The Oxidation of N-Aminoheterocyclic Compounds

By

Jeffrey Adamson

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The University of Leicester

ProQuest LLC
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106-1346

Statement

The work described in this thesis was carried out by the author in the Department of Chemistry of King's College, University of London, and the University of Leicester under the supervision of Professor C.W.Rees. No part of it is concurrently being submitted for any other degree.

October 1964-August 1967

Signed

J. Adamson.

(J. Adamson)

Acknowledgements

The author would like to record his sincere thanks to Professor C.W.Rees for his supervision and constant encouragement, to Professor D.H.Hey for the provision of research facilities at King's College, and to the Science Research Council for the award of a Research Studentship.

Summary

The oxidation of all 1,1-disubstituted hydrazines is reviewed as a model for the oxidation of N-aminoheterocyclic compounds and the mechanism of the reactions discussed.

The oxidation of N-aminotriazoles is studied with a wide range of oxidants and shown to proceed most efficiently with lead tetraacetate. The products are shown to be acetylenes or nitriles, depending on the structure of the triazole. Highly reactive medium-ring cyclic acetylenes are also produced by this method and may be trapped by tetraphenylcyclopentadienone. The acetylenes are also shown to be produced efficiently from 1,2-bis-hydrazones by lead tetraacetate oxidation.

The oxidation of N-amino-1,2,3-benzotriazin-4-ones is studied and shown to proceed in part through benzocyclopropenones and in part through indazolones. Both types of reactive intermediate are powerful electrophiles. The oxidation of indazolinones is shown to be a related reaction.

The direction of opening of the cyclopropenone ring is markedly influenced by the electronic character of substituents in the benzene ring, leading to products of predictable structure. The relationship between benzocyclopropenone and the known cyclopropenones is discussed.

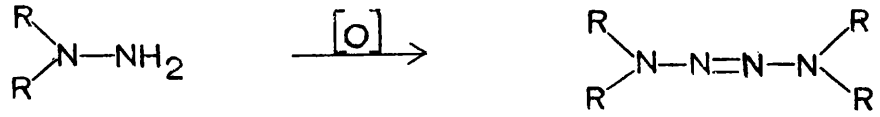
Contents

Section II

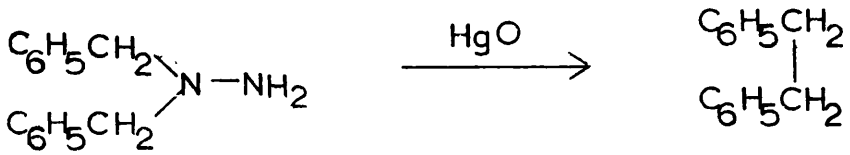
Introduction

N-Aminoheterocyclic compounds may be conveniently considered as 1,1-disubstituted hydrazines. The oxidation of these compounds, and related reactions, have been studied in some detail and various reaction pathways have been elucidated.

1,1-Disubstituted hydrazines are readily prepared from the disubstituted amine either by nitrosation and reduction or by direct amination. The "normal" oxidation product of a 1,1-disubstituted hydrazine is a tetrazene.[1,2,3,4]

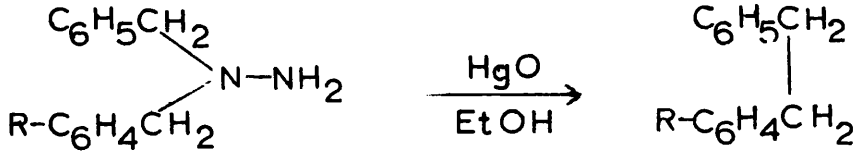


The first anomalous oxidation reported was by Busch and Weiss[5] in 1900. They found that 1,1-dibenzylhydrazine was oxidised to dibenzyl.



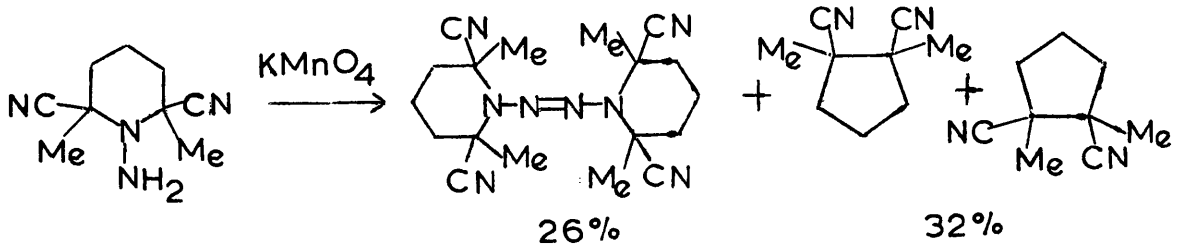
This did not occur with alkyl or aryl substituents, but was peculiar to benzyl groups. Many symmetrically substituted analogues have since been oxidised[6] to give the symmetrically substituted dibenzyls. Hinman and Hamm[7] prepared and oxidised a number of 1,1-dibenzylhydrazines where one aromatic ring only was substituted. They showed that unsymmetrical

dibenzyls were produced and could find no evidence for symmetrical cross over products.



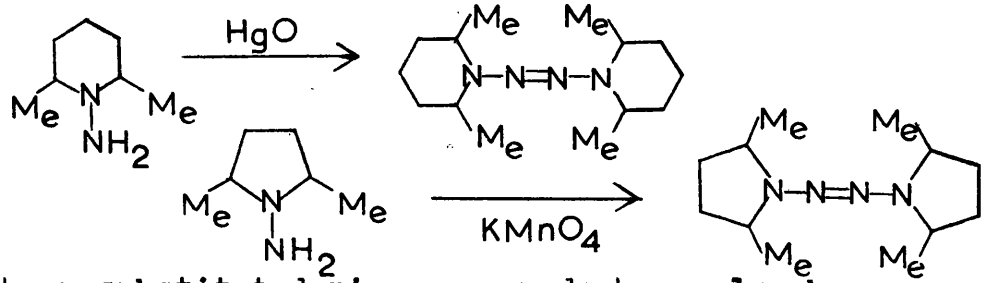
One of the benzyl groups was replaced by furfuryl and the reaction shown to proceed similarly. This reaction is therefore intramolecular. The yields of dibenzyls were shown to depend on the nature of the substituents, which are probably affecting the stability of an intermediate in the oxidation. The reaction course was shown also to depend on the oxidising agent. Thus, benzoquinone or mercuric acetate gave the tetrazene, in agreement with the work of Curtius.[3]

Recently, this reaction has attracted a great deal of interest and Overberger and his colleagues, working on related systems, have done much to elucidate its mechanism. Oxidation of 1-amino-2,6-dicyano-2,6-dimethylpiperidine[8] with potassium permanganate gave the tetrazene and <u>cis</u> and <u>trans</u>-1,2-dicyano-1,2-dimethylcyclopentane.



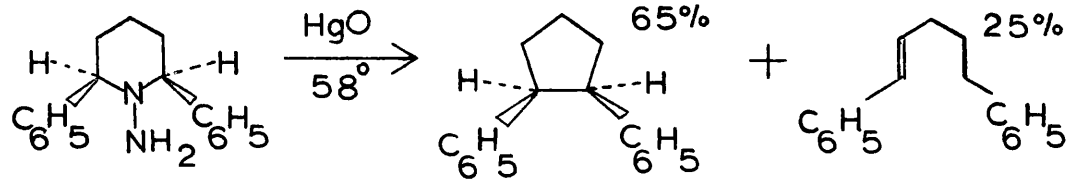
Here, the nitrogen substituents are not benzylic, but do carry cyano groups, and the retention of nitrogen to form a tetrazene, and loss of nitrogen to form a coupled product

are still observed. When the cyano groups are removed, the oxidation proceeds as for a normal dialkyl hydrazine. Thus 1-amino-2,6-dimethylpiperidine and 1-amino-2,5-dimethylpyrrolidine gave the tetrazenes on oxidation.

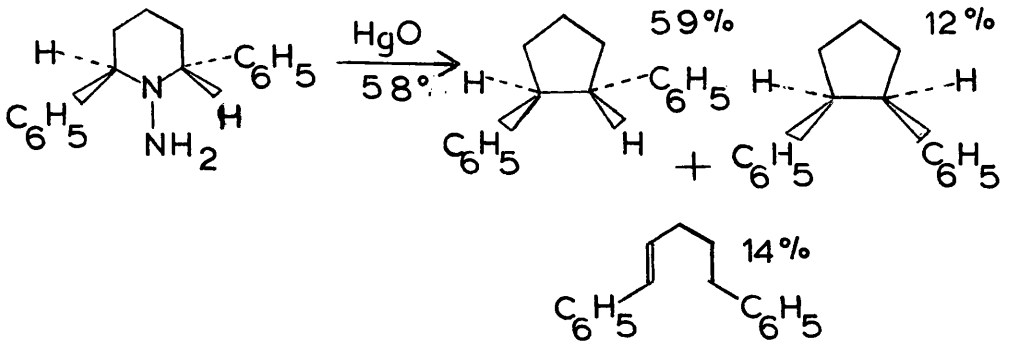


The unsubstituted ring compounds have also been reported to give tetrazenes.[9]

Overberger next synthesised cis and trans-1-amino-2,6-diphenylpiperidine and studied the oxidation with mercuric oxide.[10] The cis isomer gave cis-1,2-diphenylcyclopentane and 1,5-diphenylpent-1-ene; nitrogen loss was instantaneous.

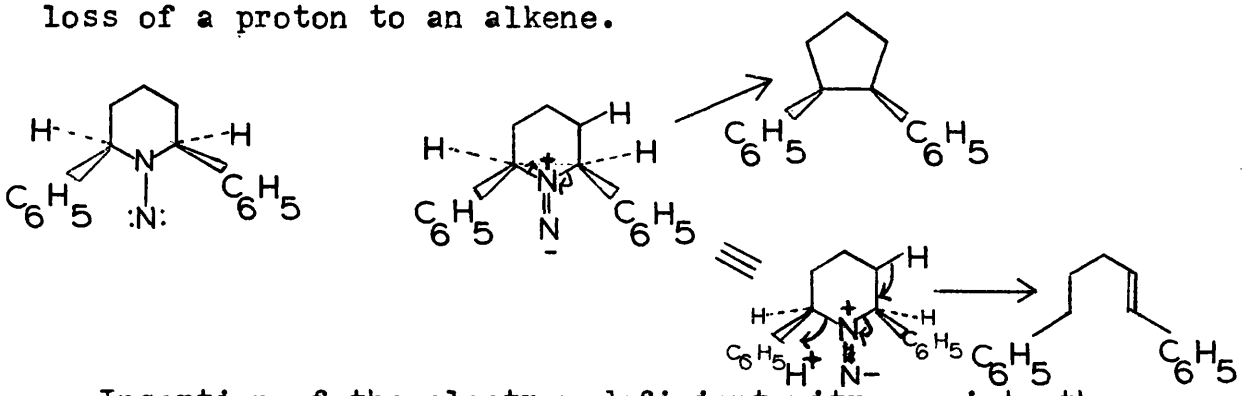


The trans isomer gave trans-1,2-diphenylcyclopentane, with some cis and 1,5-diphenylpent-1-ene.

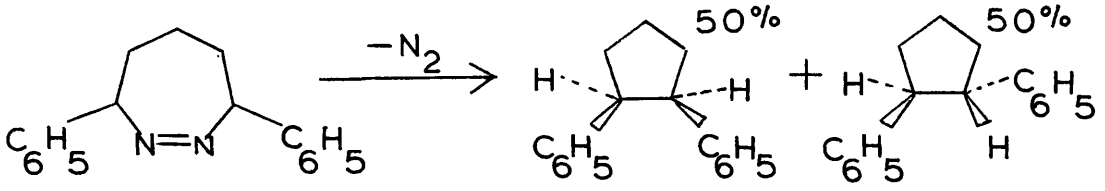


Overberger argued that the cis isomer came from isomerisation prior to oxidation, and showed that this was possible. The reaction therefore appears to be stereospecific.

The reaction proceeds, then, by a concerted loss of nitrogen from the nitrene[11] (evidence for this intermediate to follow) with collapse of the carbon skeleton to a ring structure or loss of a proton to an alkene.

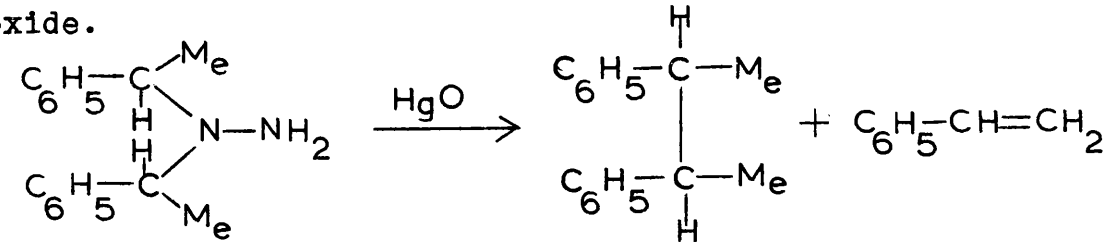


Insertion of the electron deficient nitrogen into the ring to form an azo compound was considered.[10] An authentic sample of the appropriate azo compound was shown to be too stable to be an intermediate, having a half life of five hours; nitrogen was lost to give the cis and trans isomers equally.



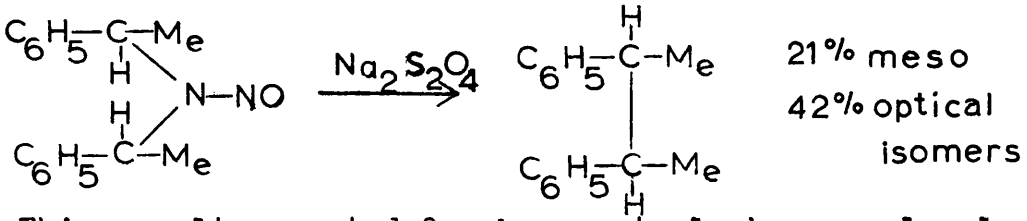
It may be argued that the observed stereoretention of configuration in the piperidine series is not the result of a truly concerted process but is a manifestation of the geometric restrictions placed on the system by a cyclic

structure. For this reason, Overberger[12] thought it important to determine the stereochemical fate of a linear hydrazine. He prepared a pure optical isomer of α,α'-dimethyl-1,1-dibenzylhydrazine and studied the oxidation with mercuric oxide.



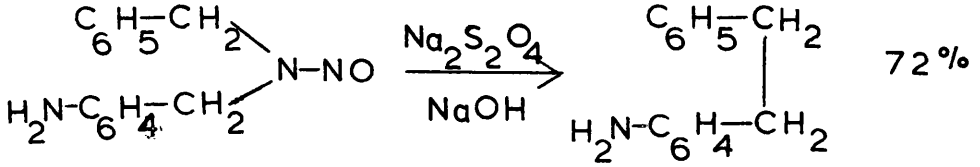
The product, 2,3-diphenylbutane, was shown to be 31% of the mesoform and 45% of optical isomers which showed a predominance of the enantiomer expected. A trace of styrene was found.

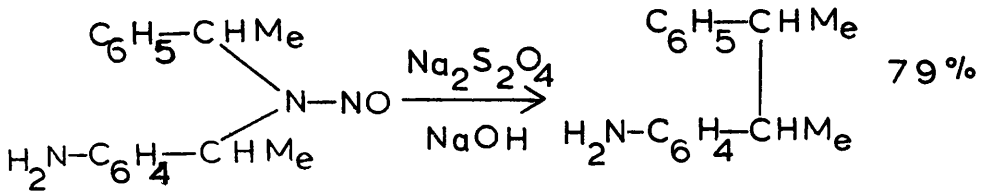
So the reaction was not truly concerted, and some fragmentation must have occurred. This is supported by the products of reduction of the N-nitroso compound with sodium hydrosulphite, a reaction also thought to proceed via a nitrene, being almost identical to those from the oxidation.



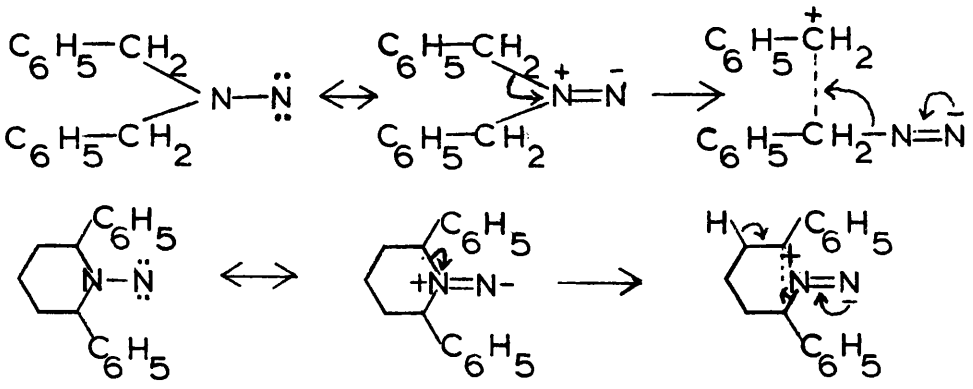
This result prompted Overberger to look more closely for "cross over" products in the dibenzyl series. If one aromatic ring is substituted with an amino group, the uncrossed product would be basic, but one of the crossed products would be neutral thus making separation simple and

efficient. In fact, no crossed products were found from N-nitroso-m-amino-1,1-dibenzylamine or its α,α'-dimethyl homologue.

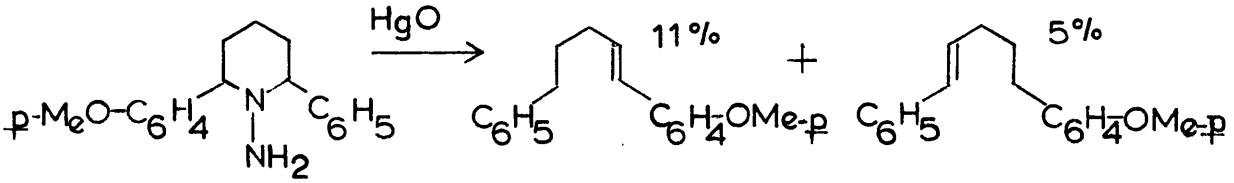




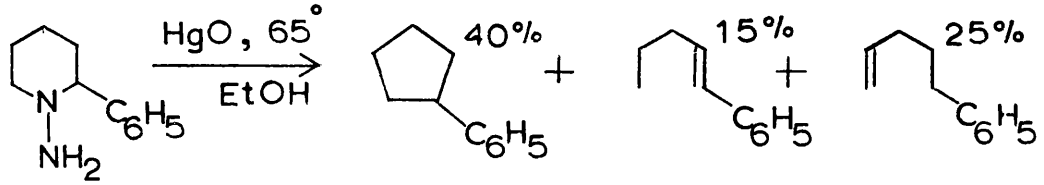
The reaction must therefore proceed by fragmentation within a solvent cage.



This would explain the facility with which benzyl substituted hydrazines decompose, a benzylic carbonium ion being stabilised. If one benzyl group carried a p-methoxy group, this should stabilise the carbonium ion still further, and the direction of opening should then be predictable. This oxidation[13] gave hydrocarbon products in quantitative yield, with the ring closed product predominating.

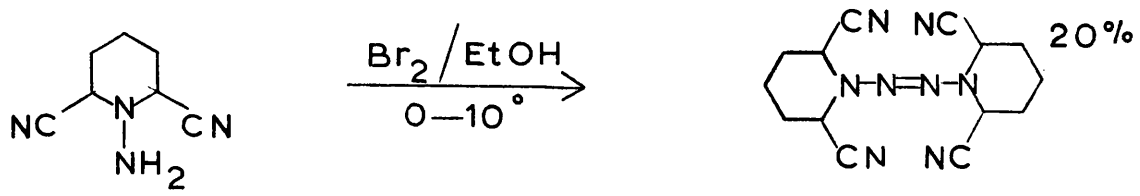


Surprisingly, the alkenes produced were not all conjugated with the p-anisyl function, and so a discrete carbonium ion is an unlikely intermediate in the reaction. Similarly, if only one α-carbon is substituted with a phenyl group, the double bond is expected to be conjugated with this ring in the product. However, when 1-amino-2-phenylpiperidine was added slowly to the mercuric oxide slurry,[14] hydrocarbon products were obtained in 80% yield but the olefin fraction was mainly unconjugated. This again appears to preclude a discrete carbonium ion intermediate.

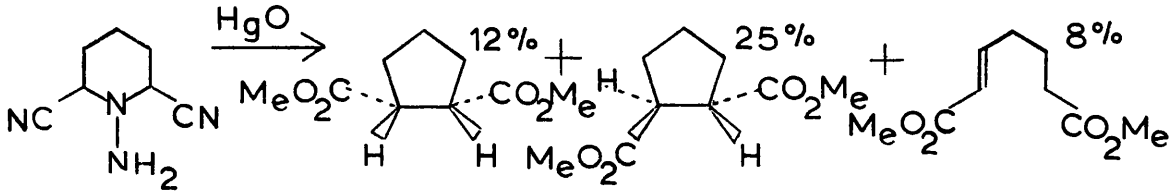


It was noted in this reaction that rapid addition of the aminopiperidine gave the tetrazene (58%) and the three hydrocarbons (17%).

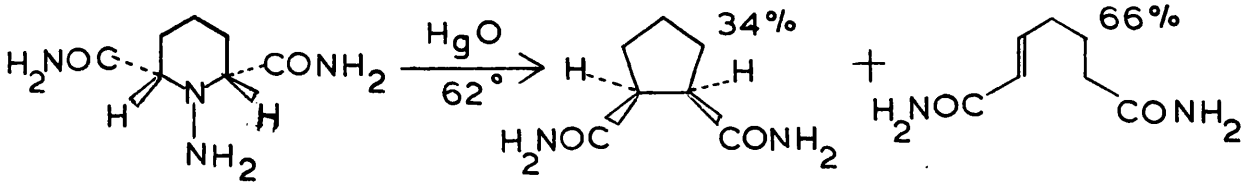
Since the reaction is little affected by electron releasing groups, Overberger[15] studied electron withdrawing substituents. 1-Amino-2,6-dicarboxamidopiperidine was synthesised, as was the dicyano compound. Oxidation of the latter with bromine or potassium permanganate gave the tetrazene.



Mercuric oxide in ethanol gave no reaction, but a dimethylsulphoxide-water mixture (2:1) as solvent gave a rapid oxidation. Products were isolated as the methyl esters by hydrolysis and esterification.



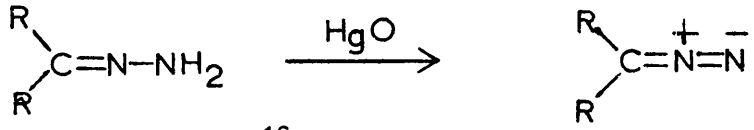
The dicarboxamide was oxidised smoothly in ethanol, giving a quantitative yield of diamides.



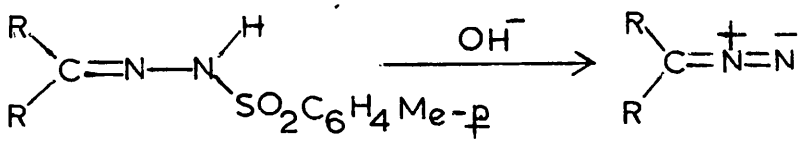
These results were explained as follows. A radical path is the most likely process for the formation of unsaturated linear products by disproportionation. If the process went through a carbonium ion, dimethylsulphoxide would favour olefin formation over cyclisation by nucleophilic attack on a β proton. This was not found. The direction of nitrene collapse is thus governed by steric considerations. Cyclisation will be preferred unless steric factors predominate. The cyano group, being small, allows cyclisation to occur readily at the expense of olefin formation. The

carboxamido group which is much more bulky hinders cyclisation and olefin formation predominates.

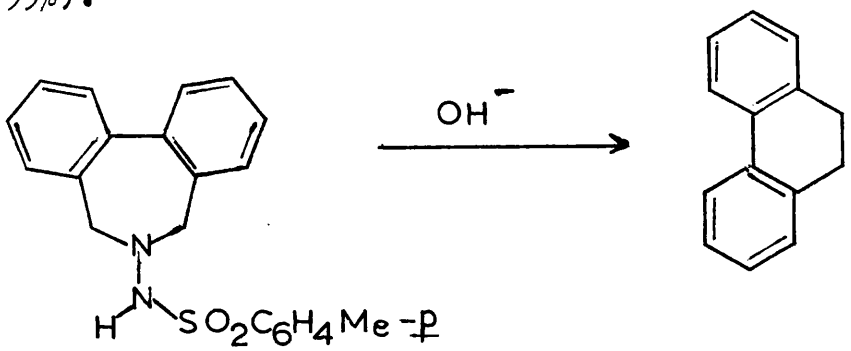
The oxidation of aliphatic hydrazones is a well known and synthetically important reaction, giving aliphatic diazo compounds.



Bamford and Stevens[16] showed that the same reaction could be achieved by the base catalysed decomposition of toluene-p-sulphonylhydrazones.

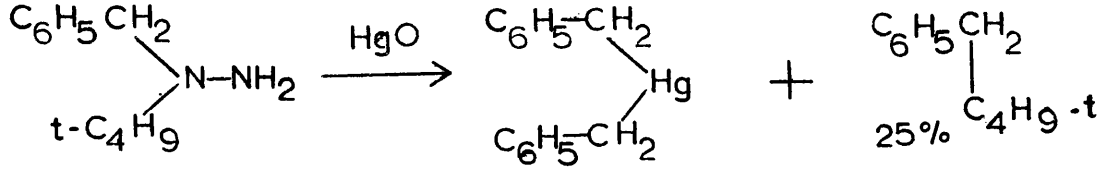


Carpino[17] extended this reaction to generate nitrenes from 1,1-disubstituted hydrazines and compared it with direct oxidation of the hydrazine. N-Toluene-p-sulphonylamidodibenzazepine when treated with base gave 9,10-dihydrophenanthrene (95%).



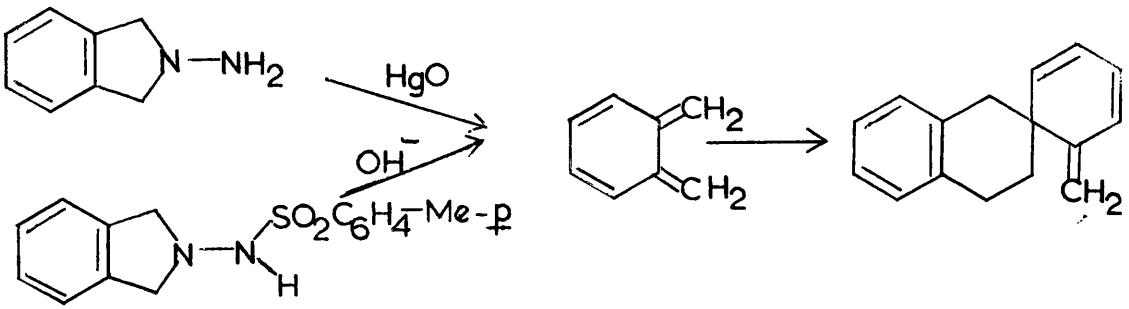
N-Toluene-p-sulphonylamido-1,1-dibenzylhydrazine[18] gave dibenzyl, in complete analogy with the oxidation.

Carpino replaced one benzyl group by various alkyl groups in this reaction and also studied the corresponding oxidation. He found that 1-benzyl-1-t-butylhydrazine gave dibenzylmercury and neo-pentylbenzene.

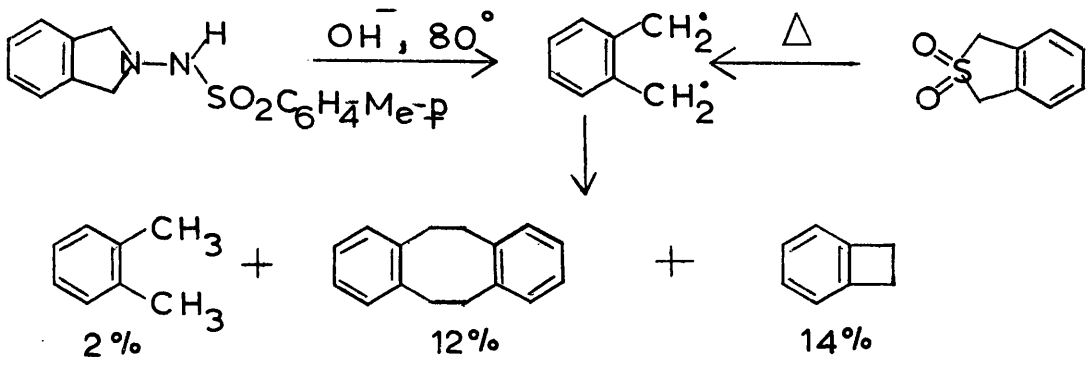


With a n-butyl group, n-amylbenzene (20%) was produced, with methylene chloride as solvent. Ethanol as solvent produced the tetrazene and silver oxide[19] as an oxidant produced the parent amine. Production of the amine from a hydrazine had been previously noted.[20] Thus, 1,1-diphenylhydrazine gives diphenylamine with mercuric oxide.

N-Aminodihydroisoindole was oxidised with mercuric oxide and the toluene-p-sulphonyl derivative cleaved with base. Carpino[21] reported identical results from the two reactions.

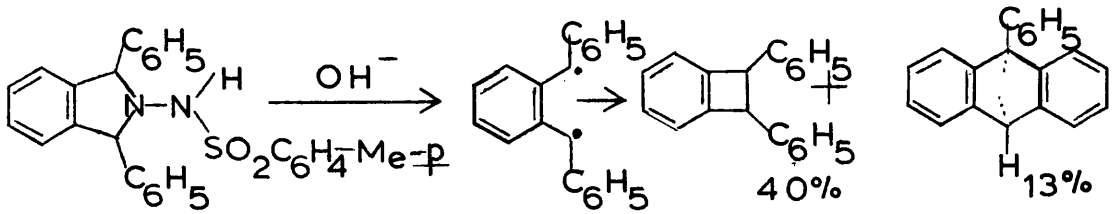


The dimeric product was characterised as its dibromide. This second reaction had previously been studied with different results.[22] Three hydrocarbon products were reported and it was suggested that they derived from the diradical remaining after nitrogen loss.

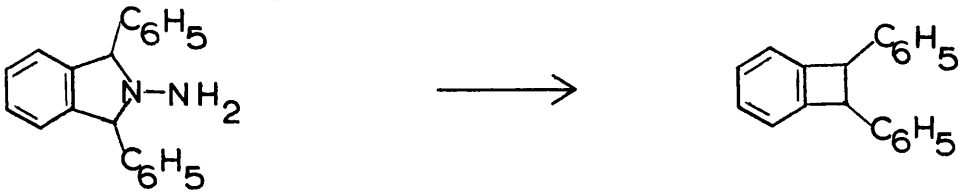


This was supported by the thermal decomposition of 2-thia-indane dioxide which gave these three hydrocarbons in almost the same yield. The thermal decomposition was also supposed to proceed through the diradical.

The 1,3-diphenyl homologue was also studied and shown to behave similarly. Diphenylbenzocyclobutene (40%) and 9-phenyl-9,10-dihydroanthracene (13%) were produced.



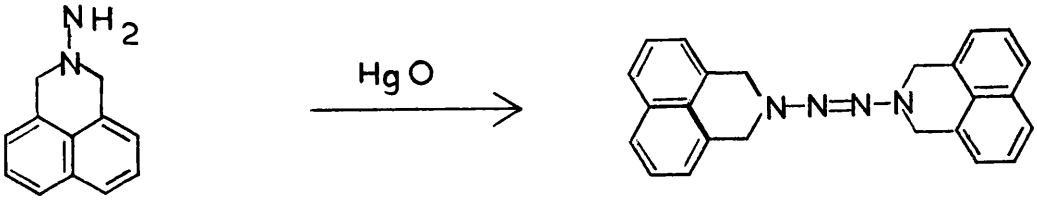
A more elegant study of this reaction was made by Carpino. He synthesised the <u>cis</u> and <u>trans</u> isomers of 2-amino-1,3--diphenyldihydroisoindole and carefully oxidised them with mercuric oxide.



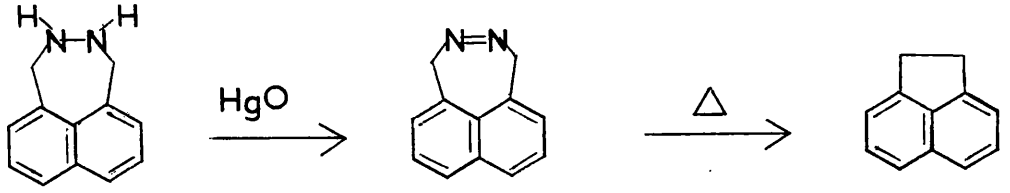
trans	$\xrightarrow{HgO}$	trans benzodiphenyl cyclobutene	81%
cis	$\xrightarrow{HgO}$	trans and cis	low yield
cis	$\xrightarrow{MnO_2}$	cis	27%

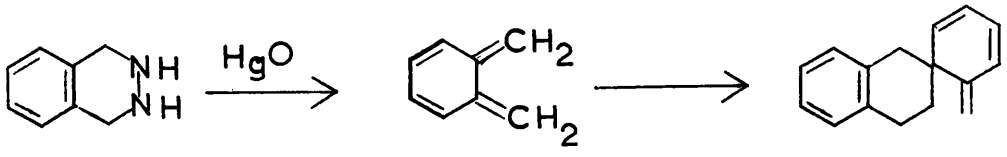
The trans-isomer gave trans-product in high yield, but the cis-compound gave both cis- and trans- in low yield. Active manganese dioxide[23] however gave the cis-product only, but in low yield.

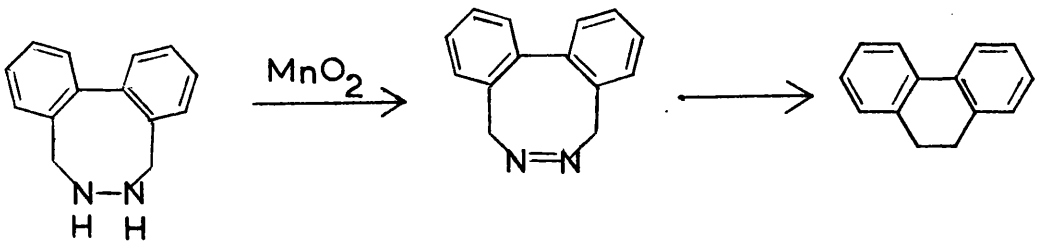
The importance of the o-dimethylene compound as an intermediate in this reaction was shown by Carpino[24] by extending the ring system to rule out contributions from this type of intermediate. 2-Amino-2,3-dihydro-1H-benz(de)isoquinoline on oxidation failed to lose nitrogen but formed a tetrazene.



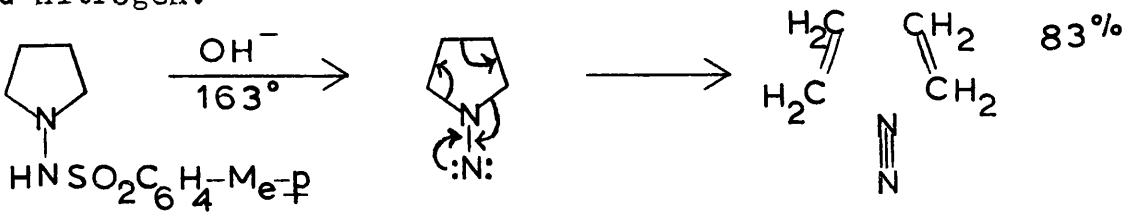
Other oxidants were tried but failed to produce acenaphthene. A number of hydrazo systems were studied for comparison in an attempt to clarify the mechanism; they all lost nitrogen to give hydrocarbon products.



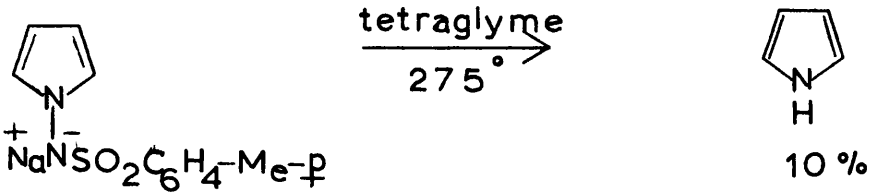




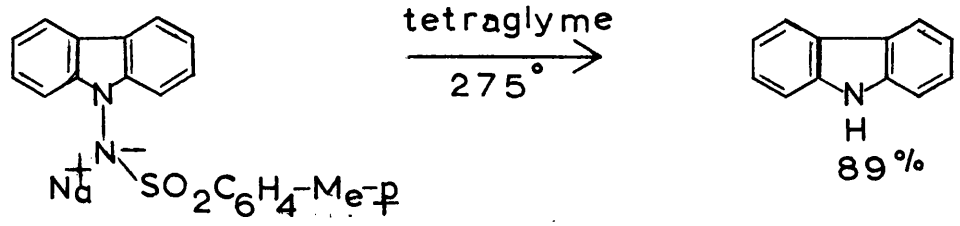
In an elegant study of the pyrrole and pyrrolidine ring systems, Lemal[25] has demonstrated the importance of the basicity of the substituted nitrogen. He found that the toluene-p-sulphonyl derivative of N-amino pyrrolidine decomposed smoothly in base to give two molecules of ethylene and nitrogen.



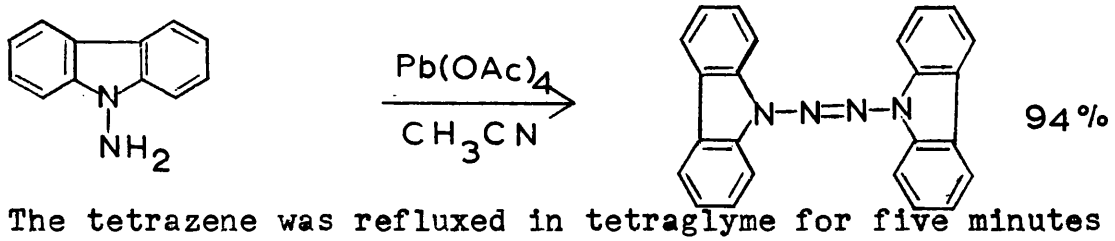
The ethylene was trapped at liquid nitrogen temperatures and characterised as the dibromide. Lemal supposed that the lone pair on the ring nitrogen was used to stabilise the nitrene, making its generation energetically more favourable. For the pyrrole analogue, this is not possible since the lone pair is delocalised into the aromatic system. The decomposition proved to be less facile and nitrogen loss was not complete.



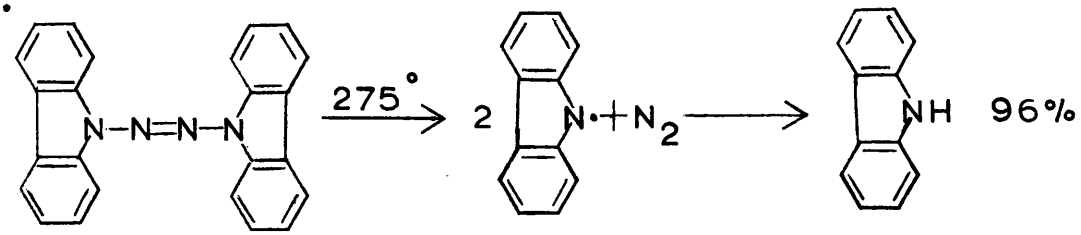
Carbazole is more basic than pyrrole since the lone pair is more available. The carbazole analogue was shown to decompose more readily, but it gave carbazole in high yield.



Lemal argued that the amine was derived from the tetrazene which should decompose under the experimental conditions. Oxidation of N-aminopyrrolidine itself and various substituted analogues was known to give the tetrazene. N-Amino carbazole was oxidised to the tetrazene with lead tetraacetate in high yield.

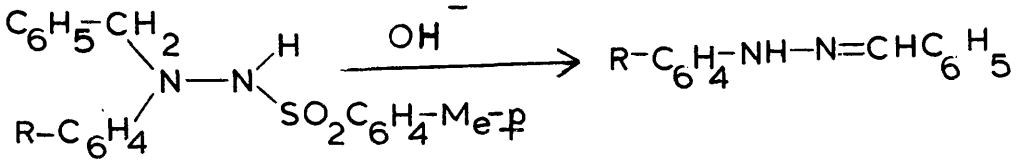


The tetrazene was refluxed in tetraglyme for five minutes then drowned out in water. Carbazole was produced in high yield.

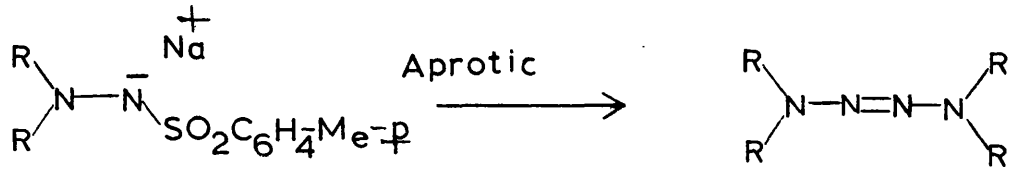


However, the availability of the lone pair on the ring nitrogen is not alone sufficient to determine whether nitrogen is lost. The derivative of N-amino piperidine was shown not to lose nitrogen under conditions where the five membered ring fragments. Here there is no obvious breakdown route for the nitrene.

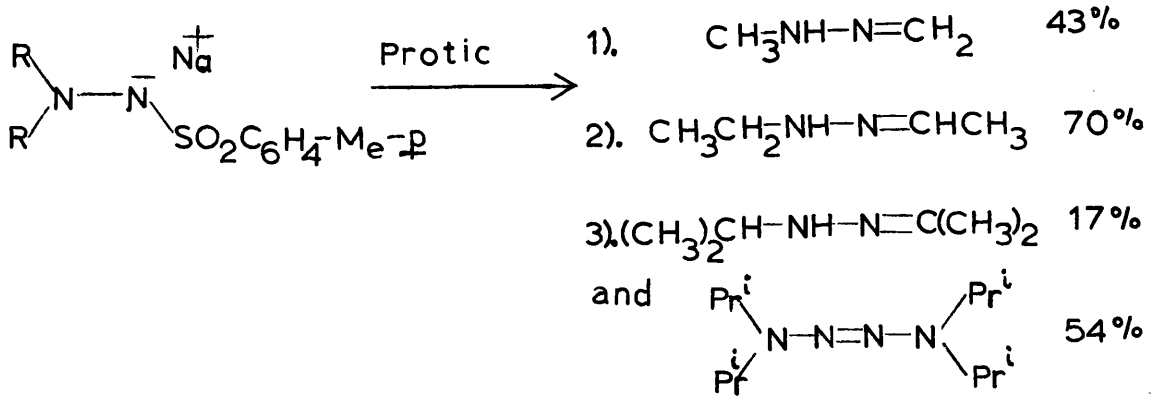
In further studies, Lemal[26] noted that many anomalous products arose from these base catalysed decompositions. Thus, 1-aryl-1-benzylhydrazine was shown to yield a hydrazone. This had also been reported by Carter and Stevens.[27]



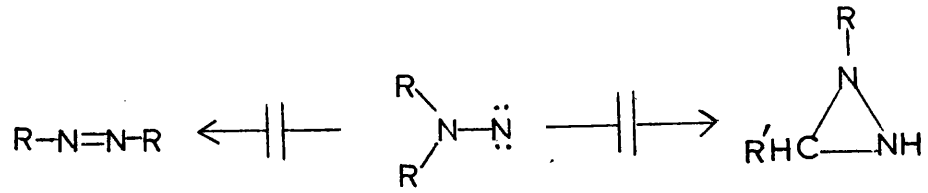
The oxidation of the hydrazine with mercuric oxide gave the hydrazone and/or the tetrazene, depending on the experimental conditions. The nature of the solvent was shown to be of utmost importance in deciding which products were produced. Aprotic solvent led to the tetrazenes while protic solvents gave the hydrazones.



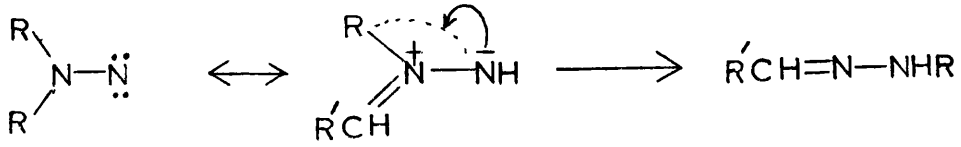
$R=CH_3$, 74%: $R=CH_2CH_3$, 80%: $R=CH(CH_3)_2$, 72%



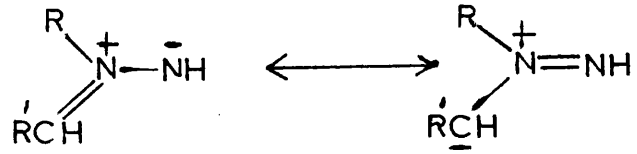
The formation of hydrazones was studied in some detail. Firstly it was shown that azo compounds were not intermediates since the corresponding azo compounds were shown not to rearrange under the experimental conditions. Then the corresponding diaziridines were synthesised and also shown not to rearrange under the experimental conditions.



The only obvious mechanism remaining for the rearrangement is a tautomerism by a prototropic shift from the initially formed nitrene, with subsequent migration of an alkyl group.

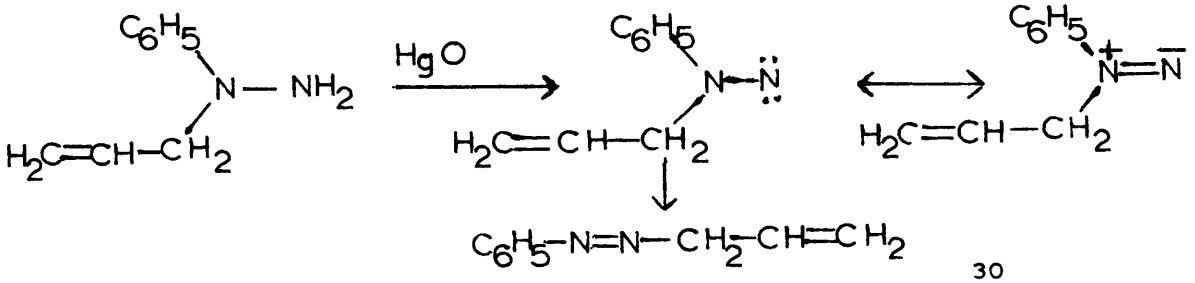


This mechanism has some rather dubious features. Migration of an alkyl group in the zwitterion is reminiscent of the Stevens rearrangement,[28] but the latter reaction ordinarily fails when only simple[28] alkyl groups are available for migration. A typical Stevens' ylid intermediate has a negative charge residing only on carbon. Here, nitrogen can share the anionic charge by delocalisation and both resonance forms place opposite charges on adjacent atoms.

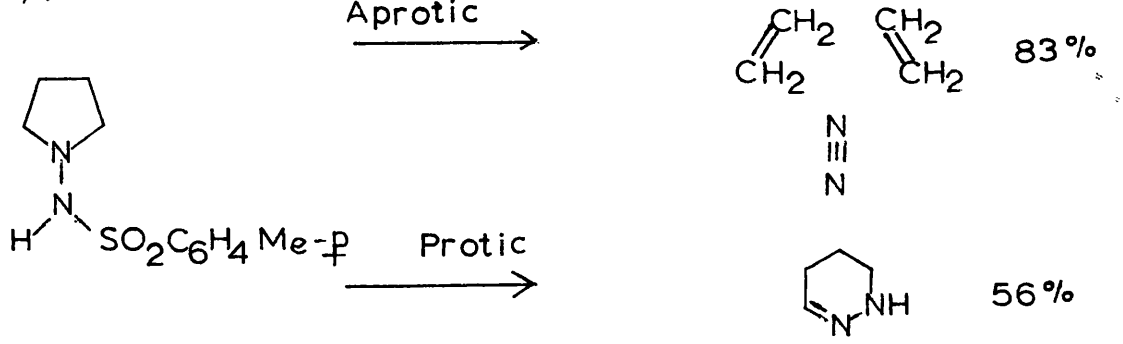


For this mechanism to be correct, rearrangement must be very rapid relative to simple ring closure to a diaziridine.

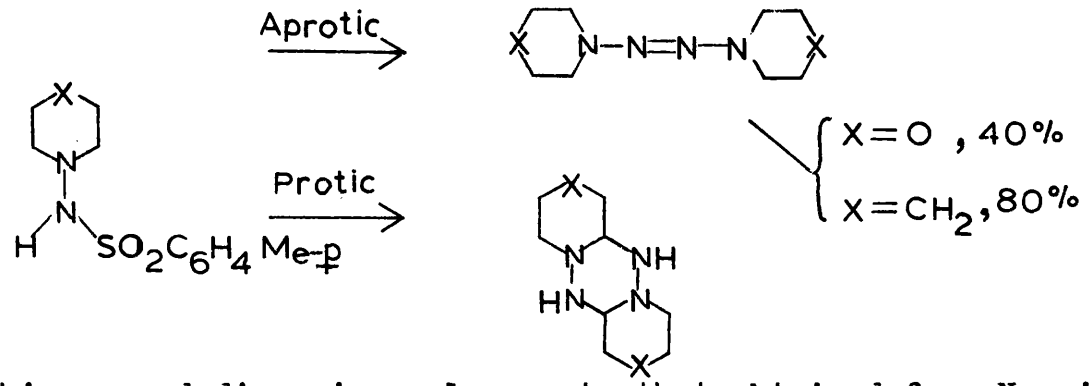
A related rearrangement is that reported by Michaelis.[29] He showed that an allyl-phenylhydrazine was oxidised to an azo compound, benzeneazoprop-2-ene, with mercuric oxide. Ferric chloride as oxidant gave the unrearranged tetrazene however.



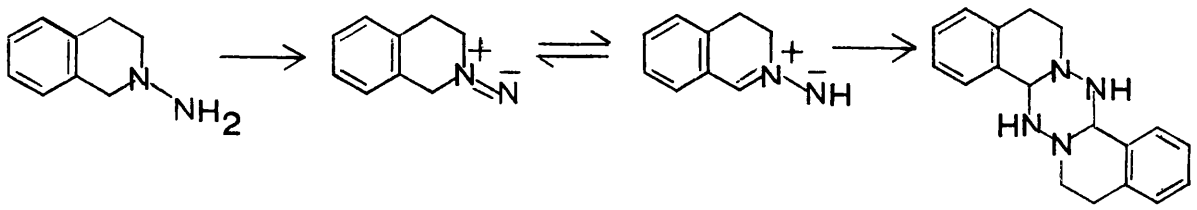
Continuing the study of solvent effects, Lemal[30] re-examined the N-tosylamidopyrrolidine decomposition. In aprotic solvents, it was shown to give ethylene in high yield, but protic solvents changed the reaction course. The nitrene inserted into the ring giving 2,3,4,5-tetrahydropyridazine (56%).



Other ring systems also showed dependence on the nature of the solvent in their reactions. N-Toluene-p-sulphonyl-amidopiperidine and the morpholine analogue were shown to give tetrazenes in aprotic solvents, but another dimer was formed in protic solvents.[31]



This second dimer is analogous to that obtained from N-amino-tetrahydroisoquinoline, with a wide variety of oxidising agents.[32]

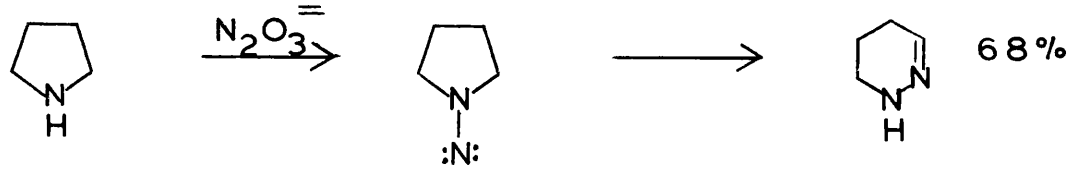


The dimerisation is supposed to be preceeded by a prototropic shift in the initially formed diazene, the resonance stabilised zwitterion formed may then last long enough to meet another zwitterion. The formation of tetrazenes, however, is supposed to be an attack of a nitrene on the starting material initially, followed by oxidation or loss of toluene-p-sulphinic acid. Direct dimerisation

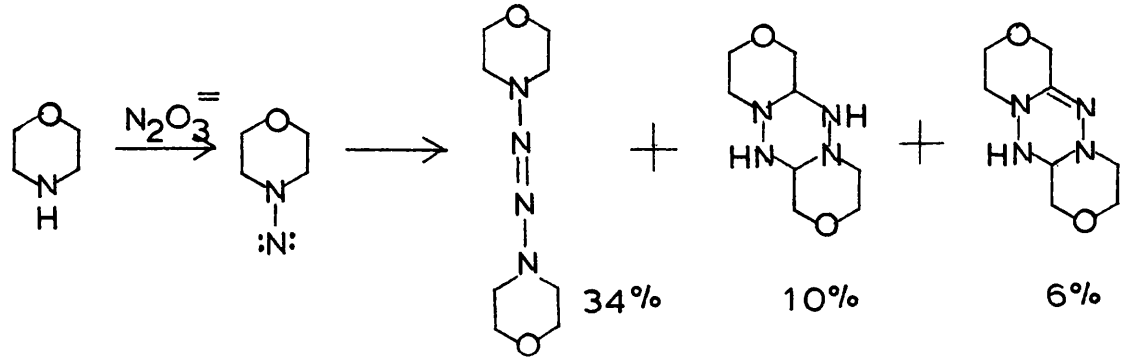
of two nitrenes is less likely, though still a possibility.

A further route to the nitrene was investigated by Lemal[33] by treating secondary amines with Angeli's salt[34] (sodium nitrohydroxylamate, $Na_2N_2O_3$) in acid. This intermediate had been considered by Angeli[34] before 1900, when he discovered that this salt transformed secondary aliphatic amines into their tetrazenes. He isolated other products as well but did not formulate their correct structures.[35]

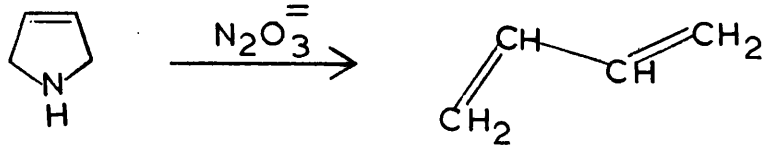
Lemal showed that dibenzylamine gave dibenzyl(70%) on treatment with Angeli's salt. The ring compounds previously studied were re-examined for comparison, though protic solvents are essential for this reaction. Thus, pyrrolidine gave tetrahydropyridazine (68%).



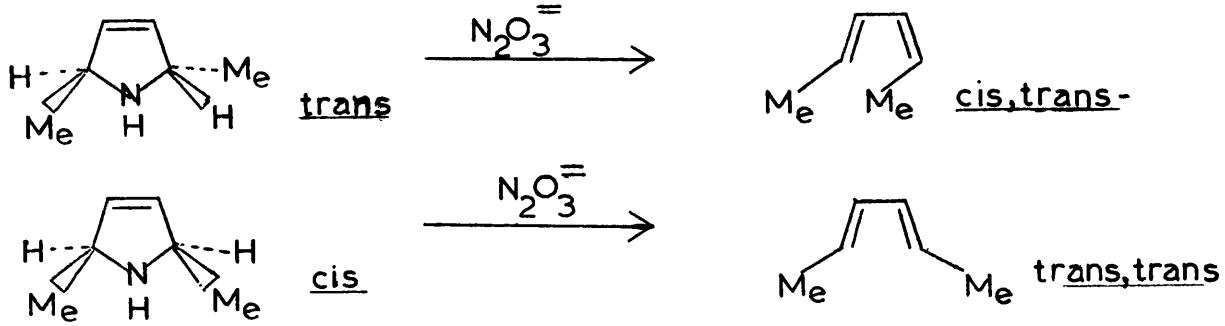
Piperidine and morpholine gave at least three compounds, a tetrazene, a tricyclic isomer and a dehydro derivative of this isomer. This is shown for morpholine below.



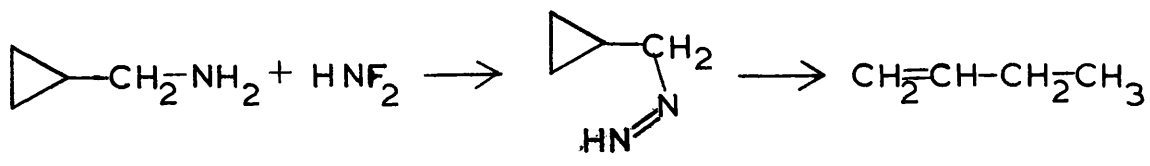
It is of interest that pyrrolidine does not fragment under these conditions. However, the 3-pyrrolines do show nitrogen expulsion and form dienes with complete stereospecificity.[33] The parent, 3-pyrroline, reacts with Angeli's salt to give 1,3-butadiene(86%).



trans-2,5-Dimethyl-3-pyrroline similarly gave cis,trans-2,4-hexadiene, and the cis-2,5-dimethyl-3-pyrroline gave trans, trans-2,4-hexadiene. No traces of the corresponding other isomer were detected in either experiment.

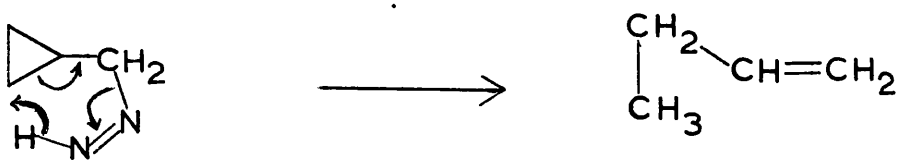


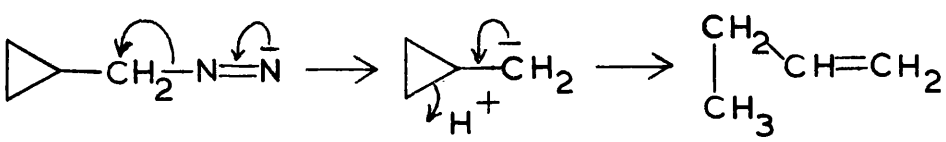
Bumgardner[36] introduced a further method of preparation of nitrenes as a result of his work on cyclopropylmethylamine.



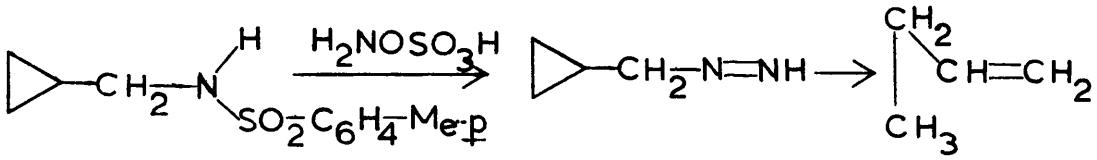
When treated with difluoramine, nitrogen was lost and but-1-ene was produced (46%). No cyclobutane was found, so we can

suppose that there is no heterolytic cleavage of the C-N bond to give a carbonium ion. No methylcyclopropane was found, so homolytic cleavage is also ruled out. The reaction is therefore concerted or possibly a carbanion decomposition. Carbanions generated next to a cyclopropane ring are known to interact with the ring;[37] so we may have mechanism (i) or (ii)

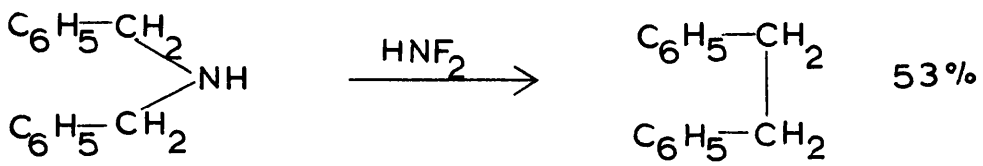
(i) 

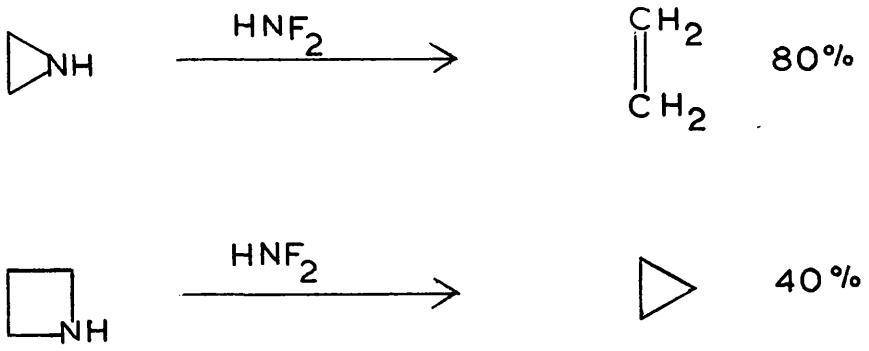
(ii) 

This is very much like the deamination of the toluene-p-sulphonyl derivative of cyclopropylmethylamine with hydroxylamine-O-sulphonic acid reported by Nickon and Sinz.[38]

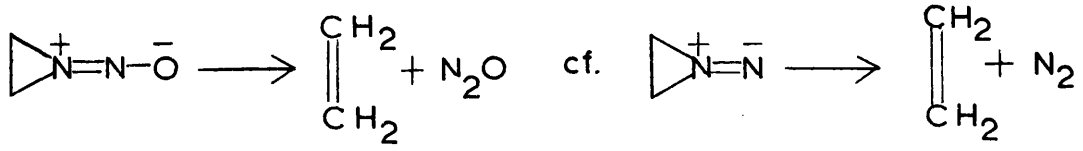


Thus, treatment of secondary amines with difluoramine should generate a nitrene. Dibenzylamine, aziridine and azetidine, when treated with difluoramine, lose nitrogen and give the expected hydrocarbon products, dibenzyl, ethylene and cyclopropane.

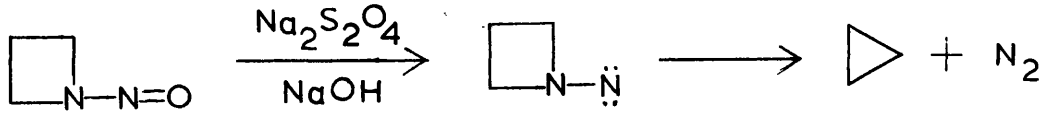




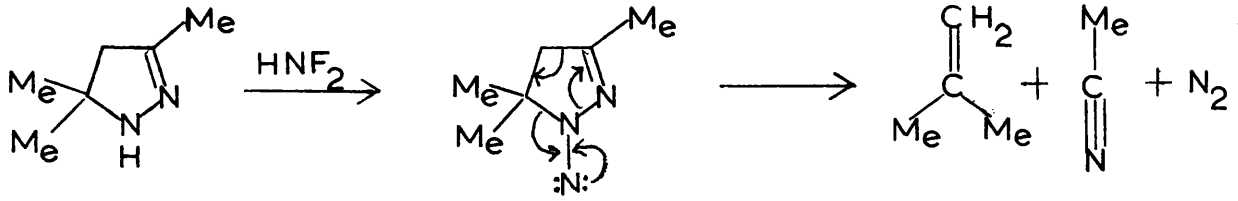
These reactions may be compared with the decomposition of the corresponding N-nitroso compounds. N-Nitrosoaziridine[39] spontaneously loses nitrous oxide to give ethylene.



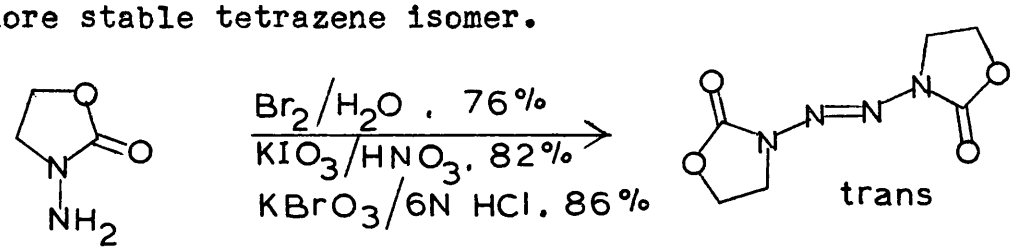
N-Nitrosoazetidine is stable, like the dibenzyl analogue, but sodium hydrosulphite in basic solution generates the nitrene which decomposes, as before, to cyclopropane.



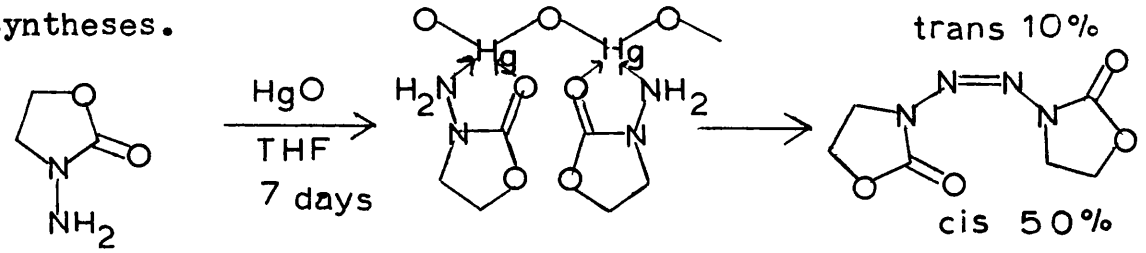
A more complicated fragmentation occurred when 3,3,5-trimethyl pyrazoline was treated with difluoramine, to give isobutylene, acetonitrile and nitrogen.



The ring system has been extended to include many other heterocycles. Forgione et al.[40] studied the oxidation of 3-amino-2-oxazolidinone and isolated both cis and trans tetrazenes. They demonstrated the effect of the oxidant on the isomer produced. With most oxidants, the nitrene is considered to be formed initially, and then dimerises to the more stable tetrazene isomer.

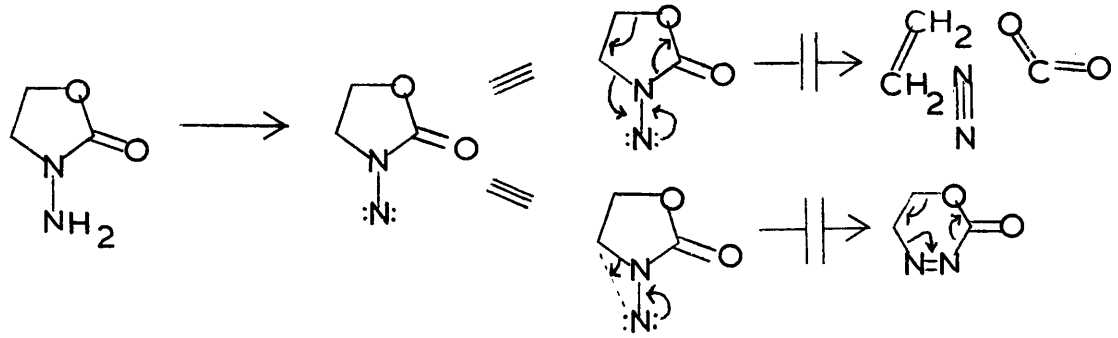


Mercuric oxide oxidation, however, is thought to proceed by the formation of a highly ordered stereospecific intermediate chelate. Under these conditions, the oxidation and coupling of molecules occurs while they are held in the syn position, resulting in the formation of the cis-tetrazene. Only single isomeric products have been reported for all other tetrazene syntheses.

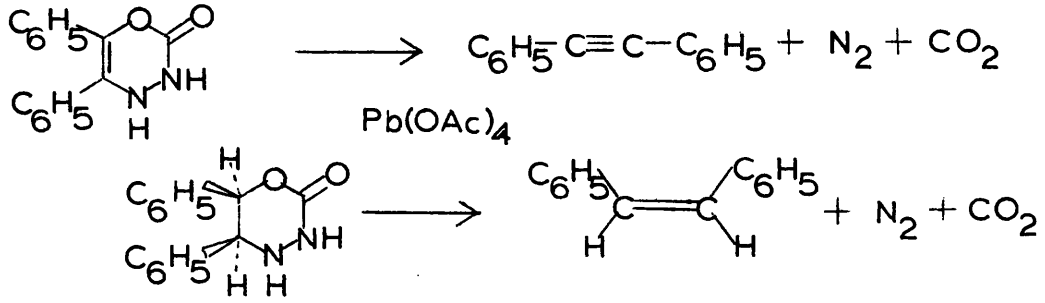


It is of interest that nitrogen is not lost from this nitrene, since a thermodynamically acceptable breakdown pathway is available. Loss of nitrogen and carbon dioxide would give ethylene. Insertion of the nitrene into the ring should

still result in loss of carbon dioxide and nitrogen.

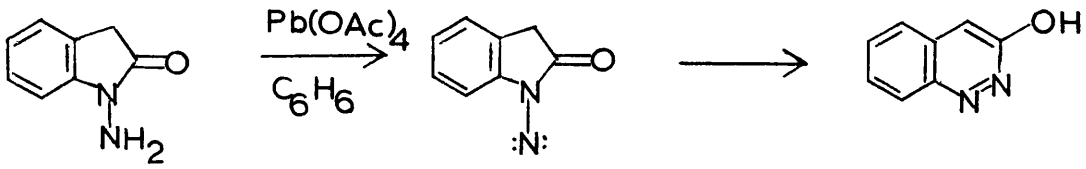


The dihydro and tetrahydrooxadiazinones studied by Rosenblum[41] show this fragmentation.



The base catalysed fragmentation of N-nitrosooxazolidinone[42] does not proceed via a nitrene and is therefore not directly comparable, though it would be expected that the facile loss of nitrogen and carbon dioxide would be mirrored in the oxidation.

Insertion of the nitrene produced by oxidation has been observed with "Neber's lactam". N-Aminooxindole is oxidised by lead tetraacetate to 3-cinnolinol.[43]



1-Aminobenzimidazole, however, is merely deaminated[44] on oxidation, without insertion or nitrogen loss. This is reminiscent of the fate of 1,1-diphenylhydrazine on oxidation by mercuric oxide.[20] N-Aminophthalimide is also deaminated[45] when oxidised with lead tetraacetate; but oxidation of this, N-aminobenzoxazolone, and N-aminodiphenyloxazolone in the presence of tetraphenylcyclopentadienone results in yellow adducts of as yet unspecified structure.[45]

Evidence for the intermediacy of a nitrene has been given by McBride.[46] He studied the oxidation of 1,1-dimethylhydrazine in acid solutions where he assumed the nitrene would be protonated to give its conjugate acid. Four points of interest arose from his investigation.

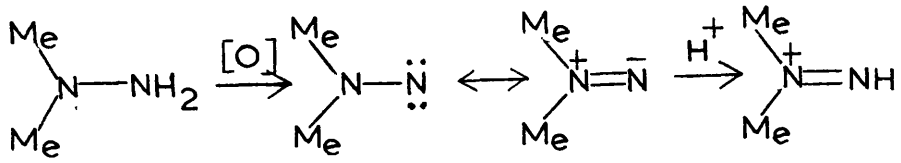
(i) No tetrazene was seen in solution after the oxidation was complete, using spectrophotometric detection methods of high sensitivity, but a tetrazene was formed when the solution was neutralised.

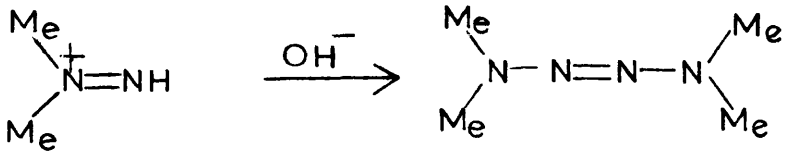
(ii) The addition of stannous chloride to the oxidised acid solution resulted in reduction back to the hydrazine.

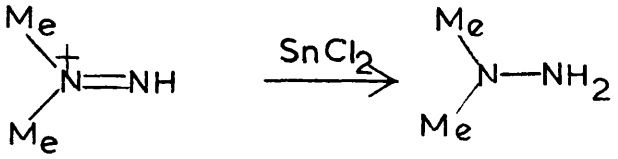
(iii) When the oxidation was performed with perchloric acid in ether, a stable perchloric salt was isolated.

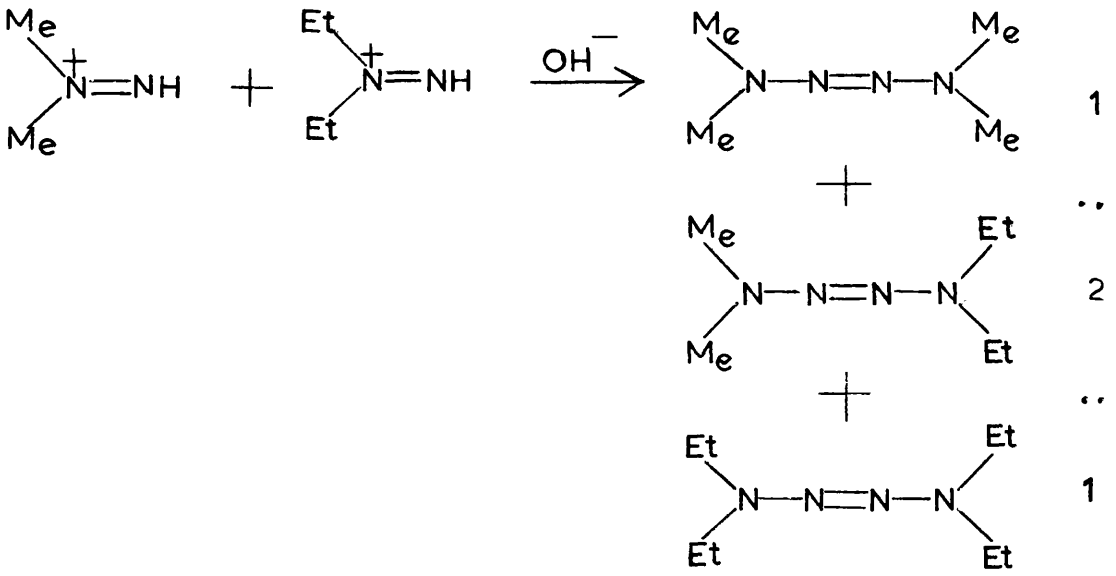
(iv) Oxidation of 1,1-dimethyl and 1,1-diethylhydrazine separately in acid solutions gave three tetrazenes when the solutions were subsequently mixed and neutralised. These were the tetramethyl, tetraethyl and diethyl-dimethyltetrazene, produced in the ratio of 1:1:2 as expected for random

dimerisation.



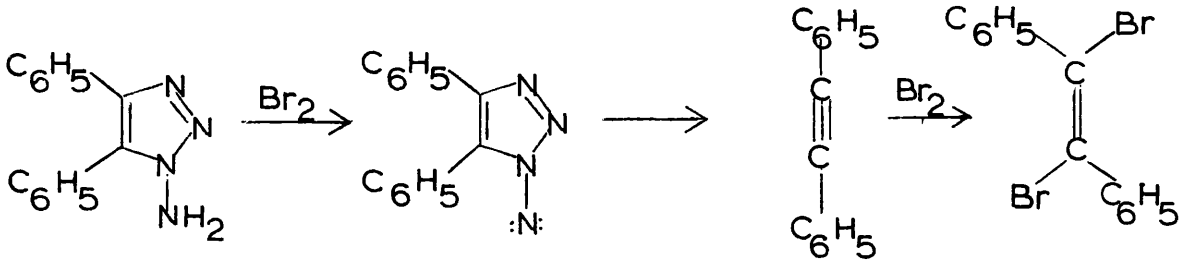




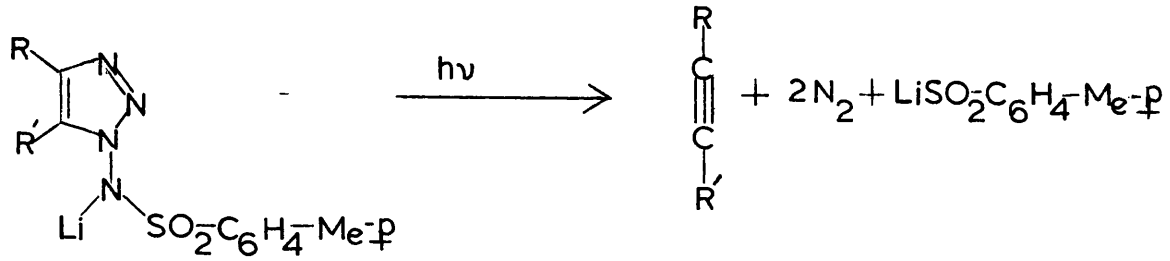


In the present work we have been interested in oxidations similar to those discussed, but where the intermediate nitrene would be more likely to fragment completely. Thus attention was focussed on N-aminotriazoles and the remainder of this introduction will discuss work already reported on these compounds.

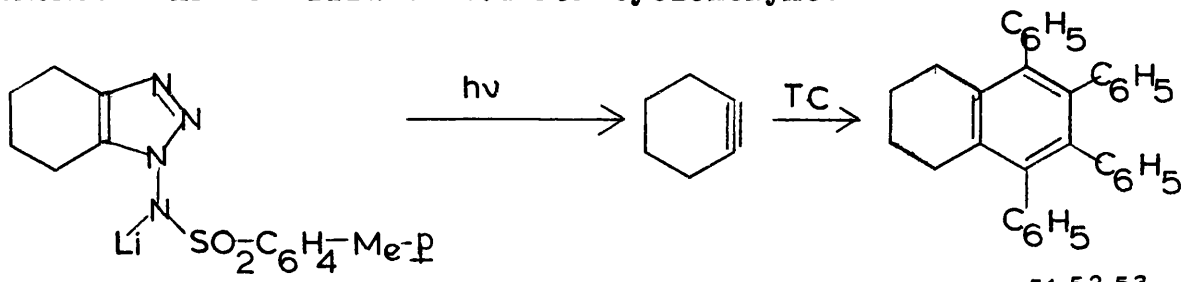
N-Amino-1,2,3-triazoles were first prepared by von Pechmann[47] in 1900 and Stollé[48] in 1904, though they both assigned the wrong structure to these compounds. Stollé reported the oxidation of 1-amino-4,5-diphenyl-1,2,3-triazole with bromine giving trans-dibromostilbene.[49] The oxidation of the dimethyl analogue was reported by von Pechmann; using bromine this gave 2,2,3,3-tetrabromobutane. No mechanism was suggested for these oxidations.



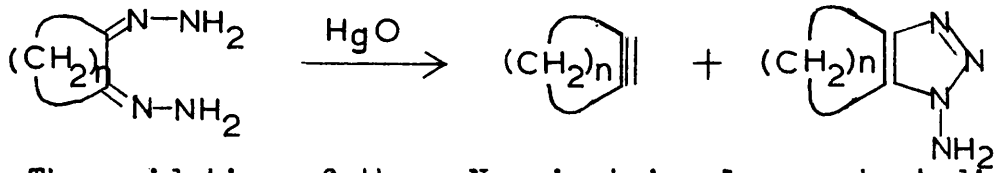
A number of toluene-p-sulphonylamido-1,2,3-triazoles were studied by Willey.[50] He showed that the lithium salts of these compounds were thermally stable, but decomposed photolytically to give the corresponding acetylenes, usually in high yield.



Where the two alkyl groups (R and R') formed a ring, Willey showed that the strained ring alkynes were very reactive and could be trapped with tetraphenylcyclopentadienone. This is illustrated for cyclohexyne.



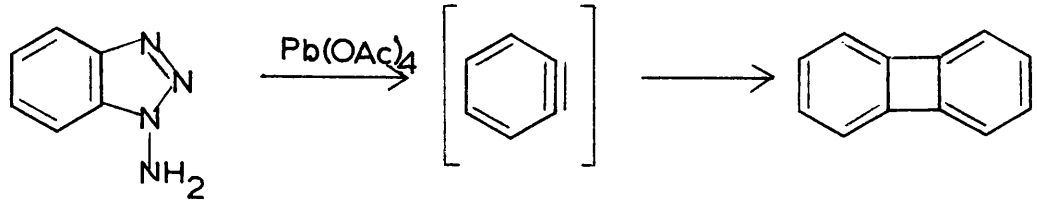
Cycloalkynes were studied extensively by Wittig using[51,52,53] various synthetic pathways. Oxidation of 1,2-bis-hydrazones with mercuric oxide was reported to give cycloalkynes in low yield.[51] A by-product was shown to be the N-aminotriazole.



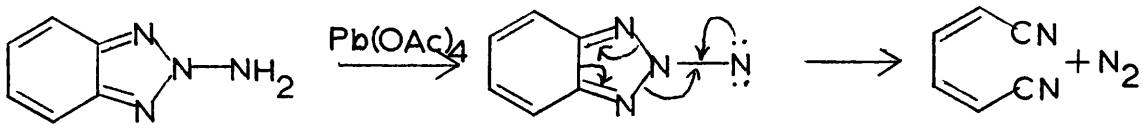
The oxidation of these N-aminotriazoles, not studied by Wittig, will be reported in this thesis and shown to give cycloalkynes in high yield. The work of Wittig follows that of Cope,[54] who oxidised benzil-bis-hydrazone to diphenylacetylene with mercuric oxide, in high yield.

1-Aminobenzotriazole was first prepared by Trave and

Bianchetti.[55] Campbell and Rees[56] used an extensive modification of the published synthesis to prepare the parent compound and many substituted analogues. These workers showed that oxidation of 1-aminobenzotriazole with lead tetraacetate resulted in the very rapid production of the transient intermediate, benzyne, in high yield. This benzyne has the remarkable property of readily dimerising to biphenylene in high yield, unlike benzyne generated by other methods.[57,58]

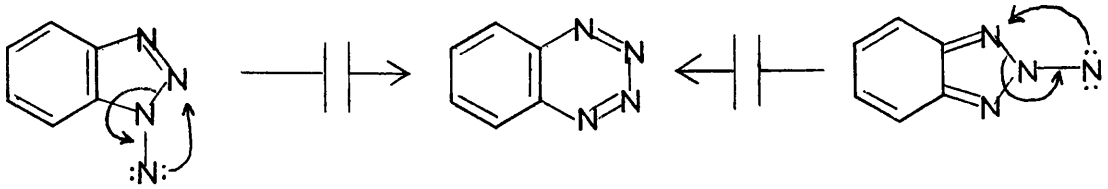


Direct amination of benzotriazole with hydroxylamine-O-sulphonic acid was shown to give the 1- and 2-amino substituted isomers.[59] Oxidation of 2-aminobenzotriazole, with lead tetraacetate or phenyl iododiacetate, was shown to give cis, cis-muconodinitrile.[60]

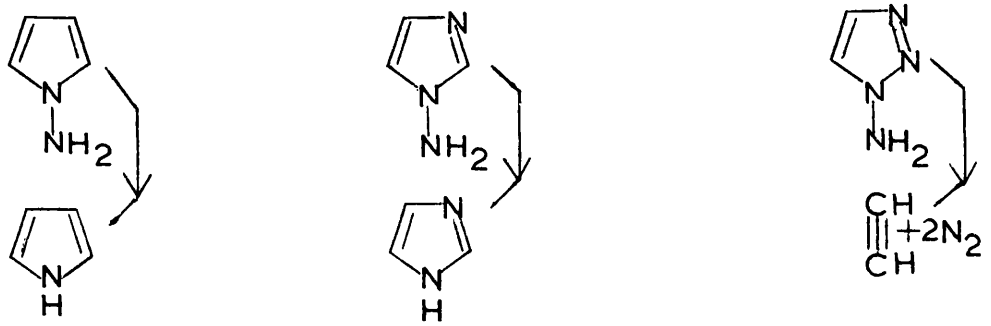


Presumably, the oxidation of 1- and 2-aminobenzotriazole proceeds via a nitrene intermediate. This nitrene cannot insert into the triazole ring before nitrogen is lost, otherwise the same products would be expected from both

isomers.



Fragmentation, with loss of nitrogen, must be preferred to tetrazene formation since no tetrazene, or parent triazole which could be derived from a tetrazene, was found. This differs sharply from the behaviour of the isoelectronic carbon analogues, N-aminopyrrole and N-aminobenzimidazole, both of which are deaminated to their corresponding parent compound on oxidation.



Concerted pathways for fragmentation are possible for these analogues.

The aromatic system has now been extended to the naphthalene series to give precursors of 1,2- and 2,3-naphthalyne.[61] A related compound described by Rees and Storr[62] is 1-aminonaphtho(1,8)triazine. Oxidation of this with lead tetraacetate results in a transient intermediate, 1,8-dehydro naphthalene. Being, in effect, a meta-aryne, the chemistry of this very reactive intermediate differs markedly from ortho-arynes and has been extensively studied.[61]

The first section of this thesis will describe a detailed study of the oxidation of 1-aminotriazoles with the aim of generating both cyclic and acyclic alkynes. Extensions to other systems will also be reported.

N-Aminobenzotriazinones, though a well known class of compounds, have never been studied with a view to their oxidative breakdown. The second section of this thesis will deal with the oxidation of these compounds. The close relationship with 1-aminotriazoles will be demonstrated, and a new reactive intermediate, benzocyclopropenone, derived from these oxidations will be discussed.

Instrumentation and Experimental Techniques.

1. Infrared (i.r.) spectra were run in the range 4000-650 $cm.^{-1}$ on a Perkin-Elmer 237 spectrophotometer, equipped with sodium chloride optics. Routine spectra of solids were taken as Nujol mulls and liquids as capillary films. Quantitative work was performed on a Perkin-Elmer 225 high resolution spectrophotometer, using liquid cells of 1mm. path length and solutions of accurately known concentration. The solvents employed were carbon tetrachloride, carbon disulphide, acetonitrile and dioxan, all of spectroscopic grade, dried and stored over molecular sieves (type 4A).
2. Proton magnetic resonance (p.m.r.) spectra were taken on a Perkin-Elmer R.10 60 Mc/s or Varian A.60 instrument, and are quoted in τ values throughout this thesis. Carbon tetrachloride, deuterochloroform or hexadeuterodimethyl-sulphoxide were used as solvents, with tetramethylsilane as internal reference.
3. Mass (m/e) spectra were taken on an Associated Electrical Industries M.S.9 spectrometer at 70 e.v., unless otherwise stated.
4. Gas-liquid chromatography (g.l.c.) was performed on a Perkin-Elmer F11 gas chromatograph, with nitrogen carrier gas and a flame ionisation detector. A Honeywell recorder

fitted with a disc integrator was used.

5. Thin-layer chromatography (t.l.c.) was used extensively for qualitative analyses of reaction products and for testing the purity of compounds. Samples were eluted with suitable solvent mixtures on glass plates coated with a 250μ thickness of Kieselgel G (E. Merk), and detected with an iodine spray.

6. Column chromatography was carried out using silica-gel (Hopkin and Williams M.F.C.), basic alumina (Spence type H) and neutral or acidic alumina (Woelm).

"Wet-columns" were prepared by packing the absorbent under petrol, and the eluant was gradually replaced by ether and then by methanol. Where separation of products proved difficult, an automatic gradient elution technique was employed using a very small polarity gradient.

"Dry-columns" were prepared by the method of Loev and Snader[63] and the same eluants employed as before.

In all experiments only chromatographic fractions which gave significant amounts of material are recorded.

7. Solvents used in oxidation experiments:

Benzene (A.R.) was dried over sodium wire, refluxed over and distilled from calcium hydride, and stored over phosphorus pentoxide.

Methylene chloride was refluxed over and distilled from

calcium hydride and stored over molecular sieves (type 4A).

Anhydrous ether was dried with sodium wire and stored over molecular sieves.

Methanol was dried by the magnesium method, distilled and stored over molecular sieves.

Acetonitrile was dried by prolonged storage over molecular sieves.

Petrol refers to light petroleum, b.p. 40-60°.

Ether and chloroform extracts were dried over anhydrous magnesium sulphate.

Solvents were removed under reduced pressure in a rotary film evaporator.

8. Lead tetraacetate (B.D.H.) was dried by filtration from acetic acid and stored <u>in vacuo</u> over concentrated sulphuric acid.

9. Melting points (m.p.) were taken in capillary tubes in an electrically heated block apparatus using corrected thermometers.

10. Reaction products were identified by comparison of i.r. spectra and mixed m.p. determinations with authentic compounds wherever possible. Literature m.p. and b.p. values are given with the appropriate reference, except for common or well-authenticated compounds, when the values are taken from the Heilbron Dictionary of Organic Compounds (3rd. and 4th. Editions).

Section I

Experimental

Preparation of 1-amino-4,5-diphenyl-1,2,3-triazole

1. From benzil-bis-benzoylhydrazone

a) Benzil (21g.) and benzhydrazide (27.2g.) were intimately mixed and fused at 120° for 2hr. The resultant solid was powdered under ethanol (50ml.), filtered and dried. Crystallisation from ethanol afforded benzil-bis-benzoylhydrazone (93%) as a white fluffy mass, m.p. 210-212° (lit.[64] m.p. 204-206°).

bi) The bis-benzoylhydrazone (22.3g.) was dissolved in ethanol (500ml.) containing sodium ethoxide (6.8g.) under reflux. Mercuric chloride (27.2g.) in ethanol (50ml.) was added and the solution cooled and filtered. The insoluble bis-mercuric chloride complex was suspended in anhydrous ether (50ml.) and iodine (25.4g.) in anhydrous ether (50ml.) was added dropwise with stirring. The precipitate was filtered off, washed with ether to remove iodine and the bis-hydrazone, with potassium iodide solution to remove mercuric chloride and finally washed with water to remove any salts and dried *in vacuo*. Crystallisation from ethanol afforded 1-benzoylamido-4,5-diphenyl-1,2,3-triazole enol benzoate (35%), flocks, m.p. 183-184° (lit.[65] m.p. 189°).

bii) The bis-benzoylhydrazone (44.6g.) was dissolved in ethanol under reflux with dioxan (300ml., 2:1). Lead dioxide (24g.) was added over 15min., the solution refluxed

for a further 15 min. and then taken to dryness. The residue was taken up in conc. HCl (50ml.), filtered, diluted and neutralised. The white precipitate was filtered off and washed with hot water. Crystallisation from ethanol afforded 1-benzoylamido-4,5-diphenyl-1,2,3-triazole (64%), m.p. 249-251°, (lit.[65] m.p. 248°).

Similar experiments with other oxidants yielded the enolbenzoate as in bi), when no acid was involved in the work up.

c) The enolbenzoate (4.4g.) was shaken with conc. HCl (20ml.) for 5 min., neutralised and the precipitate filtered off. Crystallisation from ethanol afforded 1-benzoylamido-4,5-diphenyl-1,2,3-triazole (89%), needles, m.p. and mixed m.p. 251-253° (Found: C, 73.8; H, 4.9; N, 16.3. Calc. for $C_{21}H_{16}N_4O$: C, 74.1; H, 4.7; N, 16.5%).

d) The benzoylamido triazole (3.4g.) was dissolved in ethanol (20ml.) and conc HCl (20ml.) under reflux. The solution was taken to dryness, the residue washed with sodium hydroxide solution (20ml., 2N), water (20ml.) and dried <u>in vacuo</u>. Crystallisation from benzene/petrol (1:4) afforded 1-amino-4,5-diphenyl-1,2,3-triazole (85%), white flocks, m.p. 134-135°, (lit.[65] m.p. 135°) (Found: C, 70.9; H, 5.1; N, 23.5. Calc. for $C_{14}H_{12}N_4$: C, 71.2; H, 5.1; N, 23.7%).

ν max. 3320, 3150 (NH_2); 1255 (triazole ring); 745, 690 cm^{-1}. (mono-substituted benzene ring.)

Benzylidene derivative, needles from ethanol, m.p. 182-184° (lit.[65] m.p. 184°).

2. From benzil-bis-toluene-p-sulphonylhydrazone

a) Benzil (42g.) and tosylhydrazide (74g.) in benzene (200ml.) were refluxed for 1hr. with one drop of conc. H_2SO_4, using a Dean and Stark reflux head. The solution was taken to dryness and the oily residue triturated with ether. Crystallisation from ethanol afforded benzil-bis-tosyl-hydrazone (73%), m.p. 173-175° (lit.[16] m.p. 184°).

bi) The tosylhydrazone (51.4g.) was refluxed in ethylene glycol (250ml.) with potassium hydroxide (6g.) for 1hr. The solution was poured into water (500ml.), neutralised and filtered. Crystallisation of the residue from ethanol afforded 1-toluene-p-sulphonylamido-4,5-diphenyl-1,2,3-triazole (68%)as plates, m.p. 232° (Found: C, 64.5; H, 4.7; N, 15.4. $C_{21}H_{18}N_4O_2S$ requires: C, 64.6; H, 4.6; N, 14.4%).

bii) The tosylhydrazone (51.4g.) was refluxed in propionic acid (250ml.) for 20min., poured into water (500ml.) and the solid filtered off. Crystallisation from benzene-petrol (b.p. 60-80°) (1:4) afforded the crude product. Recrystallisation from ethanol afforded 1-tosylamido-4,5-diphenyl-1,2,3-triazole (77%), m.p. and mixed m.p. 232-233°.

c) The tosylamidotriazole (20g.) was suspended in water (100ml.) and sulphuric acid (400ml., 98%) was added dropwise with

stirring, keeping the temperature below 150°. The suspension was held at 150° until dissolution was complete; the solution was cooled, poured onto ice and neutralised. The precipitate was filtered off and dried in vacuo. Crystallisation from benzene-petrol (1:4) afforded the 1-aminotriazole (92%), m.p. and mixed m.p. 132-133° (lit.[65] m.p. 135°).

3. From benzil-bis-hydrazone

a) Benzil-bis-hydrazone was prepared by the literature method.[54]

bi) Benzil-bis-hydrazone (23.8g.) was dissolved in ethanol (500ml.) under reflux. Selenium dioxide (6.7g.) in water (25ml.) was added dropwise over 1hr. The solution was refluxed for 1hr., filtered and the filtrate taken to dryness. The residue was extracted with sodium hydroxide solution (2×100ml., 2N), with water (2×25ml.) and dried in vacuo. Trituration with petrol (100ml.) followed by crystallisation from petrol (b.p. 60-80°)-benzene (4:1) afforded the 1-aminotriazole (73%), m.p. 131-133°.

bii) Benzil-bis-hydrazone (23.8g.) was dissolved in benzene (100ml.) and pyridine (7.9g.). Tosyl chloride (19.5g.) was added in portions with shaking and cooling. The solution was taken to dryness, washed with water (50ml.) and taken up in propionic acid (100ml.) with refluxing for 20min.,

then poured into water (200ml.), neutralised and filtered. The residue was washed with water (50ml.) and dried in vacuo. Crystallisation from petrol (b.p. 60-80°)-benzene (4:1) afforded the 1-aminotriazole (71%), m.p. and mixed m.p. 132-133°.

The intermediate benzil-monohydrazone-monotosylhydrazone was not characterised, though it was also prepared from benzil-monohydrazone and from benzil-monotosylhydrazone by the direct routes. The above method, however, gave maximum yields in this preparation.

4. Attempted Method.

α-Phenylazoacetophenone was prepared by the standard route.[66] The diazoketone (2.2g.) was dissolved in dry methanol (40ml.) and cooled to 0°. Freshly distilled hydrazine hydrate (5ml.) was added and the solution stirred over anhydrous calcium sulphate for 2hr. Analysis (t.l.c.) showed no reaction had occurred. The solution was stirred at room temperature for 24hr., filtered and taken to dryness. Crystallisation of the residue afforded diphenyl acetichydrazide (82%), needles from ethanol, m.p. 132-134° (lit.[67] m.p. 135°) (Found: C. 74.4; H, 6.2; N, 12.4. Calc. for $C_{14}H_{14}N_2O$: C, 74.3; H, 6.2; N, 12.4%) [Hydrochloride, m.p. 295-297° (lit.[67] m.p. 298°)]

$\nu_{max.}$ 3390, 3300 (NH_2); 1635 (C=O); 730, 695 cm^{-1}. (monosubst. benzene ring).

Oxidation of 1-amino-4,5-diphenyl-1,2,3-triazole.

The general procedure in this series of experiments was to dissolve the aminotriazole in the dry solvent (10ml. per mmole.) and to add this solution dropwise over 5-10min. to a magnetically stirred solution (or suspension) of oxidising agent (1.5mmole. per mmole. of aminotriazole) in the solvent (ca. 10ml.), at room temperature. If no reaction occurred the solution was refluxed and the oxidation followed by t.l.c. Work-up procedure involved filtering off any insoluble residue, evaporation of the filtrate onto a suitable chromatographic adsorbent, followed by column chromatography. Tolan was eluted with petrol, sublimed (150°/10mm.), and recrystallised from ethanol as plates, m.p. 59-60° (lit. m.p. 60°). trans-Dihalogenostilbenes were eluted with petrol-ether and recrystallised from petrol as trans-dichlorostilbene, cubes, m.p. 140-141° (lit. m.p. 140-142°), trans-dibromostilbene, plates, m.p. 203-204° (lit. m.p. 206°), trans-diiodostilbene, cubes, m.p. 201-203° (lit.[68] m.p. 204°).

Results are summarised in table I.

TABLE I

Oxidant	Solvent	Temp.	C.A. [a]	Product	Yield (%)
$Pb(OAc)_4$	C_6H_6	20°	B	tolan	80
$Pb(OAc)_4$	C_6H_6	20°	B	tolan	78 [b]
$Pb(PrCO_2)_4$	C_6H_6	20°	B	tolan	93 [c]
$PhI(OAc)_2$	C_6H_6	20°	N	tolan	93 [d]
$PhIO_2$	C_6H_6	80°	S	1-aminotriazole	84
$PhICl_2$	C_6H_6 - C_5H_5N	20°	N	trans-dichloro-stilbene	33 [h]
MnO_2	C_6H_6	60°	B	tolan	93 [e]
PbO_2	C_6H_6	80°	B	tolan	2
PbO_2	C_6H_6	80°	N	4,5-diphenyl-1,2,3-triazole	60 [f]
NBS	C_6H_6	60°	N	trans-dibromo-stilbene	90 [h]
$NaIO_4$	C_6H_6 - AcOH	80°	B	tolan	45
$NaIO_4$	AcOH	80°	B	tolan	80
$NaIO_3$	AcOH	80°	B	tolan	35
I_2	C_6H_6	80°	B	trans-diiodo-stilbene	17 [h]
SeO_2	C_6H_6	80°	N	1-aminotriazole	87
SeO_2	C_6H_5Cl	134°	S	tolan	85 [g]

C.A. refers to the chromatographic adsorbent employed in the work-up procedure.

Notes to Table I

a) N = neutral alumina; B = basic alumina; S = silica-gel.

b) In the presence of tetraphenylcyclopentadienone (tetracyclone) (2 mmole per mmole of aminotriazole).

c) Lead tetra-iso-butyrate was prepared by the method of Bachman and Wittmann[69] and the drying procedure for lead tetraacetate employed.

d) Iodosobenzene diacetate was prepared by the standard route.[70] Iodoxybenzene and iodobenzene dichloride were obtained during this synthesis.

e) Active manganese dioxide prepared by the method of Morrison.[23]

f) Active lead dioxide prepared by the method of Gattermann.[71]

g) Selenium dioxide was sublimed before use. The chlorobenzene solution deposited a pale green solid on cooling. Crystallisation from benzene afforded an unknown compound (10%), m.p. 226° (Found: C, 73.4; H, 4.8; N, 12.7%). i.r. ν max. 3373 (NH); 1715 (CO); 705, 690 cm^{-1}. (monosubst. benzene ring).

h) Authentic samples of trans-dihalogenostilbenes were synthesised for comparison with the reaction products. Mixed m.p's. showed no depression.

Cognate Oxidation

Benzil-bis-hydrazone was oxidised with lead tetraacetate using the same procedure as for the aminotriazole. Diphenylacetylene (100%), m.p. and mixed m.p. 59-60° was produced in the absence or presence of tetracyclone.

Preparation of 1-amino-4,5-dimethyl-1,2,3-triazole

The synthetic routes available are the same, in general, as those for the diphenyl analogue.

a) Diacetyl (47.3g.) was added dropwise to a refluxing solution of hydrazine hydrate (200ml.) and sodium carbonate (150g.) in water (2l.). The solution was refluxed for 5hr., then water distilled off until crystallisation commenced. On cooling, the solution deposited diacetyl-bis-hydrazone. Crystallisation from methanol gave needles (90%), m.p. 154-157° (lit.[72] m.p. 158°).

b) Diacetyl-bis-hydrazone (23g.) was dissolved in methanol (250ml.), stirred and cooled to 0-5°. Selenium dioxide (23g.) in methanol (50ml.) was added dropwise, keeping the temperature below 5°. The solution was stirred for 12hr. at room temperature, filtered and the filtrate evaporated. The residue was extracted with sodium hydroxide solution (2 x 50ml., 2N), washed with water and dried in vacuo. Chromatography on basic alumina, with methanol as eluant, gave a black oil. Distillation (150° / 0.001mm.) and crystallisation from aqueous ethanol afforded 1-amino-4,5-dimethyl-1,2,3-triazole (5%), needles, m.p. 94-95° (lit.[73] m.p. 95°) (Found: C, 43.0; H, 7.1; N, 49.9. Calc. for $C_4H_8N_4$: C, 42.9; H, 7.1; N, 50.0%).

i.r. ν max. 3270, 3130 (NH_2); 1645 (C=C); 1585 (N=N);

1220 (triazole ring); 1180; 1130; 990; 770; 710 cm^{-1}. (cis-R-C=C-R).

Benzylidene derivative, needles from ethanol, m.p. 80-82°, (lit.[73] m.p. 80°).

The major product was eluted from the column with ether as needles (80%), m.p. 130-133° of 1,1'-bis-(4,5-dimethyl-triazolyl) (Found: C, 50.3; H,6.9; N, 42.8. $C_8H_{12}N_6$ requires: C, 50.0; H, 6.3; N, 43.7%).

m/e: 164, 136, 82, 54, 41. $C_8H_{12}N_6$ (P)=192; P-N_2 =164; P-2N_2 =136; dimethylacetylene =54; acetonitrile =41.

i.r. νmax. 1585 (N=N); 1250, 1230 (triazole ring); 1050; 925; 710 cm^{-1}. (cis-R-C=C-R).

p.m.r. τ 7.64 singlet (3 protons); 7.89 singlet (3 protons);

Oxidation of 1-amino-4,5-dimethyl-1,2,3-triazole

The general procedure in this series of experiments was the same as with the diphenyl analogue. Temperatures were usually lower to prevent loss of dimethylacetylene from the oxidised solution. Bromine was added when necessary to the solution when the oxidation was complete, to trap the acetylene as 2,2,3,3-tetrabromobutane. This was eluted with petrol and crystallised from ethanol as stout rods, m.p. 242-243° (lit. m.p. 243°).

Results are summarised in Table II.

Cognate Oxidation

Diacetyl-bis-hydrazone was oxidised similarly. 2,2,3,3-Tetrabromobutane (80%), m.p. and mixed m.p. 241-243°, was isolated.

Table II

Oxidant	Solvent	Temp.	C.A.[a]	Product	Yield (%)
$Pb(OAc)_4$	C_6H_6[d]	-60°	S	dimethylacetylene	84[b]
$Pb(OAc)_4$	C_6H_6[d]	-60°	B	dimethylacetylene	79[b,c]
NBS	C_6H_6	20°	N	2,2,3,3-tetra-bromobutane	87

Notes to Table II

a) C.A. refers to the chromatographic adsorbent employed in the work-up: N = neutral alumina; B = basic alumina; S = silica-gel.

b) Isolated as the tetrabromobutane (84%).

c) In the presence of tetracyclone; no trapped product was detected.

d) Exactly similar results were obtained in CH_2Cl_2.

Preparation of 1-amino-4,5-tetramethylene-1,2,3-triazole

a) Cyclohexane-1,2-dione was prepared by the literature method.[74] The product was redistilled and the fraction, b.p. 75-77°/ 16mm. collected, m.p. 34-36° (lit.[74] m.p. 38-40°)

b) The dione (11.2g.) in ethanol (150ml.) was added dropwise over 1hr. to hydrazine hydrate (75ml.) in ethanol (300ml.) at -10°. The solution was stirred a further 1hr. at -10°, and the solvents then removed by freeze drying. The oily residue on trituration with ether and crystallisation from ether afforded cyclohexandione-bis-hydrazone (53%), yellow amorphous solid, m.p. 57-59° (lit.[51] m.p. 60-62°).

c) The bis-hydrazone (14g.) in benzene (150ml.) was added dropwise to a suspension of yellow mercuric oxide (30g.) and anhydrous sodium sulphate (20g.) in benzene (100ml.), with stirring and cooling. The suspension was stirred overnight at room temperatures, filtered and the filtrate evaporated. Chromatography on basic alumina, with methanol as eluant, gave a yellow oil which on distillation at 131-133°/ 0.01mm. and crystallisation from benzene-hexane (1:4) afforded 1-amino-4,5-tetramethylene-1,2,3-triazole (43%), plates, m.p. 93-94° (lit.[51] m.p. 94-95°, b.p. 128-130°/ 0.01mm.). i.r. ν max. 3275, 3170, 3130 (NH_2); 1650 (C=C); 1580 (N=N); 1495 ($-CH_2-$); 1200 (triazole ring); 1090; 990; 920; 840; 820; 755 ($-[CH_2]_4-$ skeletal vibration); 705 cm^{-1}.

Oxidation of 1-amino-4,5-tetramethylene-1,2,3-triazole

a) The 1-aminotriazole (138mg.) was dissolved in dry methylene chloride (10ml.) and added dropwise over 5-10min. to a magnetically stirred solution of lead tetraacetate (500mg.) and tetracyclone (400mg.) in dry methylene chloride (10ml.), at room temperature. The solution was filtered from the insoluble lead salts, the solvent evaporated and the residue chromatographed on basic alumina. Petrol-benzene (9:1) eluted 1,2,3,4-tetrahydro-5,6,7,8-tetra-phenylnaphthalene, cubes from ethanol (21%), m.p. 284-286° (lit.[75] m.p. 271-272°) (Found: C, 93.5; H, 6.3. Calc. for $C_{34}H_{28}$: C, 93.6; H, 6.4%).
i.r. ν max. 1600 (aromatic unsaturation); 1490 ($-CH_2-$); 1065; 1025; 800, 785; 740 [$-(CH_2)_4-$ skeletal vibration]; 730, 695 cm^{-1}. (monosub. benzene ring).
p.m.r. τ 3.0 singlet, 3.3 singlet (20 aromatic protons); 7.5 multiplet, 8.3 multiplet (8 aliphatic protons).
Benzene eluted tetracyclone (77% recovery), dark lustrous cubes from benzene-ethanol (1:20), m.p. 220-221° (lit. m.p. 222°). No other products could be eluted from the column. Gas chromatographic analysis of the evaporated solvent from the oxidation revealed no volatile products except for acetic acid.

b) The 1-aminotriazole (138mg.) was dissolved in dry methylene chloride (10ml.) and added dropwise over 5-10min.

to a magnetically stirred solution of lead tetraacetate (500mg.) in dry methylene chloride (10ml.), at room temperature. The solution was filtered from the insoluble lead salts, the solvent evaporated and the residue chromatographed on basic alumina. No solid products were obtained, but an acetoxy compound was eluted with methanol. Molecular distillation at 10 mm. afforded 2-acetylcyclohexanone enol acetate, mobile liquid, (Found: C, 66.3; H, 8.2. $C_{10}H_{14}O_3$ requires: C, 65.9; H, 7.7%).
i.r. ν max. 2940 (CH_3); 2840 (CH_2); 1750 (enol ester); 1685 (ketone); 1435 (CH_2); 1360 (CH_3); 1210 (enol ester); 1120 (vinyl ketone); 900, 850, 800 cm^{-1}.
p.m.r. τ 7.95 multiplet (4 allyl protons); 8.05 singlet (6 methyl protons); 8.40 multiplet (4 aliphatic protons).
Gas chromatographic analysis of the evaporated solvent again revealed no volatile products. The solution gave no reaction with bromine nor maleic anhydride.

Cognate Oxidation

Cyclohexandione-bis-hydrazone was oxidised with lead tetraacetate with tetracyclone present during the oxidation. From basic alumina, petrol-benzene (9:1) eluted 1,2,3,4-tetrahydro-5,6,7,8-tetraphenylnaphthalene (10%), cubes from ethanol, m.p. 283-284°. No other products were detected.

Preparation of 1-amino-4,5-pentamethylene-1,2,3-triazole

The synthetic sequence was the same as that used for the tetramethylene analogue. The products obtained were:

a) Cycloheptane-1,2-dione, yellow oil, b.p. 107-109°/ 17mm. (lit.[76] b.p. 107-109°/ 17mm.)

b) Cycloheptane-1,2-dione-bis-hydrazone, white amorphous solid, m.p. 71-73° (lit.[51] m.p. 74-75°)

c) 1-Aminotriazole, plates from benzene-hexane (1:4), m.p. 57-58° (lit.[51] m.p. 58-59°), b.p. 151-153°/ 0.01mm. (lit.[51] b.p. 145-148°/ 0.01mm.).

i.r. ν max. 3300, 3170 (NH_2); 2910, 2840 ($-CH_2-$); 1630 (C=C); 1575 (N=N); 1445 ($-CH_2-$); 1220 (triazole ring); 790cm^{-1}. [$(-CH_2-)_5$ skeletal vibration].

Oxidation of 1-amino-4,5-pentamethylene-1,2,3-triazole

The experimental procedure was as described previously.

a) Lead tetraacetate oxidation in methylene chloride, in the presence of tetracyclone: from basic alumina, petrol-benzene (4:1) eluted 1,2-pentamethylene-3,4,5,6-tetra-phenylbenzene (78%), cubes from ethanol, m.p. 225-226° (lit.[77] m.p. 215-216°) (Found: C, 93.3; H, 6.7. Calc. for $C_{35}H_{30}$: C, 93.4; H, 6.6%).
i.r. ν max. 1600 (aromatic unsaturation); 1490 ($-CH_2-$); 1065, 1025, 800, 770; 725 $\left[-(CH_2)_5-\right]$ skeletal vibration; 730, 695cm^{-1}. (monosubst. benzene).
p.m.r. τ 3.04 singlet, 3.35 singlet (20 aromatic protons); 7.35 multiplet (4 allylic protons); 8.30 multiplet (6 aliphatic protons).

Benzene eluted tetracyclone (20% recovered), m.p.219-221°. No other products were obtained. The same results were obtained in this reaction when performed at 20° or at -60° in a drikold-acetone bath.

b) The same oxidation without tetracyclone present: no solid products were obtained. Methanol eluted an uncharacterised acetoxy compound.

Cognate oxidation

Cycloheptanedione-bis-hydrazone was oxidised with lead tetraacetate in the usual manner, in the presence of

tetracyclone. From basic alumina, petrol-benzene (4:1) eluted 1,2-pentamethylene-3,4,5,6-tetraphenylbenzene (17%), cubes from ethanol, m.p. and mixed m.p. 224-225°. Gas chromatographic analysis of the oxidised solution revealed no volatile products and the solution gave no reaction with bromine nor maleic anhydride.

Attempted preparation of 1-amino-4,5(9,10-d)-phenanthro-1,2,3-triazole

From phenanthro-(9,10-d)-triazole

a) Phenanthrene was oxidised to the quinone, and this was converted to the dioxime, by standard procedures.[78,79]

b) The dioxime (72g.) was dissolved in ethanol (1 litre) at 60°. Stannous chloride (300g.) in conc. HCl (750ml.) was added dropwise with stirring, the solution cooled and the crystalline mass filtered off. The solid was washed with ethanol (20ml.) and ether (200ml.) leaving 9,10-diamino-phenanthrene hydrochloride (73%) as fine needles.

c) The hydrochloride (14g.) and anhydrous sodium acetate (8.2g.) were shaken with warm ethanol (1 litre) for 15min., then filtered from the sodium chloride residue. The filtrate was cooled to 5°, and isoamyl nitrite (6.4g.) in ethanol (20ml.) was added dropwise with stirring. The solution was stirred at room temperature for 1hr., and on a steam bath for 1hr., and then diluted with water (1 litre) and filtered. Crystallisation of the residue from acetic acid-water afforded phenanthro-(9,10-d)-triazole (50%), m.p. 325-328° (lit.[80] m.p. 306°) (Found: C, 76.6; H, 4.2. Calc. for $C_{14}H_9N_3$: C, 76.7; H, 4.1%).

i.r. νmax. 3000 (NH); 1625, 1615 (aromatic unsaturation); 1195 (triazole ring); 750, 720 (1,2 disubst. benzene) cm^{-1}.

m/e: P = 219; P-HN_2 = 190; P-CHN_3 = 164.

Methylation with dimethyl sulphate in alcoholic sodium hydroxide and crystallisation from ethanol afforded 1-methylphenanthrotriazole, fine needles, m.p. 174-176° (lit.[80] m.p. 160°) (Found: C, 77.2; H, 4.9; N, 17.9. Calc. for $C_{15}H_{11}N_3$: C, 77.2; H, 4.7; N, 18.0%).

The yellow insoluble residue, m.p. $\gg$ 400°, from the crystallisation of the triazole, which gave a cornflower blue colouration with conc. H_2SO_4, was presumed to be tetrabenzophenazine (lit. m.p. 487°).

The preparation of phenanthrotriazole reported[80] in the literature gave only tetrabenzophenazine and an azide in our hands. On standing, or attempted crystallisation, decomposition of the azide occurred (i.r.) and so characterisation was not attempted.

di) The triazole (219mg.) was dissolved in dry dimethyl formamide (20ml.) and dry benzene (20ml.). Sodium hydride (30mg.) was added and the solution refluxed for 1hr. The mixture was cooled and ethereal chloramine[81] solution (60mg. in 15ml.) was added with stirring. After stirring overnight, the triazole (89%) was recovered unchanged.

dii) The triazole (876mg.) in ethanol (25 ml.) and potassium hydroxide solution (600mg. in 2ml.) was stirred at 60° and hydroxylamine-O-sulphonic acid (1.1g.) was added in small portions. The solution was stirred at room temperature overnight. On work-up, the triazole (97%) was recovered unchanged.

diii) The attempted amination with hydroxylamine-O-sulphonic acid was repeated using sodium methoxide in methanol. Again, the triazole (76%) was recovered unchanged.

From 1-hydroxyphenanthrotriazole

a) Phenanthrenequinone monoxime (2.2g.) and tosylhydrazide (1.9g.) were refluxed in ethanol (25ml.) and conc. HCl (0.5ml.) for 15min. The precipitate was filtered off, washed with hot water (50ml.), hot ethanol (50ml.) and dried, to give 1-hydroxy-4,5(9,10-d)-phenanthro-1,2,3-triazole (100%), white amorphous solid, m.p. 275° (dec.) (Found: C, 71.6; H, 3.9; N, 18.1; MW by mass spec. 235. $C_{14}H_9N_3O$ requires: C, 71.5; H, 3.8; N, 17.9%; MW 235).
i.r. ν max. 2500 (NOH); 1625, 1615 (aromatic unsaturation); 1265 (triazole ring); 1140; 1085; 1010; 950; 770, 740cm^{-1}. (1,2 disubst. benzene).
m/e: P = 235; P-O = 219; P-HN_2O = 190; P-CHN_3O = 164.

b) The hydroxytriazole (235mg.) was dissolved in hydrazine hydrate (2ml.) and boiled under reflux for 3days. The solution was taken to dryness, the residue dissolved in ethanol (10ml.) and acidified. Filtration and washing gave the hydroxytriazole (97% recovery).

From 9-diazophenanthrenequinone

a) Phenanthrenequinone (2g.) and tosylhydrazide (1.9g.)

were refluxed in ethanol (20ml.) for 10min. The solution was diluted with water (100ml.), made slightly basic (solution self indicating; bright green end point), filtered and the precipitate dried in vacuo. Chromatography on basic alumina, with methylene chloride as eluant, afforded 9-diazophenanthrenequinone (55%), yellow plates from cyclohexane, m.p. 106-108° (lit.[83] m.p. 107-109°).

b) The diazoketone (220mg.) in ethanol (2ml.) and hydrazine hydrate (2ml.) was refluxed for 15min. The solution was taken to dryness and the residue crystallised from ethanol-water to give phenanthrenequinone.

From 4,5-diphenyltriazole

Attempts were first made to convert the diphenyltriazole into the phenanthrotriazole, with a view to extending the reaction to substituted 1-aminotriazoles.

a) 4,5-Diphenyl-1,2,3-triazole (200mg.) was intimately mixed with anhydrous aluminium chloride (2g.) and fused to a dull red heat. The diphenyltriazole (79%) was recovered unchanged.

b) The experiment was repeated using nitrobenzene, cf[84] as solvent and oxidant, under reflux. The solution solidified to a deep red complex which was unaffected by acids or organic solvents.

c) The triazole (221mg.) was dissolved in acetic acid (10ml.)

and added to potassium permanganate (500mg.) in acetic acid (10ml.).[cf 85] The solution was refluxed for 30min., then poured into water (100ml.). The diphenyltriazole (92%) was recovered unchanged.

d) The triazole (1.2g.) and iodine (32mg.) were dissolved in cyclohexane (500ml.) and photolysed for 2hr. while a current of air was blown through the solution.[cf 86] The diphenyltriazole (100%) was recovered unchanged.

Preparation of 4-amino-3,5-diphenyl-1,2,4-triazole

Using the literature method,[87] the following compounds were prepared from benzonitrile and hydrazine hydrate:

4-amino-3,5-diphenyl-1,2,4-triazole, (43%), plates from ethanol, m.p. 258-260° (lit.[87] m.p. 263°)
i.r. νmax. 3360, 3280, 3210 (NH_2); 1630 (C=N); 770, 700cm^{-1}. (monosubst. benzene ring).
Benzylidene derivative, needles from ethanol, m.p. 208-209° (lit.[87] m.p. 207°).

1,2-dihydro-3,6-diphenyl-1,2,4,5-tetrazine (46%), orange needles from ethanol, m.p. 189-190° (lit.[87] m.p. 190-192°).
i.r. νmax. 3310 (NH); 1655 (C=N); 1350; 1110 (triazole ring); 1065; 1025; 980; 870; 770, 700 (monosubst. benzene ring); 680cm^{-1}.
Nitrous acid oxidised the dihydrotetrazine to 3,6-diphenyl-1,2,4,5-tetrazine (93%), purple needles from ethanol-water, m.p. 190-192° (lit.[87] m.p. 190-192°), and hydrochloric acid converted it into the aminotriazole, m.p. and mixed m.p. 258-260°.

Oxidation of 4-amino-3,5-diphenyl-1,2,4-triazole

The experimental procedure was as outlined previously, using lead tetraacetate in methylene chloride. The oxidised solution was filtered and made upto 25ml.

G.l.c. on polyethyleneglycol-celite: retention time, 3min. 7sec.; authentic PhCN 3min. 7.5sec.; mixture 3min. 7.5sec.; estimated yield 97%.

G.l.c. on apiezon L-chromosorb P: retention time, 2min. 25sec. authentic PhCN and mixture, 2min. 25sec.; estimated yield 97%.

i.r. (CH_2Cl_2) νmax. 3040 (OH); 2240 (C≡N); 1720 (C=O); 1500, 1455; 1300 (C-O); 765, 695cm^{-1}. (monosubst. benzene ring).

Miscellaneous Reactions

Deamination of 1-amino-4,5-diphenyl-1,2,3-triazole

Sodium nitrite (0.7g.) in water (5ml.) was added dropwise with stirring to the 1-aminotriazole (2.4g.) in acetic acid (20ml.) cooled in an ice bath. The solution was stirred for 1hr., diluted with water (100ml.) and the precipitate filtered off and dried. Crystallisation from benzene-petrol (1:4) afforded 4,5-diphenyltriazole (97%), m.p. 135-137° (lit.[48] m.p. 138°) (Found: C, 75.7; H, 5.1; N, 19.4. Calc. for $C_{14}H_{11}N_3$: C, 76.0; H, 5.0; N, 19.0%).
i.r. νmax. centred on 3000 (v. broad) (triazole NH); 1610 (C=C); 1590 (N=N); 1190 (triazole ring); 1010; 990; 770, 700-680 (monosubst. benzene ring) cm^{-1}.

Amination of 4,5-diphenyl-1,2,3-triazole

i) Sodium hydride (0.3g.) was added to the triazole (2.2g.) in benzene (10ml.) under reflux for 1hr. Ethereal chloramine solution[81] (0.6g. in 15ml.) was added to the cold suspension with stirring, and the whole stirred for 12hr. The solvents were removed and the residue chromatographed on silica, with ether as eluant, to give 1-amino-4,5-diphenyl-1,2,3-triazole (80%), m.p. and mixed m.p. 133-134° (lit.[48] m.p. 135°)

ii) The triazole (2.2g.) was dissolved in warm sodium

hydroxide solution (1g. in 20ml.). On cooling, colourless plates crystallised out of solution. Filtration, washing with ethanol and drying in vacuo afforded the hydrated sodium salt of diphenyltriazole, m.p.$\gg 300^{\circ}$, (Found: C, 64.5; H, 4.7. $C_{14}H_{12}NaN_3O$ requires: C, 64.4; H, 4.6%). i.r.νmax. 3620, 3480, 3350, 3000 (v. broad) (OH and NH); 1610 (C=C); 1510; 1255 (triazole ring); 1175; 1090; 990; 920; 765, 705 cm^{-1}. (monosubst. benzene ring).
The salt redissolved on warming. Hydroxylamine-O-sulphonic acid[82](2.4g.) was added in portions to the solution at 60° with stirring over 1hr. Chromatography on silica afforded the triazole (87%) unchanged.

Attempted nitrosation of 4,5-diphenyl-1,2,3-triazole

Sodium hydride (0.3g.) was added to the triazole (2.2g.) under reflux in benzene (10ml.). isoAmyl nitrite (1.5g.) was added and the solution stirred for 2hr. Analysis (t.l.c.) showed the parent triazole unreacted. After refluxing for 12hr., chromatographic work-up afforded the unchanged triazole (98%).

A similar experiment with ethyl nitrate also failed.

4,5-Diphenyl-1,2,3-triazole with Angeli's salt

Angeli's salt (2g.) was added to diphenyltriazole (2.2g.) in acetic acid (10ml.) with stirring at room temperature.

No nitrogen was evolved, and chromatographic work-up afforded the diphenyltriazole (88%) unchanged.

The same experiment with 3,5-diphenyl-1,2,4-triazole also failed.

Attempted preparation of 4,5-dimethyl-1,2,3-triazole

Diacetyl-bis-hydrazone (6.5g.) was pyrolysed at 170° for 3hr. The polymeric residue was extracted with ethanol. No triazole was found, contrary to the report by Boyer.[88] Benzil-bis-hydrazone under the same conditions affords benzylphenylketazine.[89]

Preparation of benzotriazole-1-carboxamide

Potassium cyanate (12.1g.) was added portionwise to benzotriazole (11.9g.) in acetic acid (75ml.), with stirring for 1hr. The precipitate was filtered off and dried. Crystallisation from ethanol afforded 1-carboxamido-benzotriazole (88%), stout rods, m.p. 150°c (dec.) (lit.[90] m.p. gradual decomposition above 130°)

i.r. νmax. 3320, 3220, 3140 (NH_2); 1735 (C=O); 1600 (arom. unsaturation); 1235 (triazole ring); 1045; 920; 780, 745, 720cm^{-1}. (1,2 disubst. benzene).

An analoguous compound was made from 4,5-diphenyltriazole, m.p. gradual decomposition above 120°.

i.r. ν max. 3440, 3260 (NH_2); 1775, 1730 (C=O); 1685 (arom.

unsaturation); 1565 (N=N); 1235 (triazole ring); 970; 760, 685cm^{-1} (monosubst. benzene).

On recrystallisation from ethanol, the compound decomposed to the parent triazole.

Benzotriazole-1-carboxamide was unaffected by lead tetraacetate in toluene under reflux, nor did it undergo a Hofmann rearrangement with sodium hypochlorite in sodium hydroxide solution.

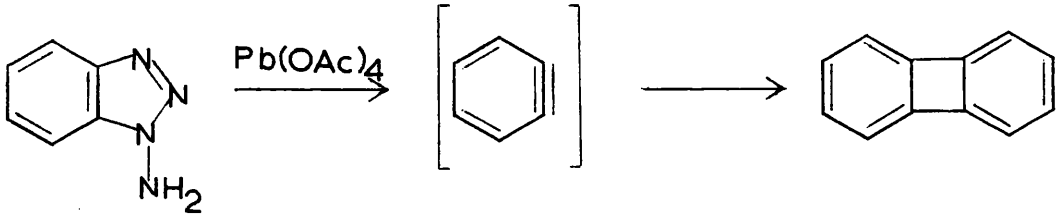
Discussion

Foreword

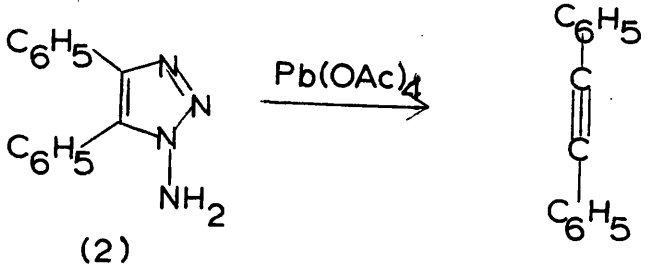
It has been reported[56] that the oxidation of 1-amino-benzotriazole (1) results in the production of the transient intermediate, benzyne, in high yield. This benzyne has the remarkable property of readily dimerising, unlike benzyne generated by other methods,[57,58] to give biphenylene in high yield.

This prompted an investigation concerned firstly with a detailed study of this oxidation and secondly with its extension to include other alkynes, both cyclic and acyclic.

Attention was first focussed on the preparation and oxidation of 1-amino-4,5-diphenyl-1,2,3-triazole (2) which is closely related to (1), but its corresponding oxidation product, tolan (diphenylacetylene), is a stable compound and would not have to be "trapped" like benzyne.



(1)

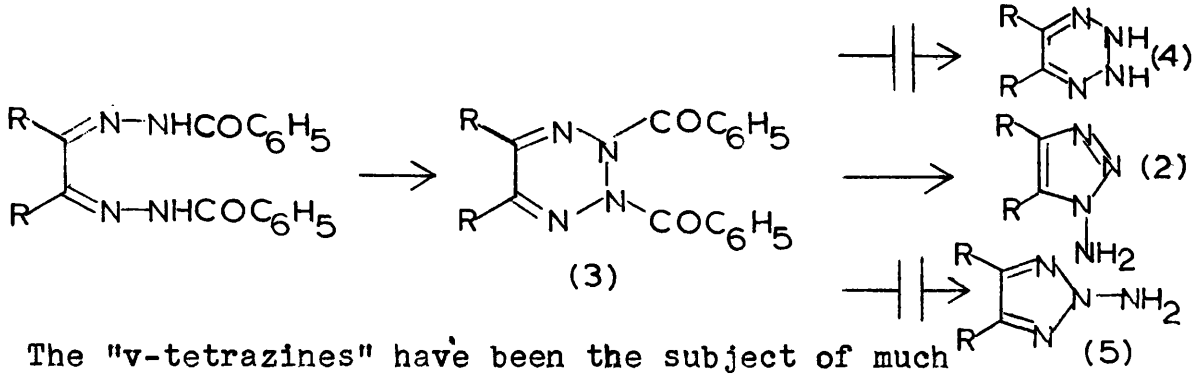


(2)

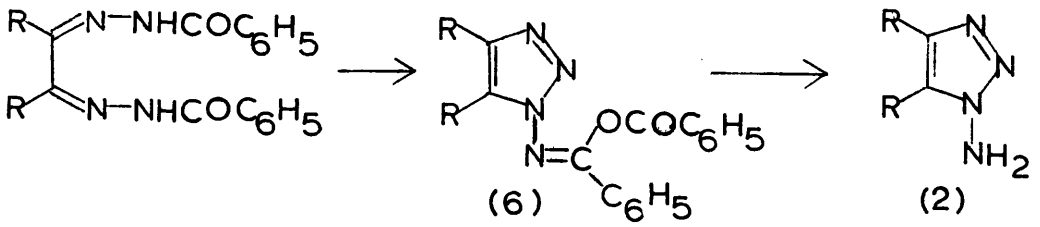
Preparation of 1-amino-4,5-diphenyl-1,2,3-triazole.

1. From benzil-bis-benzoylhydrazone.

1-Amino-1,2,3-triazoles were first prepared by von Pechmann[47] in 1900 and Stollé[48] in 1904. Both used the same synthetic route, starting from 1,2-diketo compounds. The bis-benzoyl hydrazones were readily prepared and oxidised in a variety of ways to "dibenzoyl-v-tetrazines" (3) which were hydrolysed to the amino triazoles, as described in the Experimental section. Both workers initially described aminotriazoles as "dihydro-v-tetrazines" (4), but Stolle changed this to a 2-aminotriazole structure[49] (5), before finally proposing the correct structure[91] (2) in 1926.



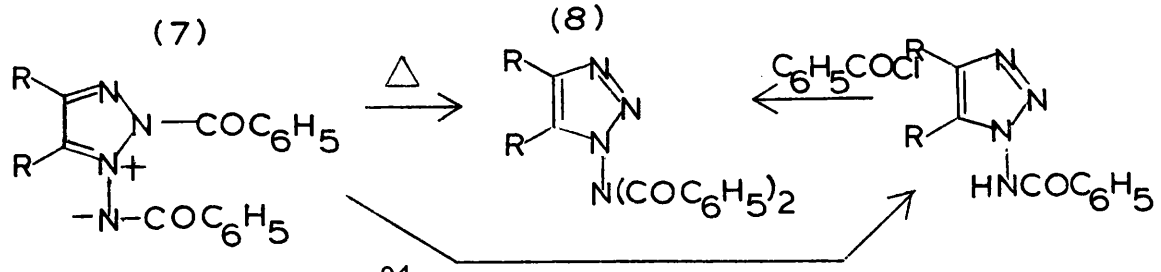
The "v-tetrazines" have been the subject of much discussion. Alexandrou[92] has proposed an enolbenzoate structure (6) for (3), on the basis of the ready hydrolysis of one benzoyl group followed by the more difficult hydrolysis of the second. The spectral properties of (6) are in complete agreement with this structure.



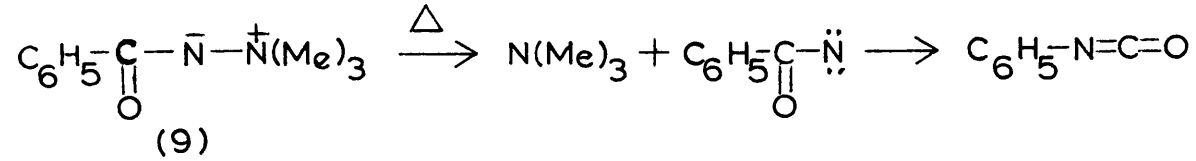
(6) (2)

However, Katritzky[93] favours a zwitterionic structure (7) for (3). Chemical and spectral evidence quoted by Katritzky is also in agreement with this structure. Katritzky proposes that on pyrolysis, a 1,3 benzoyl migration occurs to give the 1-dibenzoylamidotriazole (8) reported by Stollé[91] as the product of this reaction. Benzoylation of the benzoylamidotriazole affords an identical compound.

(7) (8)

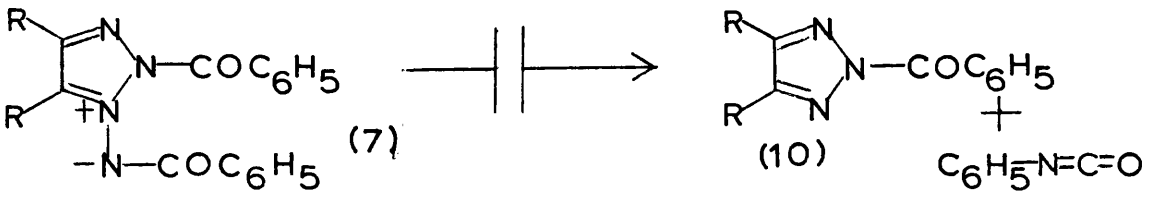


Gibson and Murray[94] showed that trimethylamine-benzimido (9), which has an analogous zwitterionic structure, decomposes at 185° into trimethylamine and phenylisocyanate.



(9)

The structure proposed by Katritzky[93] should, by analogy, yield phenylisocyanate and 2-benzoyl-1,2,3-triazole (10), on pyrolysis.

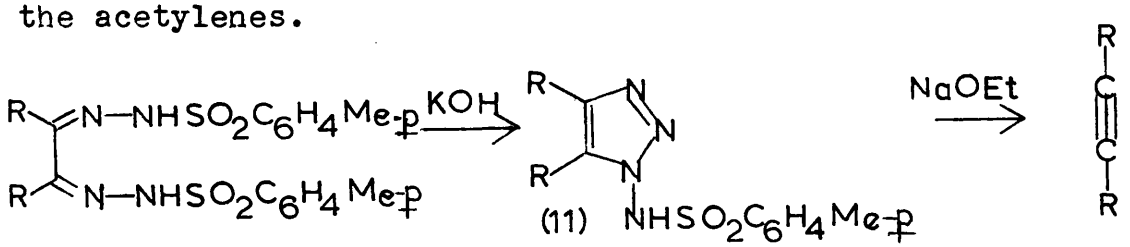


(7) (10)

The fact that this does not occur suggests this structure is less likely to be correct than the enolbenzoate (6) structure adopted in this thesis.

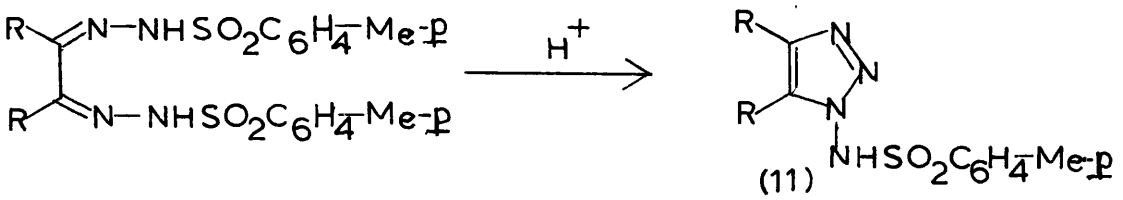
2. From benzil-bis-toluene-p-sulphonylhydrazone.

Bamford and Stevens[16], in 1952, prepared a number of toluene-p-sulphonylamidotriazoles (11) by treating 1,2-bis-tosylhydrazones with potassium hydroxide in ethylene glycol. These were sufficiently stable to resist the base catalysed decomposition to the nitrene, the reaction developed by Carpino[17]. Sodium ethoxide, however, was shown[16] to decompose the bis-tosylhydrazones rapidly through to the acetylenes.



(11)

The rearrangement of a bis-tosylhydrazone to a tosyl-amidotriazole is also accomplished by acid catalysis, as demonstrated by Wittig[51]. Here there is no problem of further decomposition to the acetylene, so yields are usually higher.

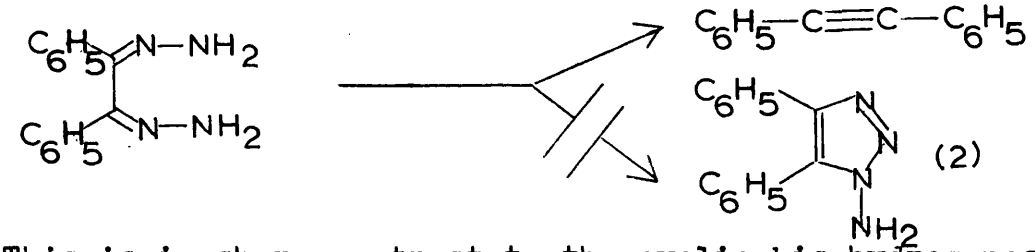


(11)

This is a general reaction, having been applied to cyclic[51] as well as acyclic 1,2-bis-tosylhydrazones. Acetic acid will accomplish the reaction for cyclic compounds, but a higher boiling acid, such as propionic, is necessary for the acyclic compounds.

3. From benzil-bis-hydrazone.

The oxidation of benzil-bis-hydrazone with mercuric oxide has been shown to give tolan in high yield.[54] Since the 1-aminotriazole (2) is inert to mercuric oxide, this cannot be an intermediate in the oxidation.

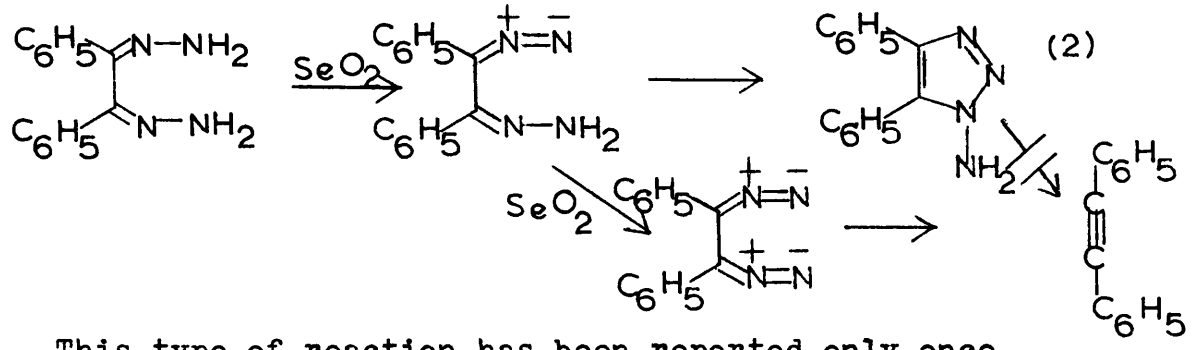


(2)

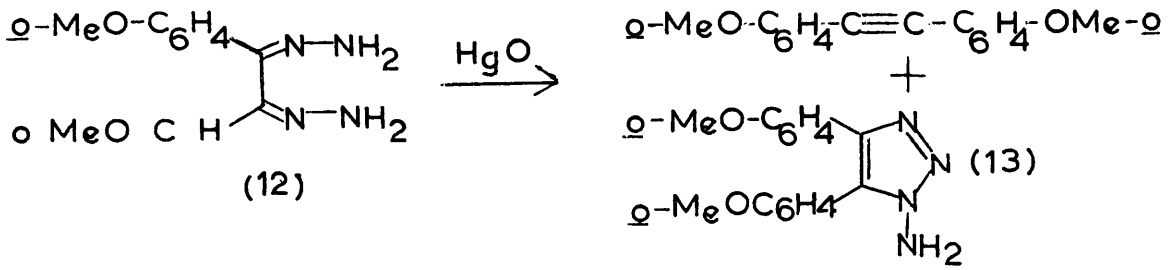
This is in sharp contrast to the cyclic-bis-hydrazones to be discussed later. Manganese dioxide also oxidises this bis-hydrazone quantitatively to tolan.[95]

Selenium dioxide, however, oxidises the bis-hydrazone to the 1-aminotriazole (2) which is then inert to further oxidation under the experimental conditions. Tolan (9%)

is produced presumably by further oxidation before ring closure occurs.

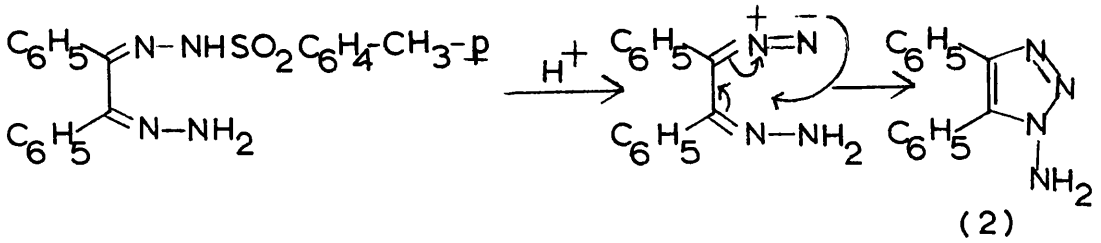


This type of reaction has been reported only once previously. Weygand and Siebenmark[96] found that 2,2'-dimethoxybenzil-bis-hydrazone (12), on oxidation with mercuric oxide, gave only a low yield of the acetylene, but a reasonable yield of the 1-aminotriazole (13) which they wrongly described as a dihydro-v-tetrazine.



(12)

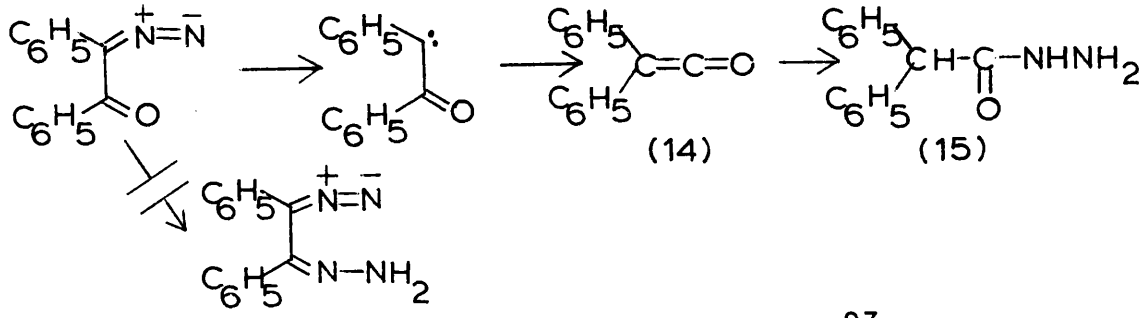
When one hydrazone function is substituted with a tosyl group, acid catalysed loss of toluene-p-sulphinic acid generates a diazo group next to the hydrazone; this ring closes to form a 1-aminotriazole (2).



(2)

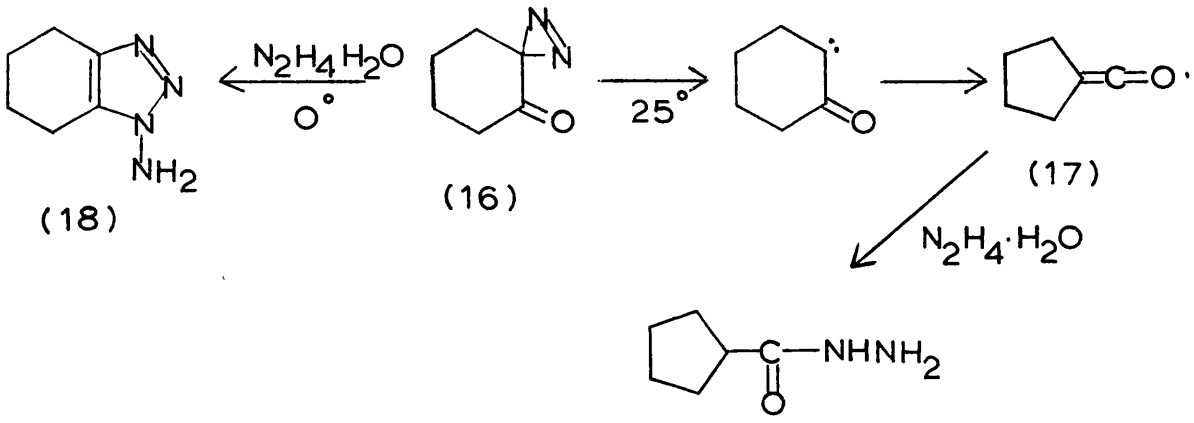
4. From α-Phenylazoacetophenone

The final attempted preparation of 1-amino-4,5-diphenyl-1,2,3-triazole (2) was by introducing the hydrazone function after formation of the diazo group. The diazoketone, however, is not sufficiently reactive to condense with hydrazine, instead loss of nitrogen occurs, with the generation of diphenyl ketene (14). This then reacts with hydrazine to form the acid hydrazide (15).



(14) (15)

A related reaction is reported by Schmitz[97] for the cyclic azo compound (16). At room temperatures it loses nitrogen to form a ketene (17) which then reacts with hydrazine, but at lower temperatures it will condense with hydrazine to form the 1-aminotriazole (18).

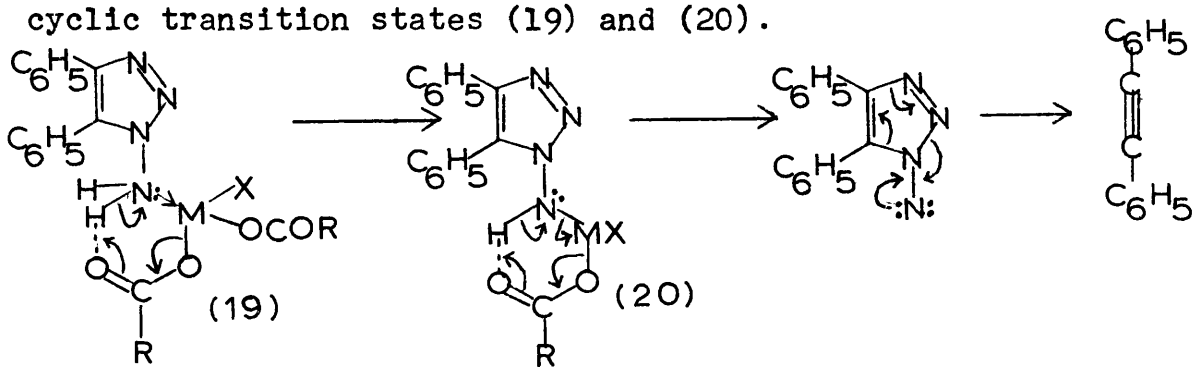


(18) (16) (17)

Oxidation of 1-amino-4,5-diphenyl-1,2,3-triazole.

The reaction of the 1-aminotriazole (2) with several oxidants was studied. It was unaffected by potassium persulphate, potassium ferricyanide, sodium bismuthate, sodium perborate and mercuric oxide from room temperature upto reflux in solvents such as benzene.

Lead tetraacetate, lead tetra-isobutyrate and phenyl iododiacetate all gave tolan in high yield. A reasonable mechanism for these oxidations involves two six-membered cyclic transition states (19) and (20).



(19) (20)

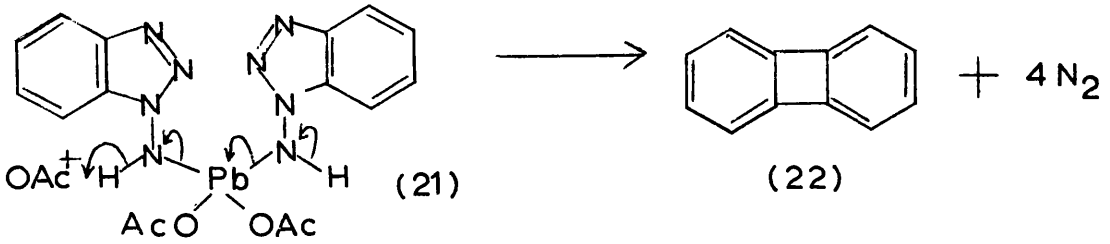
(a) M = Pb; X = $(OCOCH_3)_2$; R = $-CH_3$

(b) M = Pb; X = $(OCOCHMe_2)_2$; R = $CHMe_2$

(c) M = I; X = C_6H_5; R = CH_3

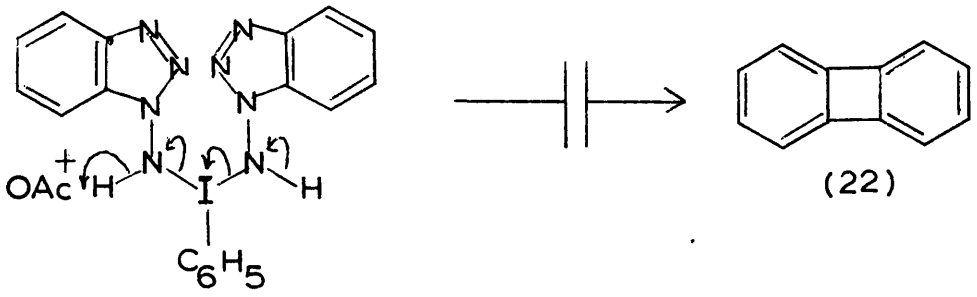
An alternative mechanism has been proposed[58] to explain the ready dimerisation of benzyne generated by lead tetraacetate oxidation of 1-aminobenzotriazole. This involves the initial attack of the oxidant on two molecules of the aminotriazole. The bridged intermediate (21) on further oxidation should then yield two molecules of

benzyne in close proximity, which may dimerise.

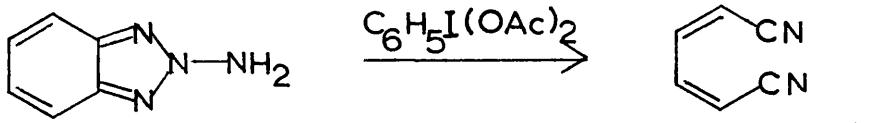


(21) (22)

However, phenyl iododiacetate is equally capable of performing the same reaction; but no biphenylene (22) is found[58] in this oxidation, though the 2-amino isomer (23) is oxidised[60] quantitatively to cis, cis-muconodinitrile (24).

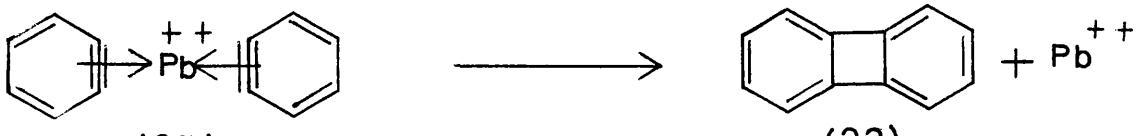


(22)



(23) (24)

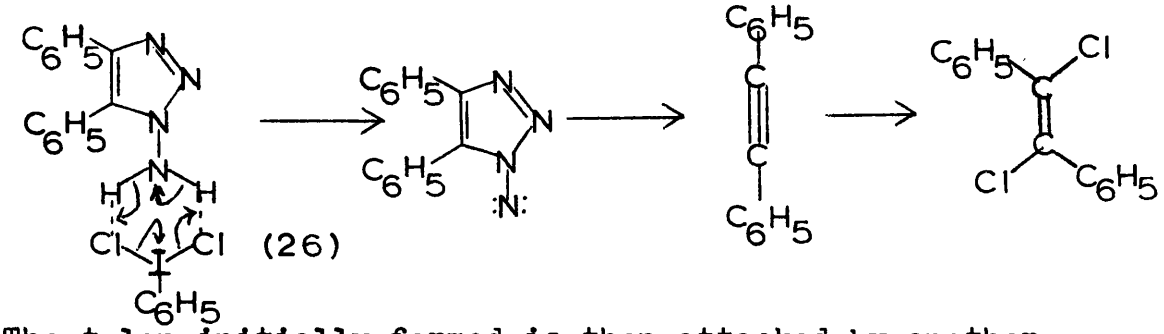
It would appear that the lead salt is affecting the course of the reaction in some other way. One possibility is that a benzyne-lead-benzyne complex (25) is formed in solution. The two benzyne molecules held in close proximity in this way may then dimerise.



(25) (22)

A related benzyne-silver complex has been reported, and the effect of the silver ion on the course of benzyne reactions studied.[98]

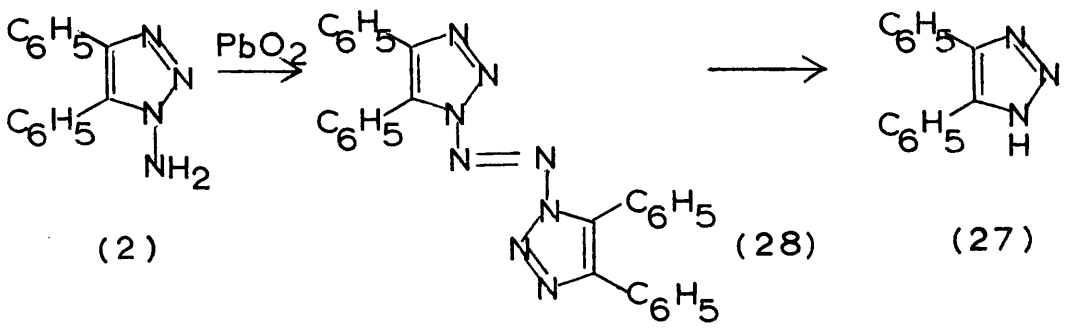
Phenyl iododichloride may oxidise the aminotriazole by the intermediacy of a six-membered cyclic transition state (26), only by the simultaneous removal of both hydrogens from the amine.



(26)

The tolan initially formed is then attacked by another molecule of oxidant to form trans-dichlorostilbene.

There is a rather surprising difference in the behaviour of the 1-aminotriazole towards various metal oxides. Thus, mercuric oxide has no effect on the amine, and lead dioxide very little. Active lead dioxide[71] produces the parent triazole (27), presumably via a tetrazene (28).



(2) (28) (27)

Active manganes dioxide,[23] however, produces tolan in high yield, though it does not form biphenylene from 1-amino-benzotriazole.[58]

N-Bromosuccinimide oxidises ~~exides~~ the aminotriazole by a free radical chain reaction. An induction period is observed prior to a rapid evolution of nitrogen. This is explained by the following scheme.

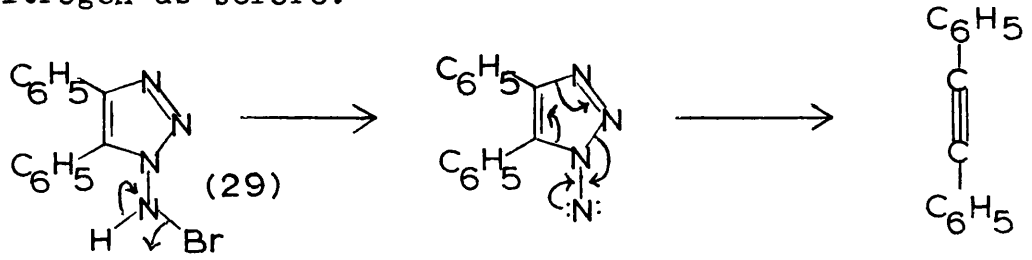
$$NBS \longrightarrow Br\cdot + S\cdot$$

$$-NH_2 + Br\cdot \longrightarrow HBr + -NH\cdot$$

$$HBr + NBS \longrightarrow SH + Br_2$$

$$Br_2 + -NH\cdot \longrightarrow Br\cdot + -NHBr$$

The new N-bromocompound (29) then spontaneously loses hydrogen bromide, affording the nitrene which loses nitrogen as before.



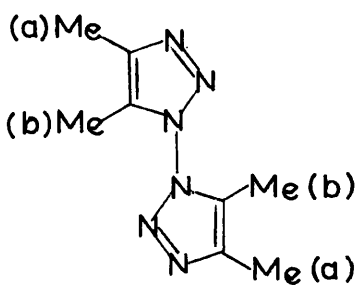
The chain may be terminated by the acetylene removing a bromine molecule or radical, to give trans-dibromo-stilbene, the observed product.

The oxidation of the aminotriazole with selenium dioxide is very dependent on the experimental conditions. No reaction occurs in benzene under reflux, but the reaction proceeds explosively when the two solids are

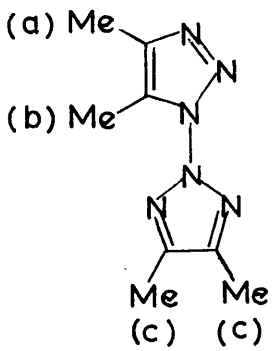
heated to the melting point of the amine (135°). The reaction is controllable in chlorobenzene under reflux (134°), and tolan is produced in high yield. An unknown, high melting solid is also produced which was not characterised since it appeared to be semi-polymeric.

Preparation of 1-amino-4,5-dimethyl-1,2,3-triazole.

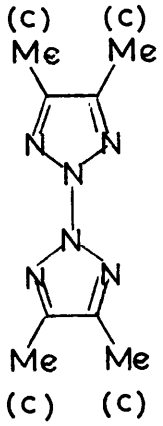
Using the synthetic route described for the diphenyl analogue, von Pechmann[47] prepared this compound from diacetyl-bis-benzoylhydrazone. Our preparation from diacetyl-bis-hydrazone proceeded in very low yield in cold methanol, and not at all in ethanol or water, or where heating was employed. In these cases, a yellow polymer was the only product. In the successful preparation, the major product was 1,1'-bis (4,5-dimethyltriazolyl) (30). This structure was assigned from a consideration of the analysis and spectral data. Two non-equivalent methyl groups (a:b = 1:1) were shown to be present in the p.m.r., and these were the only protons present in the molecule. If the triazole rings were linked 1-2 (31), then there would be three types of methyl groups, (a:b:c = 1:1:2) and a 2-2 linkage (32) would result in only one type of methyl group (c).



(30)

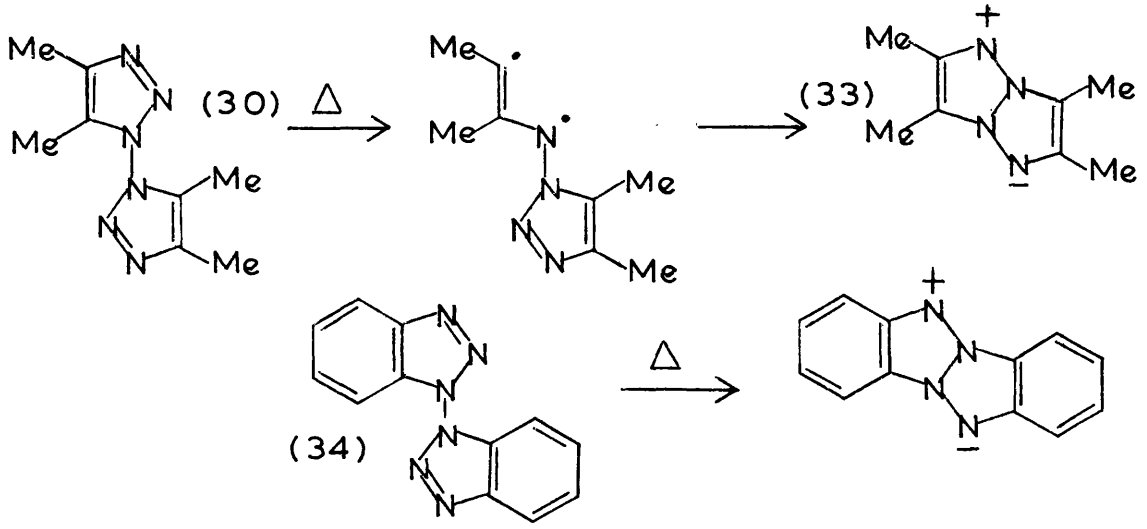


(31)



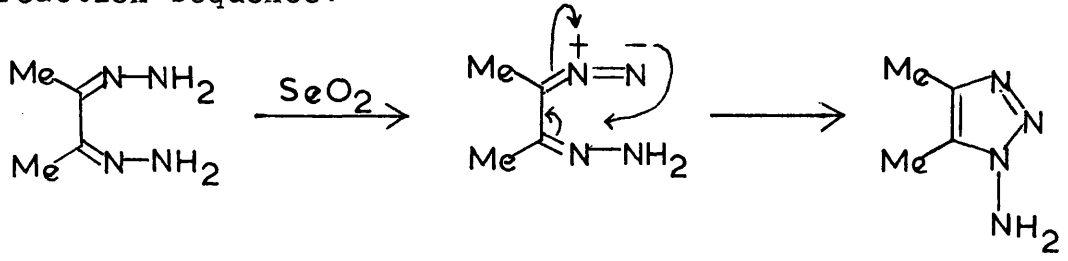
(32)

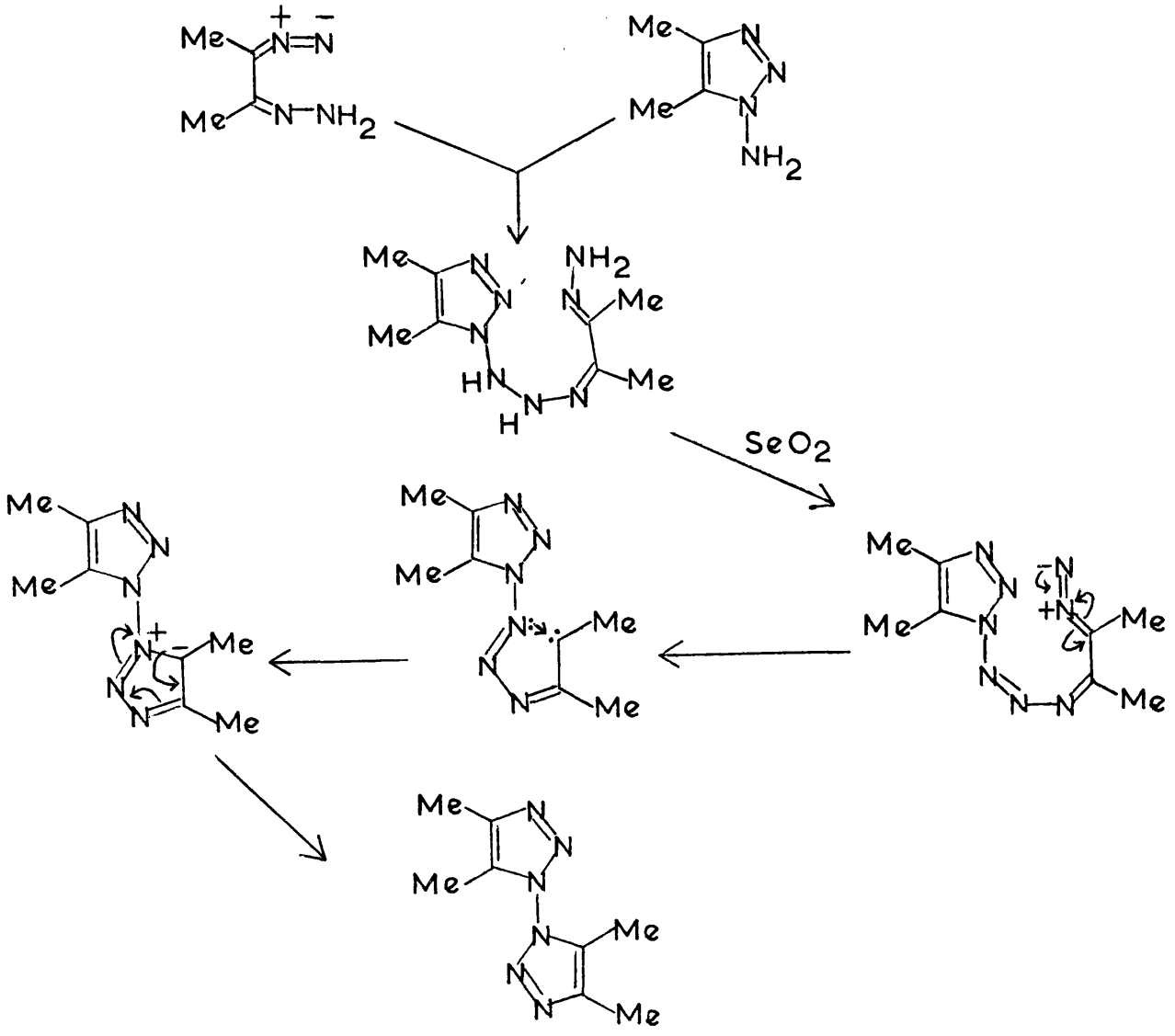
The molecular ion (P) was not observed in the mass spectrum, but this is explained by the facile loss of nitrogen which has been reported for the corresponding 1,1-dibenzotriazolyl[59] (34).



Mass spectral fragmentation generates the 2,3,5-6-tetramethyl-1,3a,4,6a-tetraazapentalene (33), which is the peak of highest m/e seen in the mass spectrum. The remainder of the breakdown pattern is derived from the decomposition of this molecular species.

The 1,1-bis (4,5-dimethyltriazolyl) (30) may possibly be formed from diacetyl-bis-hydrazone by the following reaction sequence.



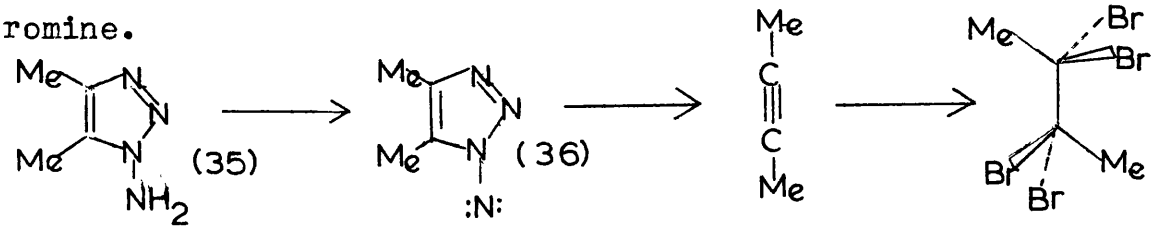


(30)

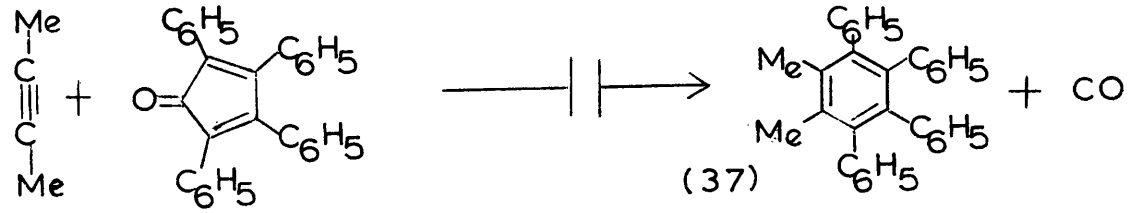
Many other reaction sequences may also be invoked to explain this novel reaction.

Oxidation of 1-amino-4,5-dimethyl-1,2,3-triazole

The oxidation of this compound by bromine was reported by von Pechmann[47] to give 2,2,3,3-tetrabromobutane. This is in complete agreement with our results. The oxidation proceeds in the same way as the diphenyl analogue with lead tetraacetate and NBS; the nitrene initially generated (36) fragmenting to form dimethylacetylene which then adds bromine.



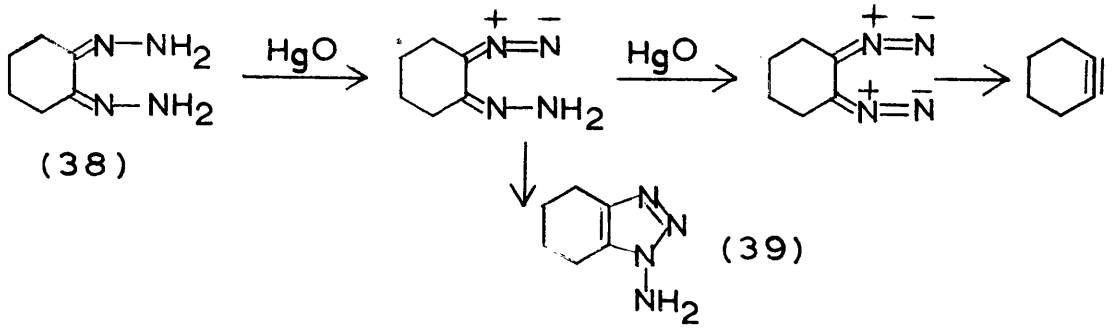
Willey[99] reported that dimethylacetylene produced by the photolysis of the lithium salt of the tosylamidotriazole could be trapped with tetracyclone (2%) in the cold. Our results gave no evidence of this reaction, since no 1,2-dimethyl-3,4,5,6-tetraphenylbenzene (37) was isolated.



The oxidation of diacetyl-bis-hydrazone with lead tetraacetate gave the same results as the aminotriazole, producing dimethylacetylene which was trapped with bromine (80%).

Preparation of 1-amino-4,5-tetramethylene-1,2,3-triazole

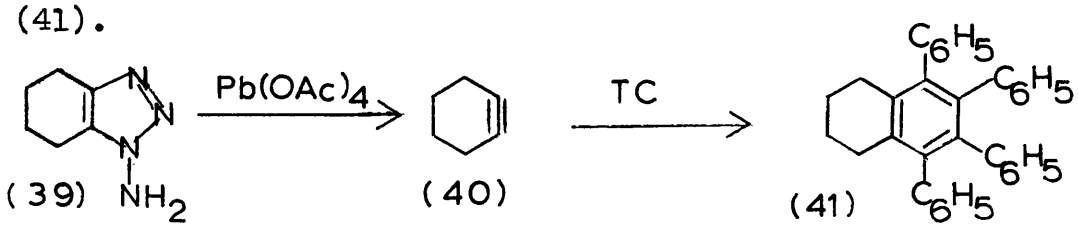
Wittig[51] and his colleagues have oxidised a number of 1,2-bis-hydrazones to prepare alkynes. In the course of their study, they discovered that cyclohexan-1,2-dione-bis-hydrazone (38) was oxidised by mercuric oxide in boiling benzene in low yield to cyclohexyne, but in fair yield to the corresponding 1-aminotriazole[51](39). The latter was inert to mercuric oxide.



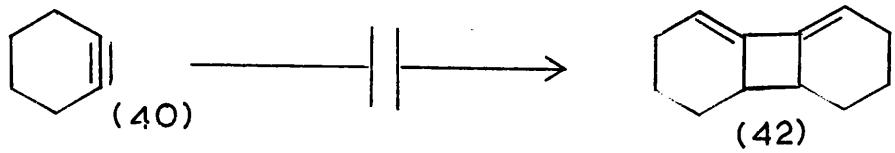
The bis-hydrazone is thermally unstable and readily loses nitrogen in refluxing benzene. Thus, by using Wittig's method but keeping the temperature at 5-10° the aminotriazole was prepared in good yield in benzene.

Oxidation of 1-amino-4,5-tetramethylene-1,2,3-triazole

The oxidation of the 1-aminotriazole (39) with lead tetraacetate generated cyclohexyne (40) as shown by the isolation of the product (21%) of its reaction with tetracyclone, 1,2,3,4-tetrahydro-5,6,7,8-tetraphenylnaphthalene (41).



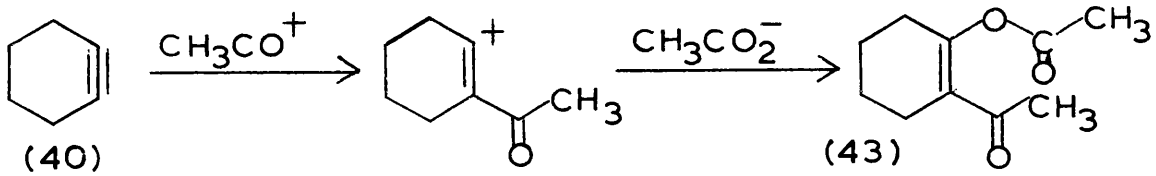
The p.m.r. spectrum of this compound showed aromatic protons (20) and aliphatic protons (8). Other spectral and analytical data agreed with this structure. Not surprisingly, no evidence was obtained for the dimerisation of cyclohexyne e.g. none of the rearranged product (42) was detected, hence its behaviour is not analogous to benzyne.[56]



The oxidation of cyclohexan-1,2-dione-bis-hydrazone (38) with lead tetraacetate gave similar results. In all the oxidations studied, there was an appreciable amount of starting material unaccounted for. Gas chromatographic analysis of the evaporated solvent from these oxidations failed to indicate any volatile products; in particular,

there was a noticeable absence of cyclohexene and cyclohexa-1,3-diene. This was confirmed by the failure of the evaporated solvent to react with bromine and maleic anhydride.

The cyclohexyne could therefore have reacted with lead tetraacetate and acetic acid to give the enolacetate of 2-acetylcyclohexanone (43).



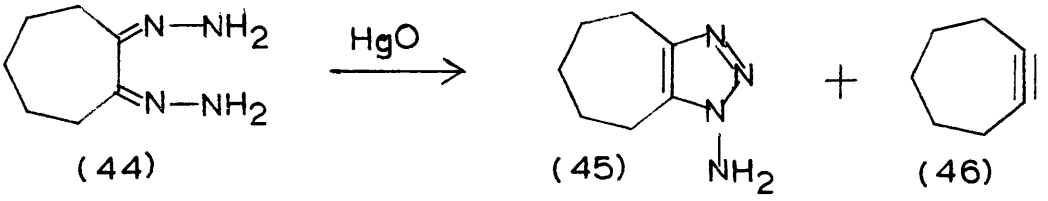
(40) (43)

In agreement with this the p.m.r. spectrum of the liquid acetoxy compound performed on 5mg. in a Japanese cell, showed 4 allylic protons, 6 methyl protons and 4 aliphatic protons. Analytical and i.r. data also agreed with this structure.

The reactivity of cyclohexyne (40), because of the strain imparted on the six-membered ring by the triple bond, is demonstrated by its very short life-time; it does not survive long enough to meet another cyclohexyne molecule,to dimerise, but indiscriminately attacks tetracyclone and lead tetraacetate. In this respect, it shows greater reactivity than benzyne which does enjoy some aromatic stabilisation.

Preparation of 1-amino-4,5-pentamethylene-1,2,3-triazole

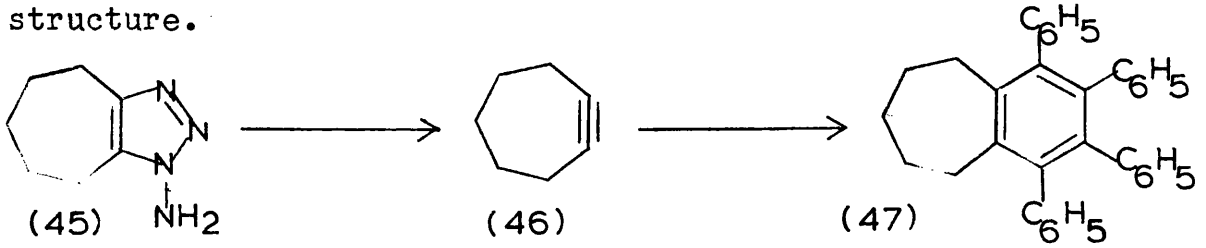
The preparation of this aminotriazole was completely analogous to that employed for the tetramethylene homologue (39). A modification of the method of Wittig[51] afforded the aminotriazole (45) in good yield.



(44) (45) (46)

Oxidation

Its oxidation with lead tetraacetate gave cycloheptyne which readily reacted with tetracyclone to afford 1,2-pentamethylene-3,4,5,6-tetraphenylbenzene (47). The p.m.r. spectrum showed 20 aromatic protons and 10 aliphatic protons and other spectral and analytical data supported this structure.



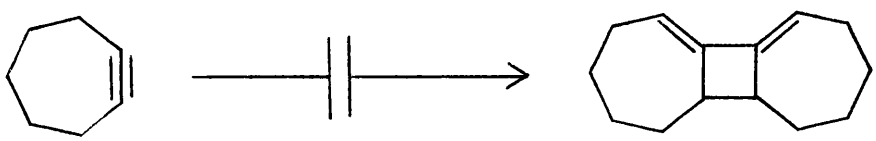
(45) (46) (47)

With the increase in ring size from six to seven members, there is obviously less strain placed on the ring by the triple bond. Thus, the acetylene is less reactive

and survives its oxidative environment to be trapped by tetracyclone. Willey[99] determined the half-life of cycloheptyne at -25° to be two minutes, but cyclohexyne was too short lived for its half-life to be estimated.

The yields of these two cycloalkynes generated by the photolysis of the lithium tosylamidotriazoles by Willey[99] were comparable to those obtained from our lead tetraacetate oxidation of the aminotriazoles. The mercuric oxide oxidation, quoted by Wittig,[51] and the lead tetraacetate oxidation of the bis-hydrazones in general gave much lower yields of the cycloalkynes.

No evidence was obtained for the dimerisation of cycloheptyne, and it was presumed that reaction with lead tetraacetate and acetic acid occurred when no diene was present to trap the reactive intermediate. A very small yield of a liquid acetoxy (i.r.) compound was obtained, but in insufficient amount to be characterised. Gas chromatographic analysis of the oxidised solution gave no evidence for the production of cycloheptene or cyclohepta-1,3-diene, or of rearranged dimers like (48).

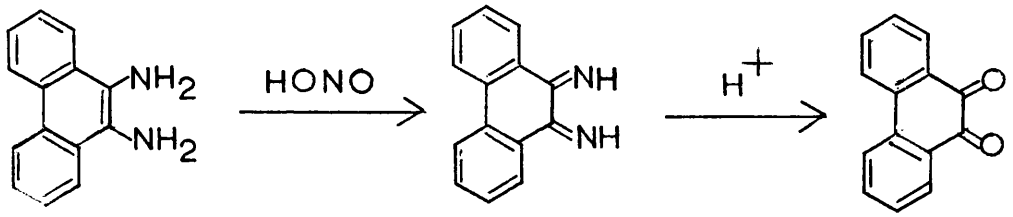


(46) (48)

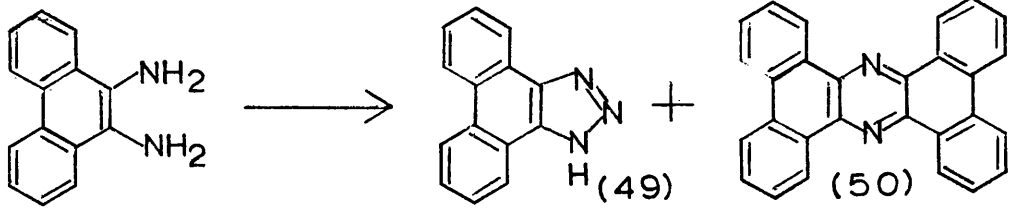
Attempted preparation of 1-amino-4,5(9,10-d)-phenanthro-1,2,3-triazole

From 4,5(9,10-d)-phenanthrotriazole

The diazotisation of 9,10-diaminophenanthrene has been reported to give phenanthrotriazole.[80] The pH of the diazotised solution is most important, since in solutions with pH5 or less, phenanthrenequinone is produced exclusively.



When the literature preparation[80] was followed, tetrabenzophenazine (50) and a yellow azide were produced, with none of the expected triazole. However, when isoamyl nitrite was substituted for sodium nitrite, the triazole (49) was produced in good yield, under initially anhydrous conditions.

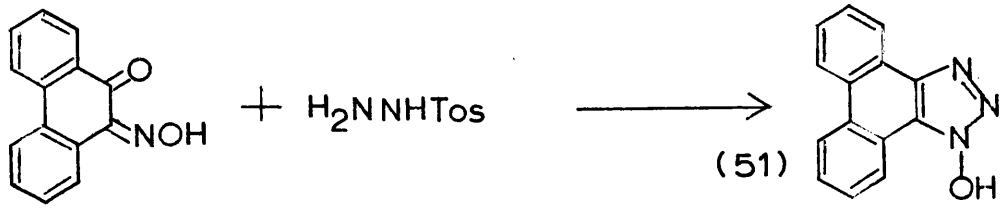


Direct amination of the triazole with hydroxylamine-O-sulphonic acid,[82] which was successful with benzotriazole,[59] or with chloramine, which was successful with 4,5-diphenyl-1,2,3-triazole, failed to give the aminotriazole. Only

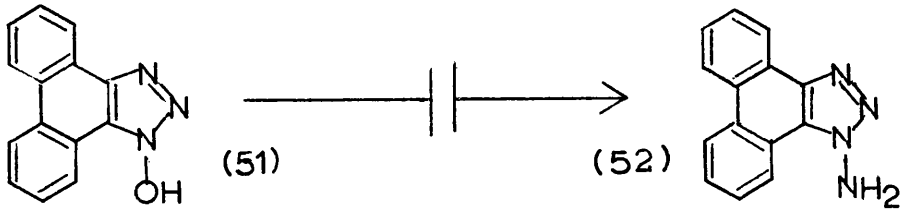
small amounts of mixtures of polyaminated compounds were isolated.

From 1-hydroxy-4,5(9,10-d)-phenanthrotriazole

The preparation of the 1-hydroxytriazole (51), from phenanthrenequinone monoxime and tosylhydrazide, proved to be much simpler than the parent triazole (49).[cf 100]



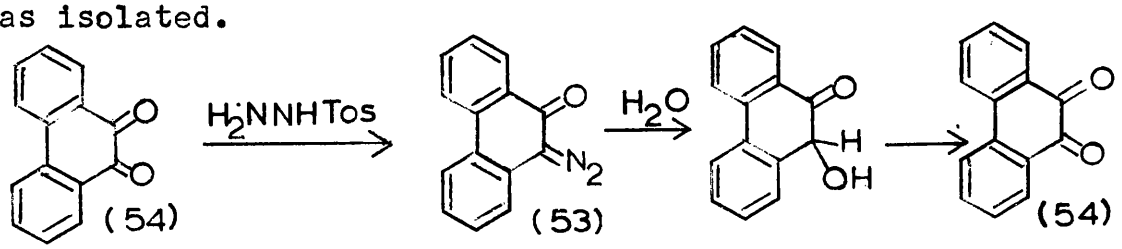
Analytical and infrared data fitted well for this compound, and the mass spectrum showed the parent peak at 235, the triazole at 219 and a breakdown pattern the same as the triazole. However, substitution of an amino group for the hydroxy group by vigorous treatment with hydrazine could not be achieved (cf. ref. 58 and 61).



From 9-diazo-9,10-phenanthrenequinone

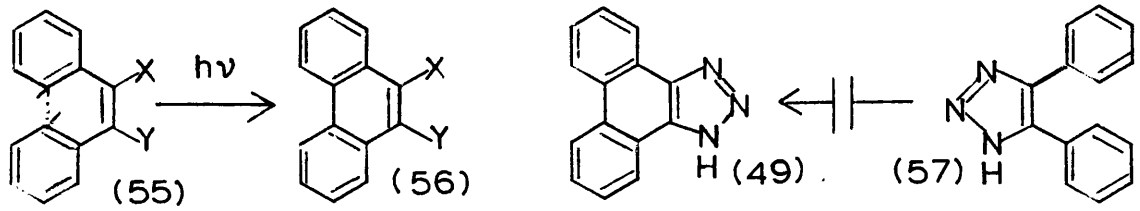
Following the work of Schmitz[97] (p. 72), reaction of the diazoketone (53) with hydrazine should give the

aminotriazole, if condensation occurs before loss of nitrogen from the diazo compound. Treatment of the diazoketone with hydrazine did not follow either of the expected routes (p. 72); instead phenanthrenequinone (54) was isolated.



From 4,5-diphenyl-1,2,3-triazole

The oxidative conversion of cis-stilbenes (55) to phenanthrenes (56) has been widely studied; with aluminium chloride alone or in nitrobenzene,[84] with potassium permanganate in acetic acid,[85] and with iodine by photolysis.[86] Following these experimental techniques, 4,5-diphenyl-triazole (57) was always recovered unchanged.

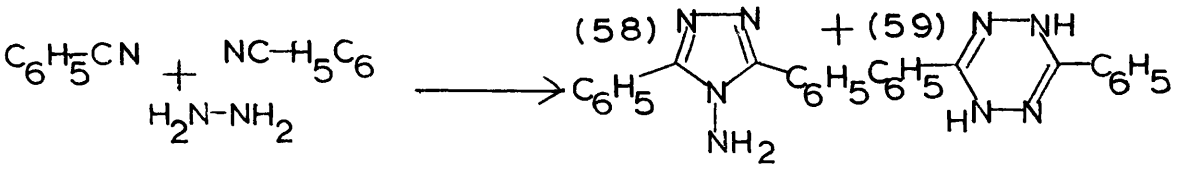


Had the conversion of 4,5-diphenyl-1,2,3-triazole (57) into the phenanthrene triazole been possible, it was hoped to extend the synthesis to a suitably substituted 1-amino-4,5-diphenyl-1,2,3-triazole to obtain a derivative of 1-amino-4,5(9,10-d)-phenanthro-1,2,3-triazole which could be degraded to the amine.

Had the aminotriazole been synthetically available, it was hoped that its oxidation would produce the much sought dimer of phenanthryne, tetrabenzobiphenylene. Theoretical considerations predict a decrease in stability from biphenylene through the benzobiphenylenes to tetrabenzobiphenylene, as more cyclobutadienoid character is imposed on the central 4-membered ring. The work so far reported on these compounds[101] is in complete agreement with this prediction.

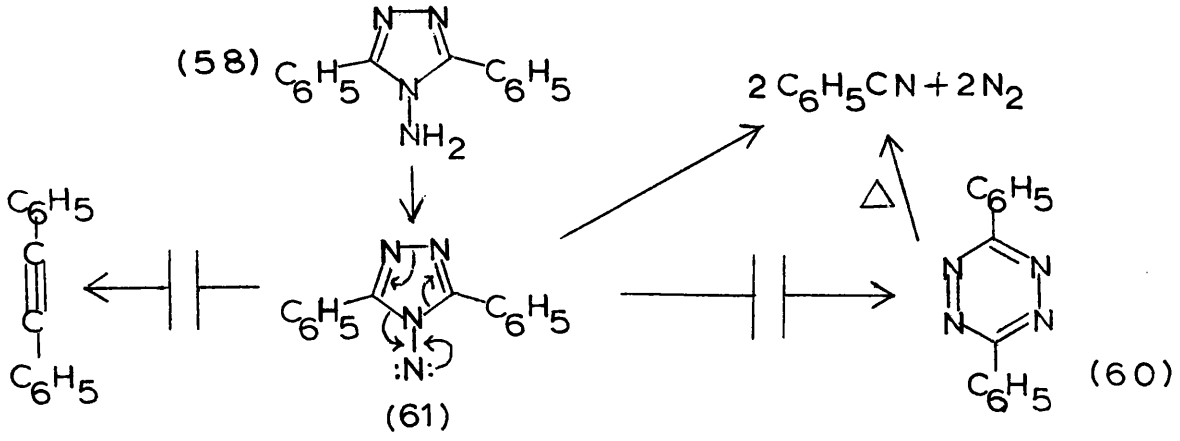
Preparation of 4-amino-3,5-diphenyl-1,2,4-triazole.

Following the literature procedure,[87] benzonitrile and hydrazine hydrate at 100° for 3 days afforded the amino triazole (58) and the isomeric dihydro-1,2,4,5-tetrazine (59).

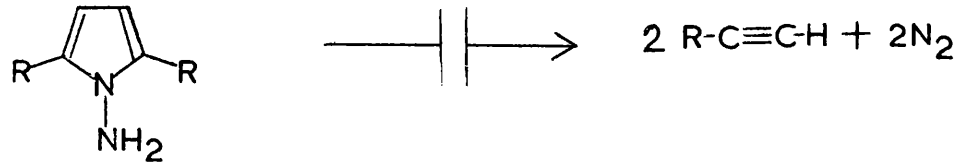


The dihydrotetrazine was converted into the aminotriazole (58) with dilute acid, and to the tetrazine (60) with nitrous acid.

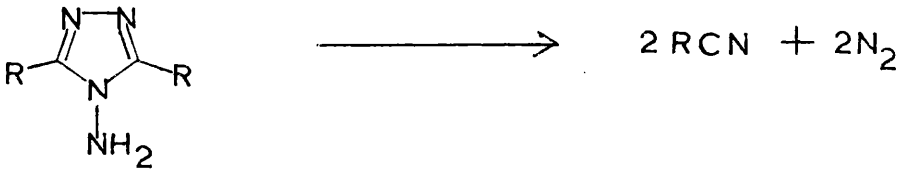
Oxidation of the aminotriazole (58) with lead tetracetate afforded benzonitrile in high yield, characterised and estimated by g.l.c. The intermediate nitrene (61) produced in the oxidation cannot insert into the ring, as this would have produced the stable tetrazine (60). The tetrazine (60) was shown to give benzonitrile only on pyrolysis at 200°. An alternative mechanism for fragmentation could produce tolan, but this route is obviously not favoured.



The oxidation of N-aminopyrroles (62), which has been reported,[25] does not lead to fragmentation though the system is iso-electronic with 4-amino-1,2,4-triazoles (58). The reason for this difference in behaviour is not clear, since the thermodynamic stabilities of the corresponding products, an acetylene and a nitrile are comparable.



(62)

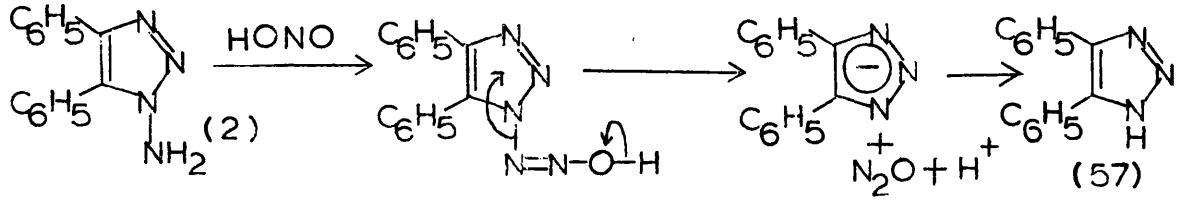


(58)

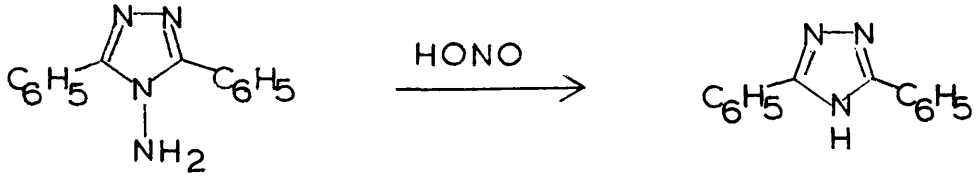
Miscellaneous Reactions

Deamination of 1-amino-4,5-diphenyl-1,2,3-triazole

Deamination with nitrous acid is a general reaction of N-amino compounds.[102] The aminotriazole (2) afforded the parent triazole (57) quantitatively.



4-Amino-3,5-diphenyl-1,2,4-triazole (58) was deaminated similarly to 3,5-diphenyl-1,2,4-triazole (63) (97%).

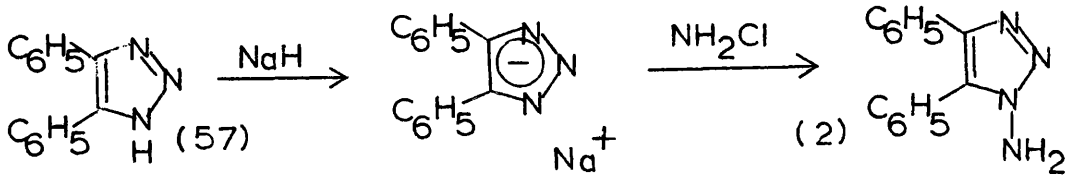


(58) (63)

Amination and attempted nitrosation of 4,5-diphenyl-1,2,3-triazole

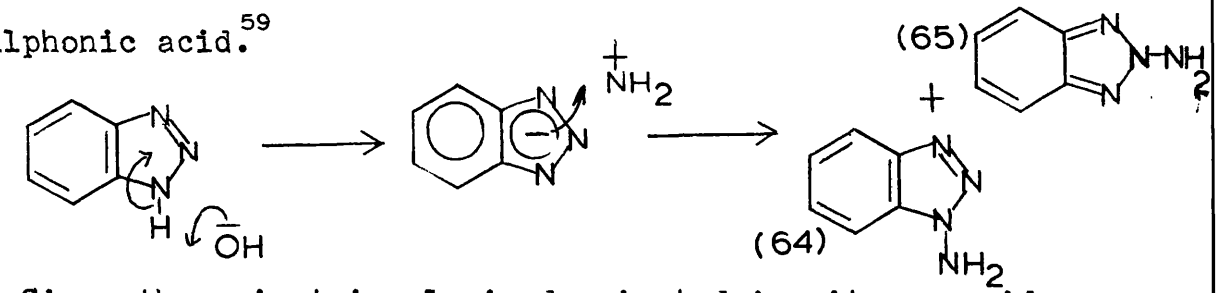
Because of the availability of this triazole (57), its amination was studied as a model for other triazoles, and phenanthrotriazole (49) in particular. The triazole (57) is acidic, as shown by its formation of a hydrated sodium salt in sodium hydroxide solution. The reaction of the triazole with sodium hydride gave the anhydrous sodium salt, which then reacted with chloramine[81] to give the 1-

aminotriazole (80%).



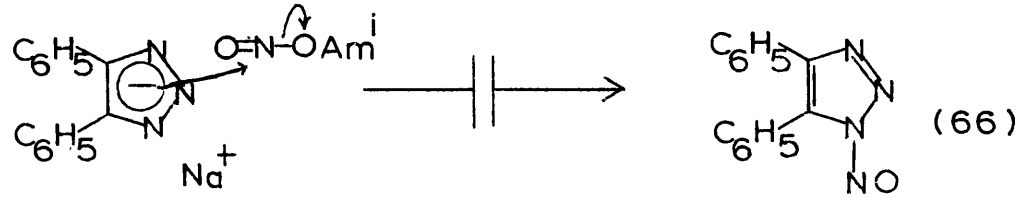
The negatively charged triazole ring should show aromatic character. Substitution could therefore proceed in two positions to give 1-amino and 2-aminotriazoles. None of the 2-amino isomer was detected. A preference for substitution at the 1-position has also been observed in naphtho(1,8)triazine.[61]

Amination with hydroxylamine-O-sulphonic acid[82] failed to give isolable quantities of the 1-amino or 2-aminotriazoles. This behaviour is surprising since benzotriazole is not aminated[58] with chloramine but gives fair yields of 1-amino (64) and 2-aminobenzotriazole (65) with hydroxylamine-O-sulphonic acid.[59]



Since the aminotriazole is deaminated in nitrous acid, and the triazole is then inert to the excess of nitrous acid, the N-nitroso compound (66) is obviously not easily formed. It was hoped that the reaction of the anhydrous sodium salt of the triazole with isoamyl nitrite would afford the N-nitrosotriazole (66). This compound was considered

to be of interest since it could formally decompose to tolan, N_2, and N_2O, and since its deoxygenation, e.g. with trimethyl phosphite, could generate the same nitrene as that proposed in the oxidation of the N-amino compound.

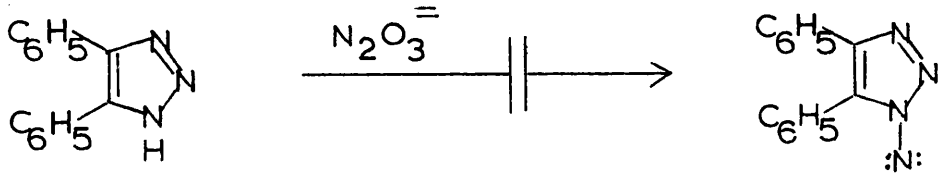


(66)

However, the triazole was recovered unchanged. A similar reaction with ethyl nitrate also failed, a reaction known to give nitramines with primary amines.[103]

Reaction of 4,5-diphenyltriazole with Angeli's salt.

The reaction of Angeli's salt[34] ($Na_2N_2O_3$) with secondary amines has been shown[33] to give the N-nitrenes directly. However, under the same experimental conditions, 4,5-diphenyltriazole (57) was completely inert.

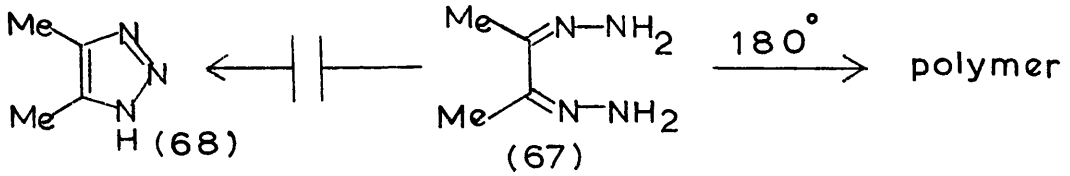


Similarly, 3,5-diphenyl-1,2,4-triazole (63) was also inert.

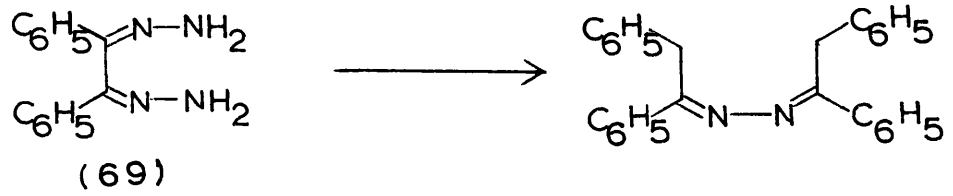
Attempted preparation of 4,5-dimethyltriazole.

It has been reported[88] that the pyrolysis of diacetyl-

bis-hydrazone (67) at 180° affords 4,5-dimethyltriazole (68). We found no evidence that this triazole is produced, polymeric material only being isolated.

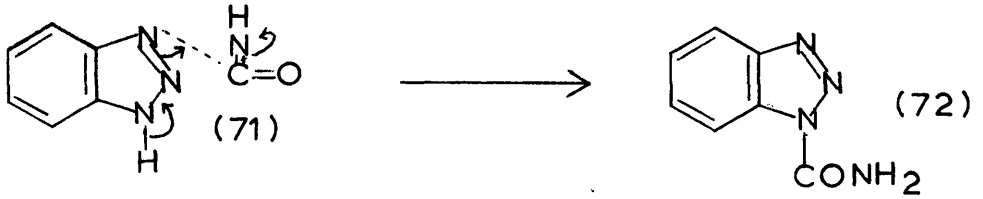


Under similar conditions, benzil-bis-hydrazone (69) affords benzylphenylketazine[89] (70).

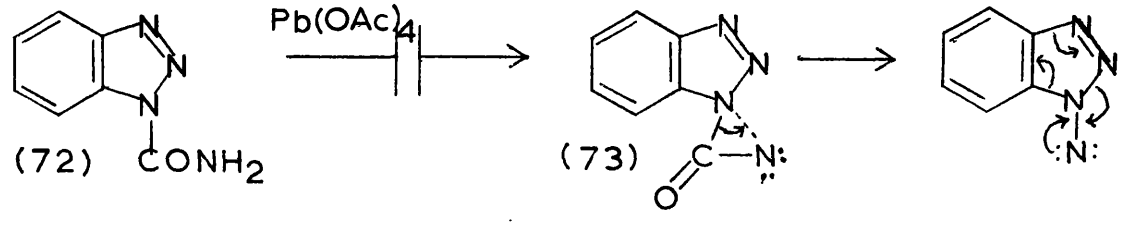


Preparation of benzotriazole-1-carboxamide.

Benzotriazole (71) reacts in acid solution with cyanate salts, giving benzotriazole-1-carboxamide.[90]



This amide (72) is surprisingly inert to lead tetra-acetate oxidation which was expected to produce complete fragmentation in aprotic solvents.[cf 104]



The isocyanate, a possible intermediate in the oxidation sequence shown, was not produced by the Hofmann method either, though it was hoped that this might prove a useful route to the N-amino compound.

The synthesis of the diphenyl analogue afforded what appeared to be a similar compound, but attempted crystallisation resulted in the regeneration of the parent triazole, so characterisation was not attempted.

Conclusion

The oxidation of N-aminotriazoles with lead tetraacetate results in fragmentation of the ring with complete loss of nitrogen. 1-Aminobenzotriazole, the first compound of this type to be studied,[56] has been shown to give benzyne in high yield, which dimerises readily, or is trapped by a 1,3-diene. 1-Amino-4,5-diphenyl-1,2,3-triazole, and the dimethyl analogue, give the acetylene which does not dimerise, nor can it be trapped with 1,3-dienes. 1-Amino-4,5-tetramethylene-1,2,3-triazole, and the pentamethylene analogue, give the acetylene which does not dimerise, but can be trapped by a 1,3-diene. The greater reactivity of the cyclic acetylenes is due to the strain exerted by the ring on the triple bond; the smaller the ring, the greater the reactivity.[105] 1-Amino-4,5(9,10-d)-phenanthro-1,2,3-triazole could not be synthesised and thus its oxidation could not be studied. 4-Amino-3,5-diphenyl-1,2,4-triazole also fragmented similarly on oxidation, with the production of benzonitrile.

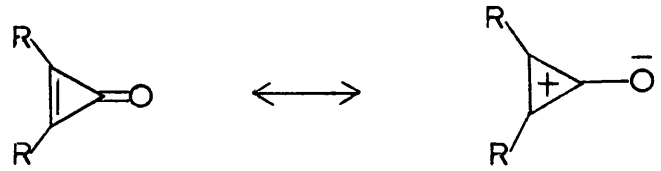
If fragmentation of the triazole ring resulted in a singlet intermediate, this would be expected to degenerate to a stable acetylene, where possible, faster than any other reaction. But, if a triplet intermediate was formed, this might be trapped before a spin transition afforded the singlet, which could then degenerate to an acetylene.

The failure to trap the intermediate in the oxidation of 1-amino-4,5-diphenyltriazole (and the dimethyl analogue) suggests that the intermediate is generated in a singlet state. Benzyne and cyclohexyne, generated by the same method, do not have a stable acetylenic ground state, and so the singlet intermediate here may be trapped.

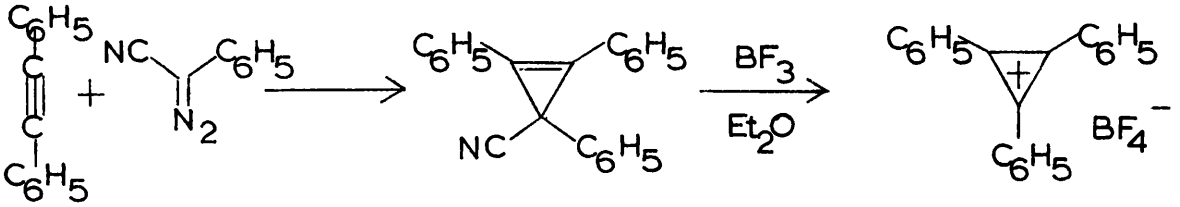
Section II

Introduction

Prior to 1959, no three membered ring containing a carbonyl group had been reported, though their stability had been predicted[106] because of the potential aromatic character of the ring [based on Hückel's $(4n + 2)\pi$ electrons rule, where $n = 0$].

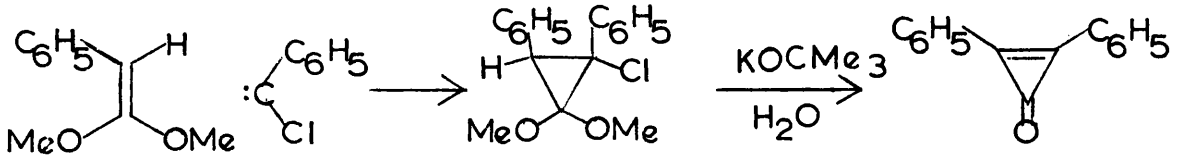


Stability due to this aromaticity had been found in triphenylcyclopropenylium tetrafluoroborate.[107]

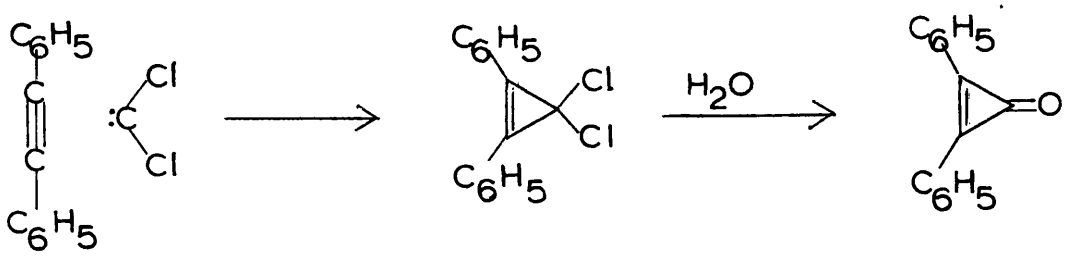


The stability of this ion may be due in part to the conjugation of three phenyl groups with the positive charge.

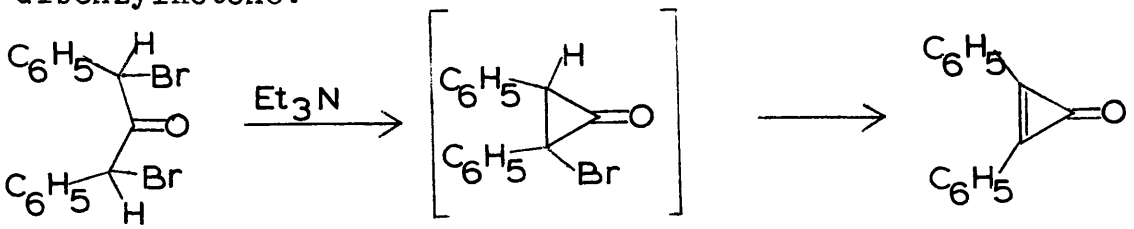
Breslow[108] and Vol'pin[109] independently isolated diphenylcyclopropenone in 1959. Breslow added phenylchlorocarbene to a ketene dimethylketal.



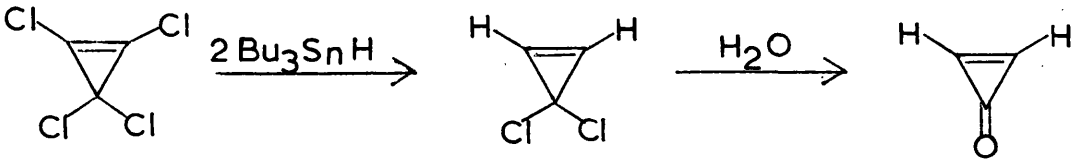
Vol'pin added dichlorocarbene to tolan and hydrolysed the gem-dichloro product.



Breslow introduced a better synthetic method in 1963,[110] which was a modified Favorskii reaction, from α,α'-dibromodibenzylketone.

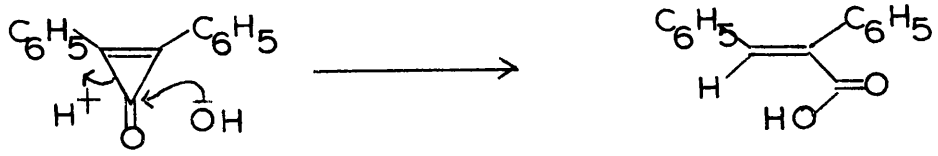


This method has now been extended to the preparation of many other disubstituted cyclopropenones.[111,112] Monosubstituted cyclopropenones have been prepared[113] by the action of lithium trichloromethide on an acetylene at -100°. The unsubstituted parent, cyclopropenone, resisted the usual methods of preparation, but has finally been made, though not yet isolated, from tetrachlorocyclopropene by reduction with tri-n-butyltin hydride followed by hydrolysis.[114]

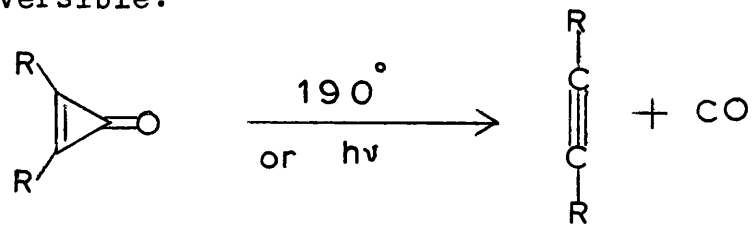


The extent of the contribution of the zwitterionic form to the overall structure of cyclopropenones is shown by the high dipole moments. Cyclopropenone is not hydrated in water, though salts are formed with strong acids, and

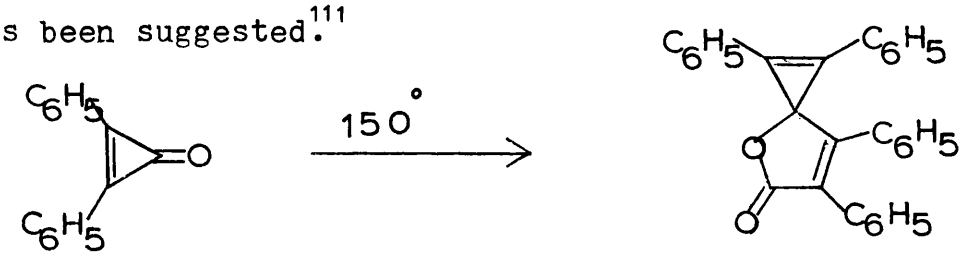
this is indicative of the stability of the ring system and its inertness to nucleophilic attack. Strong alkali, however, opens the ring to give an acrylic acid.[111]



Pyrolysis, or photolysis, of cyclopropenones affords the acetylene and carbon monoxide, and the reaction is irreversible.[111]



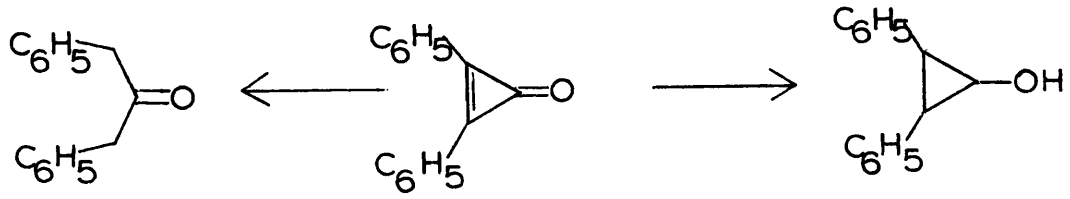
However, if diphenylcyclopropenone is heated to just above its melting point, dimerisation occurs rather than decarbonylation. A provisional structure for the dimer has been suggested.[111]



This does not give tolan on heating at higher temperatures, so cannot be an intermediate in the normal decomposition. This structure has also been suggested for the methyl analogue, and p.m.r. evidence supports this structure.

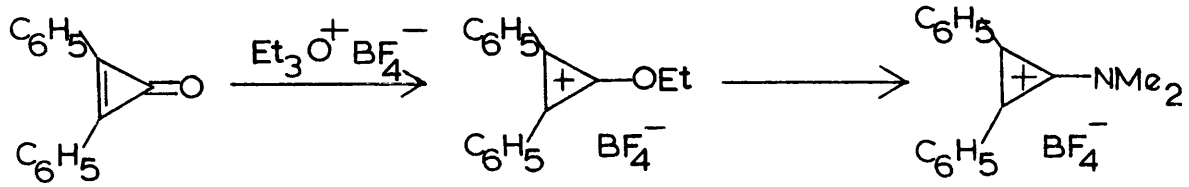
Catalytic hydrogenation of diphenylcyclopropenone has been reported to give dibenzyl ketone[111] and 2,3-diphenyl-

-cyclopropan-3-ol.[109]

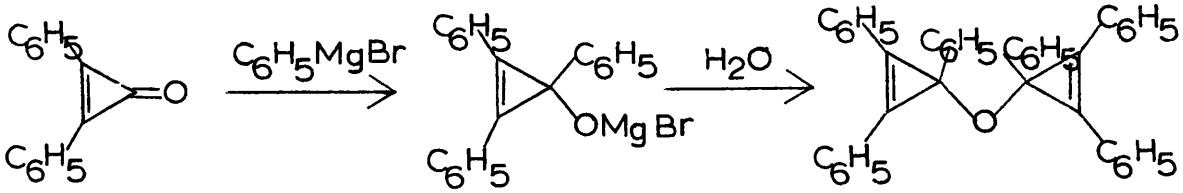


Lithium aluminium hydride reduction of the cyclopropenone affords the cyclic alcohol only, no ring opening having been detected.[115]

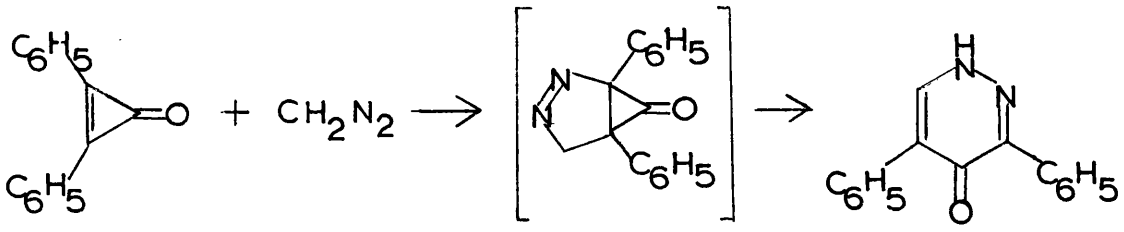
Triethyloxonium fluoroborate converts diphenyl cyclopropenone into ethoxydiphenylcyclopropenyl fluoroborate, which reacts with dimethylamine to give dimethylamino diphenylcyclopropenyl fluoroborate.[111]



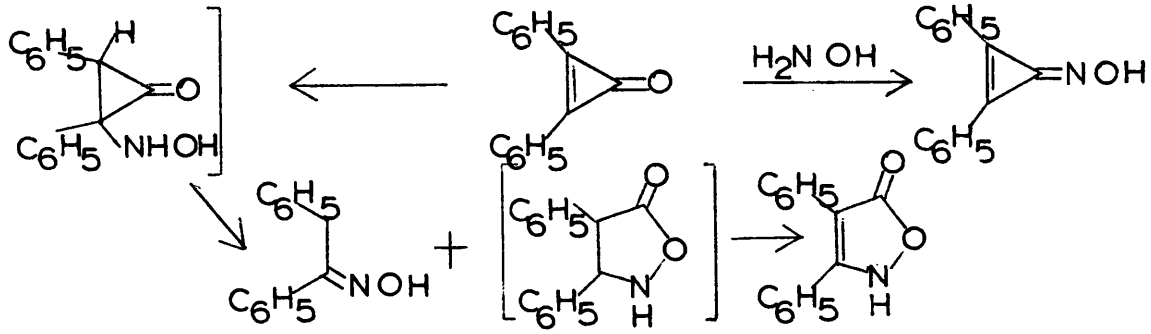
The carbonyl group reacts with Grignard reagents to give ethers which are cleaved with perchloric acid to cyclopropenyl perchlorates.



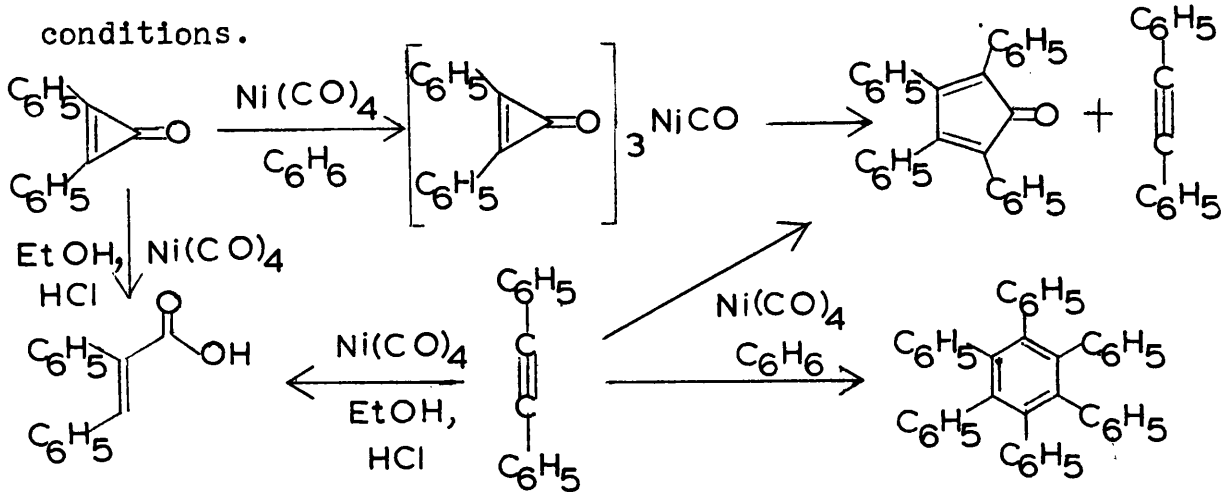
Diazomethane does not insert into the ring in the normal way, but adds across the double bond, the cyclopropanone then ring opening to afford 3,5-diphenyl-4-pyridazinone.[111]



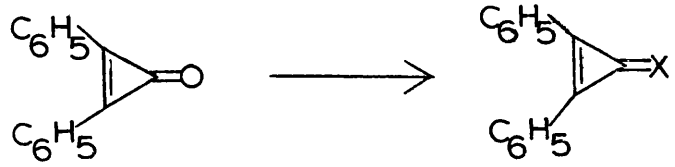
The reaction of hydroxylamine with the carbonyl group has been variously stated to afford deoxybenzoin oxime,[111] 3,4-diphenyloxazolone[111] and the normal oxime.[116]



Reppe proposed that diphenylcyclopropenone was an intermediate in the carbonylation of tolan to acrylic acid with nickel tetracarbonyl.[117] This appears quite likely in view of the reactions of diphenylcyclopropenone with nickel tetracarbonyl, which affords <u>trans</u>-α-phenylcinnamic acid or tolan and tetracyclone, or tris(diphenylcyclopropenone) nickel carbonyl, depending on the reaction conditions.

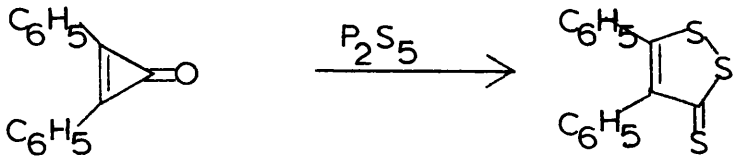


The carbonyl group can be replaced by various other functions: phosphorus pentachloride,[116] thionyl chloride[118] and phosgene[119] afford the gem dichloro cyclopropene, malononitrile affords the 3-dicyanomethylenecyclopropene[117] and phosphorus pentasulphide affords the thione.[116]



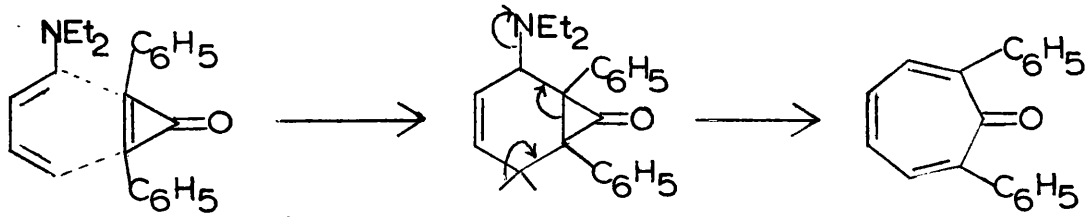
X = Cl_2
X = $C(CN)_2$
X = S

This last reaction has also been stated to give 4,5-diphenyltrithione.

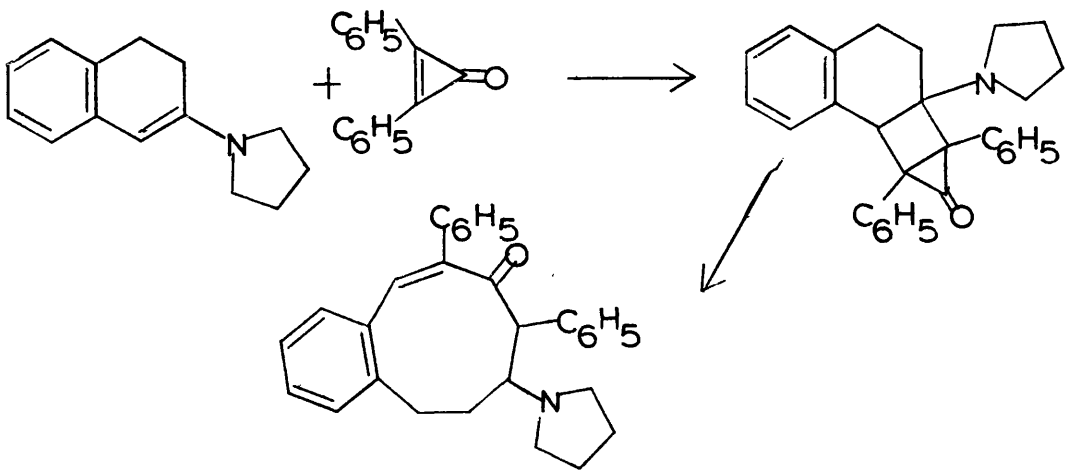


The ketone does not form a tosylhydrazone directly and there is doubt concerning the structure of the 2,4-dinitrophenylhydrazone reported.[109]

The final reaction reported of this system is the 1,4- and 1,2-cycloaddition of enamines to the double bond. 1-Diethylamino-1,3-butadiene gives 2,7-diphenyltropone with diphenylcyclopropenone.

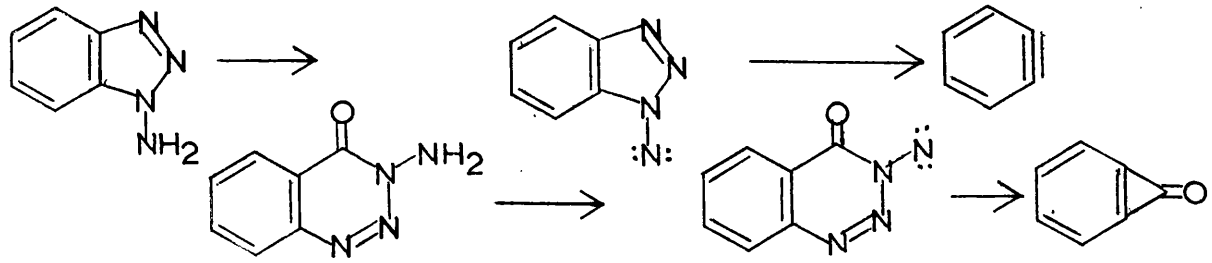


2-(N-Pyrrolidino)-3,4-dihydronaphthalene gives a 9-membered ring product after 1,2-addition to the double bond.



Some work has been published on the related methylene cyclopropenes, quinocyclopropenes and calicenes (a formal combination of the cyclopropenylium cation and the cyclopenta-dienyl anion) and this has been reviewed.[121]

The oxidation of 1-aminobenzotriazole has been thoroughly investigated,[56] and it seemed reasonable to suppose that the reaction course would be little altered by the insertion of a carbonyl group into the ring.



3-Amino-1,2,3-benzotriazin-4-one is reported in the literature,[122] and so was synthesised, and its oxidation studied. Our intention was to prepare benzocyclopropenone in solution where its reactions might be studied, and eventually to attempt to isolate this reactive compound, in order to determine its physical properties. At present,

few benzocyclopropenes have been reported. The parent,[123] and various 1,1-disubstituted benzocyclopropenes,[124] have been prepared by the photolysis of indiazenes, but in low yield.

Experimental

Preparation of 3-amino-1,2,3-benzotriazin-4-one

a) Methyl anthranilate (100g.), hydrazine hydrate (40ml., 100%) and water (40ml.) were heated at 140-150° for 3.5hr. The mixture became homogeneous but separated into layers again on cooling. Trituration gave a solid which was filtered and washed with water and cold ethanol. The solid was crystallised from a large volume of chloroform to give colourless needles of o-aminobenzoylhydrazide (70%), m.p. 123-125° (lit.[122] m.p. 120-122°).

b) o-Aminobenzoylhydrazide (18g.) was dissolved in acetic acid (28ml.) and water (100ml.), and sodium nitrite (8.8g.) in water (120ml.) was added dropwise over 15min. to the well-stirred solution at 3-5°. The yellow precipitate was filtered, washed with water and dried *in vacuo*. The solid was treated with cold ethanol (2x50ml.) and filtered. The insoluble portion was crystallised from ethanol (charcoal) to give 3-amino-1,2,3-benzotriazin-4-one (41%) as long grey needles, m.p. 154-155° (dec.), (lit.[125] m.p. 152-153°).

3-Toluene-p-sulphonylamido-1,2,3-benzotriazin-4-one, (cf. ref. 128), plates from ethanol, m.p. 193-195° (dec.), (Found: C, 53.0; H, 4.0; N, 17.7. $C_{14}H_{12}N_4O_3S$ requires: C, 53.2; H, 3.8; N, 17.7%).

The alcohol-soluble component was precipitated from

solution with water, filtered and crystallised from petrol (b.p. 60-80°)-benzene (5:1) to give o-aminobenzoylazide (35%) as bright yellow plates, m.p. 81-83°(dec.), [lit.[125] m.p. 82-83°(dec.)].

By exactly analogous routes, 3-amino-6-chloro- and-7-chloro-1,2,3-benzotriazin-4-one were synthesised from methyl 5-chloro- and 4-chloroanthranilate respectively. In these cases, the esters were produced by treatment of the corresponding acids with an equimolar amount of diazomethane in ethereal solution.[126] The compounds obtained were:

2-amino-4-chlorobenzoylhydrazide, needles from chloroform, m.p. 150-151°, (lit.[127] m.p. 151°).

3-amino-7-chloro-1,2,3-benzotriazin-4-one, needles from ethanol, m.p. 184-185°, (Found: C, 42.8; H, 2.8; N, 28.3; MW by mass spec. 196. $C_7H_5ClN_4O$ requires: C, 42.8; H, 2.5; N, 28.5%; MW 196).

i.r. νmax. 3420, 3220, 3150 (NH_2); 1680 (C=O); 1590 (N=N); 1320, 1200, 1130, 1070, 870 (1,2,4 subst. benzene); 780cm^{-1}. (C-Cl).

m/e: P=198 and 196 (two chlorine isotopes); P-NH=183, 181; P-N_2 =170, 168; P-HN_4 =141, 139.

2-amino-4-chlorobenzoylazide, needles from petrol (b.p. 60-80°)-benzene (4:1), m.p. 107.5°(dec.), (Found: C, 42.9; H, 2.7; N, 28.5; MW by mass spec. 196. $C_7H_5ClN_4O$ requires: C, 42.8; H, 2.5; N, 28.5%; MW 196).
i.r. νmax. 3480, 3350 (NH_2); 2130 (N_3); 1750 (C=O); 1685 (aromatic unsaturation);1610; 1230 (N_3); 1200, 1030, 975, 880 (1,2,4 subst. benzene); 840; 800 (C-Cl); 720cm^{-1}.
m/e: P=198, 196; P-NH=183, 181; P-N_2=170, 168.

2-amino-5-chlorobenzoylhydrazide, needles from chloroform, m.p. 140-142°, (Found: C, 45.5; H, 4.2; N, 22.4. $C_7H_8ClN_3O$ requires: C, 45.3; H, 4.3; N, 22.6%).
i.r. νmax. 3440, 3410, 3270 (NH_2 and NH); 1610 (C=O); 1570 (aromatic unsaturation); 1290, 1245, 950, 885 (1,2,4 subst. benzene); 825cm^{-1}. (C-Cl).

3-amino-6-chloro-1,2,3-benzotriazin-4-one, needles from ethanol, m.p. 163-164°, (Found: C, 42.8; H, 2.7; N, 28.3; MW by mass spec. 196. $C_7H_5ClN_4O$ requires: C, 42.8; H, 2.5; N, 28.5%; MW 196).
i.r. νmax. 3440, 3380, 3270 (NH_2); 1670 (C=O); 1580 (N=N); 1150,1040, 940, 830 (1,2,4 subst. benzene); 815cm^{-1}. (C-Cl).
m/e: P=198, 196; P-NH=183, 181; P-N =170, 168; P-HN =141, 139.

2-amino-5-chlorobenzoylazide, needles from petrol (b.p. 60-80°)-benzene (4:1), m.p. 106°(dec.) (Found: C, 43.0; H, 2.6; N, 28.3; MW by mass spec. 196. $C_7H_5ClN_4O$ requires: C, 42.8; H, 2.5; N, 28.5%; MW 196).

i.r. νmax. 3480, 3350 (NH_2); 2130 (N_3); 1750 (C=O); 1685 (aromatic unsaturation); 1610; 1230 (N_3); 1200, 1030, 975, 880 (1,2,4 subst. benzene); 840; 800 (C-Cl); 720cm^{-1}.

m/e: P = 198, 196; P-NH = 183, 181; P-N = 170, 168.

Oxidation of the 3-amino-1,2,3-benzotriazin-4-ones

The general procedure in this series of experiments was to dissolve the aminotriazinone in the dry solvent (10ml. per mmole), and to add this solution dropwise over 5-10min. to a magnetically stirred solution (or suspension) of lead tetraacetate (1.5mmole per mmole of aminotriazinone) in the solvent (ca. 10ml.), at various temperatures. Work-up procedure involved the addition of reagents to trap the reactive intermediates produced, unless such traps were present initially, then filtering off any insoluble residue. Gas chromatographic analysis was used for liquid products and evaporation of the filtrate onto a suitable chromatographic adsorbent followed by column chromatography for solid products.

Results are summarised in Tables III, IV and V.

Oxidation of 3-amino-1,2,3-benzotriazin-4-one

Table III

Solvent	Temp.	Trap initially present	Traps added after oxidation	Products	Yield (%)
MeOH	20°	MeOH		methyl benzoate [a]	77
CH_2Cl_2	20°		MeOH	methyl benzoate [a]	14.5
CH_2Cl_2	40°		MeOH	methyl benzoate [a]	19.5
CH_3CN	20°		MeOH	methyl benzoate [a]	15
CH_3CN	80°		MeOH	methyl benzoate [a]	18.4
CH_2Cl_2	20°		H_2O [c]	benzoic acid [b]	57
CH_2Cl_2	20°		1) Tetracyclone [d]	i) benzoic acid [b]	15
			2) H_2O	ii) indazolone adduct [e]	20
CH_2Cl_2	20°	Tetracyclone [d]	H_2O [c]	i) benzoic acid	15
				ii) indazolone adduct [e]	30

Notes to Table III

a) Methyl benzoate was characterised and estimated by gas chromatographic analysis on a diethyleneglycol succinate ester-chromosorb P column, by comparison with standard solutions.

b) Benzoic acid eluted from a silica column with petrol-ether (5:1), was sublimed and crystallised from water, m.p. and mixed m.p. 120-121°.

c) Water was added to the reaction as moist ether to keep the reaction homogeneous.

d) Tetracyclone was eluted from the column with benzene and crystallised from benzene-ethanol (1:5) as dark lustrous plates (d_1, 55%; d_2, 50% recovery), m.p. 219-221°.

e) The indazolone adduct was characterised as 1,4-carbono-1,2,3,4-tetraphenyl-4a,9a-bisazafluorenone, yellow solid, m.p. 180-182°, (Found: C, 83.0; H, 5.0; N, 5.8; MW by mass spec. 516. $C_{36}H_{24}N_2O_2$ requires: C, 83.7; H, 4.7; N, 5.4%; MW 516).

i.r. νmax. 1720 (ketone C=O); 1630 (amide C=O); 1560 (C=C); 1500, 1450, 1405, 1340, 1265; 1220, 1120, 1035-1025, 965, 760 (1,2 disubst. benzene); 1165-1150, 1110, 1070, 745, 690cm^{-1}. (monosubst. benzene).

m/e: P=516; Tetracyclone = 384; Indazolone = 132.

On heating the adduct at 200°/ 1mm. tetracyclone (95%)

sublimed, leaving an intractable tar, presumably derived from indazolone.

Oxidation of 3-amino-7-chloro-1,2,3-benzotriazin-4-one

Table IV

Solvent	Temp.	Trap initially present	Traps added after oxidation	Products	Yield (%)
MeOH	20°	MeOH		methyl p-chlorobenzoate [a]	68
CH_3CN	80°		MeOH	methyl p-chlorobenzoate [a]	16
				p-chlorobenzoic acid [b]	6
CH_2Cl_2	20°		H_2O [c]	p-chlorobenzoic acid [b]	24
CH_2Cl_2	20°	Tetracyclone [e1]	H_2O [c]	p-chlorobenzoic acid [b]	20
				6-chloro-3-indazolone adduct [d]	35
CH_2Cl_2	20°		1) Tetracyclone [e2] 2) H_2O [c]	m-chlorobenzoic acid [f]	0.2
				p-chlorobenzoic acid [b]	21
				6-chloro-3-indazolone adduct [d]	17

Notes to Table IV

a) Methyl p-chlorobenzoate was estimated by gas chromatographic analysis on a diethyleneglycol succinate ester-chromosorb P column, with reference to a standard solution. No column was found which was capable of resolving methyl m- and p-chlorobenzoate.

The ester was characterised by chromatography on silica, with petrol as eluant, followed by high resolution i.r. analysis, which proved capable of resolving an authentic mixture of isomers.

b) p-Chlorobenzoic acid was eluted from silica with petrol-ether (20:1), sublimed and crystallised from petrol-ether as needles, m.p. and mixed m.p. 240-242°(lit. m.p. 243°). i.r. Comparison with an authentic sample confirmed the structure.

c) Water was added to the reaction as moist ether.

d) The 6-chloro-3-indazolone adduct was characterised as 1,4-carbono-6-chloro-1,2,3,4-tetraphenyl-4a,9a-bisazafluorenone, yellow solid, m.p. 198-199°(dec.), (Found: C, 78.7; H, 4.4; N, 5.2; MW by mass spec. 550. $C_{36}H_{23}ClN_2O_2$ requires: C, 78.5; H, 4.2; N, 5.1%; MW 550).

i.r. $\nu_{max.}$ 1730 (ketone C=O); 1635 (amide C=O); 1500 (C=C); 1440, 1390, 1340; 1220, 1150, 1120, 1040, 970, 910, 840 (1,2,4 subst. benzene); 1150, 1110, 1030, 710, 690cm^{-1}. (monosubst. benzene).

m/e: P=552 and 550 (two chlorine isotopes); P-CO=524, 522; P-CO_2=508, 506; Tetracyclone = 384; 6-chloro-3-indazolone = 168, 166.

On heating the adduct at 200°/ 1mm. tetracyclone (92%) sublimed, leaving an intractable tar, presumably derived from 6-chloro-3-indazolone.

e) Tetracyclone was eluted from silica with benzene and crystallised from benzene-ethanol (1:5) as dark lustrous plates, (e_1, 64%; e_2, 52% recovery), m.p. 222°.

f) m-Chlorobenzoic acid was eluted from silica with petrol-ether (50:1) and sublimed as needles, m.p. and mixed m.p. 156-157°, (lit. m.p. 158°), with i.r. identical to that of an authentic specimen.

Oxidation of 3-amino-6-chloro-1,2,3-benzotriazin-4-one

Table V

Solvent	Temp.	Trap initially present	Traps added after oxidation	Products		Yield (%)
MeOH	20°	MeOH		methyl m-chlorobenzoate	a)	58.5
				methyl p-chlorobenzoate	a)	11.5
CH_3CN	80°		MeOH	methyl m- and p-chlorobenzoate	b)	17
				m- and p-chlorobenzoic acid	c)	6
CH_3CN	-80°		$CH_2N_2/Et_2O/H_2O$	methyl chlorobenzoates	b)	2
				chlorobenzoic acids	c)	21
CH_3CN	-80°		D_2O	deuterated chlorobenzoic acids	d)	35
CH_2Cl_2	20°		H_2O	m-chlorobenzoic acid	e)	2
				p-chlorobenzoic acid		7

Table V cont.

Solvent	Temp.	Trap initially present	Traps added after oxidation	Products	Yield (%)
CH_2Cl_2	20°	Tetracyclone[f1]	H_2O	m-chlorobenzoic acid[e]	0.3
				p-chlorobenzoic acid	3
				5-chloro-3-indazolone adduct[g]	10.5
CH_2Cl_2	20°		1) Tetracyclone[f2] 2) H_2O	m-chlorobenzoic acid[e]	1
				p-chlorobenzoic acid	15
				5-chloro-3-indazolone adduct[g]	2

Notes to Table V

a) The total yield of esters was estimated by gas chromatographic comparison with an authentic mixture of the same isomeric composition. The isomer ratio was obtained by high resolution i.r. analysis of the esters after chromatography on silica.

b) The yield of esters is based on a comparison with a standard solution of methyl p-chlorobenzoate. Low resolution i.r. showed the two isomers to be present, but no high resolution analysis was attempted, due to the low yield of esters obtained.

c) The two acids were not separated on a silica column with petrol-ether (20:1) as eluant, but low resolution i.r. showed the two isomers to be present.

d) Deuterium oxide in ether was added to the reaction mixture. The acids were not separated by chromatography on silica, but low resolution i.r. showed the two isomers to be present, and comparison of the mass spectrum of this mixture with that of an undeuterated mixture demonstrated that deuterium had been incorporated on the benzene ring.

e) Chromatography on silica with an automatic gradient elution technique, using a low polarity gradient (petrol-ether; 50:1-20:1; 10 litre) resulted in the separation of the two acids. m-Chlorobenzoic acid was eluted first

and sublimed as needles, m.p. and mixed m.p. 156-157°(lit. m.p. 158°). p-Chlorobenzoic acid was eluted shortly after its isomer and sublimed as needles, m.p. and mixed m.p. 240-242°(lit. m.p. 243°).

f) Tetracyclone was eluted from silica with benzene and crystallised from benzene-ethanol (1:5) as dark plates, (f_1, 50%; f_2, 87% recovery) m.p. 220°.

g) The 5-chloro-3-indazolone adduct was characterised as 1,4-carbono-7-chloro-1,2,3,4-tetraphenyl-4a,9a-bisazafluorenone, yellow solid, m.p. 190-192°(dec.) (Found: C, 78.4; H, 4.4; N, 5.1; MW by mass spec. 550. $C_{36}H_{23}ClN_2O_2$ requires: C, 78.5; H, 4.2; N, 5.1%; MW 550).

i.r. νmax. 1730 (ketone C=O); 1650 (amide C=O); 1500 (C=C); 1450, 1340; 1220, 1140, 1030, 970, 855 (1,2,4 subst. benzene); 1150, 1025, 710, 680cm^{-1}. (monosubst. benzene).

m/e: P = 552, 550; P-CO = 524, 522; P-CO_2 = 508, 506; Tetracyclone = 384; 5-chloro-3-indazolone = 168, 166.

On heating the adduct at 200°/ 1mm. tetracyclone (95%) sublimed, leaving an intractable tar.

Preparation of 3-Indazolinones

All the 3-indazolinones were prepared from the anthranilic acids by diazotisation at 0°, reduction with SO_2 and ring closure in boiling dil. HCl, following the literature preparations exactly.[129] The compounds obtained were:

3-indazolinone, needles from methanol, m.p. 249-251° (lit.[129] m.p. 250-252°).

5-chloro-3-indazolinone, needles from methanol, m.p. 273-274° (lit.[130] m.p. 275-276°).

6-chloro-3-indazolinone, needles from methanol, m.p. 284-286° (lit.[131] m.p. 289°).

6-nitro-3-indazolinone, orange needles from ethanol, m.p. 244-245° (lit.[131] m.p. 244°).

Oxidation of 3-Indazolinones

The general procedure in this series of experiments was as described for the aminotriazinones.

Results are summarised in Table VI.

Table VI

Compound	Solvent	Temp.	Trap initially present	Traps added after oxidation	Products	Yield (%)
3-indazolinone	MeOH	20°	MeOH		methyl benzoate [a]	46
	CH_3CN	80°		MeOH	methyl benzoate	18.4
5-chloro-3-indazolinone	MeOH	20°	MeOH		methyl m-chlorobenzoate [b]	52
	CH_2Cl_2	20°		1) Tetracyclone 2) H_2O	5-chloro-3-indazolone adduct [c]	10
6-chloro-3-indazolinone	MeOH	20°	MeOH		methyl p-chlorobenzoate [d]	53
	CH_2Cl_2	20°		1) Tetracyclone 2) H_2O	6-chloro-3-indazolone adduct [e]	25
6-nitro-3-indazolinone	MeOH	20°	MeOH		methyl p-nitrobenzoate [f]	55
	CH_2Cl_2	20°		1) Tetracyclone 2) H_2O	6-nitro-3-indazolone adduct [g]	32
	CH_2Cl_2	20°		H_2O	p-nitrobenzoic acid [h]	25

Notes to Table VI

a) Methyl benzoate was characterised and estimated by g.l.c.

b) Methyl m-chlorobenzoate was estimated by g.l.c. and chromatography on silica. Petrol eluted the ester as an oil, which crystallised on cooling to 0°, (lit. m.p. 21°). High resolution i.r. spectroscopy showed only one isomer to be present.

c) The 5-chloro-3-indazolone-tetracyclone adduct was shown to be identical with that obtained from 3-amino-6-chloro-1,2,3-benzotriazin-4-one, m.p. and mixed m.p. 190-191°(dec.).

d) Methyl p-chlorobenzoate was estimated by g.l.c. and chromatography on silica. Petrol eluted the ester as plates, m.p. 40-42° (lit. m.p. 44°). High resolution i.r. showed only one isomer to be present.

e) The 6-chloro-3-indazolone-tetracyclone adduct was shown to be identical to that obtained from 3-amino-7-chloro-1,2,3-benzotriazin-4-one, m.p. and mixed m.p. 196-197°(dec.).

f) Methyl p-nitrobenzoate was eluted from silica with petrol as plates, m.p. 93-95° (lit. m.p. 96°). High resolution i.r. showed only one isomer to be present.

g) Chromatography on silica with benzene as eluant gave tetracyclone (70%). Benzene-ether (1:1) eluted a yellow solid, m.p. 161-163°(dec.), assigned the 6-nitro-3-indazolinone-tetracyclone adduct structure (32%).

A satisfactory analysis for C and H could not be obtained, (Found: N, 7.3; MW by mass spec. 561. $C_{36}H_{23}N_3O_4$ requires: N, 7.5%; MW 561).

i.r. νmax. 1730 (ketone C=O); 1635 (amide C=O); 1550, 1345, 825, 760 (NO_2); 730, 695 (monosubst. benzene); 805cm^{-1} (1,2,4 subst. benzene).

m/e: P = 561; Tetracyclone = 384; 6-nitro-3-indazolone = 177.

h) p-Nitrobenzoic acid was extracted from the oxidised solution with base; the basic solution was acidified and extracted with ether to give the acid, m.p. and mixed m.p. 238-240° (lit. m.p. 241.5°).

Miscellaneous Reactions

Decomposition of 2-amino-4-chlorobenzoylazide

The azide (0.5g.) was heated in toluene (5ml.) under reflux for 5min. Colourless needles were deposited which were filtered off and washed with benzene (20ml.) to give 5-chloro-2-benzimidazolinone (95%), m.p. 317-318° (lit. m.p.$\gg$270°).

Decomposition of 2-amino-5-chlorobenzoylazide

The azide (0.5g.) was decomposed in the same manner as its isomer and afforded the same product, 5-chloro-2-benzimidazolinone (93%), m.p. and mixed m.p. 317-318°.

Attempted preparation of 3-amino-7-nitro-1,2,3-benzotriazin--4-one

a) 2-Amino-4-nitrobenzoic acid (Aldrich) was converted to the methyl ester quantitatively with diazomethane.[126]

b) The ester (20g.), hydrazine hydrate (20ml.) and water (20ml.) were refluxed for 3.5hr. Water (100ml.) was added to the semi-solid cold mass and the precipitate filtered off. Crystallisation from ethanol afforded 2,4-diaminobenzoylhydrazide (74%), orange prisms, m.p. 207-208° (Found: C, 50.4; H, 6.0; N, 33.0; MW by mass spec. 166. $C_7H_{10}N_4O$ requires: C, 50.6; H, 6.0; N, 33.7%; MW 166).

m/e: P = 166; P-NH_2 = 150; P-N_2H_3 = 135; P-N_3H_4 = 120.

bii) The ester (20g.), hydrazine hydrate (20ml.) and ethanol (200ml.) were shaken for 2 days at room temperature. The orange solid was filtered off and crystallised from ethanol as 2-amino-4-nitrobenzoylhydrazide (83%), m.p. 237-238°. (Found: C, 43.1; H, 4.3: N, 28.3; MW by mass spec. 196. $C_7H_8N_4O_3$ requires: C, 42.9; H, 4.1; N, 28.6%; MW 196). i.r. νmax. 3450, 3420, 3305 (NH_2); 1650 (C=O); 1580, 1350, 830, 730 (NO_2); 820cm^{-1} (1,2,4 subst. benzene).
m/e: P = 196; P-NH = 181; P-N_2H_3 = 165; P-N_3H_5 = 149; P-$N_3H_3O_2$ = 119.

c) The hydrazide (10g.) was dissolved in acetic acid (500ml.) at 0°. Sodium nitrite (3.5g.) in water (50ml.) was added dropwise over 0.5hr. with stirring, and the solution stirred for a further 1hr. Water (1 litre) was added slowly to the solution and the yellow precipitate filtered, washed with water and dried in vacuo. The solid was treated with cold ethanol (2 X 50ml.) and filtered. The alcohol soluble component was precipitated from solution with water, filtered and crystallised from petrol (b.p. 60-80°)-benzene (5:1) to give 2-amino-4-nitrobenzoylazide (63%), orange needles, m.p. 133.5°(dec.) (Found: C, 40.6; H, 2.6; N, 33.7. $C_7H_5N_5O_3$ requires: C, 40.6; H, 2.4; N, 33.8%).

i.r. ν max. 3470, 3550 (NH_2); 2160-2140 (N_3); 1735, 1670 (C=O); 1640, 1590 (C=C; N=N); 1515, 1355, 865, 735 (NO_2); 880, 825cm^{-1}. (1,2,4 subst. benzene).

The insoluble portion was crystallised from ethanol as yellow plates, m.p. 260-280° (slow dec.). Recrystallisation from ethanol afforded 5-nitro-2-benzimidazolinone (17%), m.p. 303-305° (lit.[132] m.p. 308°).

di) 2-Amino-4-nitrobenzoylhydrazide was benzoylated by the Schotten-Baumann method, and the product diazotised directly. Filtration and crystallisation from ethanol afforded 3-benzoylamido-7-nitro-1,2,3-benzotriazin-4-one (63%), m.p. 208-209°(dec.) (Found: C, 54.0; H, 3.3; N, 22.3; MW by mass spec. 311. $C_{14}H_9N_5O_4$ requires: C, 54.0; H, 3.0; N, 22.5%; MW 311).

i.r. ν max. 3200 (NH); 1720, 1655 (C=O); 1595, 1580 (C=C; N=N); 1530 (NO_2); 860, 795 (1,2,4 subst. benzene); 730, 705cm^{-1}. (monosubst. benzene).

Hydrolysis in hot HCl-ethanol (10%) afforded 5-nitro-2-benzimidazolinone (57%), m.p. and mixed m.p. 306-307°. Milder conditions gave the starting material recovered unreacted.

dii) Attempted preparation of the benzylidene derivative of 2-amino-4-nitrobenzoylhydrazide afforded a yellow solid, fine needles from ethanol, m.p. 209-211° (Found: C, 66.4; H, 4.3; N, 16.5; MW by mass spec. 253. $C_{14}H_{11}N_3O_2$ requires:

C, 66.4; H, 4.4; N, 16.6%; MW 253).
i.r. $\nu_{max.}$ 1710; 1665; 1530, 1350, 830, 740; 800; 765, 695cm^{-1}.

Decomposition of 2-amino-4-nitrobenzoylazide

The azide (0.5g.) was heated in toluene (20ml.) under reflux for 5min. Yellow needles were deposited which were filtered from the cold solution, washed with benzene and dried to give 5-nitro-2-benzimidazolinone (97%), m.p. 305-307° (lit.[132] m.p. 308°) (Found: C, 46.9; H, 2.9; N, 23.4; MW by mass spec. 179. Calc. for $C_7H_5N_3O_3$: C, 46.9; H, 2.8; N, 23.5%; MW 179).

Preparation and reactions of benzoic acetic anhydride

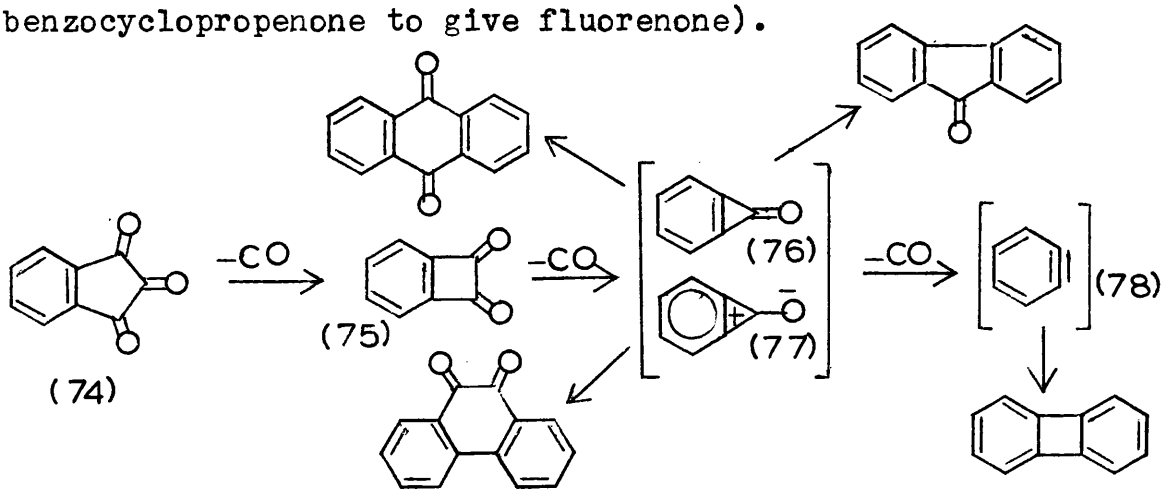
Ketene, generated from acetone with a ketene lamp previously standardised, was passed through a solution of benzoic acid (12g.) in ether (100ml.) for 17min. The ether was removed by evaporation, leaving benzoic acetic anhydride as a mobile oil.

Water converted the mixed anhydride into benzoic acid and acetic acid quantitatively. Methanol afforded a mixture of esters, shown by g.l.c. to be methyl benzoate (7.5%) and methyl acetate (92.5%).

Discussion

Benzocyclopropenone (76) has been proposed as an intermediate in the thermolytic and mass-spectral fragmentation of indanetrione[133] (74) and phthalic anhydride[134] and is also of interest as a potentially aromatic system (77) by analogy with the stable monocyclic cyclopropenones.[111]

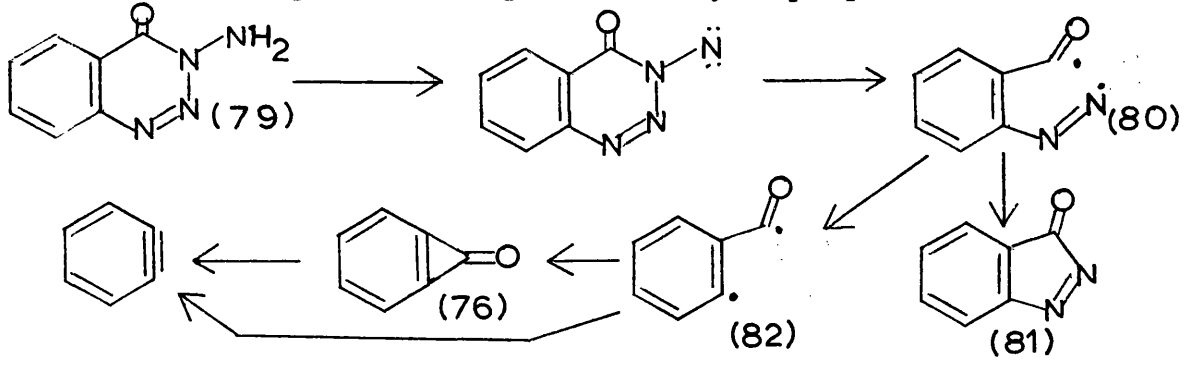
On pyrolysis, indanetrione[133] (74) has been shown to lose carbon monoxide in a stepwise manner, yielding benzocyclobutenedione (75) (which was isolated), benzocyclopropenone (76) (which dimerises to anthraquinone and phenanthraquinone) and benzyne (78) (which dimerises to biphenylene, or traps benzocyclopropenone to give fluorenone).



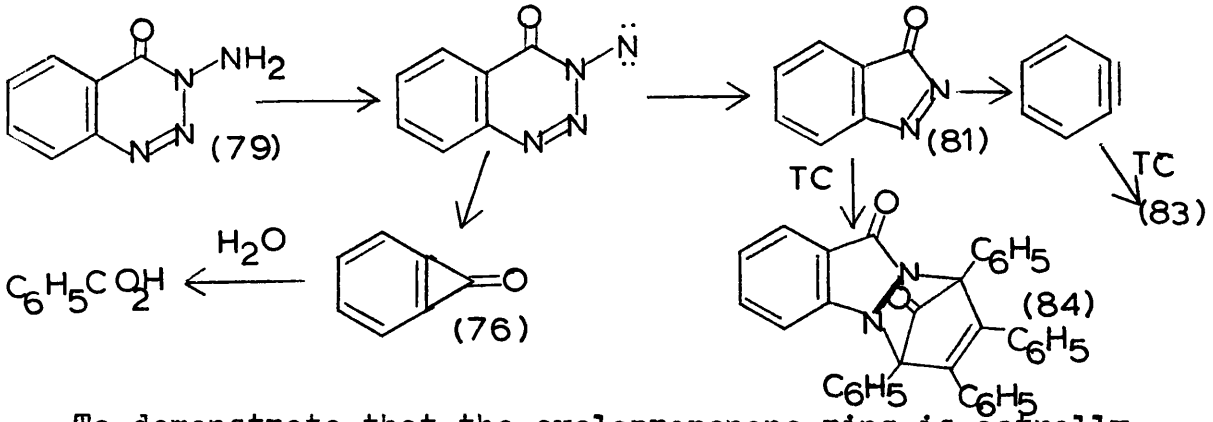
Phthalic anhydride also fragments to "benzocyclopropenone" (76) (with loss of carbon dioxide first) and benzyne (78) under similar treatment,[134] and attempts have been made to correlate this with the breakdown of molecular ions on mass spectral analyses of these compounds.

As mentioned in the introduction, it seemed that

reactions based on the oxidation of 1-aminobenzotriazole to benzyne[56] might be mild enough to allow the generation of benzocyclopropenone under more useful conditions. 3-Aminobenzotriazin-4-one (79) was synthesised in order to determine whether, on oxidation, complete fragmentation to benzyne by loss of nitrogen and carbon monoxide would occur, or whether nitrogen only would be lost, initially; this would give a diradical (80), which could ring close to indazolone (81) or lose another mole of nitrogen to give a diradical (82) (or a corresponding dipolar species) which could ring close to give benzocyclopropenone (76).

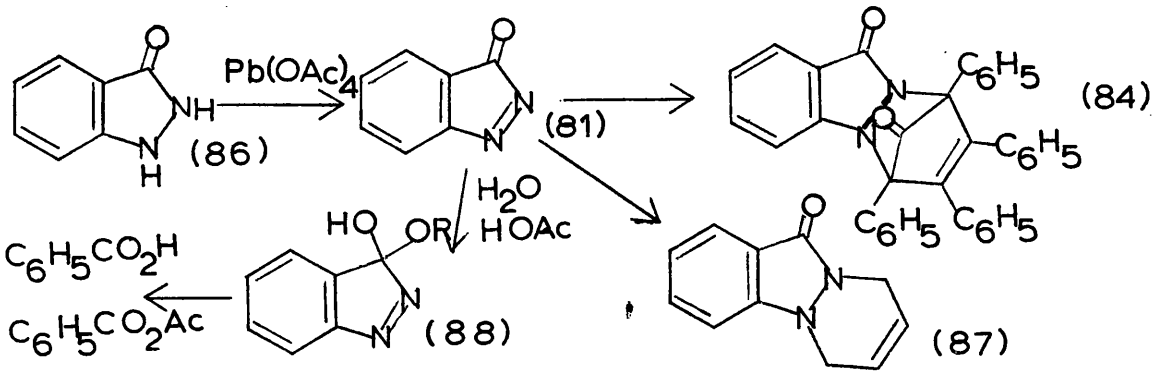


Preliminary work performed on this system showed that the three possibilities may all occur under various conditions.[58] In refluxing benzene, benzyne was generated as shown by the formation of tetraphenylnaphthalene (5%) (83) with tetracyclone. The indazolone adduct (84) with tetracyclone was formed (30%) at temperatures from -80° to 80° and benzoic acid (3%), from the nucleophilic attack of water on benzocyclopropenone, was formed under the same conditions.

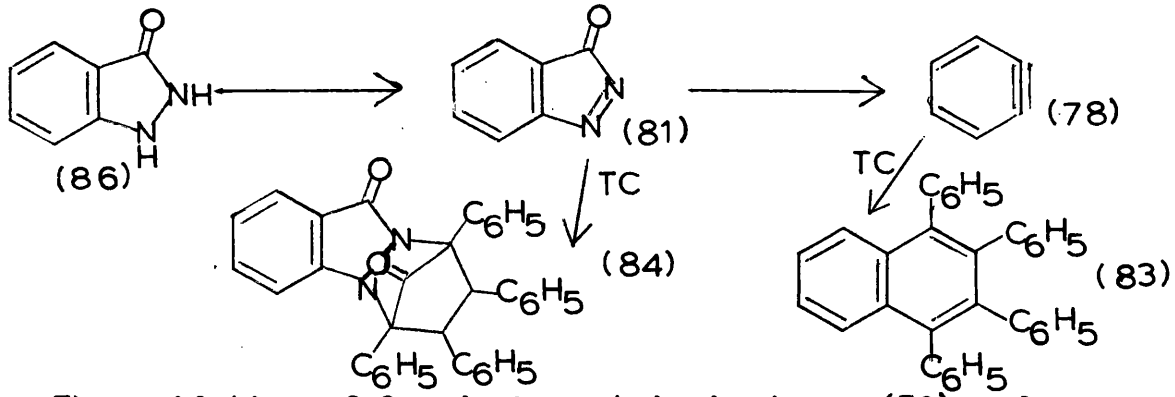


To demonstrate that the cyclopropenone ring is actually formed in the reaction, the benzene ring has to be labelled to remove the symmetry of the intermediate, so that direction of ring opening may be demonstrated. This was done by synthesising 6- and 7-chloro-3-amino-1,2,3-benzotriazin-4-one (85)[a] and (85)[b].

3-Indazolinone (86), on oxidation with lead tetraacetate, was reported, in a preliminary communication,[135] to give the unstable 3-indazolone (81) in solution at low temperatures. This compound reacts with dienes, such as butadiene, to give Diels-Alder adducts, such as (87), and with nucleophiles, such as water, methanol and acetic acid, to give benzoic acid, methyl benzoate and benzoic acetic anhydride respectively. The gradual loss of nitrogen after the addition of nucleophiles suggests that the tetrahedral intermediate (88) is initially formed, which slowly loses nitrogen to give the products.



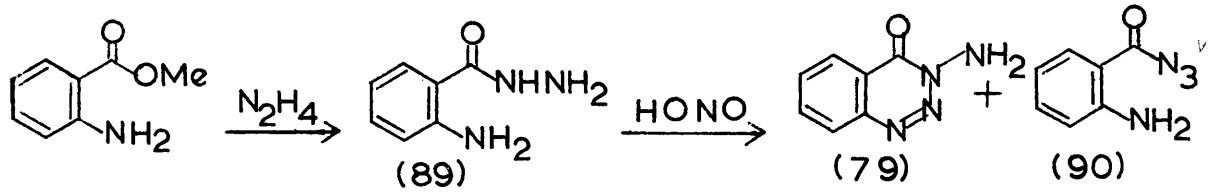
Barkhus and Ullman[135] reported that no products were formed which resulted from complete dissociation into benzyne, but the oxidation in refluxing benzene, like the 3-aminobenzotriazin-4-one, has since been reported to give tetraphenylnaphthalene (4%) (83) and the indazolone adduct (30%) (84) with tetracyclone.[58]



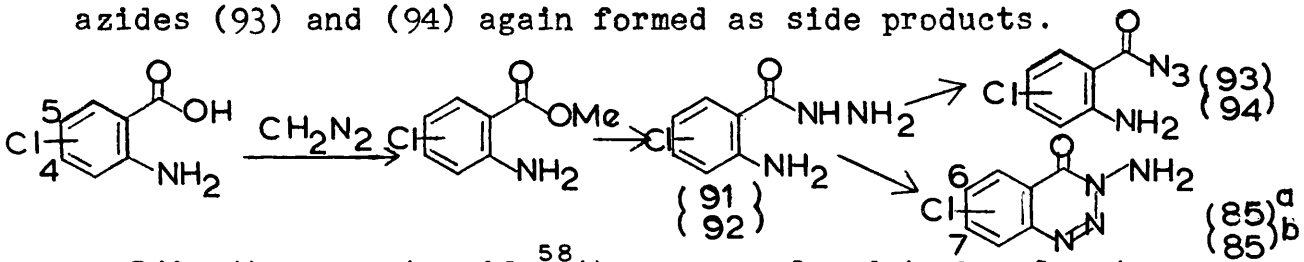
The oxidation of 3-aminobenzotriazin-4-one (79) and 3-indazolinone (86), performed under very similar conditions, are obviously closely related; thus, a comparison of the products of the two oxidations could give some insight into the mode of decomposition.

Preparation of 3-aminobenzotriazin-4-ones.

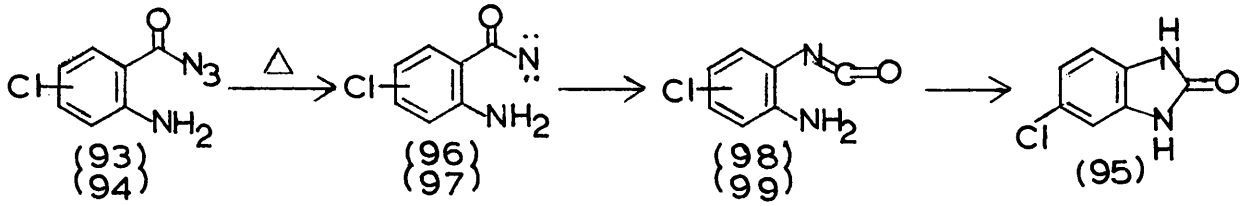
3-Aminobenzotriazin-4-one (79) was prepared[122] by the diazotisation of o-aminobenzoylhydrazide (89). O-Amino-benzoylazide (90) was also formed in this reaction.



3-Amino-6-chlorobenzotriazin-4-one (85)[a], and the corresponding 7-chloro isomer (85)[b] were prepared by an analogous method from the hydrazide (91) and (92) with the amino-azides (93) and (94) again formed as side products.



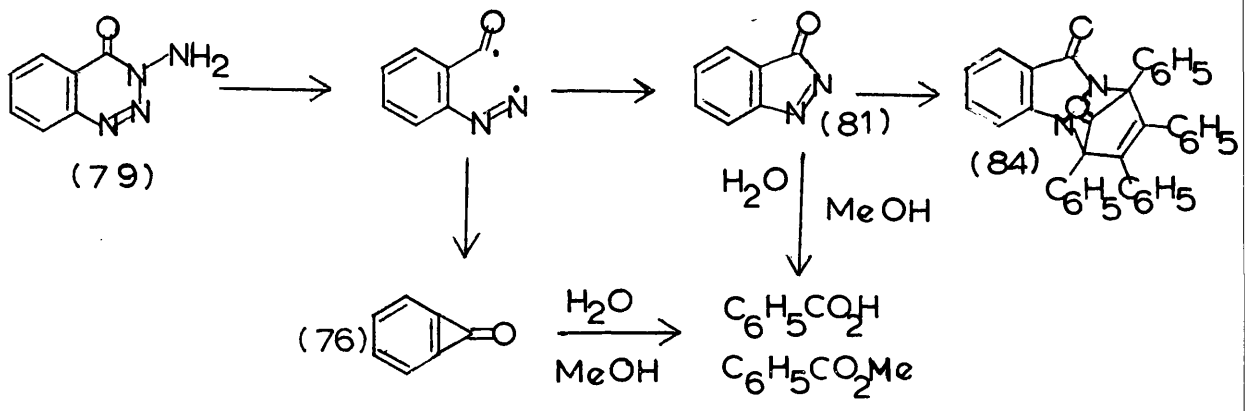
Like the parent azide,[58] these were found to be almost quantitively converted into 5-chloro-2-benzimidazolinone (95) by refluxing a solution of either in toluene. This compound presumably arose by rearrangement of the nitrenes (96) and (97) followed by intramolecular cyclisation of the isocyanates (98) and (99). It is interesting to note that the nitrene (96 or 97) rearranges faster than it can be trapped intramolecularly by the o-amino group.



Oxidation of 3-aminobenzotriazin-4-ones.

When a solution of 3-aminobenzotriazin-4-one (79) in methanol was added to a suspension of lead tetraacetate in methanol, there was an immediate gas evolution. After the addition, a gas continued to be evolved slowly. Gas chromatographic analysis of the solution showed methyl benzoate (77%) to be the product of the oxidation. Similar oxidations in inert solvents at 20° to 80°, with the addition of methanol when the reaction was complete, gave methyl benzoate (15 to 20%), demonstrating the existence of an intermediate with a reasonable lifetime. The addition of moist ether to an oxidised solution afforded benzoic acid (57%), confirming this point.

Since the reactive intermediate may be indazolone (81) and/or benzocyclopropenone (76), the amine was oxidised in methylene chloride at 20°, a solution of tetracyclone added to trap the indazolone (81), followed by moist ether to trap the benzocyclopropenone (76). The indazolone adduct (20%) (84) and benzoic acid (15%) were both produced, and thus, if the indazolone is trapped rapidly in high yield by tetracyclone, both intermediates must be present in the oxidised solution.



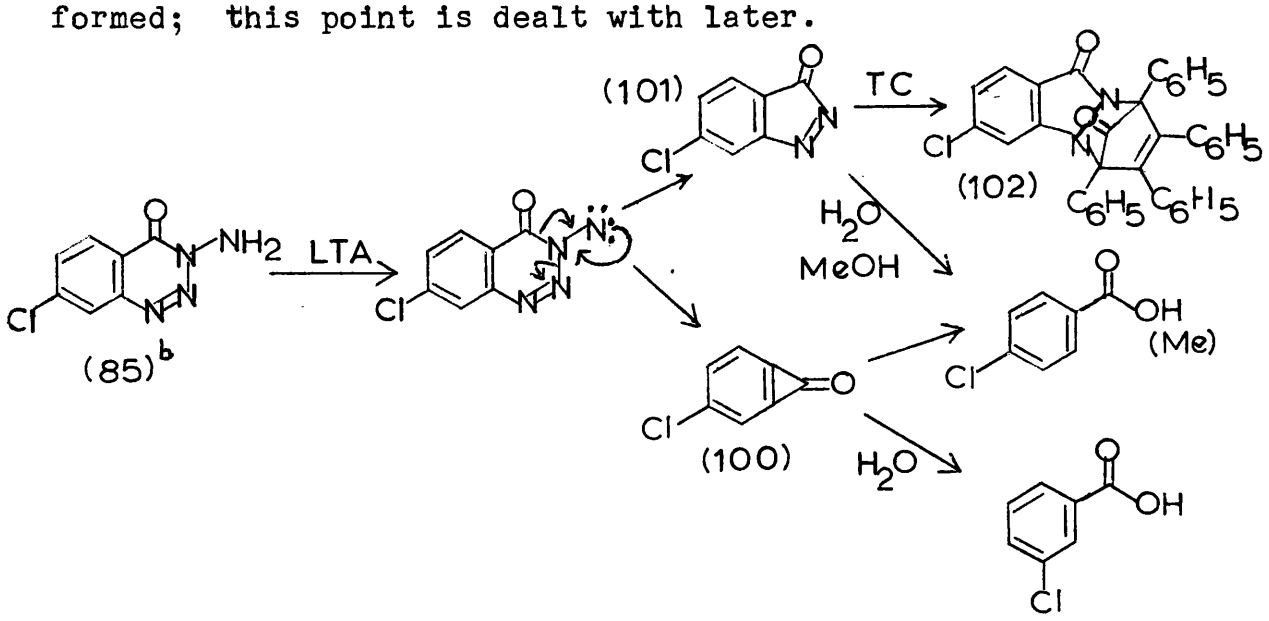
When a solution of 3-amino-7-chlorobenzotriazin-4-one (85)[b] in methanol was oxidised with lead tetraacetate, methyl p-chlorobenzoate (68%) was produced, and this same ester was formed (16%) when methanol was added to an acetonitrile solution of the oxidised amine. Chromatography on silica-gel gave, in addition to the ester, p-chlorobenzoic acid (6%) which presumably resulted from adventitious hydrolysis before the addition of methanol. When water, as moist ether, was added to the oxidised solution, p-chlorobenzoic acid (24%) was produced.

Since two reactive intermediates were shown to be formed from the unsubstituted amine, two experiments were devised to demonstrate the extent of formation of each intermediate and to show that one intermediate is not a precursor of the other.

The oxidation in methylene chloride at 20°, in the presence of tetracyclone, with the addition of moist ether to the oxidised solution afforded p-chlorobenzoic acid (20%), derived from 4-chlorobenzocyclopropenone (100), and the

tetracyclone adduct (102) of 6-chloro-3-indazolone (101). If the indazolone (101) is trapped as soon as it is formed, then the benzocyclopropenone (100) must be formed by an independent pathway, not involving the indazolone intermediate.

The oxidation in methylene chloride at 20°, with the addition of a solution of tetracyclone followed by moist ether afforded m-chlorobenzoic acid (0.2%), p-chlorobenzoic acid (21%) and the 6-chloro-3-indazolone adduct (17%) (102). This adduct is derived from 6-chloro-3-indazolone (101) remaining in solution when the oxidation is completed, and since this is trapped first, the acids must derive from 4-chlorobenzocyclopropenone (100) also remaining in solution and this would indicate a reasonable stability for the very reactive intermediate. Since the 3-membered ring may open two ways, two isomeric chlorobenzoic acids should be formed; this point is dealt with later.



When a solution of 3-amino-6-chlorobenzotriazin-4-one (85a) in methanol was oxidised with lead tetraacetate, methyl m- and p-chlorobenzoate were produced (58.5% and 11.5% respectively). Chromatography on silica-gel afforded a mixture of the esters and the isomer ratio was calculated from high resolution infrared spectroscopy. Analysis of an authentic mixture by p.m.r. failed to produce a satisfactory resolution. It was, therefore, only used as additional evidence for the structure of the esters. Methyl m-chlorobenzoate could be produced by nucleophilic attack of methanol on 5-chloroindazolone (103) and 4-chlorobenzocyclopropenone (100); methyl p-chlorobenzoate can only derive from 4-chlorobenzocyclopropenone (100).

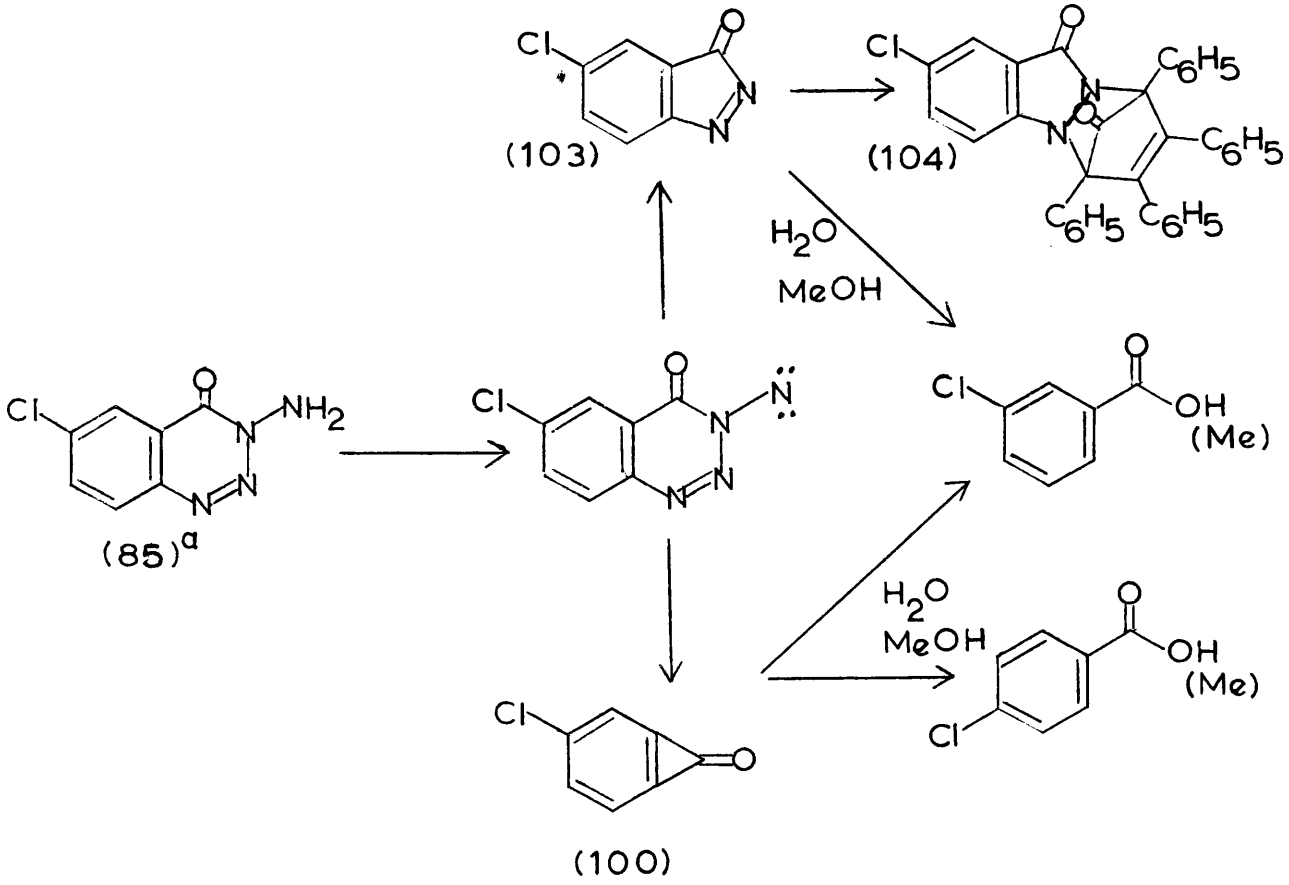
When the amine (85a) was oxidised in acetonitrile at 80°, and methanol added to the solution after the oxidation was complete, a mixture of methyl chlorobenzoates (17%) and chlorobenzoic acids (6%) was produced. No separation of isomers could be obtained by chromatography and isomer ratios were not estimated. The acids presumably arose from adventitious hydrolysis before the methanol was added.

This reaction was repeated at -80° and D_2O added in ether. Chromatography on silica-gel afforded a mixture of deuterated chlorobenzoic acids (35%) as shown by mass-spectral anaylsis and infrared spectroscopy, but isomer ratios were not estimated.

The oxidation of the amine in methylene chloride at 20° with the addition of water after completion of the oxidation afforded m-chlorobenzoic acid (2%) and p-chlorobenzoic acid (7%), separated by chromatography on silica-gel with a gradient elution technique. Here the "rearranged" acid predominates and the 3-membered ring, once formed, must open under the influence of the substituent in the same direction as for the other chloro isomer.

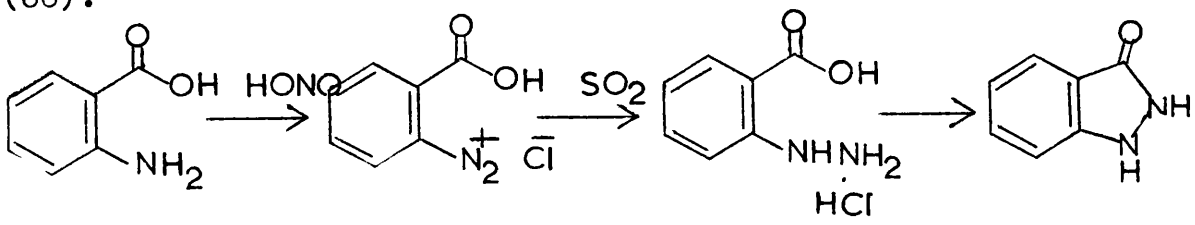
In order to differentiate the products derived from 5-chloroindazolone (103) and 4-chlorobenzocyclopropenone (100), tetracyclone was again used as a trap in two different experiments. The amine (85^{a}) was oxidised in the presence of tetracyclone, and water added when the oxidation was complete. m-Chlorobenzoic acid (0.3%), p-chlorobenzoic acid (3%) and the 5-chloroindazolone-tetracyclone adduct (10.5%) (104) were separated by a gradient elution technique on silica-gel. When the amine (85^{a}) was oxidised alone, then a tetracyclone solution added, followed by water, and using the same work-up procedure, m-chlorobenzoic acid (1%), p-chlorobenzoic acid (15%) and the 5-chloro-3-indazolone adduct (2%) (104) were obtained. These two experiments indicate that 5-chloro-3-indazolone (103) is less stable than the 6-chloro isomer (101), less being formed initially and this decays rapidly. The preponderance of rearranged

acid product demonstrates the effect of the substituent on the direction of opening of the 3-membered ring.



Preparation of 3-indazolinones.

Anthranilic acid was diazotised at 0-5°, and the solution added dropwise to dil. HCl saturated with SO_2, while SO_2 was continuously bubbled through the solution. Addition of conc. HCl to the solution precipitated o-hydrazinobenzoic acid hydrochloride (105). This hydrochloride was refluxed in water to give the ring closed product, 3-indazolinone[129] (86).

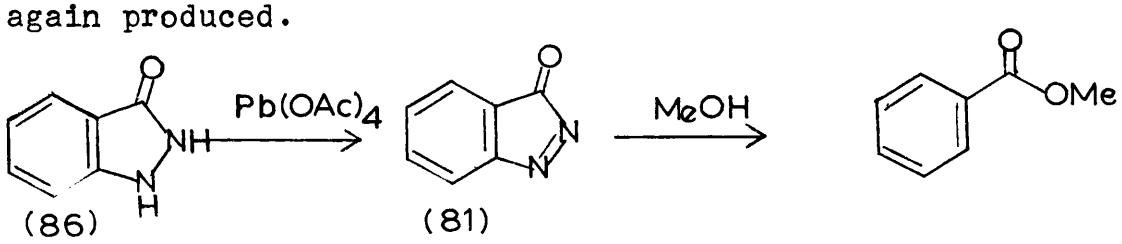


(105) (86)

The same procedure[129] was followed for 5-chloro-3-indazolinone (106), 6-chloro-3-indazolinone (107) and 6-nitro-3-indazolinone (108).

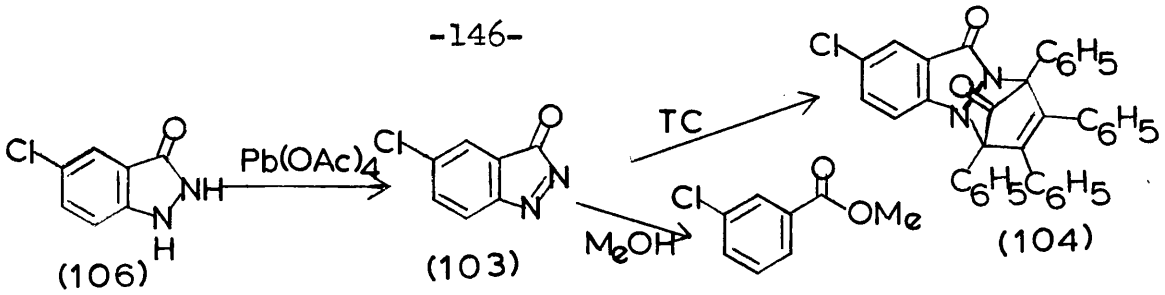
Oxidation of 3-indazolinones.

When a solution of 3-indazolinone (86) in methanol was added to a suspension of lead tetraacetate in methanol, a slow evolution of nitrogen occurred. Gas chromatographic analysis of the solution after 1hr. showed methyl benzoate (46%) to be the only volatile product. When the reaction was performed in acetonitrile at 80°, and methanol added after the oxidation was complete, methyl benzoate (18%) was again produced.

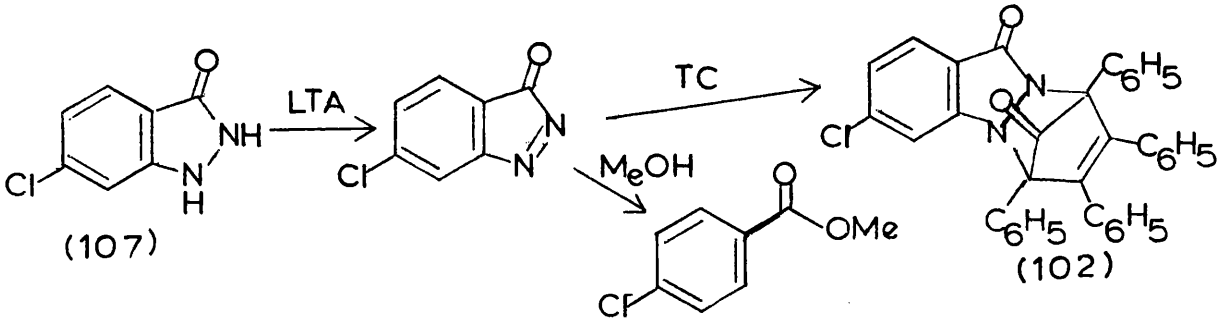


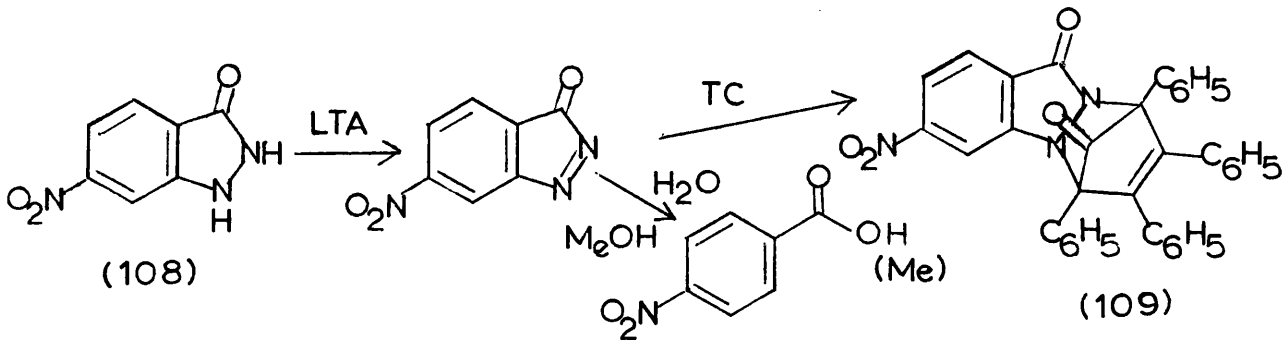
(86) (81)

A solution of 5-chloro-3-indazolinone (106) in methanol oxidised with lead tetraacetate afforded methyl m-chlorobenzoate (52%). The product was isolated by chromatography on silica-gel, and high resolution infrared spectroscopy failed to show the presence of the p-chloro ester. When (106) was oxidised in methylene chloride at 20°, and a solution of tetracyclone added, followed by moist ether, the 5-chloro-3-indazolone-tetracyclone adduct (10%) (104) was the only product isolated. The indazolone (103) does not, therefore, decay to 4-chlorobenzocyclopropenone (100), and all acid and ester products must result from nucleophilic attack on the indazolone (103).



In analogous reactions, 6-chloro-3-indazolinone (107) afforded methyl p-chlorobenzoate (53%) in methanol, and the 6-chloroindazolone adduct (102) (25%) in methylene chloride with the addition of tetracyclone followed by water. Similarly, 6-nitro-3-indazolinone (108) when oxidised in methanol afforded methyl p-nitrobenzoate (55%). When (108) was oxidised in methylene chloride and moist ether added, p-nitrobenzoic acid (25%) was the only product isolated. A careful search (t.l.c., i.r.) for m-nitrobenzoic acid proved negative. A similar reaction but with the addition of a solution of tetracyclone afforded the 6-nitro-3-indazolone adduct (109) (32%).

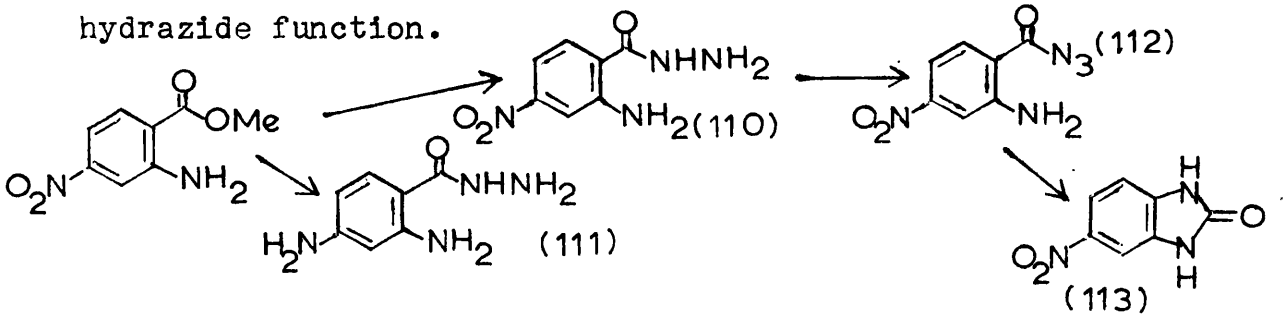




Attempted preparation of 3-amino-7-nitro-1,2,3-benzotriazin-4-one

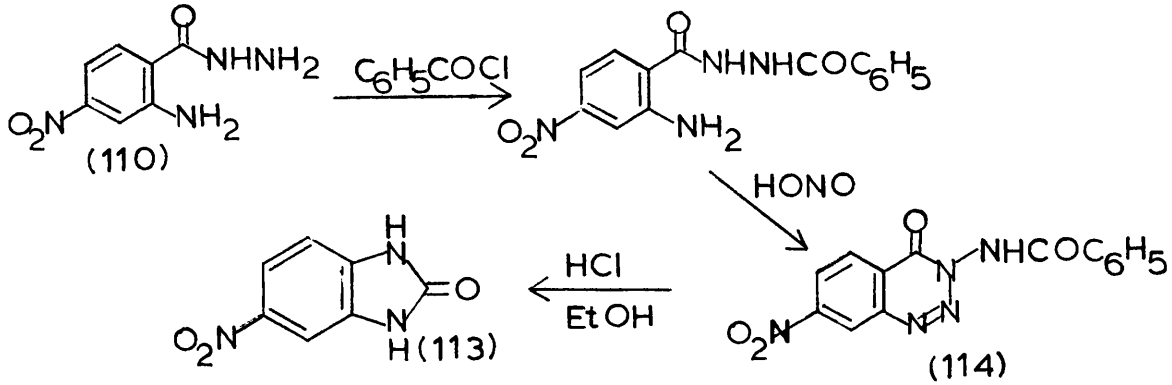
2-Amino-4-nitrobenzoylhydrazide (110) was prepared from the methyl ester with hydrazine in ethanol at room temperature. When the ester was boiled in hydrazine hydrate-water (1:1) the nitro group was reduced, to give 2,4-diamino -benzoylhydrazide (111).

Diazotisation of 2-amino-4-nitrobenzoylhydrazide (110) afforded 2-amino-4-nitrobenzoylazide (63%) (112), and 5-nitro-2-benzimidazolinone (17%) (113) which presumably arose from the decomposition of the azide (112). The nitro group in the 4-position deactivates the amino group on the aromatic ring, hence diazotisation occurs only on the hydrazide function.



3-Benzoylamido-7-nitrobenzotriazin-4-one (114) was successfully synthesised by benzoylation of the hydrazide (110) prior to diazotisation. However, attempted removal of the benzoyl group by acid hydrolysis resulted in cleavage of the triazinone ring, as described for 3-amino-1,2,3-benzotriazin-4-one by Gibson and Green,[136] and 5-nitro-2-benzimidazolinone (57%) (113) was produced. This

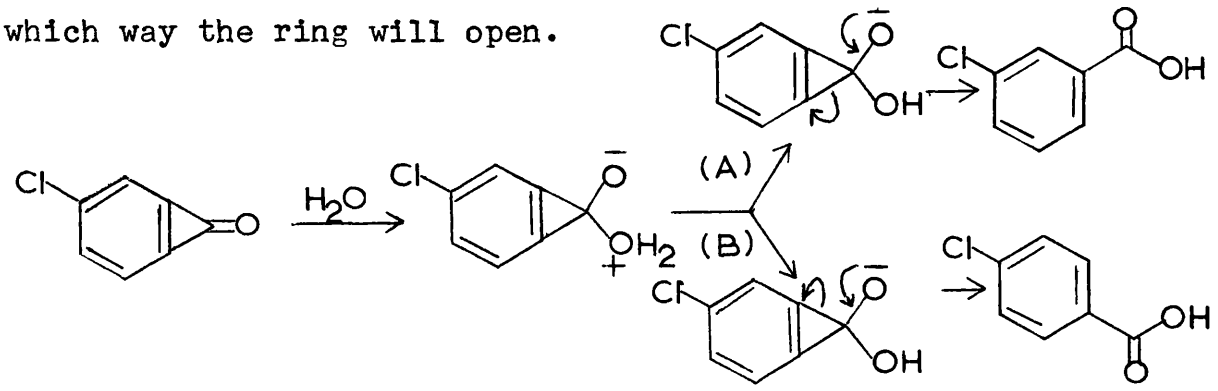
product, identical to that obtained by diazotisation of the hydrazide (110), was also produced by thermal fragmentation of 2-amino-4-nitrobenzoylazide (112).



The attempted preparation of the benzylidene derivative of the hydrazide (110) afforded an unknown yellow crystalline solid which analysed for $C_{14}H_{11}N_3O_2$ and the MW from the mass spectrum was 253 in agreement with this formula. However, no structure could be assigned to this compound.

Conclusion

The work described shows that 3-amino-1,2,3-benzotriazin-4-one is oxidised with lead tetraacetate to benzocyclopropenone and 3-indazolone by independent pathways. 3-Indazolone may be trapped with tetracyclone, or it may react with nucleophiles, with loss of nitrogen. Benzocyclopropenone is rapidly attacked by nucleophiles which open the 3-membered ring to give benzoic acid derivatives. When the benzocyclopropenone is substituted, then the cyclopropene ring can open in two ways when reacting with a nucleophile. Electronic effects of the substituent will then determine which way the ring will open.



For chlorine, there are two effects to consider, the mesomeric and inductive, and both of these should operate to destabilise a negative charge p to the chlorine more than one m to the chlorine. Hence 4-chlorobenzocyclopropenone would be expected to ring open more in one direction than the other[137], i.e. route (B) would be favoured over route (A). This is borne out by the experimental observations.

It would obviously be interesting to investigate the

reverse situation with an electron withdrawing group, particularly in the 4 position, in benzocyclopropenone. For this reason, the synthesis of 3-amino-7-nitro-1,2,3-benzotriazin-4-one was attempted.

3-Indazolinone is oxidised with lead tetraacetate to 3-indazolone, which may be trapped with tetracyclone or it may react with nucleophiles with loss of nitrogen. 3-Indazolone does not, however, lose nitrogen spontaneously to give benzocyclopropenone, since this would require the substituted indazolones prepared to give rearranged products with the addition of nucleophiles.

The reaction of benzocyclopropenone with acetic acid, produced in the oxidation, must be very small since the addition of D_2O after the oxidation results in deuterium incorporation on the benzene ring. Benzoic acetic anhydride was also shown to be attacked by methanol mainly at the aceto-carbonyl group, leading to methyl acetate and benzoic acid. The addition of methanol to the oxidised solutions affords good yields of the esters and very small yields of the acids.

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