H). The infrared spectrum showed an absorption characteristic of a highly polarised carbonyl group (1603 $cm.^{-1}$). This value is a little higher than that found for the corresponding 4 - hydroxy compound (1590 $cm.^{-1}$) in which the frequency is probably lowered by intramolecular hydrogen bonding.

Figure 8.



XXVI LXII LXIII LXIV

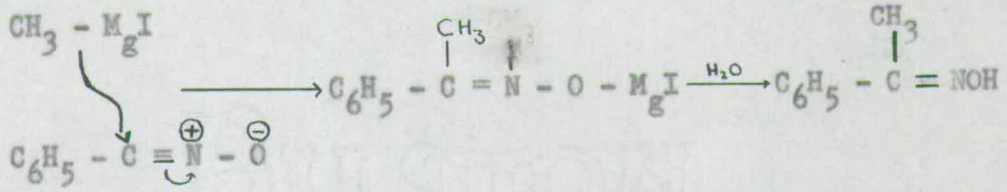


LXV

In a final approach to the synthesis of 3H-cycl [3,3,2] azin - 3 - ones, the reactions between various nitrile oxides and indolizines were studied.

The reactions of acetylenic esters with indolizines in the presence of a dehydrogenation catalyst to give derivatives of cycl [3,2,2] azine have already been mentioned. The first step is presumably a nucleophilic attack on the activated triple bond to give intermediates such as (LXII). These on cyclisation would lead to compounds such as (LXIII) which, on dehydrogenation, would give the observed products (LXIV).

In the past the study of the addition reactions of nitrile oxides has centred mainly on the 1,3-dipolar cycloadditions with unsaturated compounds. Nitrile oxides also undergo 1,3 addition reactions and Wieland[90] obtained acetophenone oxime from the reaction of benzonitrile oxide with methyl magnesium iodide.

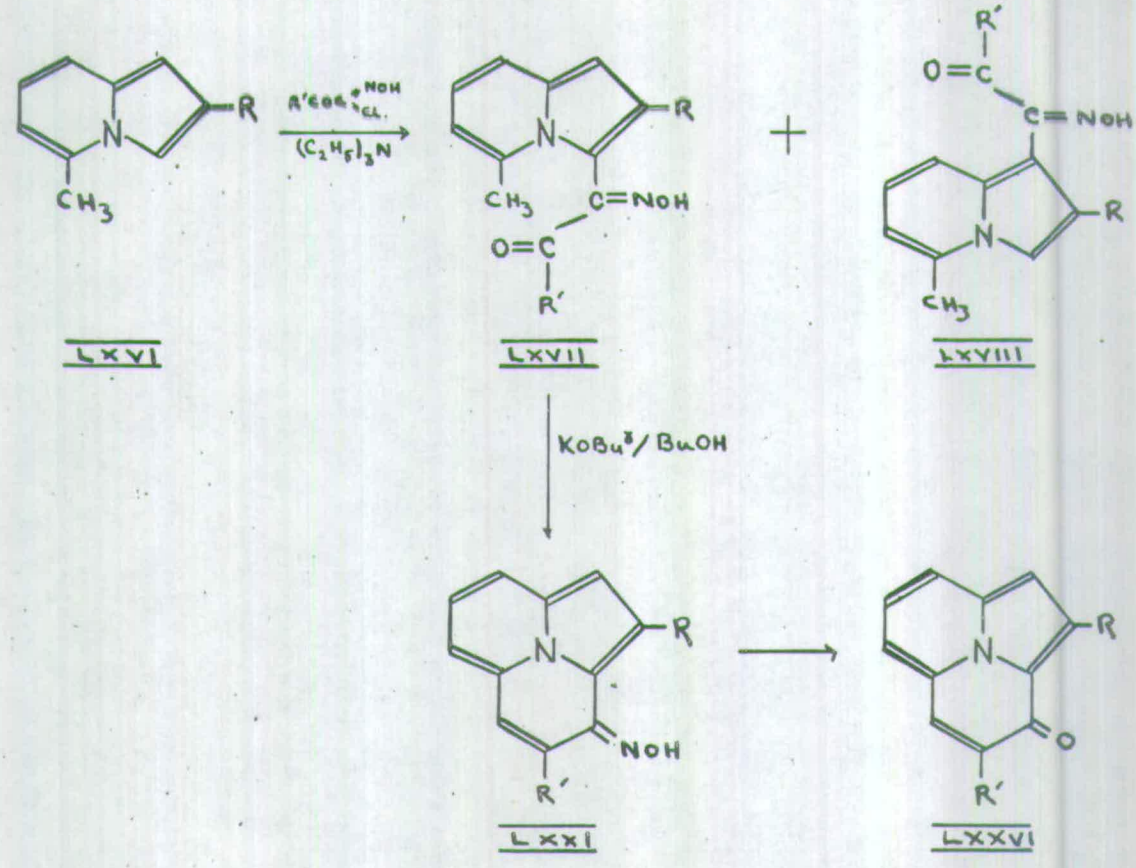


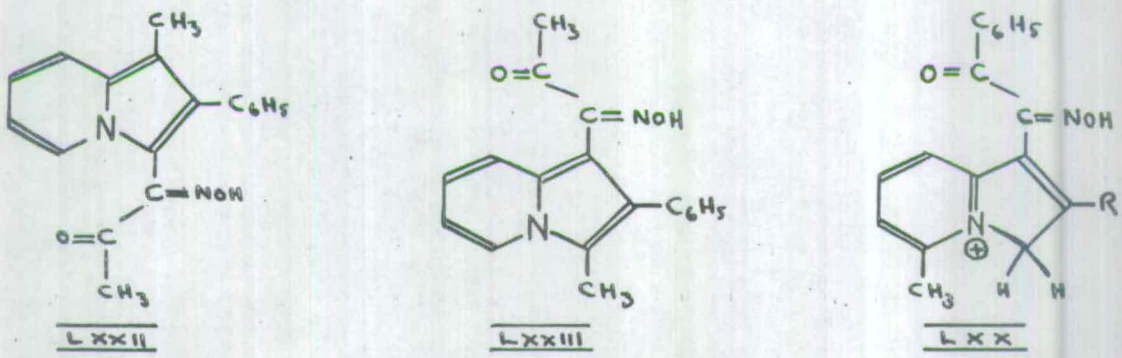
More recently other 1,3 additions of nitrile oxides have been described.[91]

Nitrile oxides are prone to polymerisation and it is necessary to use very mild conditions for these reactions and to generate the nitrile oxide *in situ*. The only known non-aromatic nitrile oxide, ethoxycarbonylformonitrile oxide, is usually prepared by treating ethyl chlorohydroxyiminoacetate with base.[92]

From these observations it was hoped that other chlorohydroxyimino compounds would react with base to give the corresponding nitrile oxides, and that the nitrile oxides would react with indolizines to give 3 - substituted indolizines such as (LXV). By choosing a suitable chlorohydroxyimino compound a 3 - substituted indolizine might be obtained which, on treatment with base,

Figure 9.


R
N
CH3
A'COCl, NOH HCl
(C2H5)3N
C=NOH
O=C
R'
KOBu^t / BuOH
LXVI
LXVII
LXVIII
LXXI
LXXVI


CH3
C6H5
N
C=NOH
O=C
LXXII
LXXIII
LXX

would cyclise to give a 3 - hydroxyimino-3H-cycl [3,3,2] azine.

A solution of 5 - methyl - 2 - phenylindolizine (LXVI, R = C_6H_5) and one equivalent of ω-chloro-ω-hydroxyiminoacetophenone, in benzene, was treated with triethylamine. Working up the reaction mixture yielded an orange crystalline compound together with a small amount of a yellow compound. The n.m.r. spectrum of the former product showed a multiplet in the region τ 2.1 - 3.7 (relative intensity 15) and a singlet at τ 7.60 (relative intensity 3). This compound was originally believed to be the pure 3 - (α - hydroxyiminophenacyl) derivative (LXVII, R = R′= C_6H_5) but was later shown to contain a small amount of the 1 - isomer (LXVIII, R = R′= C_6H_5). The other product obtained from the reaction could not be identified. The orange reaction product was heated with potassium tert - butoxide in tert - butanol and, after removal of solvent, the residual potassium salt was dissolved in water and the solution filtered. A certain amount of insoluble material was obtained and this was examined and found to be the cyclised product (LXXI, R = R′= C_6H_5), together with a small amount of a bright yellow compound. The infrared spectrum of this compound showed a hydroxyl absorption band at 3250 cm^{-1} and a carbonyl absorption band at 1663 cm^{-1}. Its n.m.r. spectrum measured in dimethyl sulphoxide, showed a multiplet in the aromatic region, the pattern of which was different from that of the starting material. A second spectrum, measured in trifluoroacetic acid, showed a multiplet in the region τ 1.4 - 2.8 (relative intensity 14) and two singlets at τ 4.12 and 6.98 (relative intensities, 2 and 3, respectively), the singlet at τ 4.12 indicating that protonation had occurred at an unsubstituted position in the indolizine nucleus. Since indolizines usually protonate in the 3-position, the spectrum was probably that of the 3H-indolizinium ion (LXX). Therefore the original reaction product must have been a mixture of the 1 - and 3 - (α-hydroxyiminophenacyl) derivatives. A large amount of

the starting material was recovered by acidification of the filtrate from the cyclisation reaction. All attempts to separate the two isomers failed, but careful recrystallisation gave a small amount of a deep orange compound which was believed to be the pure 3 - isomer. The infrared spectrum of this compound showed a hydroxyl absorption band at 3250 cm^{-1} and a carbonyl absorption band at 1640 cm^{-1}. Its n.m.r. spectrum was very similar to that of the original reaction product indicating that it was the major product present. The two isomers were each heated with potassium tert-butoxide in tert - butanol and only the compound believed to be the 3 - isomer gave the cyclised product (LXXI, R = R′= C_6H_5).

It was obvious that more strongly basic conditions were required to effect cyclisation. It has been reported [93.] that the basic strength of potassium tert-butoxide is enhanced in dimethyl sulphoxide and this is probably due to the lower degree of solvation of the tert-butoxide anion in this solvent. Treatment of the mixture of isomers with potassium tert-butoxide in boiling dimethyl sulphoxide, gave 3-hydroxyimino-2,4-diphenyl-3H-cycl [3,3,2] azine (LXXI, R = R′= C_6H_5) as the only isolable product. The formation of a certain amount of tar could be due to the decomposition of the 1 - isomer under the severe experimental conditions.

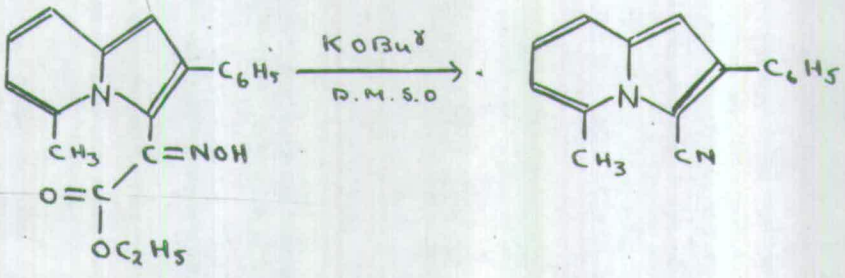
The reaction of 5-methyl-2-phenylindolizine (LXVI, R = C_6H_5) with ∝-chloro-∝-hydroxyiminoacetone, in the presence of triethylamine, gave a mixture of the 1- and 3-(∝-hydroxyiminoacetonyl) derivatives (LXVII and LXVIII, R = C_6H_5, R′= CH_3). Careful recrystallisation gave a small amount of a deep red compound which was believed to be the pure 3-isomer. Heating the mixture of isomers with potassium tert-butoxide in dimethyl sulphoxide gave 3-hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine (LXXI, R = C_6H_5, R′= CH_3).

2,5-Dimethylindolizine (LXVI, R = CH_3) and ω-chloro-ω-hydroxyiminoacetopheno in the presence of triethylamine, gave a mixture of the 1- and 3- (∝-hydroxyiminophenacyl) derivatives (LXVII and LXVIII, R = CH_3, R′= C_6H_5). Careful recrystallisation gave a small amount of an orange compound which was believed to be the pure 3-isomer. Heating the mixture of isomers with potassium tert-butoxide in dimethyl sulphoxide gave 3-hydroxyimino-2-methyl-4-phenyl-3H-cycl [3,3,2] azine (LXXI, R = CH_3, R′= C_6H_5).

Finally, the reaction of 2,5-dimethylindolizine with ∝-chloro-∝-hydroxyiminoacetone, in the presence of triethylamine, gave an oil which, on heating with potassium tert-butoxide in dimethyl sulphoxide gave a small amount of 3-hydroxyimino-2,4-dimethyl-3H-cycl [3,3,2] azine (LXXI, R = R′= CH_3).

In order to confirm the orientation of the isomers isolated during these reactions, the model compounds, 3-(∝-hydroxyiminoacetonyl) -1-methyl-2-phenylindolizine (LXXII) and 1 - (∝-hydroxyiminoacetonyl) -3-methyl-2-phenylindolizine (LXXIII) were prepared. The ultraviolet spectra of these compounds were very similar and therefore could not be used as a basis for structural identification by comparison with the spectra of compounds of unknown orientation. The n.m.r. spectra of the model compounds, measured in deuterochloroform, showed, in each case, two methyl singlets. The n.m.r. spectrum of (LXXIII), measured in trifluoroacetic acid, however, showed one singlet at τ 7.38 (relative intensity 3) and two doublets (J = 8 c.p.s.) at τ 3.78 and 8.14 (relative intensities, 1 and 3, respectively), indicating that protonation had occurred at the 3-position of the indolizine nucleus. (cf. The n.m.r. spectrum of 1-(∝-hydroxyiminophenacyl)-5-methyl-2-phenyl indolizine, in trifluoroacetic acid). The n.m.r. spectrum of (LXXII), measured in trifluoroacetic acid, did not show any evidence of protonation on the indolizine nucleus, nor did the spectra of the three isomers, which suggested that these compounds were also substituted in the 3-position. Their n.m.r. spectra

Figure 10.



LXXIV

LXXV

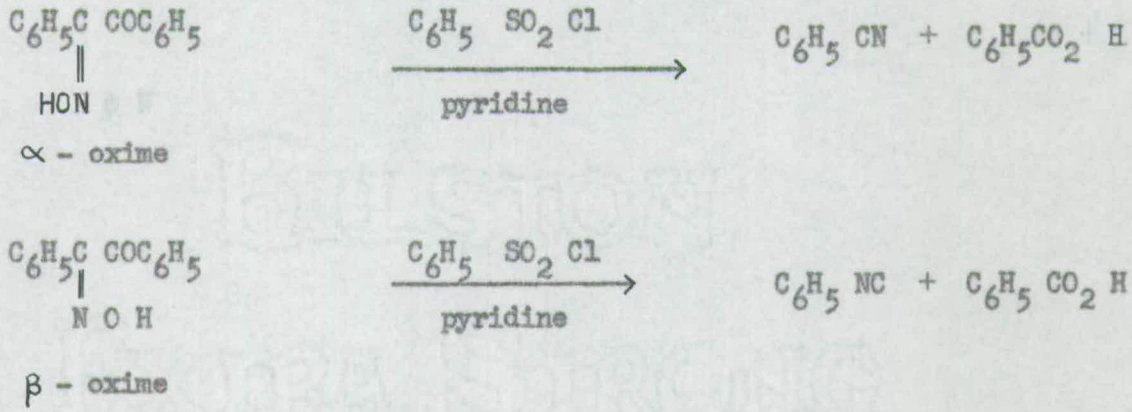
(in deuterochloroform) were then compared with the spectra of the two model compounds and, in each case, the pattern of peaks in the aromatic region was very similar to that of the 3-(α-hydroxyiminoacetonyl) derivative (LXXII). It was therefore concluded that the compounds under investigation were in fact substituted in the 3-position.

The four cyclazinone oximes were bright orange crystalline compounds which were extremely unstable to light. The infrared spectrum of each compound showed a hydroxyl absorption band at 3220 cm^{-1}, and bands at 1600 cm^{-1} and 980 cm^{-1}, due to C = N and N - O, respectively.[113] None of the spectra showed a carbonyl absorption band. The n.m.r. spectra (in deuterochloroform) were consistent with the assigned structures. The 2,4-dimethyl derivative (LXXI, R = R′= CH_3) showed aromatic-proton absorptions between τ 2.40 and 3.40, and methyl-proton absorptions at τ 7.20 and 7.78. Both the 2-methyl-4-phenyl derivative (LXXI, R = CH_3, R′= C_6H_5), and the 4-methyl-2-phenyl derivative (LXXI, R = C_6H_5, R′= CH_3), showed aromatic proton absorptions in the region τ 2.40 - 3.50, and methyl-proton absorptions at τ 7.46 and 7.82, respectively. The 2,4-diphenyl derivative (LXXI, R = R′= C_6H_5) exhibited a complex multiplet in the region τ 2.30 - 3.20. The absence of methyl-proton absorption showed that the 3-(α-hydroxyiminophenacyl) derivative (LXVII, R = R′= C_6H_5) must have cyclised under the reaction conditions. Spectra measured in trifluoroacetic acid were probably of the hydroxyamino cycl [3,3,2] azinium ions formed by protonation on the nitrogen atoms of the oximes.

The reaction of 5-methyl-2-phenylindolizine with ethyl chlorohydroxyiminoacetate, in the presence of triethylamine, gave the ethoxycarbonyl oxime (LXXIV). Its n.m.r. spectrum showed a pattern of peaks in the aromatic region very similar to that of the 3-(α-hydroximinoacetonyl) derivative (LXXII).

Heating the ethoxycarbonyl oxime (LXXIV) with potassium tert-butoxide in dimethyl sulphoxide, gave a small yield of 3-cyano-5-methyl-2-phenylindolizine (LXXV). This compound showed an infrared absorption at 2210 cm^{-1} (C ≡ N).

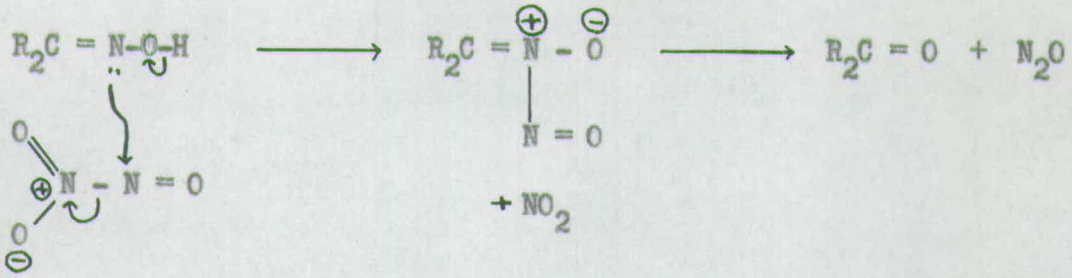
Certain oximes have been known[94.] to form nitriles on treatment with thionyl chloride, and these cleavages may be related to the more generally known cleavage of benzil-and benzoin-type oximes, which has been termed a "second order" Beckmann rearrangement. Werner, Piguet and Deutscheff found that, when the monoximes of benzil were treated with benzene sulphonyl chloride, the normal rearrangement products (N-benzoylbenzamide and benzoylformanilide) were not obtained.[95,96.] Instead a mixture of benzonitrile and benzoic acid was isolated from the rearrangement of α -benzil monoxime, and phenyl isocyanide and benzoic acid were obtained from β -benzil monoxime.[95.]



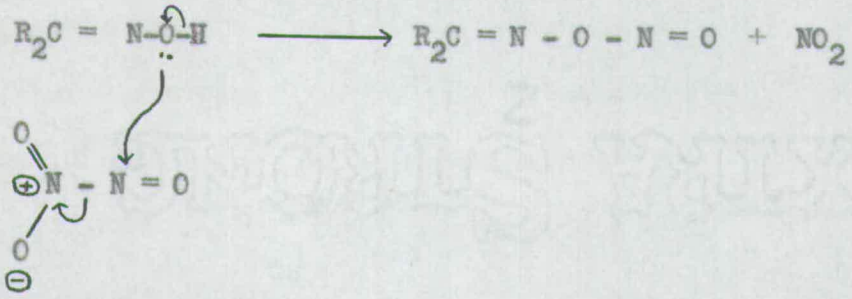
Similarly the oximes of benzoin were cleaved to benzaldehyde and benzonitrile or phenylisocyanide depending on the configuration of the oxime.

The cleavage of the ethoxycarbonyl oxime (LXXIV) is clearly an example of a "second-order" Beckmann rearrangement. All previously reported cases, however, occurred under acid conditions.

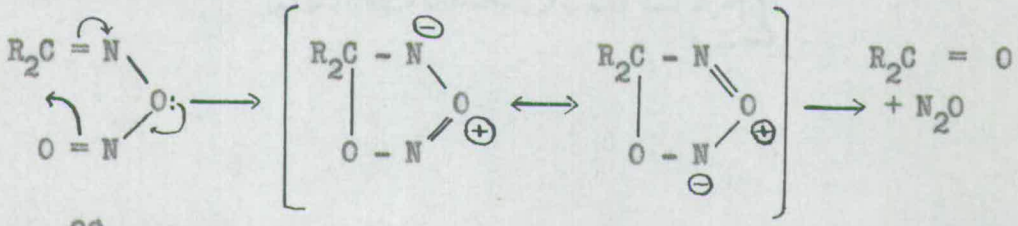
Oximes can be converted to the corresponding ketones by the action of nitrous acid.[97.] It is assumed that the nitrosating agent N_2O_3 attacks the oxime on the nitrogen atom.



In heavily susbstituted oximes approach to the nitrogen atom may be hindered so that attack at the oxygen atom predominates.



Subsequent cyclisation may then generate a mesoionic system



Barltrop[98] found that acid hydrolysis of oximes in the presence of formaldehyde gave a better yield of the ketone. De Puy and Ponder,[99] however, claimed that this method led to a certain amount of decomposition. They found that good yields of ketones were obtained by hydrolysing oximes in a 9 : 1 levulinic acid - hydrochloric acid mixture.

Heating 3-hydroxyimino-2-methyl-4-phenyl-3H-cycl [3,3,2] azine at 100° in a levulinic acid-hydrochloric acid mixture gave the corresponding cyclazinone (LXXVI, $R = CH_3$, $R' = C_6H_5$) but the 4-methyl-2-phenyl derivative (LXXI, $R = C_6H_5$, $R' = CH_3$) and the 2,4-diphenyl derivative (LXXI, $R = R' = C_6H_5$) could not be hydrolysed by this method. Treatment of these cyclazinone

oximes with sodium nitrite in acetic acid also failed to give the corresponding ketones, but gave small amounts of yellow compounds which could not be identified.

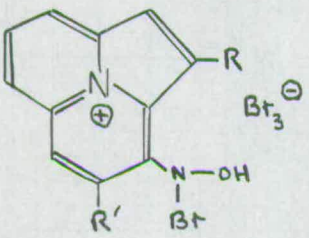
It is well established that the alkylation of oximes leads to O-alkyl oximes, or to nitrones, depending on conditions.[100.101.] It has been reported that with diazomethane the nitrone is the product obtained.[100.] The reaction in ether, of 3-hydroxyimino-2-methyl-4-phenyl-3H-cycl [3,3,2] azine (LXXI, $R = CH_3$, $R' = C_6H_5$) with diazomethane and boron trifluoride diethyletherate, gave a low yield of the ketone (LXXVI, $R = CH_3$, $R' = C_6H_5$). In a similar reaction the 2,4-diphenyl derivative (LXXI, $R = R' = C_6H_5$) also gave the corresponding ketone, while the 4-methyl-2-phenyl derivative (LXXI, $R = C_6H_5$, $R' = CH_3$) gave a deep-red crystalline compound which could not be identified. It is possible that the nitrones or the O-methyl oximes are first formed, but under the experimental conditions, these hydrolyse to the ketones.

The treatment of various benzaldoximes with methyl iodide in the presence of suspended silver oxide has been reported[102.] to yield O-methyl compounds. Under these conditions, however, 3-hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine yielded the ketone (LXXVI, $R = C_6H_5$, $R' = CH_3$). It seemed possible that this reaction was a direct oxidation and so the oxime was heated with silver oxide alone in dichloromethane. The ketone was again isolated. The reaction with silver oxide in dichloromethane proved to be the most efficient way of converting cyclazinone oximes to cyclazinones.

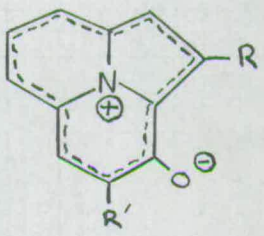
Addition of bromine to solutions of the oximes in glacial acetic acid yielded crystalline compounds which could not be purified completely but gave analytical results approximating to those required for derivatives of N-bromohydroxyaminocycl [3,3,2] azinium tribromide (LXXVII). Boiling in acetic acid converted these compounds into the corresponding cyclazinones.

To summarise, various derivatives of 3H-cycl [3,3,2] azin-3-one have been synthesised and n.m.r. spectroscopy has shown these cyclazinones to be aromatic in character. The infrared spectra of the compounds indicate highly polarised carbonyl groups and canonical structures such as (LXXVIII) must be considered to make important contributions to resonance in cyclazinones.

Attempts to prepare a derivative of the dehydrocycl [3,3,2] azinium ion from the ketone (LXXVI, R = C_6H_5, R'= CH_3) by reduction of the carbonyl group (with lithium aluminium hydride or with diborane) followed by hydride ion abstraction, were unsuccessful.

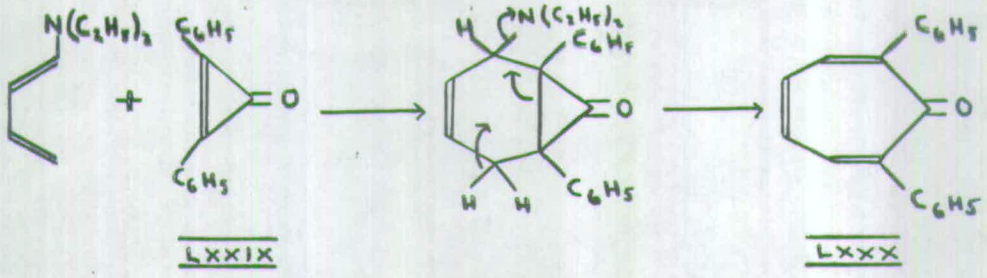


LXXVII

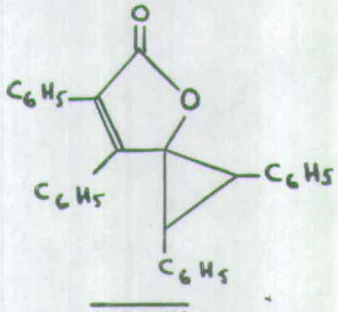


LXXVIII

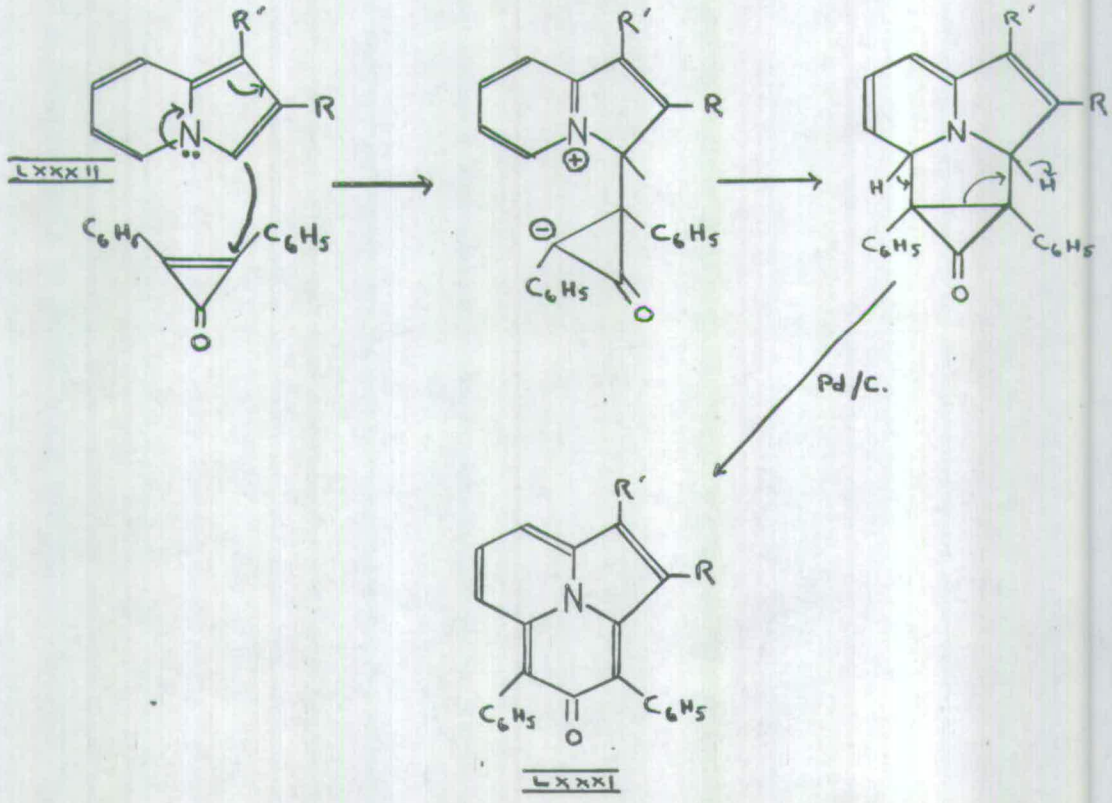
Figure 11.



LXXIX LXXX



LXXXIII



LXXXII LXXXI

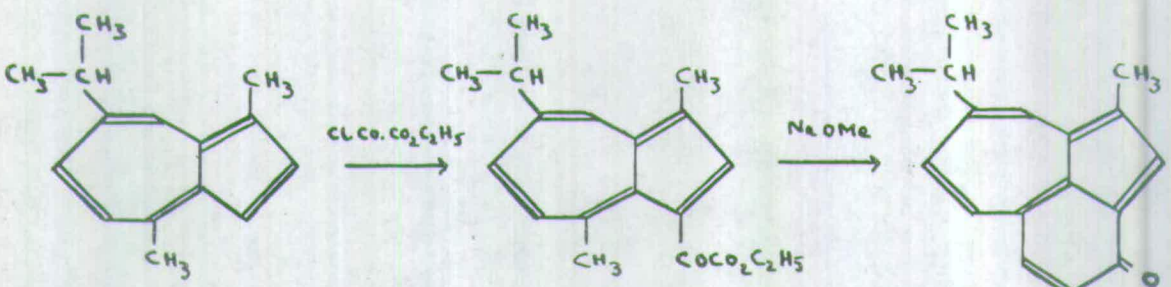
Attempts to prepare a 4H-cycl [3,3,2] azin-4-one derivative:

Enamines react with diphenylcyclopropenone (LXXIX)[103] to give products arising from a 1,2- cycloaddition of the enamine to the carbon-carbon double bond of (LXXIX). When a dienamine is employed, 1,4-cycloaddition is observed. The reactions appear to involve cyclopropanone intermediates which cleave to form ring-enlarged products. Thus the 2,7-diphenyltropone (LXXX), formed by the reaction of diethylaminobuta-1,3-diene with (LXXIX), presumably arises from a 1,4-cycloaddition to give a cyclopropane intermediate, which subsequently suffers a 1,4-elimination of the elements of diethylamine with cleavage of the cyclopropane ring.

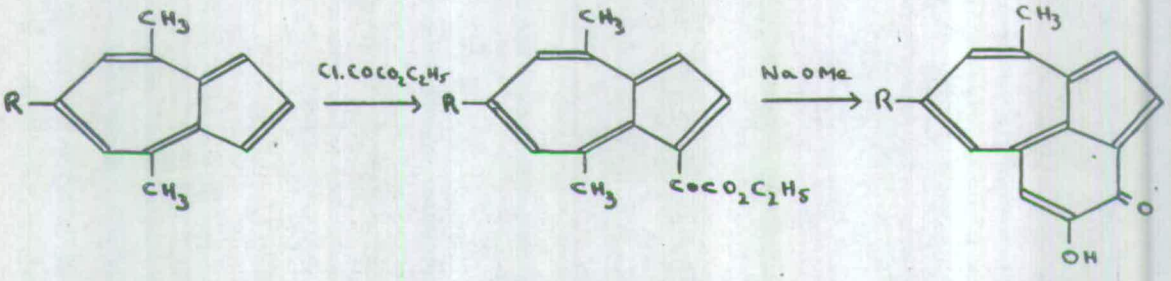
It was hoped that a suitable indolizine would undergo cycloaddition to the double bond of diphenylcyclopropenone and in the presence of a dehydrogenating catalyst yield a 4H-cycl [3,3,2] azin-4-one (LXXXI). Accordingly, equimolecular amounts of 2-phenylindolizine (LXXXII, R = C_6H_5, R′= H) and diphenylcyclopropenone (LXXIX) were heated, in benzene, with palladium on charcoal as dehydrogenating catalyst. Working up the reaction mixture yielded a small amount of a white crystalline product which did not contain nitrogen, and must therefore have arisen from intermolecular reaction of the diphenylcyclopropenone. Its infrared spectrum was not in agreement with that reported for the dimer (LXXXIII) and it could not be further identified.

Heating equimolecular amounts of 1-methyl-2-phenylindolizine (LXXXII, R = C_6H_5, R′= CH_3) with diphenylcyclopropenone in nitrobenzene, yielded a yellow crystalline product which proved to be a 1 : 1 adduct. The n.m.r. spectrum showed a low-field doublet, attributed to the proton in the 5-position of the indolizine, which showed that cycloaddition had not taken place as expected. The infrared spectrum of the compound showed a carbonyl band at 1630 cm^{-1}. No further investigation of this product was undertaken.

Figure 12.



LXXXIV LXXXV LXXXVI



LXXXVII LXXXVIII LXXXIX

The synthesis of derivatives of 3H-benz [cd] azulen-3-one:

In view of the great similarity in chemical behaviour between indolizines and azulenes, it seemed reasonable to assume that the methods used for the preparation of cyclazinones from indolizines, could be adopted to synthesise benzazulenones from azulenes.

A preliminary investigation by Mr.C.E. Cumming had already shown that guaiazulene (LXXXIV) is readily convertible into an ethoxalyl derivative (LXXXV) which, in the presence of sodium methoxide, yields a product believed to be the benzazulenone (LXXXVI) .

When a 5-methylindolizine was treated with ethoxalyl chloride, depending on conditions, either a diethoxalyl derivative or a mixture of the 1- and 3-monoethoxalyl isomers was obtained. Under basic conditions, the diethoxalyl derivative cyclised to give a mixture of a 3H-cycl [3,3,2] azin-3-one and a cycl [3,2,2] azine. It was thought that the reaction of a suitable 4,8-dimethylazulene with ethoxalyl chloride might give both the monethoxalyl- and the diethoxalyl derivatives. Treatment of these compounds with base would then lead to derivatives of 3H-benz [cd] azulen-3-one and 3,5-dihydrocyclohepta [def] fluorene-3,5-dione, respectively.

The reaction of 4,6,8-trimethylazulene (LXXXVII, R = CH_3) with ethoxalyl chloride yielded the 1-ethoxalyl derivative (LXXXVIII, R = CH_3). Heating this compound with sodium methoxide in methanol gave an insoluble sodium salt from which the 4-hydroxy-3H-benz [cd] azulen-3-one (LXXXIX, R = CH_3) was isolated. The reaction also yielded a large amount of amorphous material which appeared to be polymeric. The infrared spectrum of the benzazulenone showed absorptions characteristic of a hydrogen-bonded hydroxyl group (3360 cm^{-1}) and a highly polarised carbonyl group (1603 cm^{-1}). It was difficult to obtain an n.m.r. spectrum of the benzazulenone as it was only slightly soluble in neutral solvents. A spectrum measured in trifluoroacetic acid was probably

that of the hydroxybenzazulenium ion formed by protonation on the carbonyl oxygen. This spectrum showed all the ring proton absorptions between τ 1.2 and 2.7, in the region normally attributed to aromatic protons.

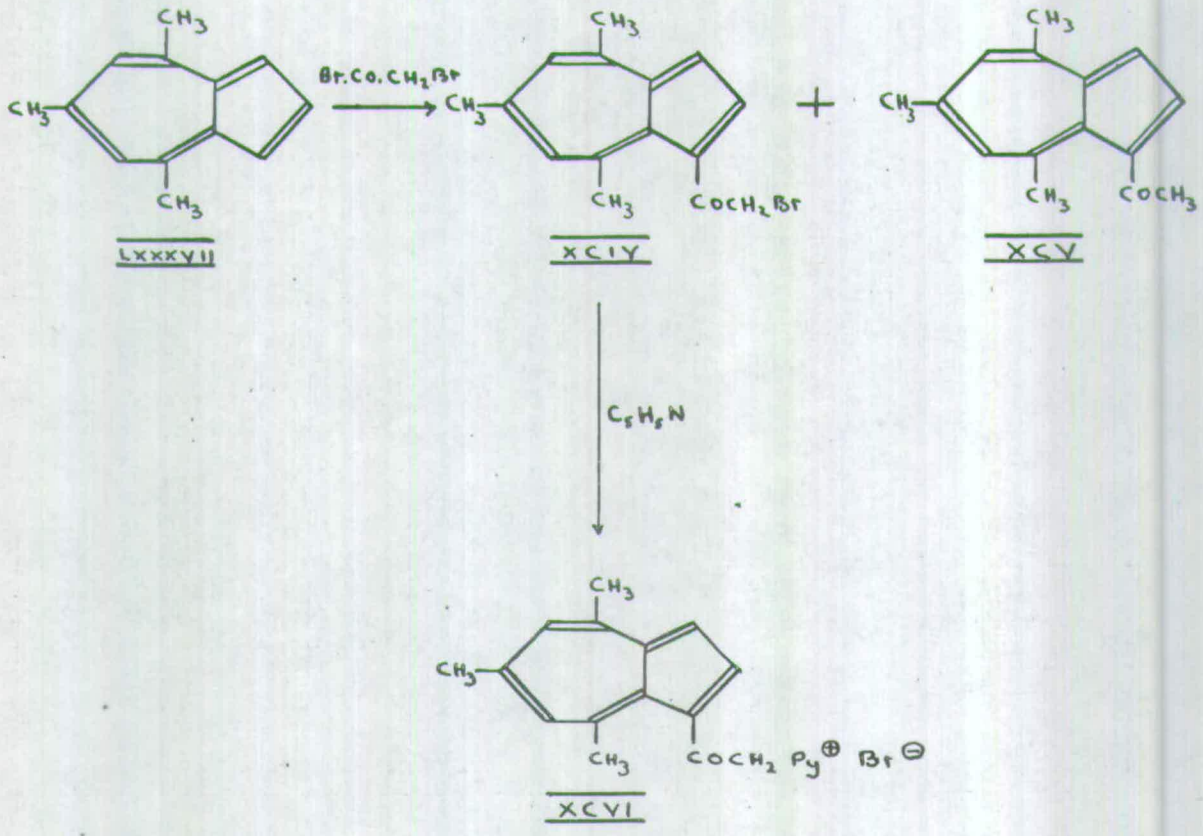
The benzazulenone could not be methylated to the 4-methoxy compound. It was recovered unchanged both after treatment with diazomethane in ether and after the addition of dimethyl sulphate to a solution of its sodium salt in methanol.

Attempts were made to prepare the 1,3-diethoxalyl derivative by using an excess of ethoxalyl chloride with anhydrous aluminium chloride, anhydrous stannic chloride, and silver perchlorate as catalysts. In all cases the monoethoxalyl compound was the only product formed. The presence of the strongly electronegative ethoxalyl group in position-1 must deactivate position-3 to such a degree, that electrophilic attack cannot take place under these conditions.

1,3-Bis-(chloromercuri) azulene has been prepared[104]. and it was thought that if a similar compound could be prepared from 4,6,8-trimethylazulene, subsequent reaction with ethoxalyl chloride could lead to the replacement of the chloromercuri groups by ethoxalyl groups. Heating 4,6,8-trimethylazulene with mercuric chloride in benzene gave a dark precipitate which could not be recrystallised. Addition of ethoxalyl chloride to a suspension of this material in refluxing dichloromethane gave no reaction and the starting material was recovered unchanged.

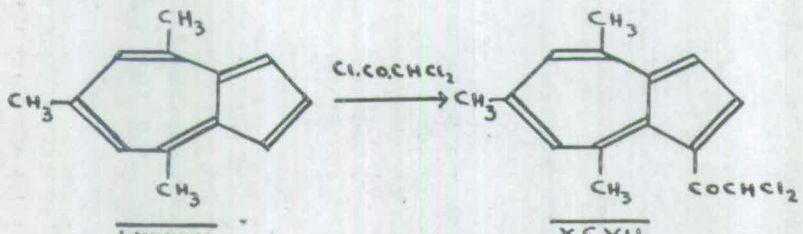
It seemed possible that derivatives of 3H-benz [cd] azulen-3-one and 3,5-dihydrocyclohepta [def] fluorene-3,5-dione might be obtained by the cyclisation of glyoxyloyl derivatives of azulenes. Guaiazulene readily forms an acetyl derivative while 4,6,8-trimethylazulene forms both monoacetyl and diacetyl derivatives. It was hoped that these acetyl groups could be oxidised to glyoxyloyl groups. Selenium dioxide has been widely used to convert active

Figure 13.



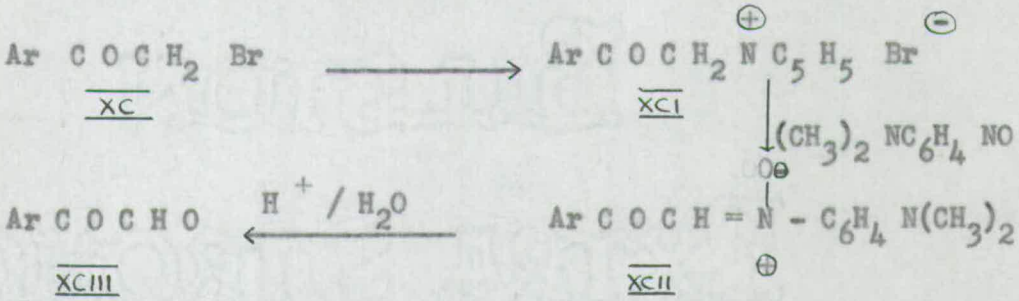
LXXXVII XCIV XCV

XCVI



LXXXVII XCVII

methyl or methylene groups to carbonyl groups,[105] and an attempt was made to oxidise 3-acetylguaiazulene to 3-glyoxyloylguaiazulene by heating with selenium dioxide in dioxan. After several hours the 3-acetylguaiazulene was recovered unchanged. The synthesis of carbonyl compounds from active methyl and methylene compounds, by way of pyridinium salts and nitrones has found wide application in recent years.[106] According to King,[107] pyridinium salts can often be prepared by the reaction of active methyl or methylene compounds with iodine in pyridine. However, the reaction of 3-acetylguaiazulene with iodine in pyridine yielded a tar, from which no definite compound could be isolated. Compounds containing reactive halogens, such as (XC), readily form pyridinium salts (e.g. XCI) which condense with p. nitrosodimethylaniline to form nitrones (XCII). These compounds may then be hydrolysed with acid to give substituted glyoxals (XCIII).[108]



4,6,8-Trimethylazulene and bromoacetyl bromide gave both 1-bromoacetyl -4,6,8-trimethyl azulene (XCIV) and 1-acetyl-4,6,8-trimethylazulene (XCV). Under similar conditions guaiazulene yielded 3-bromoacetylguaiazulene and 3-acetylguaiazulene. Since the bromoacetyl bromide was free from acetyl bromide it follows that in both reactions a certain amount of the bromoacetyl derivative had been reduced, but the mechanism of this reaction is not known. 1-Bromoacetyl-4,6,8-trimethylazulene and a slight excess of pyridine were left standing in ether for several days, during which time the pyridinium salt (XCVI) precipitated. Treatment of the pyridinium salt with p.nitrosodimethylaniline in ethanol, in the presence of sodium hydroxide solution gave a gum which could not be crystallised. Treatment of the gum with acid resulted

Figure 14.

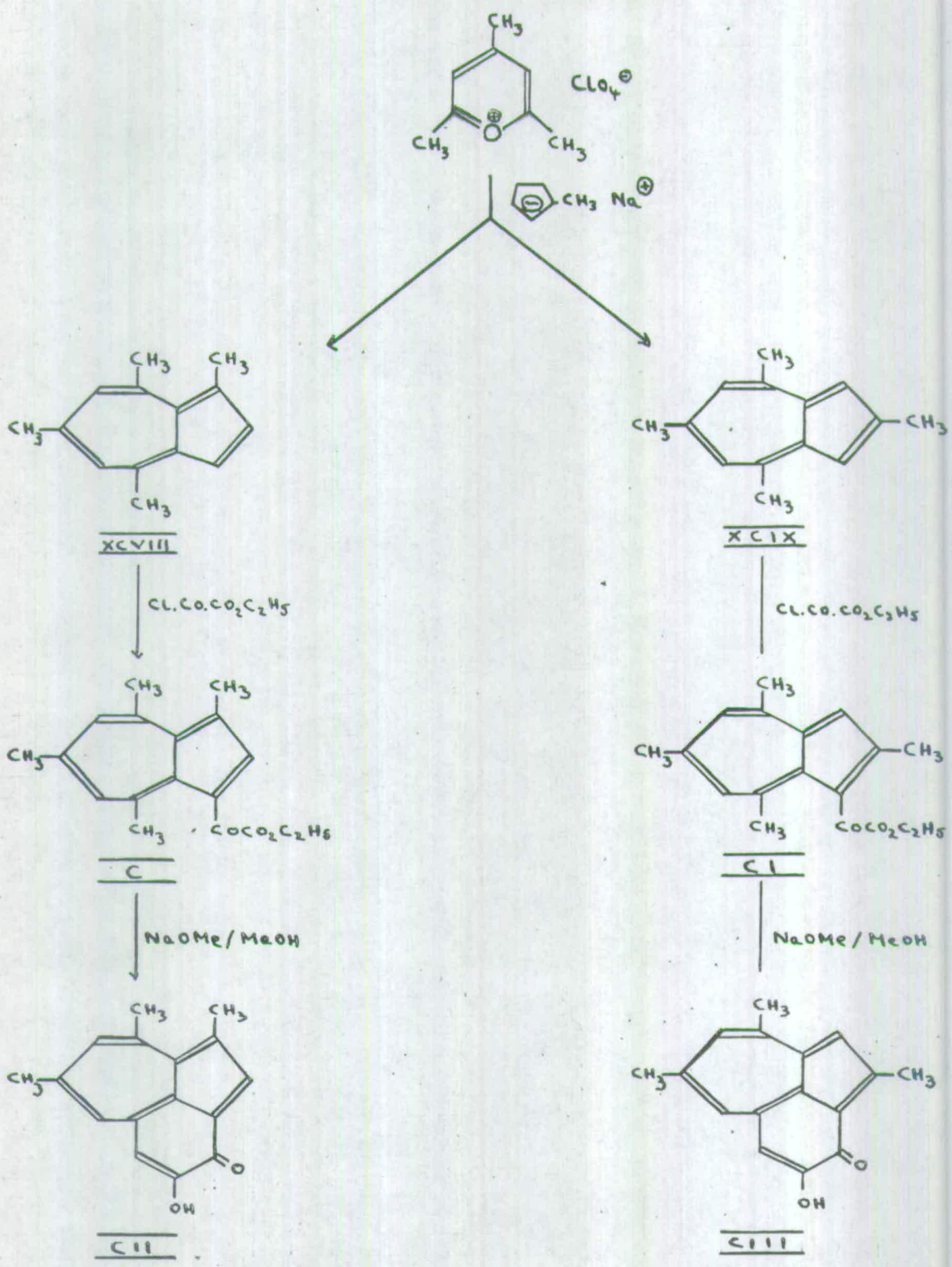
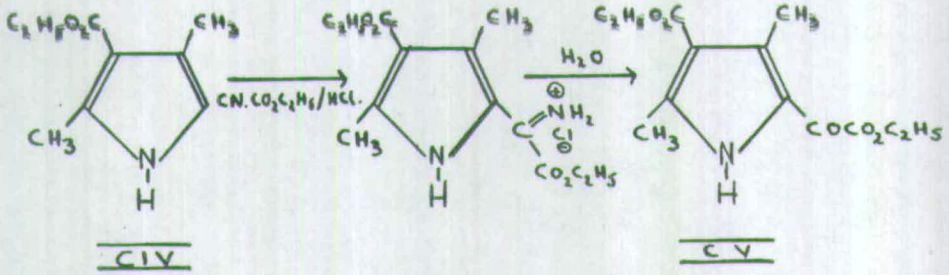
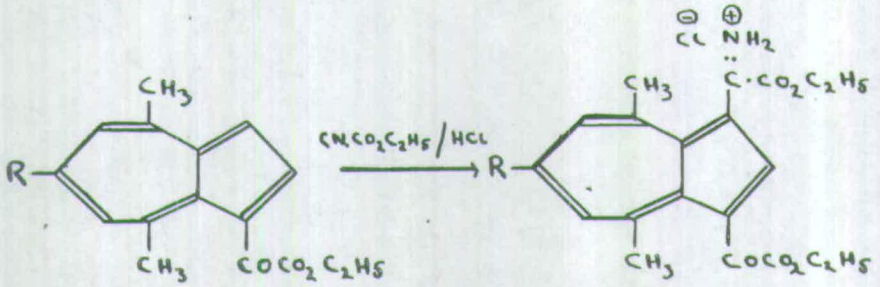


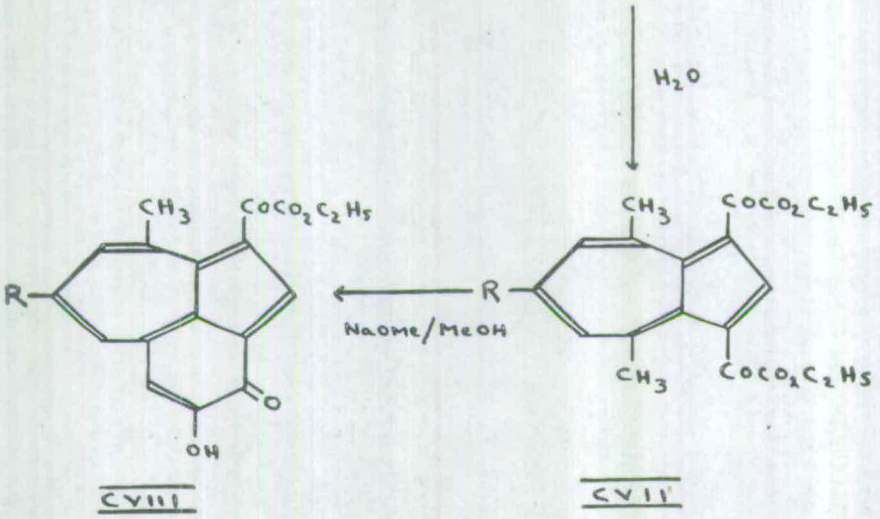
Figure 15.



CIV CV



LXXXVIII CVI



CVIII CVII

in cleavage of the side chain to regenerate the 4,6,8-trimethylazulene.

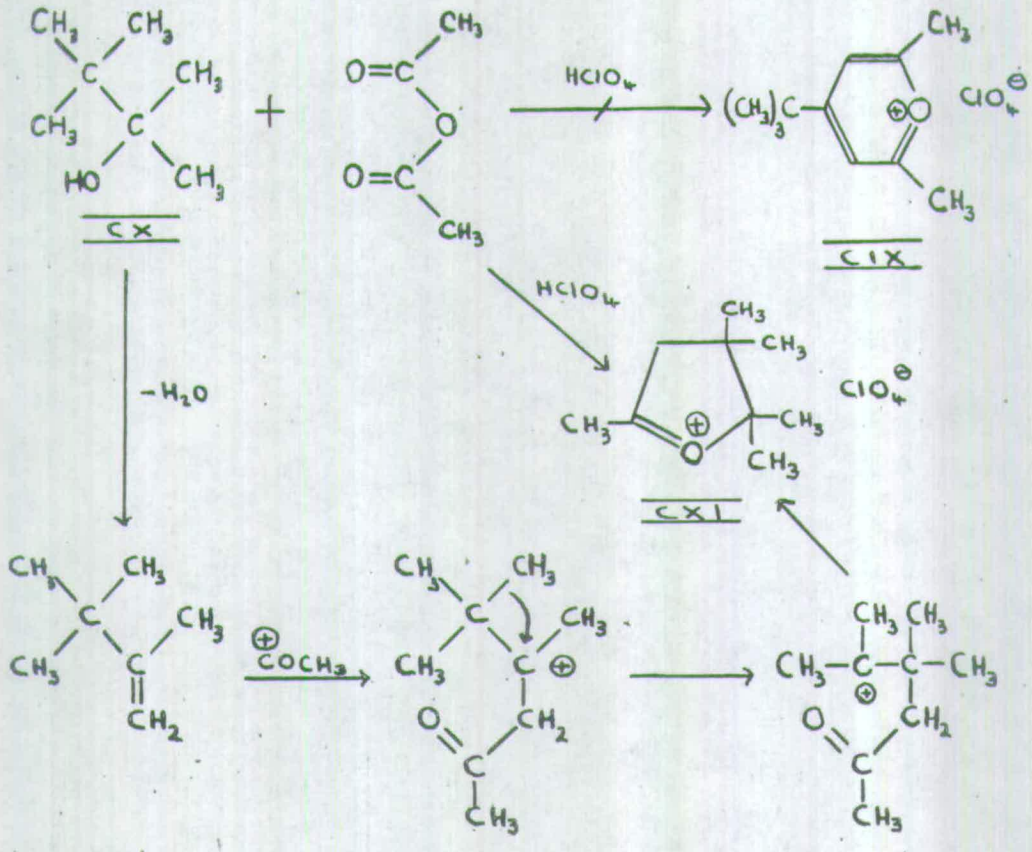
The reaction of 4,6,8-trimethylazulene with dichloroacetyl chloride gave the 1-dichloroacetyl derivative (XCVII). This might have been expected to hydrolyse and cyclise under basic conditions but, according to conditions used, either the starting material was recovered or an unidentifiable polymeric material was obtained.

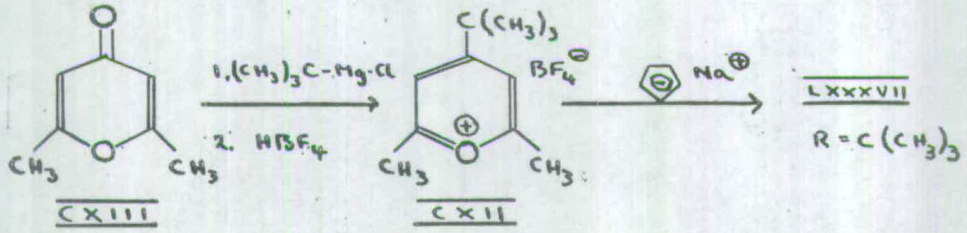
It has been reported[109] that 2,4,6,8-tetramethylazulene forms a 1,3-bis (trifluoroacetyl) derivative, whereas 4,6,8-trimethylazulene forms only a monotrifluoroacetyl derivative. It was thought possible, therefore, that a diethoxalyl derivative might be obtained from this azulene.

The reaction of 2,4,6-trimethylpyrylium perchlorate with methylcyclopentadienyl sodium gave 1,4,6,8-tetramethylazulene and 2,4,6,8-tetramethylazulene (XCVIII and XCIX), separable by chromatography on alumina. Treatment of these azulenes with ethoxalyl chloride yielded the 3-ethoxalyl derivative (C) and the 1-ethoxalyl derivative (CI), respectively. No diethoxalyl derivative could be obtained from the 2,4,6,8-tetramethylazulene. Treatment of the ethoxalyl derivatives (C) and (CI) with sodium methoxide in dry methanol gave the 4-hydroxy-3H-benz[cd]azulen-3-ones (CII) and (CIII), respectively.

The preparation of 3-ethoxycarbonyl-5-ethoxalyl-2,4-dimethylpyrrole (CV) from 3-ethoxycarbonyl-2,4-dimethylpyrrole (CIV) and ethyl cyanoformate by the Hoesch reaction, has been reported.[110] The electronegative ethoxycarbonyl group in the 3-position does not prevent attack in the 5-position and it was thought that possibly a 1,3-diethoxalyl derivative of 4,6,8-trimethylazulene might be prepared in the same way. When 1-ethoxalyl-4,6,8-trimethylazulene was dissolved in dry ether, ethyl cyanoformate added and dry hydrogen chloride passed through the solution, a precipitate, presumably the imine hydrochloride (CVI, R = CH_3), was deposited. On treating the precipitate

Figure 16





CXIII CXII LXXXVII

with water 1,3-diethoxalyl-4,6,8-trimethylazulene (CVII, R = CH_3) was formed. Base-catalysed cyclisation of the 1,3-diethoxalyl derivative yielded, according to conditions, varying amounts of 1-ethoxalyl-4-hydroxy-7,9,-dimethyl-3H-benz [cd] azulen-3-one (CVIII, R = CH_3), along with an unidentifiable polymeric material. Double cyclisation of the 1,3-diethoxalyl derivative could not be achieved.

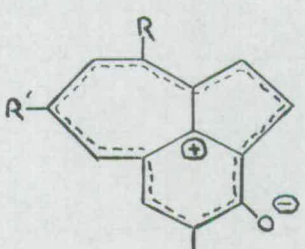
The low yields of cyclisation products in these reactions are perhaps due to the fact that the methyl group in the 6-position loses a proton more readily than those in the 4- and 8-positions owing to steric factors. Reaction would then be intermolecular rather than intramolecular, resulting in a polymeric product. It was therefore decided to synthesise the ethoxalyl derivatives of 4,8-dimethyl-6-tert-butylazulene in the hope that treatment with base would give higher yields of the cyclised products.

An attempt to prepare 2,6-dimethyl-4-tert-butylpyrylium perchlorate (CIX), from 2,3,3-trimethylbutan-2-ol (CX) and acetic anhydride, by a method similar to that used in the preparation of 2,4,6-trimethylpyrylium perchlorate gave, not the expected pyrylium salt, but 2,3-dihydro-2,2,3,3,5 - pentamethylfurylium perchlorate (CXI). The n.m.r. spectrum of (CXI) showed two singlets at τ 8.17 and 8.70 (each of relative intensity 6), due to the methyl groups at positions 3 and 2 respectively, a triplet (J = 1 c.p.s.) at τ 6.90 (relative intensity 3), due to the 5-methyl group, and a quartet (J = 1 c.p.s.) at τ 6.10 (relative intensity 2) due to the protons at position 4. The mechanism opposite (Figure 16) was proposed for the formation of this compound.

2,6-Dimethyl-4-tert-butylpyrylium fluoborate (CXII) was prepared [111] by the reaction of tert-butlmagnesium chloride with 2,6-dimethyl-4-pyrone (CXIII) in the presence of fluoboric acid. Reaction of the pyrylium salt with cyclopentadienyl sodium gave 4,8-dimethyl-6-tert-butylazulene[112] (LXXXVII , R = C $(CH_3)_3$).

The reaction of 4,8-dimethyl-6-tert-butylazulene with ethoxalyl chloride gave the 1-ethoxalyl derivative (LXXXVIII, R = $C(CH_3)_3$). Treatment of this compound with sodium methoxide in dry methanol gave 4-hydroxy-7-tert-butyl-9-methyl-3H-benz[cd] azulen-3-one (LXXXIX, R = $C(CH_3)_3$) in high yield. The n.m.r. spectrum of this compound showed a multiplet in the region τ1.9 - 3.2 (relative intensity 6) and two singlets at τ7.00 and 8.48 (relative intensities 3 and 9 respectively), due to the 9-methyl- and 7-tert-butyl groups respectively. The 1-ethoxalyl derivative was dissolved in dry ether, ethyl cyanoformate added and dry hydrogen chloride passed through the solution. The imine salt (CVI, R = $C(CH_3)_3$) was deposited and on treatment with water yielded the 1,3-diethoxalyl derivative (CVII, R = $C(CH_3)_3$). This compound cyclised extremely readily; recrystallisation from neutral ethanol yielded a mixture of the diethoxalyl derivative and the cyclised product (CVIII, R = $C(CH_3)_3$). All attempts to bring about double cyclisation, however, yielded a highly coloured amorphous material which appeared to be polymeric in nature.

To summarise, various derivatives of 3H-benz[cd] azulen-3-one have been synthesised but attempts to synthesise derivatives of 3,5-dihydrocyclohepta-[def] fluorene-3,5-dione were unsuccessful. N.m.r. spectroscopy has shown the benzazulenones to possess aromatic character, while infrared spectroscopy has shown the 3-carbonyl group to be highly polarised. It seems reasonable to assume that canonical structures such as (CXIV) make important contributions to resonance in benzazulenones.



CXIV

EXPERIMENTAL PROCEDURE AND RESULTS

Melting point determinations were carried out in a capillary tube in an n-butyl-phthalate bath and are uncorrected.

Analyses were by Weiler and Strauss of Oxford, and by Dr. Minnis of Andrew H. Baird Ltd., Edinburgh.

Infrared spectra were taken on a Unicam S.P.200 spectrophotometer and on a Perkin-Elmer P.E. 237 spectrophotometer.

N.m.r. data were obtained using a Perkin-Elmer R 10 (60 Mc/S) nuclear magnetic resonance spectrometer using tetramethylsilane (2%) as an internal standard.

Ultraviolet spectra were determined, in ethanolic solution, using a Perkin-Elmer 137 U.V. spectrophotometer and a Unicam S.P.800 spectrophotometer, and are presented in tabular and graph form at the end of the experimental procedure.

Unless otherwise stated:

Solutions were dried over anhydrous sodium sulphate or anhydrous magnesium sulphate.

Light-petroleum was the fraction distilling between 60 - 80°C.

Indolizines

All substituted indolizines were prepared by the method of Tschitschibabin,[114] which involves the quaternisation of an α-alkylpyridine with an α-haloketone, followed by intramolecular condensation of the quaternary salt in boiling aqueous sodium bicarbonate solution.

2 - Phenylindolizine[115]

Equimolecular proportions of α-picoline and phenacyl bromide were mixed together in cooled acetone. When set aside the solution deposited crystals of the quaternary salt. The quaternary salt and an equal weight of sodium bicarbonate were heated in water (100 ml. per 10 g. of quaternary salt), at 100°C. for 30 minutes. After cooling, the 2-phenylindolizine was filtered off and recrystallised from ethanol. m.p. 214-215°C.

5 - Methyl - 2 - phenylindolizine[116]

Equimolecular proportions of phenacyl bromide and 2,6-lutidine were mixed together and heated in an oven at 50°C for two days. The resultant hard crystalline mass was crushed, treated with boiling acetone, and filtered off. The quaternary salt, together with an equal weight of sodium bicarbonate, was heated in water (100 ml. per 10 g. of quaternary salt), at 100°C for 3 hours. The mixture was cooled and the solidified organic layer filtered off. Recrystallisation from methanol gave white crystals with a greenish tinge. m.p. 82 - 83°C.

Bromoacetone

Levene, Organic Synthesis X, 12. b.p. 36 - 40°C /25 mm.

2,5 - Dimethylindolizine[117].

Equimolecular proportions of bromoacetone (40 g.) and 2,6-lutidine (31 g.) were mixed together and heated in an oven at 40°C for two days. The resultant crystalline mass was crushed, treated with acetone and filtered off. The yield of quaternary salt (25 g. 35%), together with an equal weight of sodium bicarbonate, was heated in water (100 ml. per 10 g. of quaternary salt), at 100°C for 3 hours. The mixture was steam distilled, the oil extracted into ether and dried. The ether was removed and the oil fractionated; the fraction boiling at 116 - 117°C / 14 mm. being collected.

Yield 12 g. (80% from quaternary salt).

1 - Methyl - 2 - phenylindolizine

Equimolecular proportions of 2-ethylpyridine and phenacyl bromide were heated in an oven at 50°C for 20 hours. The resulting solid was triturated with acetone and filtered off. Equal amounts of the quaternary salt and sodium bicarbonate were heated in water (100 ml. per 10 g. of quaternary salt), at 100°C for 90 minutes. On cooling the mixture, the organic layer was filtered off, crushed and dried. Recrystallisation from ethanol gave 1-methyl-2-phenylindolizine. m.p. 78°C.

THE SYNTHESIS OF DERIVATIVES OF 3H - CYCL [3,3,2] AZIN - 3 - ONE

SECTION A.

1,3-Diethoxalyl-2,5-dimethylindolizine (LVII, R = CH_3):

2,5-Dimethylindolizine (14.5 g. 0.1 mole) was dissolved in dichloromethane (100 ml.) and the solution cooled to 0°C. To the rapidly stirred solution was added, dropwise, a solution of ethoxalyl chloride (41 g. 0.3 mole) in dichloromethane (50 ml.). The solution slowly turned green and, after the addition of the ethoxalyl chloride had been completed, was allowed to stand at 0°C. for 24 hours. The solution was then shaken with aqueous sodium bicarbonate solution, washed with water, and dried. The dichloromethane was removed under reduced pressure leaving a yellow oil which solidified on being rubbed with light petroleum. Recrystallisation from ethanol gave bright yellow crystals of 1,3-diethoxalyl-2,5-dimethylindolizine.

Yield 11.5 g. (33%). m.p. 73 - 74°C.

ν max: 1620, 1640, 1720, 1730 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed an aromatic multiplet at τ 1.5 - 3.2, a singlet at τ 7.6, a triplet (J = 8 c.p.s.) at τ 8.6 and a quartet (J = 8 c.p.s.) at τ 5.65, in the ratio 3 : 6 : 6 : 4.

$C_{18}H_{19}NO_6$ requires: C = 62.60%; H = 5.55%; N = 4.06%.

found : C = 62.40%; H = 5.17%; N = 3.98%.

The reaction of 1,3-diethoxalyl-2,5-dimethylindolizine with sodium methoxide in methanol:

A solution of 1,3-diethoxalyl-2,5-dimethylindolizine (6.9 g. 0.02 mole) in "super-dry" methanol (50 ml.), containing a molar equivalent of sodium methoxide, was heated under reflux for 90 minutes. On cooling a heavy precipitate

was deposited which was filtered off. The precipitate was boiled with water and filtered. The residue, yellow crystals, was recrystallised from ethanol to give 1 - methoxalyl-3-methoxycarbonyl-2-methyl-cycl [3,2,2] azine (LVIII, $R = CH_3$, $R' = COCO_2CH_3$, $R'' = CO_2CH_3$).

Yield 1.8 g. (28%). m.p. 146°C.

ν max: 1670, 1730, 1748 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed a multiplet in the region τ 1.6 - 2.4 and three singlets at τ 5.92, 5.94 and 6.9, in the ratio 4 : 3 : 3 : 3.

$C_{16}H_{13}NO_5$ requires: C = 64.21%; H = 4.38%; N = 4.68%.

found : C = 64.40%; H = 4.24%; N = 4.76%.

Acidification of the filtrate with dilute hydrochloric acid precipitated a yellow compound which was collected and recrystallised from ethanol to give yellow needles of 4-hydroxy-1-methoxalyl-2-methyl-3H-cycl [3,3,2] azin-3-one (LIX, $R = CH_3$, $R' = COCO_2CH_3$).

Yield 1.2 g. (20%) m.p. 197°C.

ν max: 3210 cm^{-1} (-OH); 1600, 1655, 1740 cm^{-1} (C = O).

Its n.m.r. spectrum showed a multiplet in the region τ 1.2 - 2.8, a broad peak at τ 3.8 and two singlets at τ 5.92 and 6.96, in the ratio 4 : 1 : 3 : 3.

$C_{15}H_{11}NO_5$ requires: C = 63.16%; H = 3.89%; N = 4.91 %.

found : C = 62.32%; H = 3.83%; N = 3.49 %.

repeat : N = 6.45 %.

Hydrolysis of 4-hydroxy-1-methoxalyl-2-methyl-3H-cycl [3,3,2] azin-3-one:

4-Hydroxy-1-methoxalyl-2-methyl-3H-cycl [3,3,2] azin-3-one (0.8 g.) was dissolved in methanol (25 ml.) containing excess of potassium hydroxide. Water (5 ml.) was added and the solution heated under reflux for 1 hour. The solvent was removed under reduced pressure, the red potassium salt dissolved in water and the solution carefully acidified with concentrated

hydrochloric acid. The resulting precipitate was filtered off, dried and recrystallised from glacial acetic acid to give 4-hydroxy-2-methyl-1-oxalyl-3H-cycl [3,3,2] azin-3-one (LIX, R = CH_3, R′= $COCO_2H$).

Yield 0.53 g. (73.1%). m.p. 252°C.

ν max: 3210 cm^{-1} broad absorption (-OH); 1590, 1673, 1700 $cm.^{-1}$ (C = O).

$C_{14}H_9NO_5$ requires: C = 62.00%; H = 3.34%; N = 5.16%.

found : C = 61.32%; H = 3.75%; N = 4.31%.

Oxidation of 4-hydroxy-2-methyl-1-oxalyl-3H-cycl [3,3,2] azin-3-one with hydrogen peroxide:

The oxalyl compound (LIX, R = CH_3, R′= $COCO_2H$) (0.5 g.) was dissolved in 2 N. aqueous sodium hydroxide (6 ml.), and 30% hydrogen peroxide (0.5 ml.) in water (1 ml.) was added to the solution, cooled to 0°C, care being taken that the temperature did not rise above 0°C. The solution was left for 40 hours at 0°C, treated with manganese dioxide to destroy excess hydrogen peroxide, and allowed to stand for 1 hour more at 0°C. After filtering, the solution was cautiously acidified with concentrated hydrochloric acid and the resulting precipitate filtered off and dried. No solvent could be found for the 4-hydroxy-2-methyl-3-oxo-3H-cycl [3,3,2] azin-1-carboxylic acid (LIX, R = CH_3, R′= CO_2H).

Yield 0.4 g. (89.2%). m.p. 360°C.

ν max: ca.3200 $cm.^{-1}$ broad absorption (-OH); 1590, 1690 $cm.^{-1}$ (C = O).

Decarboxylation of 4-hydroxy-2-methyl-3oxo-3H-cycl [3,3,2] azin-1-carboxylic acid:

The carboxylic acid (LIX, R = CH_3, R′= CO_2H) (0.2 g.) was mixed with finely ground soda-lime and strongly heated at 0.03 m.m. Rapid decomposition occurred but a small amount of a yellow compound sublimed on to a cold finger.

Yield 0.016 g. (9.8%). m.p. 148°C.

Insufficient pure product was obtained for elemental analysis but the n.m.r. spectrum of the compound showed it to be the required 4-hydroxy-2-methyl-3H-cycl[3,3,2]azin-3-one (LIX, R = CH_3, R' = H).

νmax: 3300 $cm.^{-1}$ (-OH): 1590 $cm.^{-1}$ (C = O).

SECTION B.

Attempt to prepare pyruvoyl chloride:[86]

Equimolecular proportions of pyruvic acid and anhydrous pyridine were mixed and added, dropwise, to a stirred solution of a molar equivalent of thionyl chloride in five times its weight of anhydrous ether at 0°C. Care was taken that the temperature did not rise above 10°C. After the addition of the pyruvic acid-pyridine mixture had been completed a current of dry hydrogen chloride was passed through the solution. The pyridine hydrochloride was filtered off and the ethereal solution fractionated. A small amount of acetyl chloride was collected at 51°C., but the temperature then rose steadily to 140°C. and no pure fraction could be isolated. The literature boiling point of pyruvoyl chloride is 70 - 80°C.

Attempt to prepare benzoylformyl chloride:[87,88]

Benzoylformic acid (15 g. 0.1 mole) and oxalyl chloride (50.8 g. 0.4 mole) were heated under reflux for 6 hours. After removal of unreacted oxalyl chloride, the reaction mixture was fractionated under reduced pressure. Practically all the higher boiling material distilled between 100 and 110°C. (50 mm.) and, after redistillation, was identified as benzoyl chloride by its infrared spectrum. The yield was 9.7 g. (69%). The literature boiling point of benzoylformylchloride is 91°C./9 mm. (125°C./9 mm.).

5-Methyl-2-phenyl-3-pyruvoylindolizine (LX, R = C_6H_5, R' = CH_3):

A solution of 5-methyl-2-phenylindolizine (6.21g. 0.3 mole), pyruvic acid (2.64 g. 0.3 mole) and triethylamine (6.06 g. 0.6 mole) in dichloromethane (100 ml.), was cooled in an ice-salt bath. To this stirred solution was added, dropwise, a solution of phosphoryl chloride (4.59 g. 0.3 mole) in dichloromethane (20 ml.). The solution was stirred for a further 3 hours after the addition of the phosphoryl chloride had been completed, then allowed to stand at room temperature overnight. The solution was next shaken with water, dried, and the dichloromethane removed under reduced pressure. The residue was dissolved in a minimum of benzene and chromatographed on alumina. Elution with benzene gave a large amount of starting material, which was recovered. Elution with a 50 : 50 benzene-ether mixture gave a yellow-brown band which, after removal of solvent, gave a yellow-brown solid. Recrystallisation from benzene gave 5-methyl-2-phenyl-3-pyruvoylindolizine.

Yield 1.2 g. (26.8%). m.p. 102°C.

ν max: 1600, 1705 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed a multiplet between τ 2.4 and 3.5 and two singlets at τ 7.5 and 8.04, in the ratio 10 : 3 : 3.

$C_{18}H_{15}NO_2$ requires: C = 77.96%; H = 5.45%; N = 5.05%

found : C = 77.75%; H = 5.60%; N = 5.30%

The reaction of 2,5-dimethylindolizine with pyruvic acid and phosphoryl chloride in the presence of triethylamine:

To a cooled, stirred solution of 2,5-dimethylindolizine (5.0 g.), pyruvic acid (2.93 g.) and triethylamine (6.73 g.) in dichloromethane (100 ml.), was added, dropwise, a solution of phosphoryl chloride (5.11 g.) in dichloromethane (20 ml.). The solution was stirred for a further 3 hours, then allowed to stand at room temperature overnight. The solution was next shaken with water,

dried, and the solvent removed under reduced pressure. The residue was taken up in a minimum of benzene and chromatographed on alumina. Elution with benzene gave a large amount of starting material. Elution with a 50 : 50 benzene-ether mixture gave two bands, an orange band which, after removal of solvent, gave an orange oil, and a yellow band which gave a yellow solid. The oil could not be crystallised and n.m.r. spectroscopy identified it as 2,5-dimethyl-3-pyruvoylindolizine.

The n.m.r. spectrum showed an aromatic multiplet in the region τ 2.4 - 3.6 and three singlets at τ 7.4, 7.5 and 7.62, in the ratio 4 : 3 : 3 : 3.

The yellow solid was recrystallised from benzene and gave yellow needles of 2,5-dimethyl-1-pyruvoylindolizine.

Yield 0.4 g. (5.4%). m.p. 94°C.

ν_{max}: 1600, 1710 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed a doublet at τ 1.9, a multiplet in the region τ 2.7 - 3.4 and two singlets at τ 7.5 and 7.65, in the ratio 1 : 3 : 6 : 3.

$C_{13} H_{13} NO_2$ requires: C = 72.54%; H = 6.09%; N = 6.51%.

found : C = 72.63%; H = 6.45%; N = 7.15%.

The reaction of 5-methyl-2-phenyl-3-pyruvoylindolizine with sodium methoxide in methanol:

5-Methyl-2-phenyl-3-pyruvoylindolizine (0.5 g.) was dissolved in dry methanol (30 ml.) containing a molar equivalent of sodium methoxide. The solution was heated under reflux for 90 minutes and then the solvent was removed under reduced pressure. The residue was taken up in benzene and chromatographed on alumina. Eluting with a 50 : 50 benzene-ether mixture gave two bands. The first, a yellow-brown band, gave, after removal of solvent, 0.3 g. of starting material. The second, a bright yellow band gave a small amount of an orange-yellow solid. Recrystallisation from benzene gave orange needles of 4-methyl-2-phenyl-3H-cycl $\left[3,3,2\right]$ azin-3-one (LXI, R = $C_6 H_5$, R' = CH_3).

Yield 0.07 g. (14.7%). m.p. 176°C.

ν max : 1603 $cm.^{-1}$ (C = O)

$C_{18}H_{13}NO$ requires : C = 83.38%; H = 5.05%; N = 5.40%

found : C = 83.65%; H = 4.72%; N = 5.44%

SECTION C.

α-Chloro-α- hydroxyiminoacetone

Hesse and Krehbiel Ber. 88 130 (1955). m.p.107 - 108°C.

ω-Chloro- ω -hydroxyiminoacetophenone

Levin and Hartung Organic Syntheses 24 25. m.p. 132 - 133°C.

Ethyl chlorohydroxyiminoacetate

Skinner J.A.C.S. 46 731 (1924). m.p. 80°C.

The reaction of 5-methyl-2-phenylindolizine with ω-chloro- ω -hydroxyiminoacetophenon in the presence of triethylamine:

To a stirred solution of 5-methyl-2-phenylindolizine (5.0 g.) and ω-chloro- ω -hydroxyiminoacetophenone (4.44 g.) in benzene, was added, dropwise, triethylamine (2.44g.). The solution was allowed to stand overnight, then washed with water, dried, and the solvent removed under reduced pressure. The residue was taken up in benzene and chromatographed on alumina. Eluting with benzene gave, after removal of a small amount of starting material, an orange-brown band which, after removal of solvent gave an orange solid. Recrystallisation from benzene gave a mixture of 1- and 3- (α -hydroxyiminophenacyl) -5-methyl-2-phenylindolizines.

Yield 6.1g. (71.3%)

$C_{23}H_{18}N_2O_2$ requires: C = 77.95%; H = 5.12%; N = 7.90%.

found : C = 75.29%; H = 5.20%; N = 7.38%.

Recrystallisation of a small amount of the mixture from a large volume of benzene gave a pure sample of 3-(∝-hydroxyiminophenacyl)-5-methyl-2-phenylindolizine. m.p. 161°C.

$C_{23}H_{18}N_2O_2$ requires: C = 77.95%; H = 5.12%; N = 7.90%

found : C = 77.32%; H = 4.96%; N = 7.83%

Elution with ethyl acetate gave a yellow fraction which crystallised from ethyl acetate but which could not be identified.

Yield (0.25 g.) m.p. 207°C.

ν max: 3200 $cm.^{-1}$; 1640 $cm.^{-1}$

Analysis C = 74.53%; H = 5.16%; N = 8.24%

$C_{31}H_{23}N_3O_4$ requires C = 74.24%; H = 4.62%; N = 8.38%

<u>The reaction of 5-methyl-2-phenylindolizine with ∝-chloro-∝-hydroxyiminoacetone in the presence of triethylamine</u>:

5-Methyl-2-phenylindolizine (5.0 g.) and ∝-chloro- ∝-hydroxyiminoacetone (2.94 g.) were dissolved in dry benzene (100 ml.). To the stirred solution triethylamine (2.44 g.) was added, dropwise, and the solution was allowed to stand overnight. The solution was then shaken with water, dried, and the solvent removed under reduced pressure. The residue was taken up in benzene and chromatographed on alumina. A small amount of the starting material was first eluted with benzene. A deep yellow band was then eluted and, on removal of solvent, gave a mixture of 1- and 3- (∝-hydroxyiminoacetonyl)-5-methyl-2-phenylindolizines.

Yield 6.2 g. (87.9%)

$C_{18}H_{16}N_2O_2$ requires: C = 73.96%; H = 5.52%; N = 9.58%

found : C = 73.26%; H = 5.76%; N = 10.27%

Recrystallisation of a small amount of the mixture from a large volume of benzene gave a pure sample of 3-(∝-hydroxyiminoacetonyl)-5-methyl-2-phenylindolizine. m.p. 184°C.

ν max: 3220 cm.$^{-1}$ (- OH); 1680 cm.$^{-1}$ (C = O).

Its n.m.r. spectrum showed a multiplet in the region τ 2.4 - 3.7 and two singlets at τ 7.60 and 7.66, in the ratio 10 : 3 : 3.

$C_{18}H_{16}N_2O_2$ requires : C = 73.96%; H = 5.52%; N = 9.58%

found : C = 73.42%; H = 5.77%; N = 9.48%

The reaction of 2,5-dimethylindolizine with ω-chloro-ω-hydroxyiminoacetophenone in the presence of triethylamine:

To a stirred solution of 2,5-dimethylindolizine (5.0 g.) and ω-chloro-ω-hydroxyiminoacetophenone (6.3 g.) in dry benzene (100 ml.), triethylamine (3.6 g.) was added, dropwise, and the solution allowed to stand overnight. The solution was then shaken with water, dried, and the benzene removed under reduced pressure. The residue was taken up in a minimum of benzene and chromatographed on alumina. Benzene first eluted a small amount of unreacted starting material, then a red-orange band which, after removal of solvent, gave a red-orange solid. Recrystallisation from benzene gave a mixture of 1- and 3- (α-hydroxyiminophenacyl)-2,5-dimethylindolizines.

Yield 4.0 g. (39.7%).

$C_{18}H_{16}N_2O_2$ requires: C = 73.96%; H = 5.52%; N = 9.58%.

found : C = 74.26%; H = 6.06%; N = 9.17%.

By recrystallising a small amount of the mixture from a large volume of benzene, red crystals of the 3-isomer were obtained. m.p. 142 - 144°C.

ν max: 3260 cm.$^{-1}$ (- OH); 1640 cm.$^{-1}$ (C = O).

Its n.m.r. spectrum showed an aromatic multiplet in the region τ 1.8 - 3.6 and two singlets at τ 7.66 and 7.84, in the ratio 10 : 3 : 3.

$C_{18}H_{16}N_2O_2$ requires: C = 73.96%; H = 5.52%; N = 9.55%.

found : C = 74.80%; H = 5.92%; N = 8.97%.

repeat : C = 73.59%; H = 6.08%; N = 9.43%.

The reaction of 2,5-dimethylindolizine with ∝-chloro-∝-hydroxyiminoacetone in the presence of triethylamine:

2,5-Dimethylindolizine (2.0g.) and ∝-chloro-∝-hydroxyiminoacetone (1.68 g.) were dissolved in dry benzene (50 ml.). Triethylamine was added, dropwise, to the stirred solution which was then allowed to stand overnight. The solution was then shaken with water, dried, and the benzene removed under reduced pressure. The residue was taken up in benzene and chromatographed on alumina. Elution with benzene gave first some unreacted starting material, then a red band which, after removal of solvent, gave a red oil.

Yield ca 2.2g. (72.3%)

The n.m.r. spectrum of this oil showed a complex multiplet in the region τ 2.7 - 3.9 and another multiplet in the region τ 7.4 - 8.1. Scale expansion of the latter showed six peaks indicating the presence of both the 1- and the 3- (∝-hydroxyiminoacetonyl)-2,5-dimethylindolizines.

The reaction of 5-methyl-2-phenylindolizine with ethyl chlorohydroxyiminoacetate in the presence of triethylamine:

To a stirred solution of 5-methyl-2-phenylindolizine (5.0 g.) and ethylchlorohydroxyiminoacetate (3.66 g.) in dry benzene (100 ml.), triethylamine was added, dropwise, and the solution allowed to stand overnight. The solution was then shaken with water, dried, and the benzene removed under reduced pressure. The residue was dissolved in benzene and chromatographed on alumina. Elution with benzene gave, apart from some unreacted starting material, a yellow band which, on removal of solvent, gave a yellow solid. Recrystallisation from benzene gave yellow crystals of ethyl hydroxyimino (5-methyl-2-phenylindolizin-3-yl) acetate.

Yield 5.7 g. (65.3%) m.p. 166°C.

ν max: 3300 $cm.^{-1}$ (- OH); 1700 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed a multiplet in the region τ2.3 - 3.7, a singlet at τ7.6, a triplet (J = 8 c.p.s) at τ9.05 and a quartet (J = 8 c.p.s.) at τ5.9, in the ratio 9 : 3 : 3 : 2.

$C_{19}H_{18}N_2O_3$ requires: C = 70.79%; H = 5.63%; N = 8.69%.

found : C = 70.90%; H = 5.80%; N = 8.40%.

The reaction of 1-methyl-2-phenylindolizine with α-chloro-α-hydroxyiminoacetone in the presence of triethylamine:

1-Methyl-2-phenylindolizine (0.5 g.) and α-chloro-α-hydroxyiminoacetone (0.3g.) in dry benzene (30 ml.) were treated with triethylamine (0.35 ml.) and the solution allowed to stand overnight. The solution was then shaken with water, dried, and the solvent removed under reduced pressure leaving an orange-red solid which recrystallised from benzene to give orange-red crystals of 3-(α-hydroxyiminoacetonyl)-1-methyl-2-phenylindolizine (LXXII).

Yield 0.5 g. (70%) m.p. 152°C.

ν max: 3220 $cm.^{-1}$ (-OH); 1700 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed a multiplet in the region τ1.9 - 3.6 and two singlets at τ7.60 and 7.68, in the ratio 10 : 3 : 3.

$C_{18}H_{16}N_2O_2$ requires: C = 73.96%; H = 5.52%; N = 9.58%.

found : C = 74.75%; H = 6.07%; N = 8.90%.

repeat : C = 75.78%; H = 6.40%; N = 9.85%.

The reaction of 3-methyl-2-phenylindolizine with α-chloro-α-hydroxyiminoacetone in the presence of triethylamine:

A stirred solution of 3-methyl-2-phenylindolizine (0.5 g.) and α-chloro-α-hydroxyiminoacetone (0.3 g.) in dry benzene (30 ml.) was treated with triethylamine (0.35 ml.) and the solution allowed to stand overnight. The solution was then shaken with water and dried. The benzene was removed under reduced pressure to give a yellow-orange solid which recrystallised from

benzene to give 1- (∝-hydroxyiminoacetonyl)-3-methyl-2-phenylindolizine (LXXIII).

Yield 0.46 g. (65%). m.p. 197°C.

ν max: 3220 $cm.^{-1}$ (- OH) ; 1700 (C = O).

Its n.m.r. showed a multiplet in the region τ 1.6 - 3.4 and two singlets at τ 7.54 and 7.72 in the ratio 10 : 3 : 3.

$C_{18} H_{16} N_2 O_2$ requires : C = 73.96%; H = 5.52%; N = 9.58%.

found : C = 73.75%; H = 5.70%; N = 9.59%.

The reaction of 1- and 3- (∝-hydroxyiminophenacyl) - 5 - methyl -2-phenylindolizines with potassium tert-butoxide in tert-butanol:

A solution of the 1- and 3- (∝-hydroxyiminophenacyl) derivatives (7.3 g.) in tert-butanol containing an excess of potassium tert-butoxide, was heated under reflux for 90 minutes. The tert-butanol was removed under reduced pressure and the residue boiled with water and filtered. The residue was dried and dissolved in boiling chloroform. On cooling yellow needles of 1- (∝-hydroxyiminophenacyl) -5-methyl-2-phenlindolizine were deposited.

Yield 0.7 g. m.p. 200°C.

$C_{23} H_{18} N_2 O_2$ requires: C = 77.95%; H = 5.12%; N = 7.90%.

found : C = 78.29%; H = 5.56%; N = 7.81%.

The mother liquor was evaporated to dryness and the residue recrystallised from benzene to give bright orange crystals of 3-hydroxyimino-2,4-diphenyl-3H-cycl [3,3,2] azine.

Yield 0.9 g. (13%) m.p. 198°C. (chars)

$C_{23} H_{16} N_2 O$ requires: C = 82.12%; H = 4.79%; N = 8.33%.

found : C = 82.81%; H = 5.24%; N = 9.09%.

repeat : C = 81.65%; H = 5.10%; N = 8.50%.

The aqueous filtrate was carefully acidified with dilute hydrochloric acid and the resulting precipitate filtered off and dried. From the yield of the precipitate (7.4 g.) it was obvious that the hydrochlorides of the starting

material had been formed. The precipitate was dissolved in boiling benzene and filtered. On cooling crystals of the starting material were deposited.

Yield 5.3 g.

The reaction of 1- and 3- (∝ -hydroxyiminophenacyl)-5-methyl-2-phenylindolizines with potassium tert-butoxide in dimethyl sulphoxide:

A solution of the 1- and 3- (∝ -hydroxyiminophenacyl) derivatives (5.0 g.) in dry dimethyl sulphoxide (50 ml.), containing excess of potassium tert-butoxide, was heated under reflux for 5 minutes. The dimethyl sulphoxide was removed under reduced pressure and the residue dissolved in dichloromethane and chromatographed on alumina. Eluting with dichloromethane gave a bright orange band which, after removal of solvent, gave an orange solid. Recrystallisation from benzene gave 3-hydroxyimino-2,4-diphenyl-3H-cycl [3,3,2] azine.

Yield 1.2 g. (25.3 %).

The reaction of 1- and 3- (∝ -hydroxyiminoacetonyl)-5-methyl-2-phenylindolizines with potassium tert-butoxide in dimethyl sulphoxide:

A solution of the 1- and 3- (∝ -hydroxyiminoacetonyl) derivatives (5.0 g.) in dry dimethyl sulphoxide (30 ml.), containing an excess of potassium tert-butoxide, was heated under reflux for 5 minutes. The dimethyl sulphoxide was removed under reduced pressure, the residue dissolved in dichloromethane and chromatographed on alumina. Eluting with dichloromethane gave an orange band which, after removal of solvent, gave an orange solid. Recrystallisation from benzene gave 3-hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine.

Yield 2.5 g. (53.3%). m.p. 202°C. (chars)

$C_{18} H_{14} N_2O$ requires: C = 78.81%; H = 5.14%; N = 10.21%.

found : C = 75.89%; H = 5.16%; N = 10.15%.

repeat : C = 79.15%; H = 5.15%

The reaction of 1- and 3- (∝ -hydroxyiminophenacyl) -2,5-dimethylindolizines with potassium tert-butoxide in dimethyl sulphoxide:

A solution of 1- and 3- (∝-hydroxyiminophenacyl)-2,5-dimethylindolizines (4.5g.) in dry dimethyl sulphoxide (30 ml.), was heated under reflux for 5 minutes with an excess of potassium tert-butoxide. The solvent was removed under reduced pressure, the residue dissolved in dichloromethane and chromatographed on alumina. Dichloromethane eluted an orange band which, after removal of solvent, gave an orange solid. Recrystallisation from benzene gave 3-hydroxyimino -2-methyl-4-phenyl-3H-cycl [3,3,2] azine.

Yield 2.2 g. (52.0%). m.p. 204°C. (chars)

$C_{18}H_{14}N_2O$ requires: C = 78.81%; H = 5.14%; N = 10.21%

found : C = 78.40%; H = 5.08%; N = 10.10%.

The reaction of 1- and 3- (∝-hydroxyiminoacetonyl) -2,5-dimethylindolizines with potassium tert-butoxide in dimethyl sulphoxide:

The oil (ca. 2.2 g.) obtained from the reaction of 2,5-dimethylindolizine with ∝-chloro-∝-hydroxyiminoacetone, was dissolved in dry dimethyl sulphoxide (30 ml.). An excess of potassium tert-butoxide was added and the solution heated under reflux for 5 minutes. The dimethyl sulphoxide was removed under reduced pressure, the residue taken up in dichloromethane and chromatographed on alumina. Eluting with dichloromethane gave an orange band which, after removal of solvent, gave an orange solid. Recrystallisation from benzene gave 3-hydroxyimino-2,4-dimethyl-3H-cycl [3,3,2] azine.

Yield 0.4 g. (19.7%). m.p. 110°C. (chars)

$C_{13}H_{12}N_2O$ requires: C = 73.57%; H = 5.70%; N = 13.20%.

found : C = 73.93%; H = 5.88%; N = 12.72%.

The reaction of ethyl hydroxyimino (5-methyl-2-phenylindolizin-3-yl) acetate with potassium tert-butoxide in dimethyl sulphoxide:

A solution of the ester (0.5 g.) and excess of potassium tert-butoxide in dry dimethyl sulphoxide (20 ml.) was heated under reflux for 5 minutes. The solvent was removed under reduced pressure and the residue taken up in dichloromethane and chromatographed on alumina. A light brown band was eluted with dichloromethane and, after removal of solvent, gave a solid, which recrystallised from benzene to give 3-cyano-5-methyl-2-phenylindolizine.

Yield 0.2 g. (58.3%). m.p. 114°C.

ν max: 2200 $cm.^{-1}$ (C = N).

Its n.m.r. spectrum showed a multiplet between 2.1 and 3.7 and a singlet at 7.05, in the ratio 9 : 3.

$C_{16}H_{12}N_2$ requires: C = 82.73%; H = 5.21%; N = 12.06%.

found : C = 82.52%; H = 5.18%; N = 12.30%.

Hydrolysis of 3-hydroxyimino-2-methyl-4-phenyl-3H-cycl [3,3,2] azine with levulinic acid-hydrochloric acid mixture:

3-Hydroxyimino-2-methyl-4-phenyl-3H-cycl [3,3,2] azine (0.1 g.) was stirred on a steam bath in a 9 : 1 mixture of levulinic acid and N hydrochloric acid (10 ml.) for 3 hours. The solution was diluted with water, extracted with dichloromethane and the extracts washed with sodium bicarbonate solution. The dichloromethane was removed under reduced pressure from the dried extracts and the residue chromatographed on alumina using benzene as eluent. A yellow fluorescent solution was obtained which, after removal of solvent gave an orange-yellow solid. Recrystallisation from benzene gave 2-methyl-4-phenyl -3H-cycl [3,3,2] azin-3-one.

Yield 0.05 g. (47.7%) m.p. 153°C.

ν max: 1603 $cm.^{-1}$ (C = O)

Its n.m.r. spectrum showed an aromatic multiplet in the region τ 1.9 - 3.0 and a singlet at τ 7.05 in the ratio 10 : 3.

$C_{18}H_{13}NO$ requires: C = 83.38%; H = 5.05%; N = 5.40%.

found : C = 81.96%; H = 5.91%; N = 7.61%.

repeat : C = 82.56%; H = 5.09%; N = 7.85%.

The reason for the poor analysis figures is that the cyclazinone, slowly changes into another compound. This compound has not been identified.

The reaction of 3-hydroxyimino-2,4-diphenyl-3H-cycl [3,3,2] azine with sodium nitrite in glacial acetic acid:

3-Hydroxyimino-2,4-diphenyl-3H-cycl [3,3,2] azine (0.1 g.) was dissolved in glacial acetic acid (10 ml.) and treated with a 5% aqueous solution of sodium nitrite (1 ml.). The solution darkened immediately. After 1 hour the solution was diluted with water and extracted into dichloromethane. The extracts were shaken with aqueous sodium bicarbonate solution, washed with water and dried. The solvent was removed under reduced pressure and the residue taken up in benzene and chromatographed on alumina. Benzene eluted a yellow band which, after removal of solvent, gave a yellow solid which could not be identified.

An identical reaction using 3-hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine also gave a yellow solid which could not be identified.

The reaction of 3-hydroxyimino-2,4-diphenyl-3H-cycl [3,3,2] azine with diazomethane:

3-Hydroxyimino-2,4-diphenyl-3H-cycl [3,3,2] azine (0.2 g.) was dissolved in anhydrous ether (100 ml.), and one drop of boron trifluoride diethyl etherate added. An excess of diazomethane in ether was added and the solution allowed to stand overnight. The ether was then removed under reduced pressure, the residue taken up in benzene and chromatographed on alumina. Eluting with benzene gave two bands. The first, a pink band, gave a negligible amount of product, the second, a yellow fluorescent band, gave, after removal of solvent, a yellow solid. Recrystallisation from benzene gave 2,4-diphenyl-3H-cycl [illegible]

Yield 0.08 g. (41.8%) m.p. 192°C.

max: 1603 cm.$^{-1}$ (C = O).

$C_{23} H_{15} N O$ requires: C = 85.96%; H = 4.70%; N = 4.36%.

found : C = 85.63%; H = 5.30%; N = 5.18%.

The reason for the poor analysis figures is that the cyclazinone slowly changes into another compound. The latter has not been identified.

The reaction of 3-hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine with diazomethane:

3-Hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine (0.2 g.) was dissolved in ether (100 ml.) and one drop of boron trifluoride diether etherate added. An excess of diazomethane in ether was added and the solution allowed to stand overnight. The ether was then removed under reduced pressure, the residue dissolved in a minimum of benzene and chromatographed on alumina. Eluting with a 50 : 50 benzene-light petroleum mixture gave an orange oil which could not be crystallised and could not be identified. Eluting with benzene gave a red-orange band which, after removal of solvent, gave a red solid. Recrystallisation from ethanol gave deep red needles but the compound could not be identified.

Yield 0.02 g. m.p. 161°C.

Its infrared spectrum showed an absence of C = O and -OH absorption.

Its n.m.r. spectrum showed a multiplet in the region τ 1.4 - 3.2 and two singlets at τ 6.82 and 7.74, in the ratio ~ 12 : 3 : 3.

Analysis C = 69.98%; H = 5.87%; N = 11.69%.

$C_{15} H_{15} N_2 O_2$ requires: C = 70.57%; H = 5.88%; N = 10.98%.

The reaction of 3-hydroxyimino-2-methyl-4-phenyl-3H-cycl [3,3,2] azine with diazomethane:

3-Hydroxyimino-2-methyl-4-phenyl-3H-cycl [3,3,2] azine (0.2 g.) was dissolved in ether (100 ml.) and one drop of boron trifluoride diether etherate added. An excess of diazomethane in ether was added and the solution allowed to stand overnight. The ether was removed under reduced pressure, the residue dissolved in a minimum of benzene and chromatographed on alumina. Eluting with a 50 : 50 benzene-light petroleum mixture gave two bands. The first, an orange band, gave an orange oil which could not be crystallised and could not be identified; the second band gave a negligible amount of product. Eluting with benzene gave a yellow fluorescent band which, after removal of solvent gave an orange-yellow solid. Recrystallisation from benzene gave 2-methyl-4-phenyl-3H-cycl [3,3,2] azin-3-one.

Yield 0.02 g. (9.7 %).

ν max: 1603 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed a multiplet in the region τ 2.0 - 3.1 and a singlet at τ 7.1, in the ratio 11 : 3.

The reaction of 3-hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine with silver oxide in methyl iodide:

3-Hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine (0.1 g.) and silver oxide (0.1 g.) were heated in an excess of methyl iodide for 2 hours. The solution was filtered and the methyl iodide removed under reduced pressure. The residue was taken up in benzene and chromatographed on alumina. Eluting with benzene gave a yellow fluorescent band which, after removal of solvent, gave a yellow-orange solid. Recrystallisation from benzene gave 4-methyl-2-phenyl-3H-cycl [3,3,2] azin-3-one.

Yield 0.08 g. (77.9 %).

The infrared spectrum obtained was identical to that of the cyclazinone prepared by base catalysed cyclisation of 5-methyl-2-phenyl-3-pyruvoylindolizine.

The reaction of 3-hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine with silver oxide in dichloromethane:

3-Hydroxyimino-4-methyl-2-phenyl-3H-cycl [3,3,2] azine (0.1 g.) and silver oxide (0.1 g.) were heated in dichloromethane for 2 hours. The solution was filtered and the dichloromethane removed under reduced pressure leaving a yellow solid. Recrystallisation from benzene gave 4-methyl-2-phenyl-3H-cycl [3,3,2] azin-3-one.

Yield 0.08 g. (77.9 %).

Identical reactions using the 2-methyl-4-phenyl and the 2,4-diphenyl derivatives gave equally high yields of the corresponding ketones.

Reaction of 3-hydroxyimino-3H-cycl [3,3,2] azines with bromine:

The 3-hydroxyimino-3H-cycl [3,3,2] azine (0.1 g.) was dissolved in glacial acetic acid (25 ml.) and bromine added until precipitation was complete.

3N-Bromohydroxyamino-2,4-diphenyl-dehydrocycl [3,3,2] azinium tribromide.

Yield 0.18 g. m.p. decomposes at 300°C.

$C_{23}H_{16}N_2OBr_4$ requires: C = 42.11%; H = 2.46%; N = 4.27%; Br = 48.73%

found : C = 43.12%; H = 2.41%; N = 5.57%; Br = 44.51%

3-N-Bromohydroxyamino-4-methyl-2-phenyl-dehydrocycl [3,3,2] azinium tribromide

Yield 0.22 g. m.p. 204° (chars)

$C_{18}H_{14}N_2OBr_4$ requires: C = 36.40%; H = 2.38%; N = 4.72%; Br = 53.81%

found : C = 36.90%; H = 2.66%; N = 5.72%; Br = 54.05%

3-N-Bromohydroxyamino-2-methyl-4-phenyl-dehydrocycl [3,3,2] azinium tribromide

Yield 0.24 g. m.p. decomposes at 300°C.

$C_{18}H_{14}N_2OBr_4$ requires: C = 36.40%; H = 2.38%; N = 4.72%; Br = 53.81%

found : C = 36.60%; H = 2.62%; N = 5.10%; Br = 51.64%

The tribromides were very insoluble in all common solvents and could not be recrystallised. Heating the tribromides in glacial acetic acid gradually converted them to the corresponding ketones.

ATTEMPTS TO SYNTHESISE A DERIVATIVE OF THE DEHYDROCYCL [3,3,2] AZINIUM CATION:

Reaction of 4-methyl-2-phenyl-3H-cycl [3,3,2] azin-3-one with lithium aluminium hydride:

A stirred, heated solution containing an excess of lithium aluminium hydride in absolute ether (20 ml.) was treated with a solution of 4-methyl-2-phenyl-3H-cycl[3,3,2]azin-3-one (0.1 g.) in absolute ether (20 ml.). The solution was heated under reflux for 7 hours. The excess lithium aluminium hydride was hydrolysed by the careful addition of water, the solution filtered and the filtrate dried. The ether was removed under reduced pressure, the residue taken up in a minimum of benzene and chromatographed on alumina. Eluting with light-petroleum gave a yellow band which, after removal of solvent, gave a yellow-green oil. This oil which darkened rapidly on exposure to air, was dissolved in glacial acetic acid and treated with a solution of trityl fluoborate in glacial acetic acid. On being poured into ether, the solution deposited a white flocculent precipitate. The precipitate was filtered off but on exposure to air it decomposed so rapidly that no examination could be carried out.

Reaction of 4-methyl-2-phenyl-3H-cycl [3,3,2] azin-3-one with diborane:

4-Methyl-2-phenyl-3H-cycl[3,3,2] azin-3-one (0.1 g.) was dissolved in dry tetrahydrofuran (30 ml.). Excess of diborane was bubbled through the solution in a stream of nitrogen and the solution allowed to stand overnight, during which time a flocculent precipitate was deposited. The tetrahydrofuran was removed under reduced pressure, the residue treated with dilute hydrochloric acid and extracted into ether. The ether extracts darked rapidly and a dark green precipitate was deposited, probably owing to the decomposition of the unstable reduction product.

ATTEMPTS TO SYNTHESISE A DERIVATIVE OF 4H-CYCL 3,3,2 AZIN-4-ONE

Diphenylcyclopropenone

Breslow, J.A.C.S., 1965, 87, 1320. m.p. 119 - 120°C.

The reaction of 2-phenylindolizine with diphenylcyclopropenone:

2-Phenylindolizine (1.93 g.) and diphenylcyclopropenone (2.06 g.) were heated for 3 hours in toluene with 10% palladium on charcoal (0.2 g.) as a dehydrogenating catalyst. After 3 hours the solution was filtered and the toluene removed under reduced pressure. The residue was taken up in benzene and chromatographed on alumina. Elution with benzene gave a large amount of starting material followed by a pale yellow band. This, on removal of solvent, gave a yellowish solid which recrystallised from ethanol to give small white crystals. Elemental analysis showed an absence of nitrogen in the compound. The infrared spectrum showed no resemblance to that reported for the dimer (LXXXIII).

Yield 0.8 g. m.p. 242°C.

Analysis C = 87.42%; H = 5.24%.

The reaction of 1-methyl-2-phenylindolizine with diphenylcyclopropenone:

1-Methyl-2-phenylindolizine (1.0 g.) and diphenylcyclopropenone (1.0 g.) were heated under reflux for 3 hours in nitrobenzene. The nitrobenzene was then removed under reduced pressure and the residue dissolved in benzene and chromatographed on alumina. Elution with benzene gave a bright yellow band which, after removal of solvent gave a yellow solid. Recrystallisation from ethanol gave yellow crystals of a 1 : 1 adduct of 1-methyl-2-phenylindolizine and diphenylcyclopropenone.

Yield 0.5 g. (25%). m.p. 153°C.

$C_{30}H_{23}NO$ requires: C = 87.14%; H = 5.61%; N = 3.39%.

found : C = 87.47%; H = 5.90%; N = 3.60%.

THE SYNTHESIS OF DERIVATIVES OF 3H-BENZ [cd] AZULEN-3-ONE

2,4,6- Trimethylpyrylium perchlorate

Balabin and Nenitzescu, Organic Synthesis 44, 98: m.p. 244°C.

4,6,8- Trimethylazulene (LXXXVII, R = CH_3).[112.]

To a stirred suspension of sodium hydride (50% dispersion in mineral oil; 14 g.) in anhydrous tetrahydrofuran (150 ml.), cooled to -2°C, was slowly added, in a current of nitrogen, freshly distilled cyclopentadiene (25 ml.). Addition was controlled so that the temperature did not rise above 20°C. The deep pink solution was stirred for a further 20 minutes under nitrogen, then 2,4,6 - trimethylpyrylium perchlorate (30 g.) was added to the solution in small portions so that the temperature did not rise above 40°C. Stirring under nitrogen was continued for a further 40 minutes, then 100 ml. of tetrahydrofuran was removed under reduced pressure. The residue was diluted with water, extracted into light-petroleum and the extracts dried. The solvent was removed under reduced pressure leaving an oil. Distillation under high vacuum gave a violet distillate which rapidly solidified. Recrystallisation from ethanol gave violet plates of 4,6,8 - trimethylazulene.

Yield 10.2 g. (44.5 %). m.p. 80°C. (literature m.p. 80 - 81°C.)

1- Ethoxalyl - 4,6,8-trimethylazulene (LXXXVIII, R = CH_3).

4,6,8 - Trimethylazulene (5 g.; 0.029 mole) and ethoxalyl chloride (12.3 g; 0.088 mole) were heated together in dichloromethane (40 ml.) for 90 minutes. The solution was then shaken with sodium bicarbonate solution, washed with water, and dried. The dichloromethane was removed under reduced pressure leaving a red oil which solidified on being rubbed with light-petroleum. Recrystallisation from ethanol gave red needles of 1-ethoxalyl-4,6,8-trimethylazulene.

Yield 6.7 g. (84 %). m.p. 57°C.

Its n.m.r. spectrum showed a multiplet in the region τ 2.1 - 3.2, three singlets at τ 7.2, 7.35 and 7.54, a triplet (J = 8 c.p.s.) at τ 8.65 and a quartet (J = 8 c.p.s.) at τ 5.68; in the ratio 4 : 3 : 3 : 3 : 3 : 2.

$C_{17}H_{18}O_3$ requires: C = 75.53%; H = 6.71%.

found : C = 75.50%; H = 6.61%.

4-Hydroxy-7,9,-dimethyl-3H-benz [cd] azulen-3-one (LXXXIX, R = CH_3):

A solution of 1-ethoxalyl-4,6,8-trimethylazulene (2.0 g.) in "super-dry" methanol (50 ml.), containing a molar equivalent of sodium methoxide, was heated under reflux for 30 minutes. The solution was allowed to cool and the precipitated sodium salt filtered off. The precipitate was dissolved in water and the solution acidified with dilute hydrochloric acid. The resulting green precipitate was filtered off, dried, and recrystallised from nitromethane to give dark blue-green needles of 4-hydroxy-7,9-dimethyl-3H-benz [cd] azulen-3-one.

Yield 0.6 g. (36%). m.p. 257°C.

$C_{15}H_{12}O_2$ requires: C = 80.34%; H = 5.39%.

found : C = 79.90%; H = 5.41%.

Attempts to prepare 4-methoxy-7,9-dimethyl-3H-benz [cd] azulen-3-one:

(a) To a suspension of 4-hydroxy-7,9-dimethyl-3H-benz [cd] azulen-3-one (0.1 g.) in ether, was added an excess of diazomethane in ether. On removal of the solvent the 4-hydroxy compound was recovered unchanged.

(b) To a solution of the sodium salt (0.1 g.) of 4-hydroxy-7,9-dimethyl-3H-benz [cd] azulen-3-one in methanol was added a molar equivalent of dimethyl sulphate. The solution was allowed to stand overnight, but after removal of the solvent, the sodium salt was recovered and converted into the 4-hydroxy compound.

1,3-Bis- (chloromercuri) - 4,6,8-trimethylazulene:

4,6,8-Trimethylazulene (0.5 g.) and two molar equivalents of mercuric chloride were heated under reflux in benzene for 1 hour. The dark precipitate was filtered off, but no solvent could be found for recrystallisation.

Yield 1.5 g. (79.7%). m.p. 300°C.

Addition of excess ethoxalyl chloride to 1,3-Bis- (chloromercuri)-4,6,8-trimethylazulene (0.1 g.) in boiling dichloromethane gave no reaction and the compound was recovered unchanged after several hours.

3 - Acetylguaiazulene:[118].

A solution of acetyl bromide (2.1 ml.) and guaiazulene (2.3 g.) in dichloromethane was heated under reflux for 3 hours. The solution was poured into water and extracted into ether. The ether extracts were dried and the ether removed under reduced pressure. The residue was dissolved in light-petroleum and chromatographed on alumina. Eluting with light-petroleum gave a small amount of guaiazulene. Eluting with benzene gave a purple band which, after removal of solvent, yielded a purple oil. The oil solidified on being rubbed with light-petroleum and on recrystallisation from a 50 : 50 ethanol-light-petroleum mixture gave purple crystals of 3-acetylguaiazulene.

Yield 1.2 g. (40%). m.p. 85°C. (literature m.p. 85.5 - 86°C.)

1 - Acetyl-4,6,8-trimethylazulene:[109].

A solution of 4,6,8-trimethylazulene (1.0 g.) and three molar equivalents of acetyl bromide in dichloromethane (25 ml.) were heated under reflux for 2 hours. The solution was poured into water and extracted into ether. The ether extracts were dried and the ether removed under reduced pressure. The residue was dissolved in light-petroleum and chromatographed on alumina. Unreacted 4,6,8-trimethylazulene was first eluted with light-petroleum.

Elution with benzene gave a maroon band, which after removal of solvent, gave an oil. The oil solidified on being rubbed with light-petroleum, and recrystallisation from a 50 : 50 ethanol-light-petroleum mixture yielded maroon crystals of 1-acetyl-4,6,8-trimethylazulene.

Yield 0.45 g. (56%). m.p. 67°C. (literature m.p. 67-69°C.)

1,3 - Diacetyl - 4,6,8 - trimethylazulene:[109].

A solution of 4,6,8 - trimethylazulene (1.0 g.), three molar equivalents of acetyl chloride and one molar equivalent of anhydrous stannic chloride in dichloromethane (25 ml.), was heated under reflux for 90 minutes. The solution was poured into water and extracted into ether. The ether extracts were dried, and the ether removed under reduced pressure to give an oil which solidified on being rubbed with light-petroleum. Recrystallisation from a 50 : 50 ethanol-light-petroleum mixture gave deep red crystals of 1,3-diacetyl-4,6,8-trimethylazulene.

Yield 0.52 g. (78%). m.p. 173°C. (literature m.p.173-174°C.)

The reaction of 3 - acetylguaiazulene with selenium dioxide:

3-Acetylguaiazulene (0.5 g.) was added to a solution of one molar equivalent of selenium dioxide in dioxan (30 ml.) and water (ml.). The solution was heated under reflux for 4 hours. Thin layer chromatography showed that the 3-acetylguaiazulene was still present and had not been oxidised.

The reaction of 3 - acetylguaiazulene with iodine in pyridine:

3-Acetylguaiazulene (1.0 g., 0.04 mole) was dissolved in pyridine (30 ml.). Iodine (1.06 g., 0.04 mole) was added and the solution heated for 30 minutes on a steam bath, then allowed to stand overnight. Excess pyridine was removed under reduced pressure and the reaction mixture poured into water. On decanting off the aqueous layer a red tar was obtained which could not be crystallised.

Bromoacetyl bromide:[119].

Bromine (170 g.) was gradually added to purified acetic acid (40 g.) containing red phosphorous (8 g.). The mixture was heated at 120°C. for 1 hour and fractionally distilled, the fraction boiling 147 - 150° being collected.

Yield 59 g. (44 %).

3 - Bromoacetylguaiazulene:

A solution of guaiazulene (1.0 g.) and one molar equivalent of bromoacetyl bromide in dichloromethane (25 ml.) was heated under reflux for 2 hours. The solution was then poured into water and extracted into ether. The ether extracts were dried and the ether removed under reduced pressure. The residue was taken up in light-petroleum and chromatographed on alumina. Unreacted guaiazulene was eluted with light-petroleum while elution with benzene gave two further bands. The first, a blue band gave, after removal of solvent a blue oil which solidified on being rubbed with light petroleum. Recrystallisation from ethanol-light-petroleum gave blue needles of 3-bromoacetylguaiazulene.

Yield 0.38 g. (23.5 %). m.p. 76°C.

ν max: 1640 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed a multiplet in the region τ 1.7 - 2.9 and singlets at τ 5.66, 7.16, 7.43, 8.59 and 8.7; in the ratio 4 : 2 : 3 : 3 : 3 : 3. The septuplet due to the tertiary isopropyl proton was obscured by the methyl-proton absorptions at τ 7.16 and 7.43.

$C_{17}H_{19}BrO$ requires: C = 63.95%; H = 5.99%; Br = 25.03%.

found : C = 65.46%; H = 5.95%; Br = 22.80%.

The second band gave, after removal of solvent, a purple solid which on recrystallisation from ethanol-light-petroleum yielded crystals of 3-acetylguaiazulene.

Yield 0.38 g. (31 %). m.p. 85°C. (literature m.p. 85.5 - 86°C.)

The poor analysis figures for the 3-bromoacetylguaiazulene could be due to the presence of a small amount of 3-acetylguaiazulene as an impurity.

1 - Bromoacetyl-4,6,8-trimethylazulene:

A solution of 4,6,8-trimethylazulene (1.0 g.) and one molar equivalent of bromoacetyl bromide in dichloromethane (25 ml.) was heated under reflux for 2 hours, then poured into water and extracted with ether. The ether extracts were dried and the ether removed under reduced pressure. The residue was dissolved in light-petroleum containing a little benzene and chromatographed on alumina. Light-petroleum eluted a small amount of unreacted 4,6,8-trimethylazulen Two further bands were eluted with benzene. The first was a deep red band which, after removal of solvent, gave an oil. The oil solidified on being rubbed with light-petroleum and recrystallisation from ethanol-light-petroleum gave red needles of 1-bromoacetyl-4,6,8-trimethylazulene.

Yield 0.59 g. (34.5 %). m.p. 84°C.

ν max : 1640 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed an aromatic multiplet in the region τ 2.1 - 3.1 and four singlets at τ 5.64, 7.18, 7.20 and 7.44; in the ratio 4 : 2 : 3 : 3 : 3.

$C_{15}H_{15}BrO$ requires: C = 61.89%; H = 5.19%; Br = 27.21%.

found : C = 62.08%; H = 5.07%; Br = 27.34%.

The second band gave a maroon solid which on recrystallisation from ethanol-light-petroleum gave maroon crystals of 1-acetyl-4,6,8-trimethylazulene.

Yield 0.35 g. (30.8 %). m.p. 68°C. (literature m.p. 67 - 69°C.)

The reaction of 1-bromoacetyl-4,6,8-trimethylazulene with pyridine:

1-Bromoacetyl-4,6,8-trimethylazulene (0.1 g.) was dissolved in ether (20 ml.). A slight excess of pyridine was added and the solution left for several days. The precipitate which had formed was then filtered off and

and recrystallised from water to give dark red needles of the pyridinium bromide (XCVI).

Yield 0.08 g. (60 %). m.p. 250°C. (decomposes).

ν max : 1680 cm.$^{-1}$ (C = O).

$C_{20}H_{20}BrNO$ requires : C = 64.89%; H = 5.44%; N = 3.78%; Br = 21.60%.

found : C = 61.90%; H = 5.30%; N = 3.51%; Br = 20.40%.

repeat : C = 62.10%; H = 5.91%

Attempt to prepare 1-glyoxyloyl-4,6,8-trimethylazulene:

Equimolecular proportions of the pyridinium salt (XCVI) and p - nitrosodimethylaniline were dissolved in 10% aqueous alcohol and the solution cooled to -4°C. On addition of N. sodium hydroxide solution the smell of pyridine became obvious, and addition of water to the solution gave a tar which could not be crystallised. This tar was treated with 2N. hydrochloric acid and extracted into ether. The ether extracts were bright purple in colour and thin layer chromatography showed 4,6,8-trimethylazulene to be the only product present.

1-Dichloroacetyl-4,6,8-trimethylazulene (XCVII):

A solution of 4,6,8-trimethylazulene (1.0 g.) and dichloroacetyl chloride (0.57 ml.) in dichloromethane (20 ml.) was heated under reflux for 90 minutes. The reaction mixture was poured into water and extracted into ether. The ether extracts were dried and the ether removed under reduced pressure to give an oil which solidified on being rubbed with light-petroleum. Recrystallisation from ethanol gave purple crystals of 1-dichloroacetyl-4,6,8-trimethylazulene.

Yield 0.9 g. m.p. 121°C.

ν max : 1660 cm.$^{-1}$ (C = O).

Its n.m.r. spectrum showed a multiplet in the region τ1.9 - 2.9 and four singlets at τ3.05, 7.06, 7.1 and 7.32; in the ratio 4 : 1 : 3 : 3 : 3.

$C_{15}H_{14}Cl_2O$ requires: C = 64.06%; H = 4.98%; CL = 25.27%.

found : C = 63.74%; H = 4.81%; CL = 25.50%.

The reaction of 1-dichloroacetyl-4,6,8-trimethylazulene with sodium methoxide in methanol:

A solution of dichloroacetyl-4,6,8-trimethylazulene (0.5 g.) in "super-dry" methanol (30 ml.), containing one molar equivalent of sodium methoxide was heated under reflux for 90 minutes. Thin layer chromatography showed only the 1-dichloroacetyl derivative present, no other product having been formed.

The reaction of 1-dichloroacetyl-4,6,8-trimethylazulene with sodium hydride:

To a solution of 1-dichloroacetyl-4,6,8-trimethylazulene (0.5 g.) in anhydrous benzene was added an excess of sodium hydride and the mixture (protected from moisture) boiled for 90 minutes. Excess sodium hydride was destroyed with iso-propyl alcohol and the solution washed with water. On removal of the solvent from the dried organic layer a dark residue was obtained which failed to crystallise. Thin layer chromatography could only separate a small amount of starting material.

1,4,6,8 - and 2,4,6,8-Tetramethylazulenes (XCVIII and XCIX):[109].

To a cold (-20 to -30° C.) stirred suspension of 2,4,6-trimethylpyrylium perchlorate (22.2 g. 0.1 mole) in dry tetrahydrofuran (75 ml.), in an atmosphere of nitrogen, was added, dropwise, a solution prepared by the reaction of sodium hydride (50% dispersion in mineral oil; 2.4 g.; 0.1 mole) and freshly distilled methylcyclopentadiene (9 g.; 0.11 mole) in dry tetrahydrofuran (50 ml.).

The temperature was maintained at about -20°C. during the addition. The orange-yellow mixture which resulted was cooled to -50°C. and 250 ml. of a 1 M solution of potassium tert-butoxide in tert-butanol was added, dropwise, with stirring and cooling such that the temperature did not rise above -20°C. Stirring was continued for 12 hours, the contents of the flask being allowed to come to room temperature. About 150 ml. of solvent were removed under reduced pressure, the residue poured into water (2.5 l.) and extracted several times with ether. The ether was removed under reduced pressure from the dried extracts and the residue chromatographed on alumina. Eluting with light petroleum gave two bands, a magenta band and a blue band, which partially overlapped. Repeated chromatography separated the bands and recrystallisation of the products yielded 0.27 g. (1.5 %) of 2,4,6,8-tetramethylazulene as magenta needles m.p. 100°C. (literature m.p. 100°C.), and 0.29 g. (1.6 %) of 1,4,6,8-tetramethylazulene as blue crystals m.p. 41 - 42°C. (literature m.p. 42°C.)

1- Ethoxalyl-2,4,6,8-tetramethylazulene (CI):

2,4,6,8-Tetramethylazulene (0.27 g.) was heated in dichloromethane (20 ml.) with three molar equivalents of ethoxalyl chloride for 90 minutes. The solution was then poured into water, extracted with ether, and the ether extracts dried. Removal of the solvent under reduced pressure yielded an orange oil which could not be crystallised.

Yield 0.36 g. (81 %).

Its n.m.r. spectrum showed aromatic absorptions at τ 2.92 and 3.12, two singlets at τ 7.32 and 7.5, a triplet (J = 8 c.p.s.) at τ 8.66 and a quartet (J = 8 c.p.s.) at τ 5.66; in the ratio 3 : 6 : 6 : 3 : 2.

3-Ethoxalyl-1,4,6,8-tetramethylazulene ($\overline{C}$):

1,4,6,8-tetramethylazulene (0.29 g.) and three molar equivalents of ethoxalyl chloride were heated together in dichloromethane (20 ml.) for 90 minutes. The solution was then poured into water, extracted with ether, and the ether extracts dried. Removal of the solvent under reduced pressure gave a red solid which recrystallised from ethanol to give red flakes of 3-ethoxalyl-1,4,6,8-tetramethylazulene.

Yield 0.39 g. (87.1 %). m.p. 151°C.

ν max: 1630, 1720 cm.$^{-1}$ (C = O).

Its n.m.r. spectrum showed aromatic absorptions at τ 2.18 and 2.75, four singlets at τ 7.02, 7.10, 7.28 and 7.42, a triplet (J = 8 c.p.s.) at τ 8.58 and a quartet (J = 8 c.p.s.) at τ 5.55; in the ratio 3 : 3 : 3 : 3 : 3 ; 3 : 2.

$C_{18}H_{20}O_3$ requires: C = 76.03%; H = 7.09%.

found : C = 75.99%; H = 6.95%.

The reaction of 1-Ethoxalyl-2,4,6,8-tetramethylazulene with sodium methoxide in methanol:

A solution of 1-Ethoxalyl-2,4,6,8-tetramethylazulene (0.36 g.) in "super-dry" methanol (20 ml.), containing a molar equivalent of sodium methoxide, was boiled for 30 minutes. The solvent was removed under reduced pressure and the sodium salt dissolved in water. The solution was acidified with dilute hydrochloric acid and the resulting precipitate collected and dried. Recrystallisation from tetrachloroethylene gave deep green crystals of 4-hydroxy-2,7,9-trimethyl-3H-benz [cd] azulen-3-one. ($\overline{CIII}$).

Yield 0.09 g. (29.8 %). m.p. 267°C.

ν max : 3360 cm.$^{-1}$ (-OH) ; 1603 cm.$^{-1}$ (C = O).

$C_{16}H_{14}O_2$ requires: C = 80.65%; H = 5.92%.

found : C = 79.93%; H = 5.91%.

The reaction of 3-ethoxalyl-1,4,6,8-tetramethylazulene with sodium methoxide in methanol:

3-Ethoxalyl-1,4,6,8-tetramethylazulene (0.3 g.) and an equimolecular proportion of sodium methoxide were heated together in "super-dry" methanol (20 ml.) for 30 minutes. The solvent was removed under reduced pressure and the residue dissolved in water. Acidification of the solution with dilute hydrochloric acid gave a green precipitate which was filtered off and dried. Recrystallisation from tetrachloroethylene gave green crystals of 4-hydroxy-1,7,9-trimethyl-3H-benz [cd] azulen-3-one (CII).

Yield 0.08 (31.8 %). m.p. 219°C.

ν max: 3360 cm.$^{-1}$ (-OH) ; 1603 cm.$^{-1}$ (C = O).

$C_{16} H_{14} O_2$ requires: C = 80.65%; H = 5.92%.

found : C = 79.37%; H = 5.63%.

1,3-Diethoxalyl-4,6,8-trimethylazulene (CVII, R = CH_3):

1-Ethoxalyl-4,6,8-trimethylazulene (7.0 g.) and ethyl cyanoformate (5.13 g.) were dissolved in anhydrous ether (50 ml.). Dry hydrogen chloride was passed through the solution, cooled in an ice-salt bath, for 3 hours and the solution left at 0°C. for 3 days. The imine hydrochloride was filtered off and dissolved in water. On standing an orange precipitate was deposited, which was filtered off, dried, and recrystallised from ethanol to give orange needles of 1,3-diethoxalyl-4,6,8-trimethylazulene.

Yield 6.1 (63.6 %). m.p. 125°C.

ν max : 1660, 1720 cm.$^{-1}$ (C = O).

Its n.m.r. spectrum showed aromatic absorption at τ 1.35 and 2.3, two singlets at τ 7.05 and 7.25, a triplet (J = 8 c.p.s.) at τ 8.52, and a quartet (J = 8 c.p.s.) at τ 5.48; in the ratio 3 : 6 : 3 : 6 : 4.

$C_{21} H_{22} O_6$ requires: C = 68.10%; H = 5.99%.

found : C = 67.88%; H = 6.10%.

The reaction of 1,3-diethoxalyl-4,6,8-trimethylazulene with sodium methoxide in methanol:

A solution of 1,3-diethoxalyl-4,6,8-trimethylazulene (1.0 g.) in "super-dry" methanol (25 ml.), containing a molar equivalent of sodium methoxide, was boiled for 30 minutes. The solvent was removed under reduced pressure and the residue dissolved in water. Acidification of the solution with dilute hydrochloric acid gave a reddish precipitate which was filtered off and dried. Recrystallisation from tetrachloroethylene gave reddish-brown needles of 1-ethoxalyl-4-hydroxy-7,9-dimethyl-3H-benz [cd] azulen-3-one.

Yield 0.2 g. (22.3 %). m.p. 235°C.

ν max : 1605, 1670, 1740 cm.$^{-1}$ (C = O); 3220 cm.$^{-1}$ (-OH).

Its n.m.r. spectrum (in trifluoroacetic acid) showed aromatic absorptions at τ1.2 and 2.35, two singlets at τ 6.80 and 6.88, a triplet (J = 8 c.p.s.) at τ 8.44, and a quartet (J = 8 c.p.s.) at τ 5.27; in the ratio 4 : 3: 3 : 3 : 2.

$C_{19}H_{16}O_5$ requires: C = 70.36%; H = 4.97%.

found : C = 69.90%; H = 4.69%.

The reaction of 1,3-diethoxalyl-4,6,8-trimethylazulene with sodium hydride:

A solution of 1,3-diethoxalyl-4,6,8-trimethylazulene (1.0 g.) in anhydrous benzene was boiled for 90 minutes with an excess of sodium hydride. The mixture was cooled, excess sodium hydride destroyed with iso-propyl alcohol and the solvent removed under reduced pressure. The residue was dissolved in water and the solution acidified with dilute hydrochloric acid. The resulting black precipitate was filtered off and dried but no solvent could be found for recrystallisation. The substance appeared to be polymeric.

2,3,3-Trimethylbutan-2-ol:[120].

Pinacolone (100 g. 1 mole) in anhydrous ether (250 ml.) was added with stirring to methylmagnesium iodide (prepared from 24.3 g. of magnesium and 141.9 g. of methyl iodide) in anhydrous ether (500 ml.) and the reaction

mixture (protected from moisture) set aside overnight. The reaction product was decomposed with dilute acid and ice-water. The ether layer was washed with sodium carbonate and then with water, and dried. The ethereal extract was fractionated and the fraction boiling at 130°C. collected. This fraction consisted of 2,3,3-trimethyl-butan-2-ol (m.p. 17°C.; b.p. 130°C.) and its hydrate (m.p. 80°C.).

Yield 81.7 g.

Attempted preparation of 2,6-dimethyl-4-tert-butylpyrylium perchlorate from 2,3,3-trimethylbutan-2-ol:

2,3,3-Trimethylbutan-2-ol (11.6 g. 0.1 mole) and acetic anhydride (51.0 g. 0.5 mole) were cooled to -10°C. and treated cautiously with 70% perchloric acid (13.5 g. 0.35 mole). The temperature was kept between 90 and 100°C. by controlled addition and cooling. The reaction mixture was set aside overnight and then the yellow solid filtered off. Recrystallisation from glacial acid gave small yellow needles m.p. 162°C. The literature m.p. for 2,6-dimethyl-4-tert-butylpyrylium perchlorate is 220 - 224°C. The n.m.r. spectrum of this compound showed it to be 2,3-dihydro-2,2,3,3,5-pentamethylfurylium perchlorate.

Yield 5.0 g. (22 %). m.p. 162°C.

ν max: 1100 $cm.^{-1}$ ($ClO_4^{\ominus}$)

$C_9 H_{17} ClO_5$ requires: C = 44.91%; H = 7.12%; CL = 14.75%.

found : C = 44.50%; H = 7.78%; CL = 14.90%.

2,6 - Dimethyl - 4 - pyrone:

King, Ozog and Moffat, J.A.C.S., 1951, 71, 300.

2,6-Dimethyl-4-tert-butylpyrylium fluoborate:[111].

Tert-butylmagnesium chloride (prepared from 9.74 g. of magnesium and 37 g. of tert-butylchloride) was added to a stirred solution of

2,6-dimethyl-4-pyrone (24.8 g. 0.2 mole) in dry anisole (400 ml.). The red solution was then extracted several times with dilute hydrochloric acid. The acid extracts were neutralised with potassium carbonate and the 2,6-dimethyl-4-tert-butylpyran-4-ol extracted into ether. The ether extracts were dried and the ether removed under reduced pressure. The residue was dissolved in methanol and a 40% aqueous solution of fluoboric acid (44 ml. 0.2 mole) added slowly with cooling. On the addition of ether, 2,6-dimethyl-4-tert-butylpyrylium fluoborate separated out.

Yield 35 g. (70 %).

4,8-Dimethyl-6-tert-butylazulene:[112]

2,6-Dimethyl-4-tert-butylpyrylium fluoborate (9.6 g. 0.038 mole) was added all at once to a stirred solution of cyclopentadienyl sodium in tetrahydrofuran (100 ml. of a 1 M solution) in an atmosphere of nitrogen. After being boiled for 1 hour the reaction mixture was diluted with water (100 ml.) and extracted with light-petroleum. The light-petroleum extracts were shaken thoroughly with 60% sulphuric acid. The sulphuric acid phase was shaken twice with light-petroleum to remove excess cyclo-pentadiene and then poured into ice-water. The liberated azulene was extracted into light-petroleum and the extracts washed and dried. The solvent was removed under reduced pressure leaving an oil which solidified when rubbed with ethanol in a salt-ice bath. Recrystallisation from ethanol gave violet-black crystals of 4,8-dimethyl-6-tert-butylazulene.

Yield 6.5 g. (80 %). m.p. 33°C. (literature m.p. 33 - 34°C.)

1- Ethoxalyl - 4,8-dimethyl-6-tert-butylazulene (LXXXVIII, R = C $(CH_3)_3$):

A solution of 4,8-dimethyl-6-tert-butylazulene (1 g.) and a molar equivalent of ethoxalyl chloride in dichloromethane (20 ml.) was boiled for 90 minutes. The deep red solution was poured into aqueous sodium bicarbonate

solution and extracted into ether and the ether extracts dried. The solvent was removed under reduced pressure giving an oil which solidified on being rubbed with light-petroleum. Recrystallisation from ethanol gave deep red needles of 1-ethoxalyl-4,8-dimethyl-6-tert-butylazulene.

Yield 1.3 g. (88.3 %). m.p. 90°C.

ν max : 1630, 1720 cm.$^{-1}$ (C = O).

Its n.m.r. spectrum show aromatic absorptions between τ 1.8 and 3.0, three singlets at τ 6.96, 7.10, and 8.56, a triplet (J = 8 c.p.s.) at τ 8.56 and a quartet (J = 8 c.p.s.) at τ 5.55; in the ratio 4 : 3 : 3 : 9 : 3 : 2.

$C_{20}H_{24}O_3$ requires: C = 76.89%; H = 7.74%.

found : C = 76.91%; H = 7.56%.

4-Hydroxy-9-methyl-7-tert-butyl-3H-benz [cd] azulen-3-one (LXXXIX, R = C $(CH_3)_3$):

A solution of 1-ethoxalyl-4,8-dimethyl-6-tert-butylazulene (1.0 g.) in "super-dry" methanol (30 ml.) containing one molar equivalent of sodium methoxide was heated under reflux for 30 minutes. Most of the solvent was removed under reduced pressure and the residue dissolved in water. The solution was acidified and the resulting precipitate filtered off. The precipitate was dried, boiled with a small amount of ethanol, and filtered. On cooling the filtrate deposited green-black crystals of 4-hydroxy-9-methyl-7-tert-butylbenz [cd] azulen-3-one.

Yield 0.4 g. (46.9 %). m.p. 210°C.

ν max: 3360 cm.$^{-1}$ (- OH); 1603 cm.$^{-1}$ (C = O).

$C_{18}H_{18}O_2$ requires: C = 81.17%; H = 6.81%.

found : C = 80.32%; H = 7.00%.

1,3-Diethoxalyl-4,8-dimethyl-6-tert-butylazulene (CVII, R = C $(CH_3)_3$):

1-Ethoxalyl-4,8-dimethyl-6-tert-butylazulene (2.0 g.) and ethyl cyanoformate (1.5 g.) were dissolved in anhydrous ether (50 ml.). Dry

for 3 hours and the solution was then left at 0°C. for 3 days. The imine hydrochloride was filtered off and the crystals dissolved in water which was then extracted with ether. The ether extracts were dried and the ether removed under reduced pressure giving an orange solid. Recrystallisation from ethanol gave orange needles of 1,3-diethoxalyl-4,8-dimethyl-6-tert-butylazulene. Concentration of the mother liquor gave bronze needles of 1-ethoxalyl-4-hydroxy-9-methyl-7-tert-butyl-3H-benz [cd] azulen-3-one (CVIII, R = C $(CH_3)_3$).

1,3-Diethoxalyl-4,8-dimethyl-6-tert-butylazulene

Yield 1.24 g. (47.0 %). m.p. 103°C.

ν_{max} : 1660, 1720 $cm.^{-1}$ (C = O).

Its n.m.r. spectrum showed aromatic absorptions at τ 1.34 and 2.06, two singlets at τ 7.0 and τ 8.5, a triplet (J = 8 c.p.s.) at τ 8.55 and a quartet (J = 8 c.p.s.) at τ 5.5; in the ratio 3 : 6 : 9 : 6 : 4.

$C_{24}H_{28}O_6$ requires: C = 69.89 %; H = 6.84 %.

found : C = 70.13 %; H = 7.04 %.

1-Ethoxalyl-4-hydroxy-9-methyl-7-tert-butyl-3H-benz [cd] azulen-3-one

Yield 0.38 g. (22.1 %). m.p. 232°C.

ν_{max}: 1600, 1660, 1720 $cm.^{-1}$ (C = O); 3250 $cm.^{-1}$ (-OH).

Its n.m.r. spectrum showed aromatic absorptions at τ 1.4, 1.87 and 3.0, two singlets at τ 6.88 and 8.45, a triplet (J = 8 c.p.s.) at τ 8.55 and a quartet (J = 8 c.p.s.) at τ 5.5; in the ratio 5 : 3 : 9 : 3 : 2.

$C_{22}H_{22}O_5$ requires: C = 72.12 %; H = 6.05 %.

found : C = 72.78 %; H = 6.44 %.

The reaction of 1,3-diethoxalyl-4,8-dimethyl-6-tert-butylazules with sodium methoxide in methanol:

A solution of 1,3-diethoxalyl-4,8-dimethyl-6-tert-butylazulene (0.27 g.) in "super-dry" methanol (30 ml.) containing one molar equivalent of sodium methoxide was heated under reflux for 30 minutes. The solvent was removed under reduced pressure and the residue dissolved in water. Acidification of the solution with dilute hydrochloric acid gave a deep purple precipitate which was filtered off and dried. No solvent could be found for recrystallising the product which appeared to be polymeric.

Yield 0.24 g.

The reaction of 1-ethoxalyl-4-hydroxy-9-methyl-7-tert-butyl-3H-benz [cd] - azulen-3-one with sodium methoxide in methanol:

A solution of 1-ethoxalyl-4-hydroxy-9-methyl-7-tert-butyl-3H-benz [cd] - azulen-3-one (0.18 g.) in "super-dry" methanol (20 ml.), containing a molar equivalent of sodium methoxide, was heated under reflux for 30 minutes. After removal of the solvent under reduced pressure, the residue was dissolved in water, the solution acidified with dilute hydrochloric acid and the resulting precipitate filtered off and dried. The product was again a deep purple compound which appeared to be polymeric.

Yield 0.17 g.

ULTRAVIOLET SPECTRA

ULTRAVIOLET SPECTRA

The spectra, unless otherwise stated were carried out in ethanolic solution in 1 cm. silica cells. The letter s denotes a shoulder and the letter i denotes an inflection on the curve.

Compound	λ_{max}^{mu}	$\log_{10}$
1,3- Diethoxalyl-2,5-dimethylindolizine	232.5	3.61
	264	3.32
	291	3.15
	354	3.82
1-Methoxalyl-3-methoxycarbonyl-2-methylcycl [3,2,2] azine.	216	4.30
	247.5 s.	3.72
	274	3.91
	294.5 s.	3.73
	322.5 i.	3.69
	331	3.74
	407	3.43
	430	3.93
4-Hydroxy-1-methoxalyl-2-methyl-3H- cycl [3,3,2] azin-3-one	225 i.	3.88
	244	4.35
	304	3.88
	395	3.72
	415	3.99
4-Hydroxy-1-oxalyl-2-methyl-3H-cycl [3,3,2] azin-3-one	220.5	3.87
	241.5	4.08
	299.5	3.83
	394	3.48
	415	3.73

4-Hydroxy-2-methyl-3H-cycl [3,3,2] azin-3-one	230 260 287.5 325 333 401	3.57 4.76 3.90 3.25 3.31 4.00
5-Methyl-2-phenyl-3-pyruvoyl-indolizine	234 389.5	4.23 3.51
4-Methyl-2-phenyl-3H-cycl [3,3,2] azin-3-one	226 i. 233.5 264.5 302 i. 345 412 431	3.81 3.85 4.14 3.48 2.98 3.23 3.37
5 % ethanolic perchloric acid	227 255 286.5 377	3.70 4.31 3.38 3.25
2,5- Dimethyl-1-pyruvoylindolizine	234 359.5	3.71 3.66
1- (α-Hydroxyiminoacetonyl) -3-methyl-2-phenylindolizine	215 251 376	4.07 4.34 3.21
3- (α-Hydroxyiminoacetonyl) -1-methyl-2-phenylindolizine	208 252 302.5 i. 364	4.14 4.36 3.12 2.96
1- (α-Hydroxyiminophenacyl) -5-methyl-2-phenylindolizine	251 379	4.37 3.06

3- (α-Hydroxyiminophenacyl) -5- methyl--2-phenylindolizine	246	4.27
3- (α-Hydroxyiminoacetonyl) -5 - methyl--2- phenylindolizine	248.5 300 i. 339	4.27 3.41 3.19
3- (α-Hydroxyiminophenacyl) - 2,5--dimethylindolizine	237 353	4.53 2.75
Ethyl hydroxyimino (5 - methyl-2-phenyl--indolizin-3-yl) acetate	249.5 298 i. 342	4.18 3.03 2.85
3 - Cyano-5-methyl-2-phenylindolizine	250 266 332	4.28 4.10 3.39
3 - Hydroxyimino-4-methyl-2-phenyl--3H-cycl [3,3,2] azine	232.5 268 350 367 440	4.03 4.21 3.21 3.32 3.11
5 % ethanolic perchloric acid	223 274 327.5 426	4.12 4.23 3.60 3.82
3- Hydroxyimino - 2 - methyl - 4-phenyl--3H-cycl [3,3,2] azine	277.5 360 378 462	4.16 3.06 3.12 3.00
5 % ethanolic perchloric acid	225.5 281.5 337 422	3.64 4.43 3.00 3.46

3- Hydroxyimino-2,4-dimethyl-3H-cycl [3,3,2] azine	221.5	3.60
	261 s.	3.88
	273	4.06
	315 i.	3.01
	408 s.	3.27
	421	3.30
5 % ethanolic perchloric acid	220.5	3.59
	250.5	3.74
	272.5	4.01
	327	2.99
	415	3.18
3- Hydroxyimino-2,4-diphenyl-3H-cycl [3,3,2] azine	245 i.	4.07
	274	4.29
	354	3.14
	372	3.17
	458	3.20
5 % ethanolic perchloric acid	241.5	3.86
	283	4.03
	335 i.	3.38
	432	3.65
2 - Methyl-4-phenyl-3H-cycl [3,3,2] azin - 3 - one	241 i.	4.20
	271	4.36
	293 s.	3.95
	336.5 i.	3.32
	346	3.35
	423 s.	3.43
	440	3.66
5 % ethanolic perchloric acid	247	4.20
	281	4.20
	354 i.	3.40
	388	3.35

2,4-Diphenyl-3H-cycl [3,3,2] azin--3-one	238.5	3.92
	273.5	3.94
	302 s.	3.67
	348 s.	3.24
	426 i.	3.42
	443	3.51
5 % ethanolic perchloric acid	221.5	3.78
	248.5	3.94
	282	3.81
	379	3.33
1:1 adduct of 1-methyl-2-phenylindolizine and diphenylcyclopropenone	258	4.14
	367	3.69
1-Ethoxalyl-4,6,8-trimethylazulene	243	3.75
	322	3.84
	393	3.34
1-Ethoxalyl-4,8-dimethyl-6-tert-butylazulene	243	3.80
	322	3.91
	293	3.43
1,3-Diethoxalyl-4,6,8-trimethylazulene	260	3.91
	320	3.97
	395	3.48
1,3-Diethoxalyl-4,8-dimethyl-6-tert-butylazulene	236 i.	3.67
	262	4.10
	319	4.40
	392	3.43
3-Ethoxalyl-1,4,6,8-tetramethylazulene	247.5	3.69
	300 i.	3.45
	329	3.72
	401	3.29

3- Bromoacetylguaiazulene	235		4.03
	285		3.90
	321.5		3.98
	406		3.60
1- Bromoacetyl-4,6,8-trimethylazulene	242.5		3.78
	287.5	i.	3.50
	339		3.89
	389		3.38
1- Dichloroacetyl-4,6,8-trimethylazulene	243		3.76
	284	i.	3.43
	322.5		3.85
	392		3.37
4- Hydroxy-7,9-dimethyl-3H-benz [cd] azulen-3-one	258.5		3.89
	288	i.	3.98
	294		4.18
	307		4.29
	322		4.96
	384		3.60
	572.5		2.68
5 % ethanolic perchloric acid	222	s.	3.67
	240		3.79
	271		3.90
	301.5		4.03
	318	s.	3.68
	361		3.60
	392	s.	3.47
	410		3.56
	423	i.	3.43

4-Hydroxy-9-methyl-7-tert-butyl-3H--benz [cd] azulen-3-one	232.5		3.76
	257		3.72
	277	i.	3.83
	292.5		3.92
	308.5		3.92
	320		3.98
	377		3.56
	393		3.37
	422		3.06
	441	i.	3.01
5 % ethanolic perchloric acid	223	s.	3.76
	240		3.84
	272.5		3.94
	302		4.03
	317	i.	3.81
	363		3.58
	393.5		3.42
	406	i.	3.41
	426		3.41
1- Ethoxalyl-4-hydroxy-7,9,dimethyl-3H--benz [cd] azulen-3-one	290		3.62
	323	s.	3.41
	366	i.	3.04
	450	s.	2.92
	476		3.17
5 % ethanolic perchloric acid	261		3.38
	294		3.66
	306		3.69
	370		3.07
	381		3.07
	445		2.99

1- Ethoxalyl-4-hydroxy-9-methyl-7-tert-butyl-3H-benz [cd] azulen-3-one	262	3.95
	293	4.26
	310	4.22
	382	3.66
	452	3.47
5 % ethanolic perchloric acid	261	3.98
	296.5	4.05
	307.5	4.05
	370	3.44
	386 i.	3.89
	446	3.26
4- Hydroxy-1,7,9-trimethyl-3H-benz-[cd] azulen-3-one	263	4.12
	275	4.14
	294	4.19
	311	4.10
	324.5	4.17
	391	3.76
	605	2.62
4- Hydroxy, 2,7,9-trimethyl-3H-benz [cd] azulen-3-one	252 i.	3.82
	259.5	3.90
	270 i.	3.82
	291	4.03
	308	4.11
	322	4.16
	392	3.68
	414	3.77
	572.5	2.90

Figure 17.

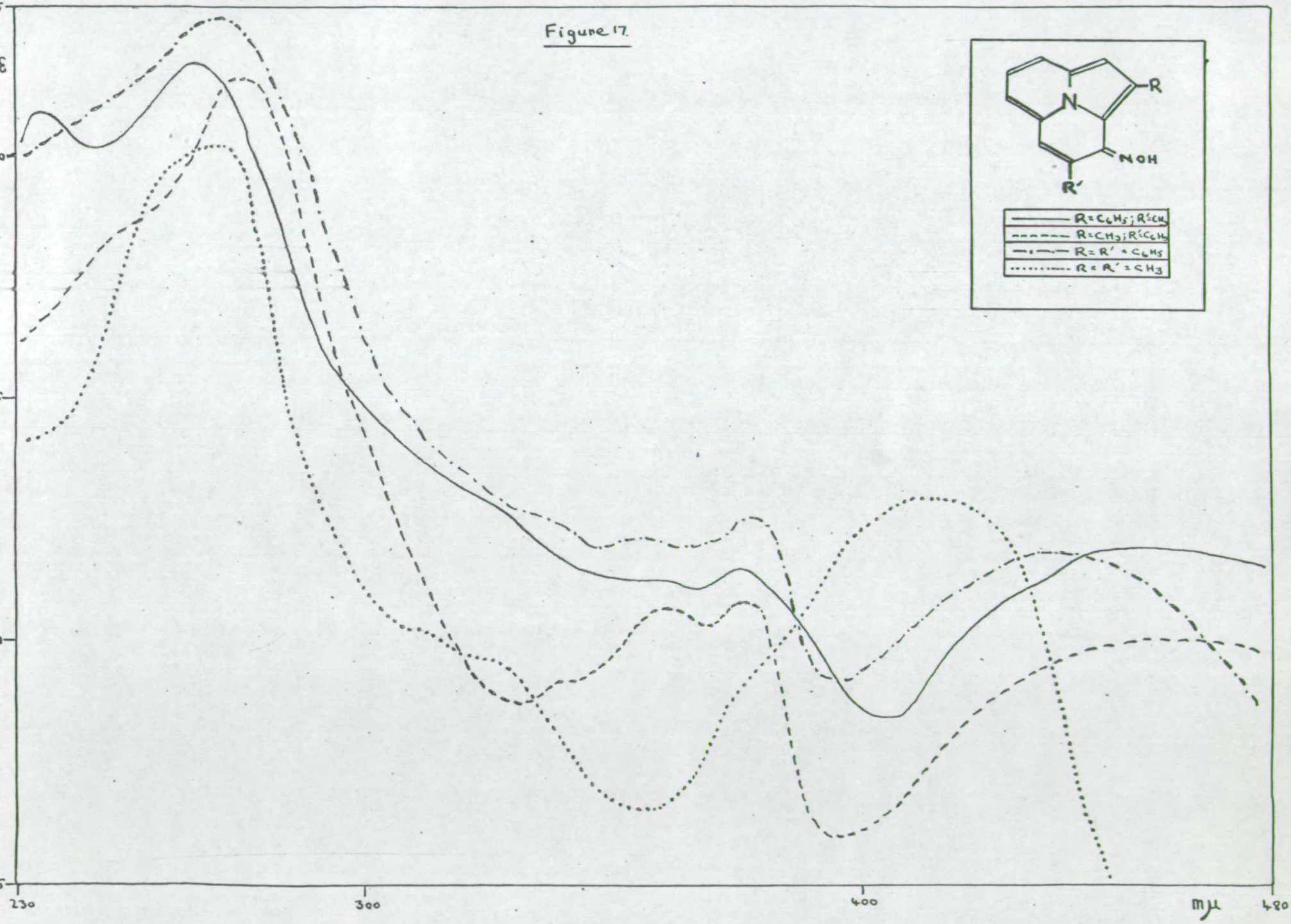


Figure 18

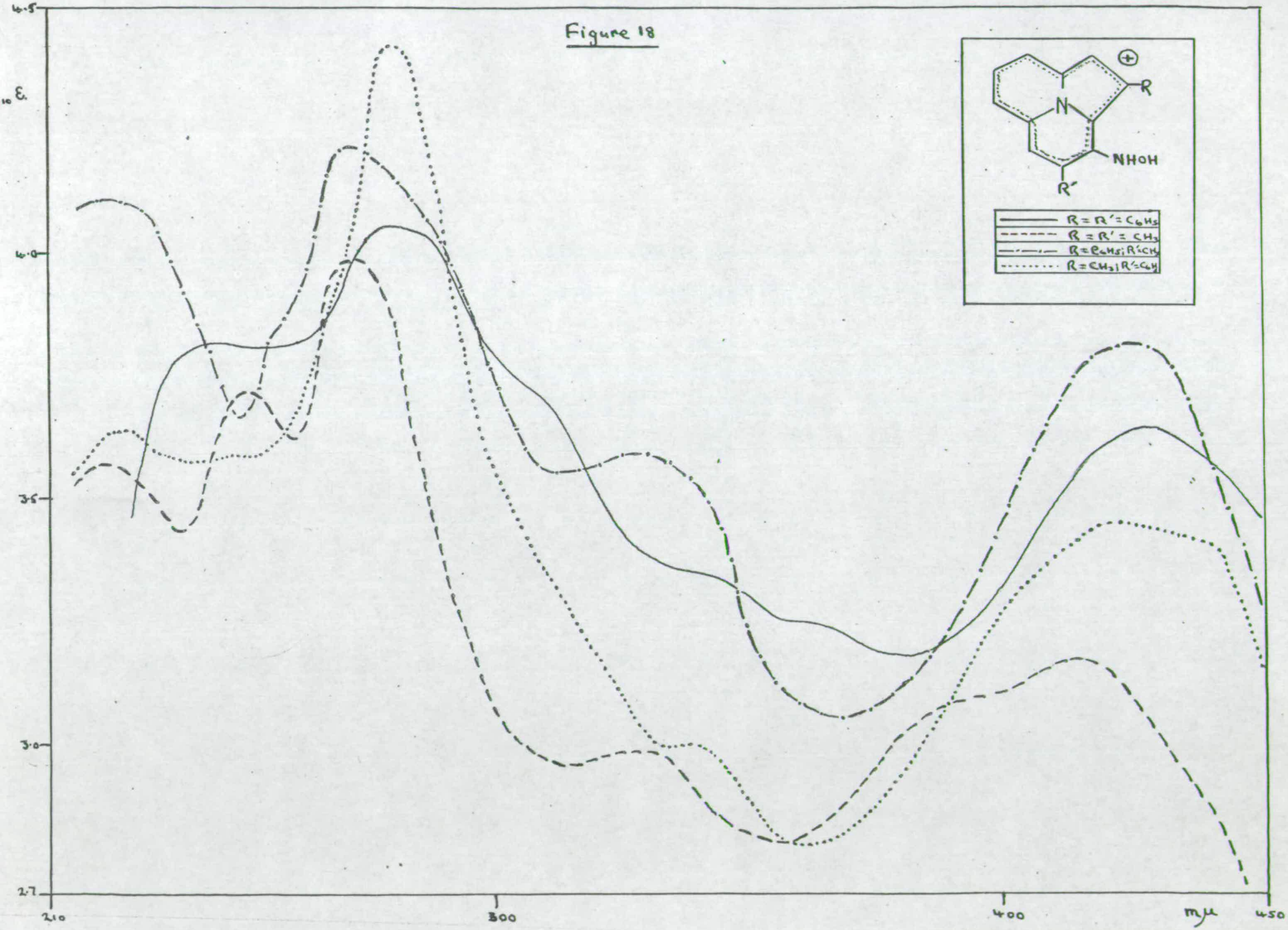
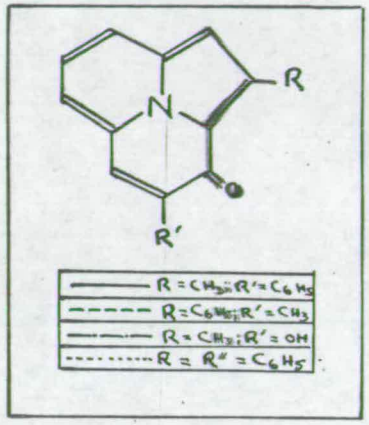
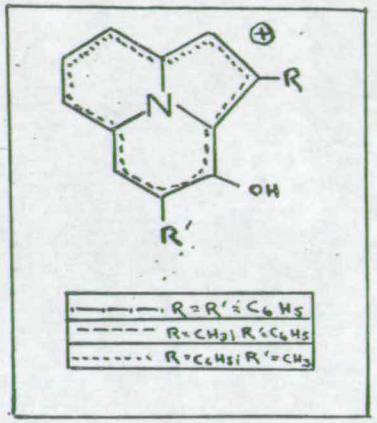

4·5
ε
10
4·0
3·5
3·0
2·7
210
300
400
mμ
450
R
N
NHOH
R′
R = R′ = C6H5
R = R′ = CH3
R = C6H5; R′ = CH3
R = CH3; R′ = C6H5

Figure 19.


R
N
R'
R = CH3; R' = C6H5
R = C6H5; R' = CH3
R = CH3; R' = OH
R = R' = C6H5

4.5
log10 ε
4.0
3.5
3.0
210
300
400
mμ
450

Figure 20.


R
N
OH
R'
R = R' = C6H5
R = CH3 ; R' = C6H5
R = C6H5 ; R' = CH3

log10 ε
4·0
3·5
3·0
2·7
220
300
400
mμ

Figure 21.

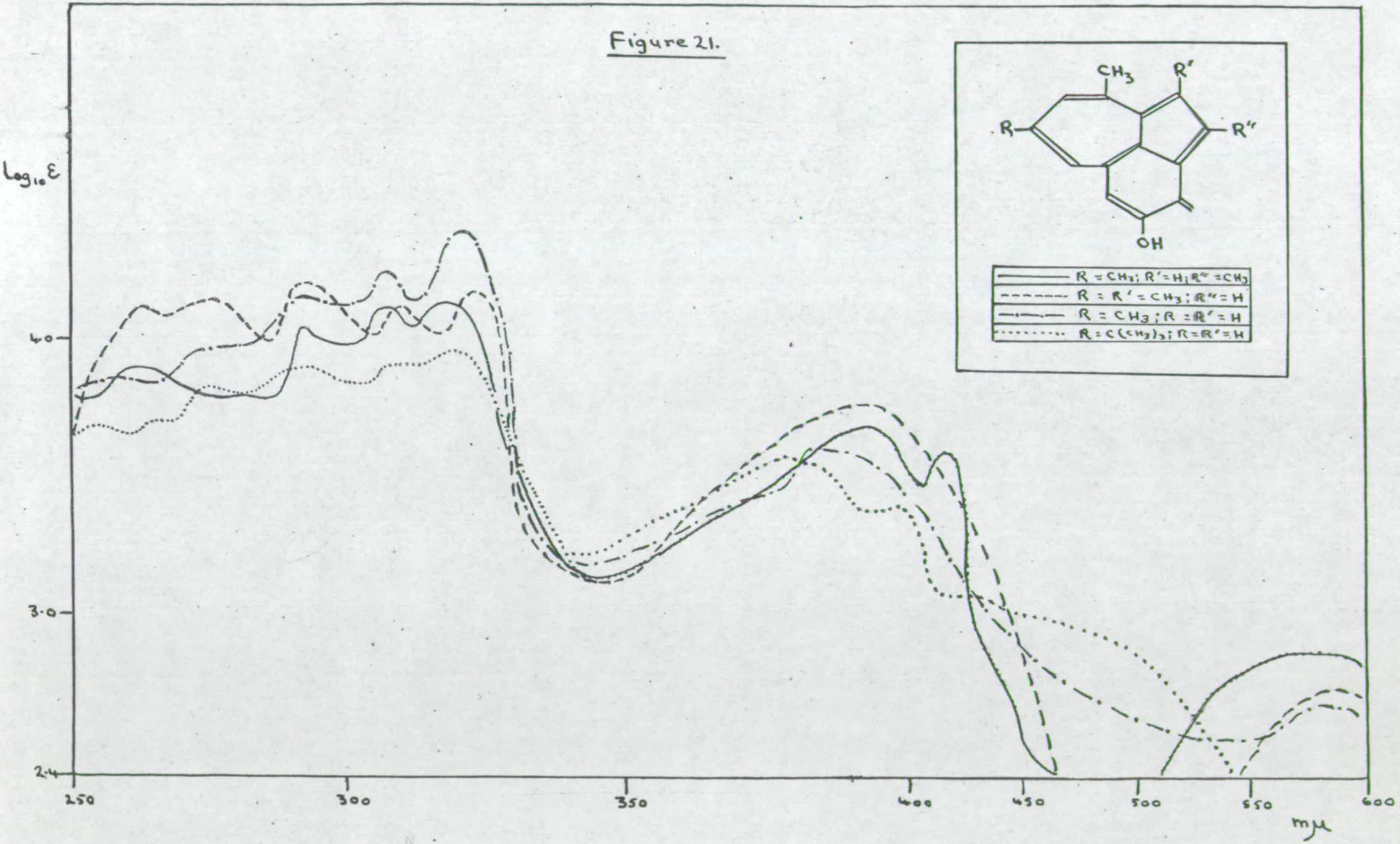

CH3
R'
R
R''
OH
R = CH3; R' = H; R'' = CH3
R = R' = CH3; R'' = H
R = CH3; R = R' = H
R = C(CH3)3; R = R' = H
Log10 ε
4·0
3·0
2·4
250
300
350
400
450
500
550
600
mμ

Figure 22.

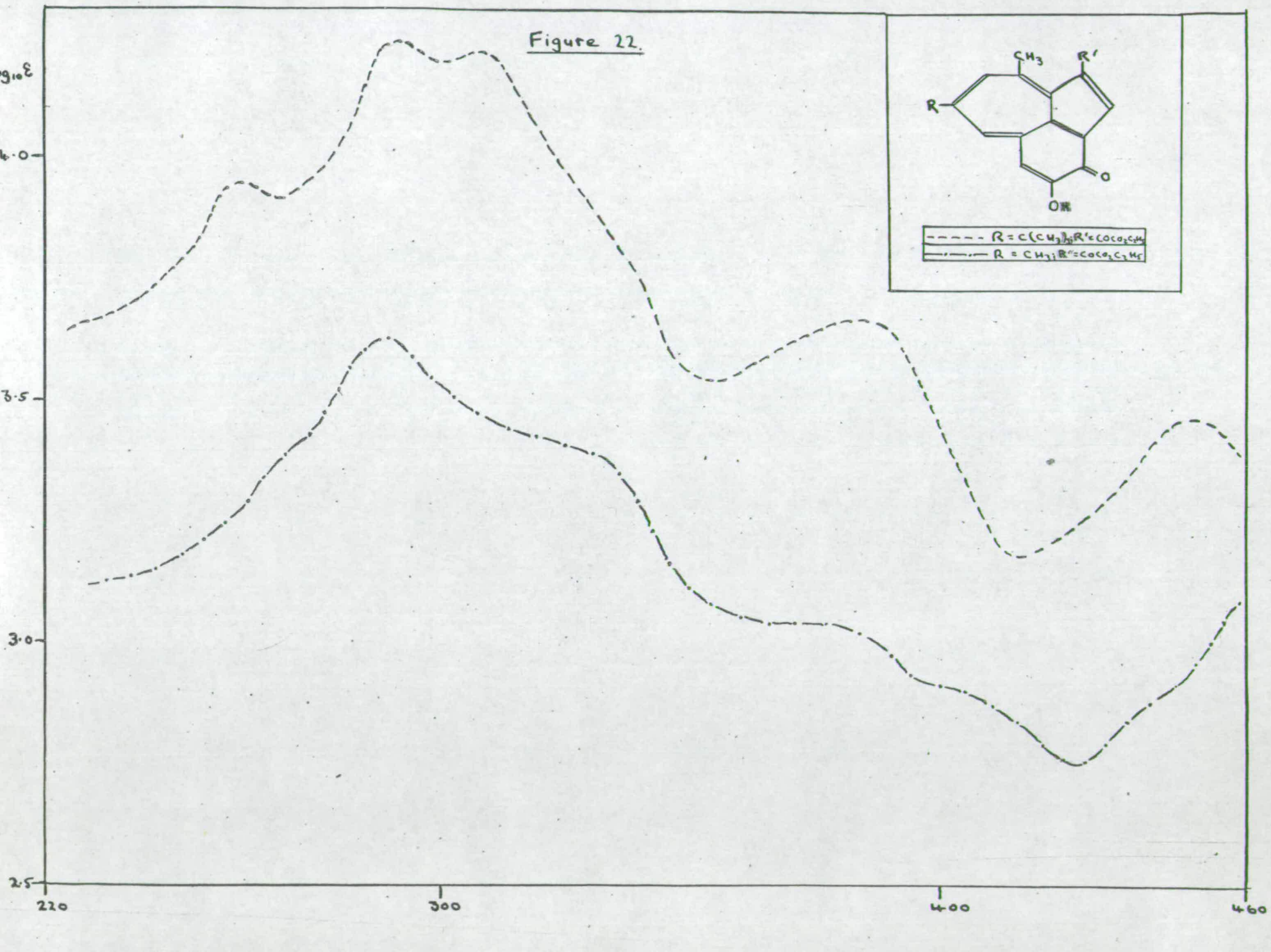
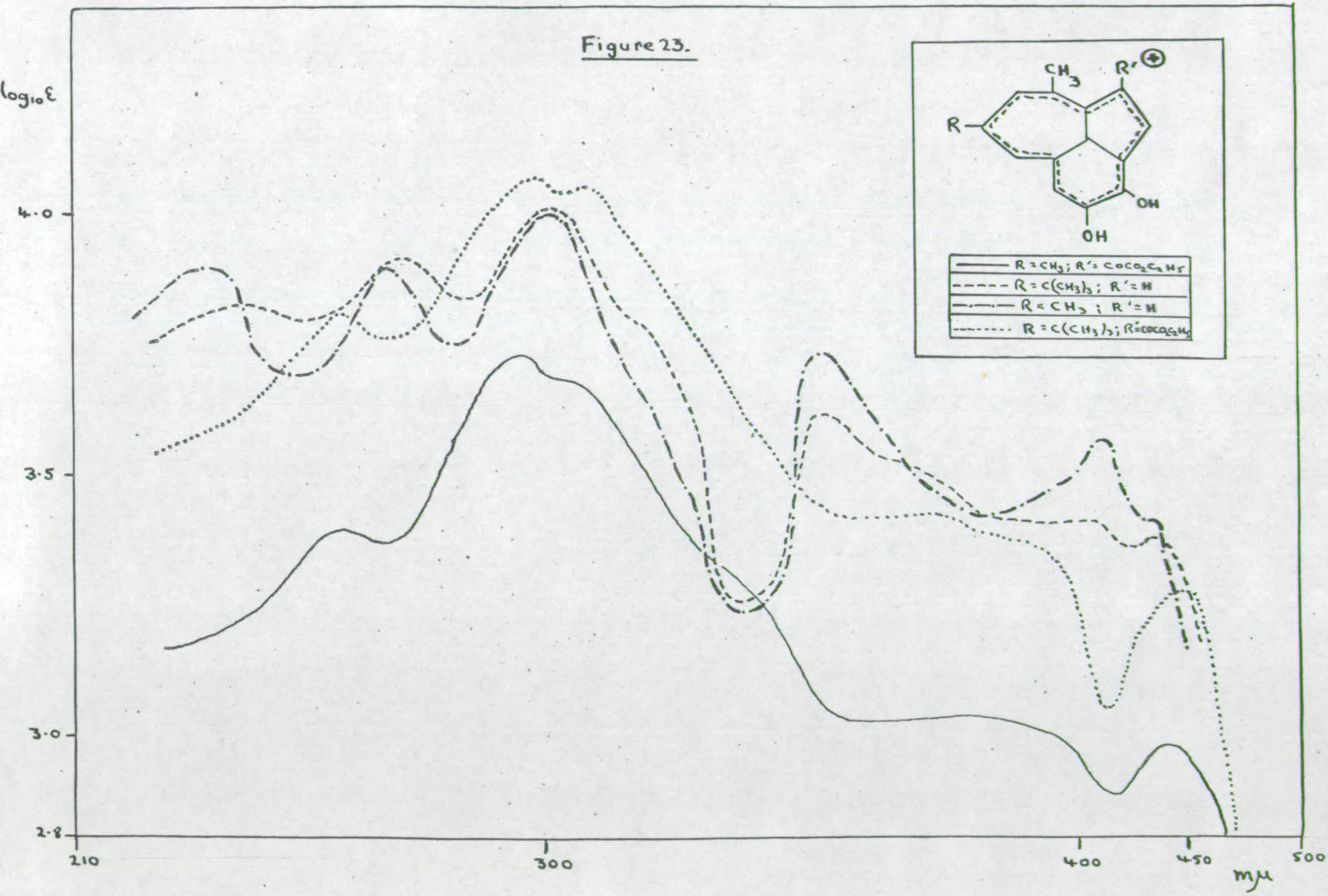

log10 ε
4·0
3·5
3·0
2·5
220
300
400
460
CH3
R'
R
O
OR''
R = C(CH3)3; R' = COCO2C2H5
R = CH3; R'' = COCO2C2H5

Figure 23.


log10 ε
4·0
3·5
3·0
2·8
210
300
400
450
500
mμ
CH3
R'
R
OH
OH
R = CH3; R' = COCO2C2H5
R = C(CH3)3; R' = H
R = CH3; R' = H
R = C(CH3)3; R' = COCO2C2H5

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Synthesis of Cycl[3,3,2]azinones and Benz[*cd*]azulenones

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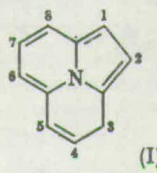
THE "second stable adduct"[1] of 2-styrylpyridine and dimethyl acetylenedicarboxylate was recently recognised[2] as the first known derivative of cycl[3,3,2]azine (pyrrolo[2,1,5-*de*]quinolizine). This ring system is potentially capable of becoming aromatic[3] but no derivatives with uninterrupted peripheral conjugation have hitherto been available for study. We now report the synthesis of derivatives which are related to the parent compound (I; 3*H*-isomer shown) in the same way as tropolone is related to cycloheptatriene.

5-Methyl-2-phenylindolizine reacted with three molar proportions of ethoxalyl chloride, in dichloromethane, to give the 1,3-diethoxalyl derivaive (II). Heating this compound with sodium ethoxide in dry ethanol converted it partly into the ethanol-soluble cycl[3,2,2]azine (III) and partly into the insoluble sodium salt of the hydroxycycl[3,3,2]-azinone (IV or V; R = CO·CO_2Et). Standard procedures of hydrolysis, decarbonylation, and decarboxylation were then used to convert the former product into 2-phenylcycl[3,2,2]azine, identical with an authentic specimen,[3] and the latter into 4(or 3)-hydroxy-2-phenyl-3(or 4)-*H*-cycl[3,3,2]azin-3(or 4)-one (IV or V; R = H). The cyclazinone was a bright yellow, crystalline compound which showed infrared absorptions (in $CHCl_3$) characteristic of a hydrogen-bonded hydroxyl group (3280 cm.$^{-1}$) and of a highly polarised carbonyl group (1590 cm.$^{-1}$). Its n.m.r. spectrum (in $CDCl_3$) showed a complex but well-resolved multiplet in the region τ 1·8—2·8 (intensity 10) and a singlet near τ 1·4 (intensity 1; OH proton) which disappeared when the solution was shaken with deuterium oxide.



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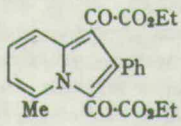

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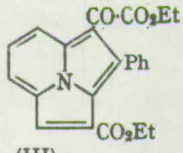
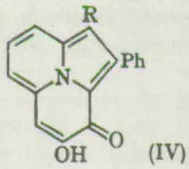


(III)



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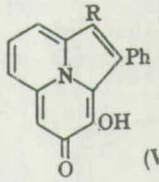

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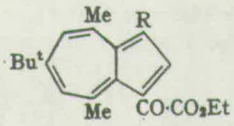
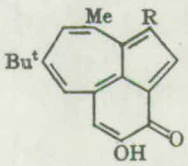


(VI)



(VII)

By making use of the well-known[4] chemical relationship between indolizines and azulenes, we were able to carry out analogous reactions leading to derivatives of benz[*cd*]azulene, a ring system which has been the subject of recent theoretical[5] and experimental[6] investigations. For example, treatment of the 1-ethoxalylazulene (VI; R=H) with sodium methoxide in boiling methanol gave an insoluble sodium salt from which the dark green 4-hydroxy-3*H*-benz[*cd*]azulen-3-one (VII; R=H) was obtained. This compound showed infrared absorptions at 3360 and 1603 cm.$^{-1}$ and its n.m.r. spectrum was fully consistent with the assigned structure.

The monoethoxalyl compound (VI; R=H) resisted further attack by ethoxalyl chloride but it reacted with ethyl cyanoformate, in the presence of dry hydrogen chloride (Hoesch reaction), to give the 1,3-diethoxalylazulene (VI; R=CO·CO$_2$Et). This compound gave the corresponding benzazulenone (VII; R=CO·CO$_2$Et) with exceptional ease (heating in neutral ethanol) but all attempts to bring about a double cyclisation yielded a deeply coloured, amorphous material which appeared to be polymeric. It is perhaps significant that the expected product of double cyclisation could be regarded as a quinone of cyclohepta[*def*]fluorene, a hypothetical hydrocarbon for which a triplet ground state or a low-lying triplet excited state has been predicted.[7]

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